RENACALL - INTERMEDIATE CARE STUDY PROTOCOL

Study information

Headline	**Evaluation of the impact of a therapy management platform on the management of patients suffering from advanced/metastatic renal cell carcinoma and receiving first line treatment with sunitinib, versus standard follow-up**
Protocol Number	**A6181213**
Protocol version	Protocol amendment no. 3.1
Date of last version	21 July 2017
Medicinal product	Sunitinib
Research question and objectives	Evaluation of the impact of a therapy management platform on the management of patients suffering from advanced/metastatic renal cell carcinoma (a/mRCC) and receiving first line treatment with sunitinib
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CONTENTS

1. LIST OF ABBREVIATIONS

List of abbreviations used in the protocol.

Abbreviations	Terms
a/mRCC	Advanced/metastatic renal cell carcinoma
ANOVA	Analysis of variance
GPP	Good Pharmacoepidemiology Practices
CATI	Computer-assisted telephone interview
CCTIRS	Comité Consultatif sur le Traitement de l'Information en Matière de Recherche dans le domaine de la Santé (Healthcare Research Data Processing Advisory Board)
CNIL	Commission Nationale de l'Informatique et des Libertés (National Data Protection Commission)
CNOM	French national medical association
CPP	Committee for the Protection of Persons
CRO	Clinical Research Organisation
PHC	Public Health Code
CTCAE	Common Terminology Criteria for Adverse Events v4.03 of June 2010
eCRF	electronic Case Report Form
ECOG	Eastern Cooperative Oncology Group
AEs	Adverse events
HTN	Hypertension
INCA	Institut National du Cancer (French national cancer institute)
INFα	Interferon alpha
ISPE	International Society for Pharmacoepidemiology
ITT	Intention To Treat
IV	Intravenous
MedDRA	Medical Dictionary for Regulatory Activities
NCI	National Cancer Institute
SOP	Standard Operating Procedure
PV	Pharmacovigilance
QC	Quality control
SPC	Summary of Product Characteristics
RECIST	Response Evaluation Criteria in Solid Tumors
CC	Call Centre follow-up
SF	Standard Follow-up

2. RESPONSIBILITIES

Pfizer medical supervisor for the study:	M. PPD Oncology medical supervisor, Pfizer Innovative Health, France Tel: PPD
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3. SYNOPSIS

Rationale

Targeted treatment therapy requires close patient monitoring to ensure that the drug is correctly used and, more specifically, to prevent and manage any adverse events. Better adverse event management helps optimise treatment duration and clinical benefit. Most targeted therapies are taken orally and adverse events frequently occur at home. Regular contact via a therapy management platform could not only reduce the proportion of patients presenting with grade 3, 4 adverse events, but could also reduce the number of unscheduled hospitalisations and consultations associated with poor tolerance.

No other studies evaluating the impact of therapy management platform follow-up versus standard follow-up on the management of patients suffering from metastatic/advanced renal cell carcinoma and treated with targeted oral therapy have yet been published. The improvement of the management of patients treated by targeted oral therapy is one of the priorities of the cancer 2 plan, drawn up by INCa (http://www.plan-cancer.gouv.fr/).

The RENACALL study aims to evaluate a real-life mode of patient management that differs from conventional management, with no additional intervention required by the physician.

All patients benefit from standard follow-up plus follow-up by a therapy management platform. Platform follow-up shall consist in regular phone calls to accompany patients in their real life home management of adverse events and their treatment with sunitinib (prevention, advice and guidance of patients towards options).

- **Objectives**

Main objective:

- Evaluation of the impact of a therapy management platform on the management of patients suffering from advanced/metastatic renal cell carcinoma (a/mRCC) and receiving first line treatment with sunitinib Main outcome measure: Proportion of patients presenting with at least one grade 3 or 4 AE (whether related to sunitinib or not).

Secondary aims:

- To describe and estimate the proportion of patients presenting with dose reductions interruptions or termination of treatment (Sutent®),
- To estimate the number of unscheduled medical procedures, whether related to Sutent® or not (number of unscheduled consultations and hospitalisations),
- To evaluate treatment compliance (Morisky scale [1, 2]),
- To estimate the objective response rate (ORR) according to RECIST V1.1 criteria,
- To evaluate patient and physician satisfaction concerning the call centre
- To describe the sequence of phone calls in terms of the number of successful calls, of actions undertaken by the call centre and/or by the physician

Methods

Physician population

The study shall be proposed to a list of 10 to 20 identified centres in Metropolitan France.

Patient population

An enrolment of 100 patients is expected for this study, i.e. approximately 10 patients enrolled per centre. These patients must meet the following inclusion and non-inclusion criteria.

- Inclusion criteria
  - Man or woman aged 18 or over;
  - Patient suffering from a/mRCC, receiving sunitinib first-line treatment, as per SPC recommendations;
  - Resolution (grade ≤ 1 according to CTCAE version 4.03 of June 2010) of all acute toxic effects due to radiotherapy or surgical procedure prior to initiation of sunitinib;
  - Patient who can be monitored for 6 months.
  - Female patient of child-bearing age using a form of contraception during treatment with Sunitinib and for at least 28 days after termination of treatment with Sunitinib;
  - Patient having signed his/her consent form;
  - Patient affiliated with a social security scheme.

- Non-inclusion criteria
  - Patient participating in a clinical trial during sunitinib treatment;
  - Patient managed by a home hospitalisation service during sunitinib treatment;
  - Patient taking part in therapeutic education programmes, or benefiting from nursing consultation, or from any other significant treatment support and likely to impact adverse event management.
  - Patient untreated and/or symptomatic brain metastases prior to sunitinib initiation;
  - Patient refusing the use of his/her personal data.
  - Patient with an ECOG performance status upon inclusion > 2;
  - Patient presenting with a serum creatinine level >1.5 times the upper limit of the normal level;
  - Patient presenting with a bilirubin level > 2 mg/dl, aspartate transaminase (ASAT) or alanine transaminase (ALAT) >2.5 times the upper limit of the normal value, or >5 times the upper limit of the normal value in the presence of liver metastases upon initiation of sunitinib treatment;
  - Patients who are staff members of a centre involved in the study, or close to one of the staff members of a centre directly involved in conducting the study, or patients employed by Pfizer and involved in conducting the study

General organisation

Prospective and multi-centre intermediate care study, conducted in metropolitan France on adult patients suffering from advanced/metastatic renal cell carcinoma and receiving first-line sunitinib treatment.

Patient therapeutic management must not be modified during the study and must conform to the SPC recommendations. The patients will receive additional follow-up by the call centre. This follow-up consists in making regular phone calls (14 during the first 4 cycles) to support the patients in the management of their sunitinib treatment.

The RENACALL study aims to evaluate a different mode of patient management from that performed during routine follow-up.

Patient management varies widely according to the physician and his/her patients' needs. To avoid interfering in follow-up practices, each physician shall follow up their own patients according to their usual practices.

Statistical methodology

Complete population justification (physicians/patients)

The estimated number of patients (n) is determined by the precision (i) required when estimating the proportion (p) of patients presenting with at least one grade 3 or 4 AE. A 95% confidence interval is associated with the estimation of this proportion.

100 patients will need to be included to estimate a percentage with a 95% confidence interval whose amplitude, calculated by the asymptotic method, does not exclude ±9.8%.

4. AMENDMENTS AND UPDATE

Amendment number	Date	Administrative or substantial amendment	Modified protocol section	Amendment summary	Rationale
Amendment no. 1	04/12/2014	Substantial amendment	Patient information note and CRF	changed the patient information note (deleted all Anglicisms) and CRF	Requested by the CPP and CNIL
Amendment no. 2	16/11/2015	Substantial amendment	Inclusion criterion and CRF	Added a non-inclusion criterion and changed the CRF	Request by the Scientific Committee coordinator to add a non-inclusion criterion Changed the medical supervisor and updated the CRF following the tests performed
Amendment no. 3	18/11/2016	Substantial amendment	Rationale, objectives, Patient information note	Deleted randomisation by scientific committee request	The study scientific committee wished to find a solution for boosting inclusions and physician interest in the project by allowing them to offer therapy management platform-based follow-up to all their patients. Thus, it will be possible to compare the cohort formed by the RENACALL study to an historical cohort.
Amendement no 3.1	21/07/2017	Non-substantial amendment	Timeline and safety update	Inclusion patient period extension. Safety process update	Following approval drom regulatory authorities, it was decided to extend the inclusion period until december 31th 2017 Following the answers from our safety service, it xas decided to keep the initial safety paragraf in the protocol.

5. STUDY SCHEDULE

Task	**Scheduled date**
Protocol submission to the Bordeaux CPP	July 2014
Protocol submission to the CCTIRS	July 2014
Protocol submission to the French national medical association (CNOM)	August 2014
Protocol submission to CNIL	August 2014
Enrolment of participating physicians	October 2014
Data collection start date	March 2016
End of data collection	November 2018
Freeze database and initial analysis	Janvier 2019
Final Report	Mars 2019

6. RATIONALE

RENACALL is a prospective intermediate care study whose main aim is to evaluate the impact of a therapy management platform on the management of patients suffering from advanced/metastatic renal cell carcinoma and receiving first line treatment with Sutent®.
100 mRCC patients treated receiving first line Sutent® treatment shall be included in the study, and shall benefit both from conventional follow-up and from additional therapy management platform-based follow-up. Platform follow-up shall consist in regular phone calls to accompany patients in their real life home management of their treatment with sunitinib (prevention, advice and guidance of patients towards options).

The study's main outcome measure is the proportion of patients presenting with at least one grade 3 or 4 AE (whether related to sunitinib or not).

6.1 RATIONALE

6.1.1. Advanced/metastatic renal cell carcinoma

In France, the incidence of renal cell carcinoma is estimated at 8,300 new cases per year since 2000 and represents 2 to 3% of adult cancer cases (7^{th} most frequent cancer in men and 9^{th} most frequent in women in France) [3-5]. It is responsible for 3,600 deaths per year. In the United States, there are a little more than 38,000 new cases of renal cell carcinoma each year, corresponding to 5% of all cancers [6]. The sex-ratio is of two men for one woman, with a median age at diagnosis of 70 years.

Renal cell carcinoma is the third urological cancer in terms of frequency, though it remains the first in terms of specific mortality, with a 40% death rate [6]. Between 10 and 40% of patients diagnosed with renal cell carcinoma display a metastatic form from the outset [6, 7]. Moreover, 10 to 30% of RCCs will become metastatic, with a mean time to detection of metastases of 36 months [6-10].

6.1.2. Therapeutic care

Before the introduction of targeted therapies, the median survival time for patients suffering from metastatic renal cell carcinoma was of ten months [11]. The development of targeted therapies, acting both on the mechanisms of angiogenesis and of cell proliferation, has revolutionised the management of renal cell carcinoma [12, 13]. These treatments have led to a progression-free survival with a median value estimated at 11 months and an overall survival of 30 months [14-16].

Sunitinib is a tyrosine kinase inhibitor indicated for the treatment of advanced and/or metastatic renal cell carcinoma. It is currently considered as reference first-line treatment [17]. The pivotal sunitinib vs. INF alpha trial demonstrated a significant improvement in progression-free survival of 11 months under sunitinib versus 5 months under INFα [18]. By virtue of their mechanisms of action, targeted therapies are accompanied by adverse events of variable severity. For sunitinib, it has been shown that certain adverse events are predictive of the patient's response to the treatment [19-22]. Common toxicities have been described for all anti-angiogenic drugs (asthenia, HTN, cardiac toxicity) [23]. In the pivotal sunitinib trial [18], 84% of patients treated with sunitinib presented with at least one grade 3 or 4 adverse event (according to CTCAE version 4.03 of June 2010), whether associated with sunitinib or not. Cardiovascular, dermatological, haematological, gastrointestinal and metabolic disorders require special

surveillance. In the Santorin study (French study of the real-life use of anti-angiogenic drugs) [16], 58% of patients treated with sunitinib presented with at least one grade 3 or 4 adverse event (according to CTCAE version 4.03 of June 2010), whether associated with sunitinib or not. In the EAP "Expanded Access Program" trial [24], 58.8% of patients treated with sunitinib presented with at least one grade 3 or 4 adverse event (according to CTCAE version 4.03 of June 2010), whether associated with sunitinib or not.

The main grade 3 events were hypertension (12.6%), hand and foot syndrome (12.3%), fatigue/asthenia (11.9%), neutropenia (10.6%) and anaemia (9.3%).

One adverse event led to hospitalisation in 35% of patients. The main grade 3 events that led to hospitalisation were anaemia (22 patients, 7.3%), deterioration of general condition (10 patients, 3.3%), hypertension (7 patients, 2.3%), fatigue/asthenia (6 patients 2.0%) and a cardiovascular event (6 patients, 2.0%). 65% of patients with at least one dose reduction, 61.6% of patients with at least one cycle postponement.

6.1.3. Management of AEs

Targeted treatment therapy requires close patient monitoring to ensure that the drug is correctly used (dosage, compliance) and, more specifically, to prevent and manage any adverse events. Better adverse event management helps optimise treatment duration and clinical benefit. Most targeted therapies are oral and adverse events frequently occur at home. Thus, for improved prevention and AE management, a link between medical personnel and the patient is necessary. Regular contact via a therapy management platform could not only reduce the proportion of patients presenting with grade 3, 4 adverse events, but could also reduce the number of unscheduled hospitalisations and consultations associated with poor tolerance.

A study conducted at the Cochin hospital in Paris [25] demonstrated the benefits of a therapy management platform in the management of patients treated by standard IV chemotherapy. The purpose of this study was to evaluate the rate and cost of unscheduled hospitalisations induced by chemotherapy in a group of patients treated by chemotherapy: patients receiving standard follow-up (96 patients) and patients benefiting from call centre follow-up (259 patients). This study revealed a decrease in the unscheduled hospitalisation rate induced by chemotherapy from 4.9% to 2.4% ($p<0.01$) in the call centre group, relative to the standard follow-up group (383-day reduction in hospitalisation), along with a cost reduction of approximately $292.089 per year. Another study [26] evaluating the effectiveness of a programme for optimisation of the chemotherapy network monitoring program (PROCHE), also demonstrated a reduction in the incidence of side effects (in particular fatigue and pain) in the group monitored by this programme.

6.1.4. Justification for the RENACALL study

No other studies evaluating the impact of therapy management platform follow-up versus standard follow-up on the management of patients suffering from metastatic/advanced renal cell carcinoma and treated with targeted oral therapy have yet been published. The improvement of the management of patients treated by targeted oral therapy is one of the priorities of the cancer 2 plan, drawn up by INCa (http://www.plan-cancer.gouv.fr/).

7. AIMS OF THE STUDY

7.1 Main aim:

Evaluation of the impact of a therapy management platform on the management of patients suffering from advanced/metastatic renal cell carcinoma (a/mRCC) and receiving first line treatment with sunitinib

Primary assessment criterion: Proportion of patients presenting with at least one grade 3 or 4 AE (whether related to sunitinib or not).

7.2 Secondary aims:

- To describe and estimate the proportion of patients presenting with dose reductions interruptions or termination of treatment (Sutent®),
- To estimate the number of unscheduled medical procedures, whether related to Sutent® or not (number of unscheduled consultations and hospitalisations),
- To evaluate treatment compliance (Morisky scale [[1, 2]),
- To estimate the objective response rate (ORR) according to RECIST V1.1 criteria,
- To evaluate patient and physician satisfaction concerning the call centre
- To describe the sequence of phone calls in terms of the number of successful calls, of actions undertaken by the call centre and/or by the physician

7.3 Evaluation criteria

7.3.1. Main outcome measure

The main outcome measure is defined by the proportion of patients presenting with at least one grade 3 or 4 adverse event (whether associated to Sutent® or not) during the first 4 treatment cycles (study follow-up period), based on the 'Common Terminology Criteria for Adverse Events' (CTCAE) version 4.03 of June 2010.

Adverse events shall be collected:

- via the e-CRF, by the physicians, during routine follow-up consultations,
- Via the CATI system, by the call centre nurses during phone calls. Declaration to the Pfizer Pharmacovigilance department within the statutory time limits by the CATI system at the end of each patient interview. AEs will also be sent to the participating physicians via the e-CRF for review and validation during the patient follow-up visits.

Adverse events precisely described to the nurses by the patients, with a proposed gradation by the nurse where applicable, shall be definitively graded by the participating physician during the patient consultations at the centre, according to the CTCAE version 4.03 of June 2010, available from the study website.

Pharmacovigilance files (AE report form and additional file generated from the CRF data) shall automatically be created from the e-CRF. One file shall be created for each AE upon completion of the visits made by the participating physician and after approval of all reported cases.

7.3.2 Secondary outcome measures

Each of these criteria shall be evaluated based on the data collected via the e-CRF by the physicians and via a self-questionnaire provided to the patients.

- **Dose reduction, treatment interruptions and termination (sunitinib)**

Description of dose reduction

- Proportion of patients having had at least one dose reduction relative to the initial dose
- Reasons for dose reduction
- Change of dose (initial dose and new dose prescribed)

Description of treatment interruptions

- Proportion of patients having temporarily interrupted their sunitinib treatment (including postponement of the start of the subsequent cycle)
- Mean interruption duration
- Cause for the interruptions

Treatment termination

- Proportion of patients having stopped taking sunitinib
- Reasons for termination

- **Unforeseen medical procedures:**

- Mean number of unforeseen consultations
- Mean number of unscheduled hospitalisations

Unforeseen medical procedures correspond to unscheduled consultations and hospitalisations, whether associated with sunitinib or not.

- **Treatment compliance**

Treatment compliance shall be evaluated directly with the patients using the standardised questionnaire validated by Morisky, available in appendix 9 of the protocol. This generic therapeutic compliance evaluation questionnaire comprises 4 questions scored as 0 for "YES" and 1 for "NO". The points for each question are added up to obtain a score ranging from 0, if all questions are answered by "yes" (reflects poor compliance) and 4, if all questions are answered by "no" (reflects good compliance).
It shall be completed, during the routine follow-up visit with the participating physician, after the sixth week of cycles 1, 2 and 4, via a self-questionnaire issued to the patient.
Similarly, the questions shall be asked orally and the answers entered into the CATI system during the W4 phone interviews of cycles 1, 2 and 4 between the platform nurse and the patient. This evaluation shall be used, on the one hand, to measure the compliance after the 4^{th} week of treatment and, on the other hand, to estimate the match between patient declarations made during the W4 measurement and the consultation with the attending physician. The match measurement shall be used for information purposes only, insofar as the questionnaire is validated for self-completion by the patient himself/herself, not for submission of the questions by a third party (potential declaration bias concerning compliance).

- **Response to treatment**

Evaluation of the objective response rate (ORR) according to RECIST V1.1 criteria,

- **Patient and physician satisfaction concerning the call centre**

The evaluation of patient satisfaction concerning the call centre shall be evaluated by a self-questionnaire issued to the patients during the final visit (appendix 11), used to determine the various dimensions of their satisfaction (overall satisfaction, satisfaction concerning advice, service and management).
This questionnaire, drawn up in the context of the study, shall consist of 8 questions, with answers in the form of a semantic measurement scale with an odd number of categories (5) and with a level of control preventing any opinion from being expressed. Each answer is assigned a positive or negative score, thus enabling the data to be processed, along with mean and standard deviation.
Similarly, physicians' satisfaction shall be collected at the end of the study via a dedicated e-CRF module (appendix 10). For the physicians, only three satisfaction dimensions will be evaluated via 5 questions (overall satisfaction, satisfaction concerning advice and management), satisfaction concerning the service does not apply to them.

- **Description of phone calls**
    - Number of successful calls,
    - Action undertaken by the patient,
    - Action undertaken by the call centre,
    - And/or action undertaken by the physician,
    - Adverse event declaration.

Each call shall give rise to an automatic call report, available to the physician on the e-CRF (action undertaken by the patient, adverse event declaration).

8. METHODS

8.1. Study design

The RENACALL study is a prospective and multi-centre intermediate care study conducted in metropolitan France on adult patients suffering from advanced/metastatic renal cell carcinoma and receiving first-line sunitinib treatment. The study shall be conducted in 10 to 20 centres in charge of renal cell carcinoma.

8.2. Methods

Patients meeting the inclusion and non-inclusion criteria shall be offered to take part in the RENACALL study.
Patient therapeutic management within the establishment must not be modified during the study and must conform to the SPC recommendations. Additionally, patients will receive supplementary follow-up by the call centre.

The RENACALL study aims to evaluate real life patient management.

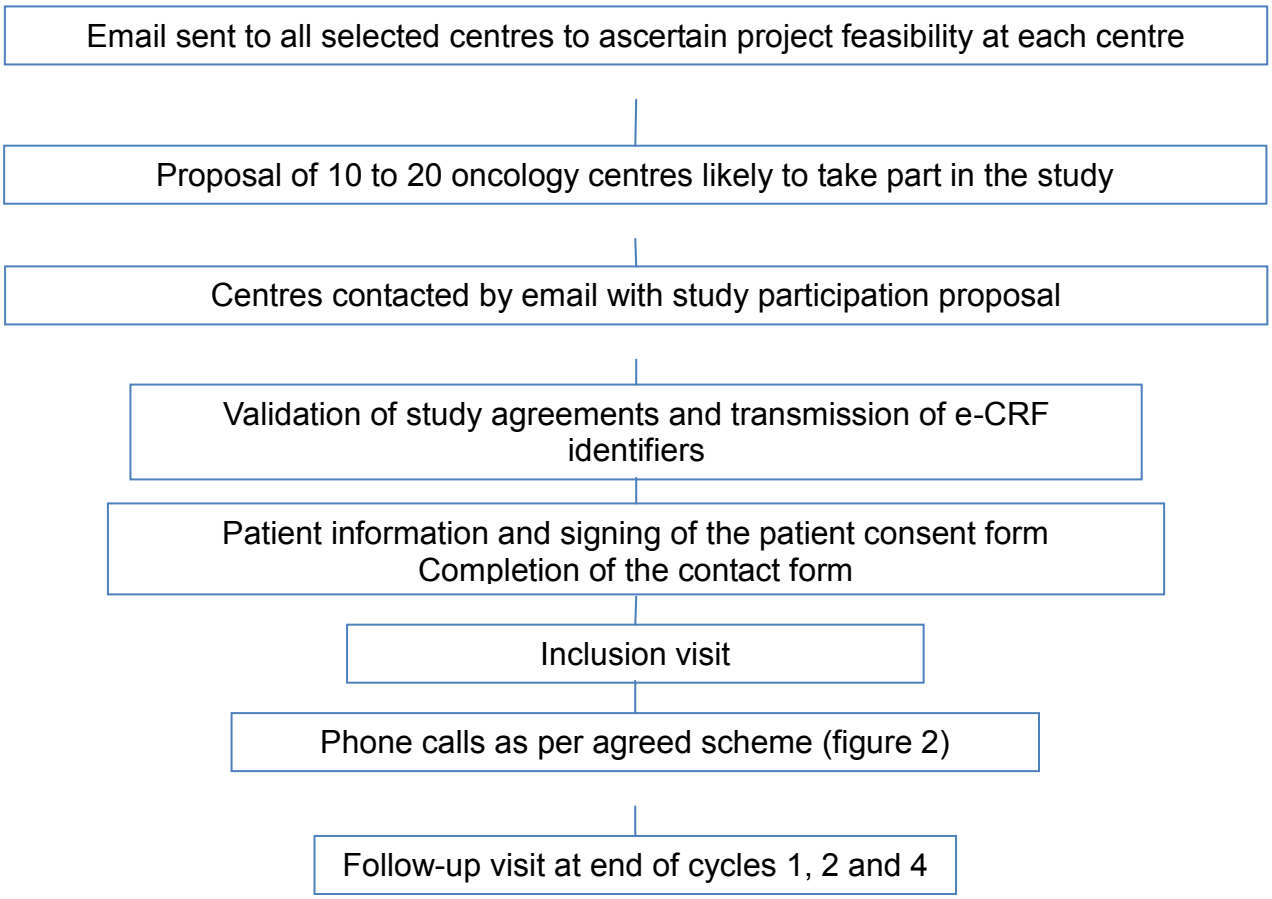

Figure 1. General study organisation

The patients included in the study will benefit from standard follow-up plus follow-up by a therapy management platform. Platform follow-up shall consist in regular phone calls (see Figure 2) to accompany patients in their real life home management of their treatment with sunitinib (prevention, advice and guidance of patients towards options).

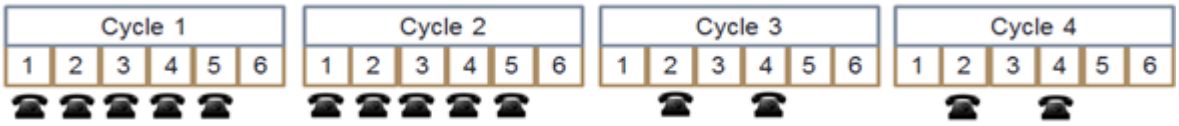

Figure 2. Phone call scheme

The study data shall be collected via an electronic case report form:

- By the physician during the inclusion and follow-up visits at the hospital,
- By the therapy management platform nurses during the phone calls, They will have special user profile access to pre-fill the data collected during the phone calls.
- The physicians will have access to the data and reports filled in the by the nurses during the phone calls.

The period for patient inclusion into the study is of 22 months. Patients shall be monitored during the first 4 cycles of sunitinib treatment, i.e. for approximately 6 months (1 treatment cycle lasts 6 weeks).

Follow-up visits shall be conducted for all study patients according to standard patient follow-up, i.e. approximately at the end of cycles 1, 2 and 4, during routine patient consultations at the centres (at approximately W6, W12 and W24).

At the end of follow-up, the patients will be asked to fill in a platform satisfaction questionnaire. The participating physicians will be asked to fill in this satisfaction questionnaire at the end of the study.

The therapy management platform will be managed via a call centre using a CATI (Computer-Assisted Telephone Interview) system. This system is used to instantly enter into the computer all the data collected in response to specific questionnaires submitted by the nurses during the telephone calls, in the context of follow-up.

Patient management varies widely according to the physician and his/her patients' needs. To avoid interfering in follow-up practices, each physician shall follow up their own patients according to their usual practices.

Population of participating physicians

The study shall be proposed to 58 physicians at 50 oncology centres in metropolitan France caring for patients suffering from metastatic/advanced renal cell carcinoma.

Each physician shall be questioned concerning the annual number of patients meeting the inclusion and non-inclusion criteria. It shall also be questioned concerning the systems in place in their centre.
Thus, each centre receiving at least 10 patients per year and that does not already possess a coordinating nurse or platform for routine patient follow-up may be selected to take part in this project, forming the list of identified physicians.

This step, conducted upstream of the study, will allow the identification of 20 to 25 physicians eligible to take part in the study.

A description of the sample of centres shall be provided subsequently, based on the identification data of the participating physicians from each centre (age, gender, geographical situation, etc.). We shall then check that the sample of participating physicians is representative of oncologists in France in terms of centre size and type, in order to guarantee external study validity.
The patients included in the RENACALL study will be monitored not only in the standard manner, but also via the therapy management platform. In the context of standard follow-up, they will be issued the usual logbooks for their treatment, along with any documents routinely used by the centres.

Patient follow-up via a therapy management platform consists in making regular phone calls (14 during the first 4 cycles) to support the patients in the management of their sunitinib treatment.

The calls shall be made from a centralised therapy management platform located in the Paris region, by nurses specifically trained for this role. If necessary, the nurses may be assisted by physicians from the platform.

The aim of these calls is to support the patients in the management of their treatment by listening to and advising them, implementing preventive measure and taking actions when deemed necessary; the purpose of these calls is to support patients in the management of their sunitinib treatment.

Call frequency is presented in the following figure:

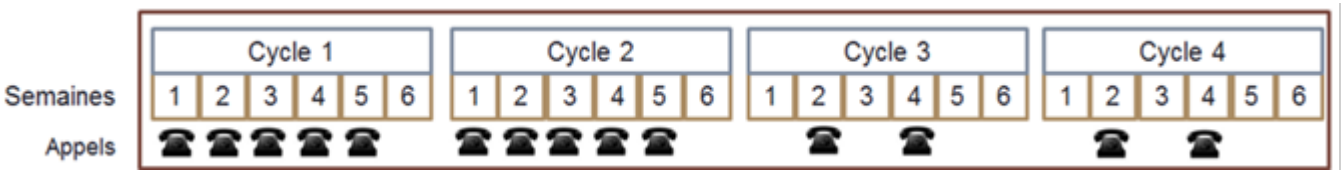

Figure 3. Call frequency

The chosen rate is of:

- For the first two cycles, C1 and C2: 5 calls during the first 5 weeks of each cycle (no call during week 6 as the patients are usually seen in consultation),
- For cycles 3 and 4: 2 calls per cycle on weeks 2 and 4.
  (decision by the CS not to make calls on weeks 1, 3 and 5).

These calls will be made for patients treated with Sutent®; in the event of termination of treatment during the follow-up period, the call following termination will close the intervention. In the event of cycle start postponement, the first call made shall be postponed to match the expected organisation (cycles 1 and 2: first call during week 1 of the cycle; cycles 3 and 4: first call during week 2 of the cycle).

Call organisation has been defined in collaboration with the concerned healthcare professionals and based on prior experience of therapy management in oncology. It shall be as follows:

- build the patient's trust by covering various aspects of the disease and/or of side effects;
- patient education to avoid serious adverse events (e.g.: dietary advice, sports exercises, etc.);
- guidance and advice when deemed necessary; for example, this may be to:
  - advise the patient to take medicinal products prescribed upstream by his/her physician,
  - guide the patient towards his/her oncologist or general practitioner or other.

The patients will also be able to contact the call centre nurses at any time during the study. A specific module will enable the nurse to record this type of "unscheduled" call.

The platform will also play a coordination role between patients and healthcare professionals, through the following actions:

- Draw up a call report on the e-CRF. This latter shall include the number of successful calls, along with the actions performed by the call centre for each call, such as: no special action, or self-medication, or consultation request to one of the physicians;
- Report adverse events identified by the platform nurses and monitor actions performed by the physicians following declaration of an adverse event by the call centre (symptomatic treatment, hospitalisation, reduction/interruption/termination of the sunitinib dose, etc.). The call centre nurses will declare, within the statutory time frame, to the Pfizer Pharmacovigilance department, any adverse events reported by the patients during a phone call.
- Access for oncologists to a call report

At the end of the follow-up cycle, those patients still treated with sunitinib and wishing to continue the therapy management, may benefit from this service until the outcome of the disease. Any adverse events are thus declared in the context of spontaneous declaration.

STUDY PROCEDURES

This is an intermediate care study; the choice of patient therapeutic strategy (implementation of sunitinib treatment) is not guided by the study.

Study period

The patient inclusion period is of 22 months. Patients shall be monitored during the first 4 cycles of sunitinib treatment, i.e. for approximately 6 months (1 treatment cycle lasts 6 weeks).

Follow-up visits shall be conducted according to standard patient follow-up, i.e. approximately at the end of cycles 1, 2 and 4, during routine patient consultations at the centres (at approximately W6, W12 and W24).

Study set-up

Enrolment of participating physicians

The study shall be proposed to 58 physicians at 50 oncology centres in metropolitan France caring for patients suffering from metastatic/advanced renal cell carcinoma.
Those physicians, accepting to take part in the study and with a suitable active file of patients, shall make up the list of eligible physicians.

Study set-up for physicians

The eligible physicians shall be invited to take part in the study. This participation shall be embodied through the signing of the financial agreement. Upon validation of this agreement, a set-up visit will be organised to present all documents to the participating physician and to appointed members of his/her staff.

After this visit, the physicians will receive an email containing a link for the study website, along with their login ID and password.
On this website, they will have access to all study elements, i.e.:

- A letter from the Scientific Coordinator,
- A synopsis and protocol, along with the various amendments
- A physician's check-list,
- The CPP ruling,
- The CCTIRS ruling,
- The CNIL authorisation,
- The file acknowledgement of receipt by the CNOM,
- The patient forms,
- The case report forms.
- A FAQ populated in real-time by the physicians' comments

During the set-up visit, they will also be issued:

- The patient information/consent forms,

- The Morisky questionnaires,
- The "patient" platform satisfaction questionnaires,
- The postage-paid envelopes required to return the questionnaires.

Each participating physician will be assigned a unique number (0001 to 00XX).
Before being issued to the patient, each patient questionnaire must be numbered with the patient number assigned during inclusion visit data input on the study website.
Moreover, the patient will also be asked to enter his/her age and gender in order to be able to correlate the questionnaires if the patient's number is omitted.

Patient selection

The physician will ensure that his/her patient meets all selection criteria. The physician will inform the patient using an information form and will ask him/her whether he/she accepts that his/her personal data be collected in the context of the RENACALL study. The patient will be asked to sign a written consent, certifying that he/she accepts to take part in the study and to provide his/her phone number for therapy management platform calls.

After signing the consent form, the physician will ask the patient to fill in a contact form (Appendix 2). This form is then sent exclusively to the therapy management platform. This form can be printed from the e-CRF. It shall contain the patient's identification number for the call platform. Thus, the patients will be assigned a research identification number, ID_{study}, (in the context of the study) and a platform identification number ID_{call} (for calls), enabling the team in charge of calls to maintain the patients personal data in plain text.

When the patient is included in the study, the physician must also fill in the physician inclusion questionnaire during the consultation.

Logistical monitoring

The participating physicians will be monitored by a team of research associates specifically trained for the project. This monitoring can be implemented in various manners: phone calls, email, specific post and newsletters.

Emphasis shall be placed on the quality of these contacts as they shall promote the involvement and quality of work performed by the participating physicians. Each physician shall, insofar as possible, be monitored by the same research associate, from enrolment to closure of the study.

The research associates shall follow up on incomplete or incoherent data (incoherence, lack of response and omission checks) and shall maintain constant contact with the participating physicians. During the patient selection period and depending on the number of inactive participating physicians (no patient selected), the research associates may be required to make follow-up calls to these latter.

Moreover, a study-specific freephone number shall be set up for the participating physicians, in order to immediately answer any queries they may have throughout the duration of the study.

In terms of traceability, all "incoming" calls via the freephone number and "outgoing" calls (selection call, follow-up call, etc.) will give rise to a written report (date, purpose of the call, steps to take, etc.) and will be entered into a log.

Receipt and input of satisfaction and compliance questionnaires

The compliance and satisfaction questionnaires completed by the patients will be sent directly to Pfizer by means of postage-paid envelopes provided to the participating physicians.

After acknowledging receipt, Pfizer sends them in batches to the CRO in charge of data input, where they are entered in duplicate into the database.

Call management

The nurse in charge of patient follow-up via the "therapy management platform", upon receipt of the contact sheet, will enter the patient's contact details into the CATI system. An call identification number (IDcall) will be assigned to the patient. This database will be secure and accessible via login and password to persons in charge of making the calls from the platform. When recording the patient's file, these data will be encrypted in the database. It will subsequently be impossible to access the complete IDstudy / IDcall / patient details chain.

Calls will then be performed according to intervention procedures (Appendix 8) defined for the patients.

End of study

A patient leaves the study in one of the following cases:
- once all 4 treatment cycles have been completed.
- when the patient stops his/her treatment with sunitinib, for whatever reason.
- when the patient withdraws from the study, or is removed by the participating physician.

A follow-up visit is conducted and an end of treatment sheet is filled in at the end of the study
The research associate will inform the physician of the end of the patient recruitment period and of the end of the follow-up period. He/she may be required to follow up on any missing documents required for remuneration, or to resolve any collected data inconsistencies identified during data management.

Roles of participants

- Logistics centre: Pfizer's Medical Operations Department, via its research associates, will be in charge of the centralised monitoring of participating physicians (use of the Pfizer non-interventional study management database).
- Participating physicians: These latter are responsible for patient selection and questionnaire data collection, while conforming to the intermediate care study protocol and agreement.
- Platform nurses: the nurses are in charge of calling the patients included in the study and for entering the corresponding data into the e-CRF.
- Monitors: The monitors are in charge of setting up the study at the centres. They are also in charge of conducting at least one follow-up visit per year and per centre, along with the closing visit. During these visits, the monitors are required to ensure that the Site Master File (SMF) is properly kept, to check e-CRF completion and to ensure that they mad the patient's source file, along with the declaration of AEs to Pfizer's pharmacovigilance department in accordance with paragraph 9 of the protocol.

8.2.1. Inclusion criteria

This study can only achieve its aims if the appropriate patients are included. The following inclusion and non-inclusion criteria are designed to select patients for whom the protocol is deemed appropriate by their physician.

- Man or woman aged 18 or over;
- Patient suffering from a/mRCC, receiving sunitinib first-line treatment, as per SPC recommendations;
- Resolution (grade ≤ 1 according to CTCAE version 4.03 of June 2010) of all acute toxic effects due to radiotherapy or surgical procedure prior to initiation of sunitinib;
- Patient who can be monitored for 6 months.
- Female patient of child-bearing age using a form of contraception during treatment with Sunitinib and for at least 28 days after termination of treatment with Sunitinib;
- Patient having signed his/her consent form;
- Patient affiliated with a social security scheme.

8.2.2. Non-inclusion criteria

- Patient participating in a clinical trial during sunitinib treatment;
- Patient managed by a home hospitalisation service during sunitinib treatment;
- Patient taking part in therapeutic education programmes, or benefiting from nursing consultation, or from any other significant treatment support and likely to impact adverse event management.
- Patient untreated and/or symptomatic brain metastases prior to sunitinib initiation;
- Patient refusing the use of his/her personal data.
- Patient with an ECOG performance status upon inclusion > 2;
- Patient presenting with a serum creatinine level >1.5 times the upper limit of the normal level;
- Patient presenting with a bilirubin level > 2 mg/dl, aspartate transaminase (ASAT) or alanine transaminase (ALAT) >2.5 times the upper limit of the normal value, or >5 times the upper limit of the normal value in the presence of liver metastases upon initiation of sunitinib treatment.
- Patients who are staff members of a centre involved in the study, or close to one of the staff members of a centre directly involved in conducting the study, or patients employed by Pfizer and involved in conducting the study

8.3. Variables

8.3.1. Table of recorded data

During the routine patient consultations at the centres:

	V1: Inclusion ***T0***	**V2: end of cycle 1** ***W6***	**V3: end of cycle 2** ***W12***	**V4: end of cycle 4** ***W24***
Data filled in by the physician via the e-CRF				
Compliance with eligibility criteria	x			
ECOG performance status	x	x	x	x
Sociodemographic characteristics	x			
History of the disease	x			
Disease progression		x	x	x
Biological, histological and metastatic examination data	x	x	x	x
Conditions of sunitinib use	x			
Modification of conditions of sunitinib use		x	x	x
Concomitant treatments	x	x	x	x
Pharmacovigilance data		x	x	x
Medical procedures (calls, consultations, hospitalisations), planned or unforeseen		x	x	x
Issuing of Sunitinib treatment support equipment	x	x	x	x
Data filled in by the patient (self-questionnaire)				
Compliance (Morisky)		x	x	x
Data filled in by the physician and the patient				
Satisfaction concerning the call centre filled in by the physician and the patient				x

8.4. Data sources

8.4.1. Data recorded by the physician:

Upon inclusion

The inclusion visit enables the physicians to document the following parameters:

- Compliance with inclusion criteria;
- ECOG performance status;
- Patient's sociodemographic characteristics;
- History of the disease;
- Biological, histological and metastatic examination data;
- Conditions of sunitinib use;
- Concomitant treatments;
- Issuing of treatment support equipment and planned support.

During the end-of-cycle 1, 2 and 4 visits

During the follow-up visits, the following parameters are recorded by the physicians, via the e-CRF:

- Disease progression;
- Biological, histological and metastatic examination data;
- Possible modifications to the conditions of sunitinib use (change of dose, treatment plan, temporary interruption or termination);
- Concomitant treatments;
- Pharmacovigilance data (recording of adverse events, degree of severity and description of the AE: intensity, symptoms, impact on patient follow-up, examinations performed, actions implemented);
- History of calls and consultations with a healthcare professional during the cycle (scheduled and unscheduled).
- Hospitalisation during the cycle (scheduled and unscheduled).
- Issuing of treatment support equipment and planned support.

The end of cycle 4 visit will represent the final visit.

At the end of the study

The participating physicians will fill in on the e-CRF a questionnaire on their level of satisfaction concerning the call platform.

8.4.2. Data recorded via the call centre:

The patients will have received phone calls on W1, W2, W3, W4 and W5 of the first two cycles, then every two weeks, W2 and W4 for cycles 3 and 4.

During the calls made by the nurses, all of the data of the specific call questionnaires (Appendix 6: Nurse intervention script) shall be recorded via a CATI system used to instantaneously enter the data collected into a software application.

The following data will be collected:

- Number of call attempts
- Patient's general condition;
- Treatment taking:
- Tolerance and occurrence of adverse events (description of the AE: intensity, symptoms, impact on the patient, examinations performed, actions implemented;
- Proposed action

A summary of calls shall be issued to the participating physicians. The adverse events collected during the calls shall be recorded in the participating physicians' CRF with a view to validating them during the follow-up visits performed by the participating physician.

8.4.3. Data recorded by the patient:

The patients shall be asked to fill in 2 self-questionnaires:

- The Morisky questionnaire (Appendix 10): 4 items used to evaluate treatment compliance with one additional item concerning the occurrence of adverse events. This questionnaire shall be filled in at the end of the 6th week of cycles 1, 2 and 4;
- A satisfaction questionnaire (Appendix 11) concerning the call platform (drawn up in the context of this study) filled in during the end-of-study visit (6th week of cycle 4), or upon treatment termination.

8.5. Complete population justification (physicians/patients)

The patients included in this study will receive support from a therapy management platform in addition to usual follow-up by their oncologist.

The estimated number of patients (n) is determined by the precision (i) required when estimating the proportion (p) of patients presenting with at least one grade 3 or 4 AE. A 95% confidence interval is associated with the estimation of this proportion. The smaller the amplitude of this confidence interval, the greater the precision. Precision is given by the following formula:

$$i = 1.96\sqrt{\frac{p(1-p)}{n}}$$

Depending on the observed proportion and on the size of the studied population, the following precision levels may be achieved:

Observed proportion	Resulting precision		
	n=75	n=100	n=125
10 – 90	6.8	5.9	5.3
20 – 80	9.1	7.8	7.0
30 – 70	10.4	9.0	8.0
40 – 60	11.1	9.6	8.6
50	11.3	9.8	8.8

[redacted]

Precision is minimum where the amplitude of the maximum confidence interval for a given proportion is equal to 50%. Failing any hypothesis concerning the value of the expected proportion, the hypothesis of a 50% proportion will be used. Thus, we can shown that 100 patients will need to be included to estimate a percentage with a 95% confidence interval whose amplitude does not exclude ±9.8%.

Between 10 and 20 centres are expected to participate in France, that shall each include 10 patients on average.

8.6. Data management

The CRO in charge of data management will process the RENACALL study data for all patients. These data will be in electronic form for data collected from the physician during the visits, along with data entered into the CATI system during calls, and in hard copy form for data collected from the patients.

All data management operations will be performed in accordance with Pfizer requirements and with CRO Standard Operating Procedures.

A data management plan, used to define and describe all biometrics activities, shall be developed by the CRO and submitted to Pfizer for validation.

8.6.1. Database construction

An annotated questionnaire shall be prepared by the CRO in charge of data management. This document will list the names of the tables and variables. For each variable, the document will give its type, length and format if applicable. The annotated questionnaire will be submitted to Pfizer for validation.

The CRO will then create a database using its own software. The structure of the database will documented and checked on printouts, comparing the attributes of the database variables to the specifications listed on the annotated questionnaire.

Before actual data entry, the database structure and input screens will be tested and validated in accordance with the CRO and Pfizer Standard Operating Procedures. For this purpose, a number of fictitious questionnaires, generally between 3 and 5, will be filled in and entered. Validation will be performed by printing out the data and comparing them to the data on the questionnaires. A validation report shall be drafted and submitted to Pfizer. The final database structure shall be submitted to Pfizer for validation before any actual data can be entered.

An audit file shall be created to save any changes made to the database. The original datum, the modified datum, the modification date and time, along with the person who made the change and the reason for the change shall be recorded in the audit file. Audit file function will be tested by altering fictitious data. A report shall be drafted and submitted to Pfizer.

8.6.2. Data input

Once the database has been validated by Pfizer, the hard copy questionnaires will be entered in duplicate using the CRO's software. Periodic input progress reports will be printed by the CRO and sent to Pfizer.

8.6.3. Data control

A list of consistency checks used to detect any inconsistencies or aberrant answers in the questionnaires shall be printed by the CRO and validated by Pfizer. These checks will be programmed using the CRO's software, then tested on fictitious data. These fictitious data, along with test-related documents, shall be kept in the study binder by the CRO and made available for review by Pfizer.

After input, the checks shall be performed continuously: a query specific to each inconsistency shall be generated electronically by the data control system. In order to limit the number of queries submitted to the participating physicians, a guide to obvious corrections can be prepared by the CRO and validated by Pfizer.

The CRO shall provide the data control documents on simple request by Pfizer. Periodic control progress reports will be printed by the CRO and sent to Pfizer.

8.6.4. Coding

All reported adverse events shall be entered using the MedDRA coding dictionary.

For other codings, a computer program shall be used to assign a code and preferred term to the verbatim text. The dictionary used shall be defined in collaboration with Pfizer.

8.6.5. Final quality control

A final quality control shall be performed on a sample of $\sqrt{n} + 1$ randomly drawn patients. This quality control shall be conducted in accordance with Pfizer's "CRF to database - QC guideline". The accepted error rate is of 0.5%. A new sample will be collected if the calculated rate exceeds this threshold value. The CRO will draft an overview of this quality control and submit it to Pfizer for review.

8.6.6. Database freeze

The database will only be frozen once the CRO has finished input, data control and possible coding. The database will be frozen in accordance with Pfizer's CT24 procedure. After validation by Pfizer, the database will be frozen by the CRO and made ready for statistical analysis.

8.6.7. Data management report

A data management report will be produced by the CRO and transmitted to Pfizer after freezing the database.

8.6.8. Data transfer

There will be no intermediate partial database transfer. At the end of the project, all paper and electronic documentation (database, programs and documents) will be transferred to Pfizer on CD-ROM.

8.7. Statistical analysis

A detailed statistical analysis plan will be drafted and submitted to the Scientific Committee members for validation before any analyses are performed.

Data for patients included in the standard follow-up group preceding amendment no. 3 will be subject to descriptive statistical analysis with respect to demographic, treatment plan and observed adverse event data.

8.7.1. Analysis strategy

The main analysis will be performed on the population of patients treated with sunitinib, taking into account all grade 3 or 4 AEs observed. Sensitivity analyses will be conducted:

- **using the "missing=failure" strategy**

Any missing values will be replaced by the value corresponding to failure, i.e. grade 3 or 4 AE. For the main outcome measure analysis, this implies that the patient shall be considered as being in a situation of failure.

- **on a population of treated patients compliant with the procedure**

The choice of a compliance threshold upon intervention must be defined in the detailed statistical analysis plan and before the final analysis is performed. This threshold shall consist in a minimum number of successful calls out of the theoretical total number of 14 calls over the entire follow-up period.

8.7.2. Statistical methods used

The descriptive analysis of qualitative and ordinal variables shall include the size and frequency of each modality, with its 95% confidence interval, along with the number of missing data.

Quantitative variables will be described in table form, displaying population size, mean and median, standard deviation, confidence interval, along with the number of missing data.

The profile of drop-out patients shall be compared to that of non-drop-out patients based on the available sociodemographic and clinical variables.

Wherever possible, the analyses will be combined with a graphical representation.

8.7.3. Analysis plan

Main outcome measure analysis

The proportion of patients presenting with at least one grade 3 or 4 AE (whether associated with sunitinib or not) shall be estimated in the overall population of patients treated with sunitinib. A 95% confidence interval will be associated with the observed proportion, using the asymptotic method, or the Clopper-Pearson exact method.

Analysis of secondary outcome measures

The analysis of secondary objectives shall be detailed in the statistical analysis plan.

8.7.4. Study report

The results will be presented in a study report. This study report will accurately and exhaustively summarise the study objectives, methods, results and their interpretation. It shall be reviewed and validated by the scientific committee. Any changes made to the statistical methods must be reported and documented in the clinical/statistical report.

A summary version of the final report will be sent to each participating physician after validation of results by the Scientific Committee.

8.8. Quality Control

During the study, Pfizer, via its CRAs, may conduct periodic monitoring visits to ensure that compliance with the protocol and with good epidemiological practice (GEP). The CRAs may examine the source documents to confirm that the data recorded on the e-CRF are accurate.
Pfizer may at any time conduct quality assurance audits on the participating physician's premises, or audits at the request of the regulatory authorities.
For the purposes of this inspection, the participating physician will provide direct source document access to the CRAs, auditors, or representatives of the competent regulatory authorities.
It is important that the participating physician and concerned staff be available during these visits and during any audits or inspections, and that a sufficient amount of time be dedicated to the process.

8.9. Study limitations

8.8.1 Selection bias

All eligible patients will be invited to take part in the study until the inclusion number is reached, in order to limit the selection of a patient profile for participation in the study.

8.8.2 Measurement bias

Upon set-up, the participating physicians will be asked not to change their patient management practices in any way during the consultations, to avoid creating a "study effect" frequently observed in studies measuring the impact of a procedure. The risk could be of more supportive management (in terms of patient follow-up) of patients, in order to provide them with the information that they would otherwise not receive in the context of the study. This effect, even though it may exist, is considered to be negligible.

The study's main outcome measure concerns grade 3 and 4 adverse events (very severe) that have the greatest impact on patients. While it is expected that patient management via the therapy management platform will globally increase the volume of events reported (more frequent contact with the patient), the hypothesis put forward is that the most severe events will be reduced by early intervention. It is therefore not expected that the double reporting of events by the physicians and nurses will have an effect on the occurrence and reporting of grade 3 and 4 adverse events in the intervention group.

8.10. Other aspects

8.9.1 CRF / e-CRF

The term CRF and/or e-CRF, as used in this protocol, refers to a hard copy questionnaire and/or to and electronic record of data, depending on the data collection method used (hard copy for the patient, electronic for the physician).
The CRF must be filled in for each patient included in the study. The original e-CRFs are the sole property of Pfizer and must not be provided to a third party in any form, with the exception of authorized Pfizer representatives, or the appropriate regulatory authorities, without Pfizer's written consent.

The participating physician is responsible for recording and reporting all collected data (clinical, pharmacovigilance, laboratory). He/she ensures that they are legible, accurate and complete. He/she must make the source data available as and when required.

The CRF must be signed by the participating physician, or by a duly authorised member of his/her staff. This signature certifies the authenticity of the data collected. Any corrections made to the e-CRF of source documents must be dated, signed and justified and must not overwrite the initially entered data.

In most cases, the source documents are the individual's file kept at the hospital or at the physician's practice. In these cases, the data recorded in the e-CRF must match those listed in these files.
In some cases, the CRF or part thereof may also serve as a source document.

8.9.2 Data storage

In order to enable inspections and/or audits by the regulatory authorities or Pfizer, the participating physician accepts to keep registers, including the identity of all participating patients (sufficient details to link for example the ERC files and those of the hospital), to inform all patients via the information/consent letter and to keep an initialled and signed copy of the consent form in the source file.
The participating physician must also keep all documents provided, along with all relevant correspondence (e.g.: letters, progress reports, meeting minutes, phone call reports). The files must be kept by the participating physician, in accordance with applicable regulations.
Should the participating physician be unable, for whatever reason, to continue keeping the study files for the required period (e.g.: retirement, change of address): The participating physician must notify this situation to Pfizer. The study files must be transferred to an appointed individual upon acceptance by Pfizer, such as another physician, another institution, or an independent third party appointed by Pfizer.
The participating physician's files must be kept for a period of at least 15 years after study termination or interruption, or for longer if required by local regulations.

The participating physician must obtain Pfizer's written consent before destroying the files, even if the storage requirements have been met.

8.9.3 CRF circuit

The data collected from the participating physicians upon inclusion and during the patient follow-up visits at the end of cycles 1, 2 and 4, shall be directly entered into the study e-CRF by the physician.

The data collected by the platform during the phone calls shall also be directly entered into the database via the CATI system. An aggregated call summary shall be made available to the participating physician on the study website (e-CRF).

via the e-CRF, by the physicians, during routine follow-up consultations,
Adverse events identified by the nurses during the phone calls shall be declared, after the calls, to the Pfizer pharmacovigilance department and shall be saved to the physician's e-CRF via the CATI system. Using the e-CRF, the participating physician review any adverse events declared by the nurses during the patient follow-up visits.

Where applicable, requests for additional information by the Pfizer pharmacovigilance department shall be sent to the person who declared the event (participating physician / nurse).
Follow-ups shall be filled in either by the nurses, or by the participating physicians, depending on the date on which the adverse event occurred.
The declarations and their follow-ups will be compiled by centre number and patient number.

The severity score (grade) estimated by the participating physician shall be entered into the e-CRF.

[redacted]

If the patient fills in a logbook (book issued according to usual patient practice), the patient logbook data will serve as the basis for the patient interviews during calls and visits. The logbook will not be transmitted to the logistics centre.

The patient compliance questionnaires (end-of-cycle 1, 2 and 4 visits) and patient satisfaction questionnaires concerning the call centre (end-of-study visit) shall be sent to the logistics centre. After acknowledging their receipt, they are sent to the CRO in batches for input.

The therapy management platform satisfaction questionnaire shall be filled in by the physician via the study website, using a specific e-CRF module accessible to the physician at the end of the study.

9. PATIENT PROTECTION

9.1. Individual information/consent

All parties are responsible for protecting the personal details of the included patients and must disclose neither the patients' names, nor any other data allowing their identification in the reports, publications and other documents.
A numerical code is assigned to the patient upon his/her inclusion in the study. This number, issued by Pfizer, shall consist of a centre number (assigned by Pfizer) and a patient number (assigned by the e-CRF). In this manner, no details are provided to Pfizer, thus guaranteeing patient anonymity.
The participating physician shall keep a confidential list of patients having taken part in the study, linking the numerical code to the patient's actual identity.

The persons participating in the study must be informed of the study's objective, its duration, the number of participants, the mode of adverse event declaration, along with their right to withdraw from the study. They must also be informed of the nature of data transmitted, of the intended use and recipients of these data, their right of access and correction, along with their right of opposition, in accordance with act 78-17 of 06 January 1978 on data protection, amended by act 2004-801 of 06 August 2004 on the protection of individuals with regard to the processing of personal data. These details are given to the patients in writing via the "Patient information leaflet" document appended to the study protocol.

The participating physician must ensure that each patient this latter's legal representative is fully informed of the nature and aims of the study, along with any possible risks associated with the patient's participation.
Each time consent is obtained from the patient's legal representative, the patient's consent must then be obtained when this latter is in a condition to do so.
Should a physician determine that his/her patients decision-making ability is so impaired that he/she cannot reasonably be consulted, then this patient cannot be included. The reasons for which the patient is unable to give his/her consent, however, must be stated in the non-inclusion register (patient refusal, impaired decision-making ability, refusal to sign the document, etc.).
The participating physician, or the person appointed by the participating physician, obtains each patient's informed consent prior to any study-specific activity. The participating physician keeps an initialled and signed original copy of the patient's consent and gives a second copy to his/her patient.

The patients will be asked to provide their phone details. These elements will be clearly explained in the information leaflet issued to the patient. The details of data storage will also be explained. The patient will

sign a consent form certifying that he/she accepts the telephone exchanges with the platform, along with the communication of his/her phone details, provided on this document.

In the case of the study, the persons in charge of the audit will have direct access to the patients' original medical data to check the study procedures and/or data. This access will be clearly stipulated in information provided to the patients who must, in this case, have signed an informed consent form.

9.2. Patient withdrawal from the study

A patient can withdraw from the study at any time, or be removed at any time by decision of the participating physician.
If a patient fails to attend a scheduled visit, all efforts must be made to contact this patient. In all cases, withdrawal from the study must be documented. The participating physician must specify the reasons for withdrawal from the study, he/she must attempt to make a further appointment for a visit and, if necessary, to monitor any unresolved adverse event.
If the patient withdraws from the study, also withdrawing his/her consent to the disclosure of future information, no other evaluations should be conducted and no additional data should be collected.
The sponsor may keep the data collected prior to withdrawal of consent.

9.3. Medical Association

Pursuant to article L.4113-6 (former L.365-1) of the Public Health Code, the following documents must be sent by the study sponsor to the CNO:

- Final protocol and amendments
- Data collection questionnaires
- List of physicians identified for participation in the study and members of the scientific committee (if available, else sent subsequently, this fact should be specified in the accompanying letter)
- Financial agreement proposed to the participating physicians and scientific committee members.
- Patient information/consent form

The study sponsor must inform the CNO in writing of all financial arrangements between the sponsor, scientific committee members and participating physicians.

A lack of response by the end of the two-month period after receipt of the dossier by the CNOM implies a favourable pronouncement. A copy of the acknowledgement of receipt shall be sent to each participating physician by the Sponsor. Each participating physician is then responsible for sending a copy of this acknowledgement of receipt, along with the signed financial agreement, to the French departmental medical association (CDO) to which he/she reports.

9.4. Data Protection: Commission Nationale de l'Informatique et des Libertés (National Data Protection Commission): "CNIL"

In accordance with act 78*17 of 06 January 1978 on data protection, amended by act 2004-801 of 06 August 2004 on the protection of individuals with regard to the processing of personal data, this protocol shall, where applicable, be submitted to the Healthcare research data processing advisory board for approval. Upon receipt of the favourable pronouncement from this board, the computer file used for this study shall be submitted to the French national data protection commission (CNIL) for authorisation. The computer file can only be used upon receipt of authorisation from CNIL.

9.5. Committee for the Protection of Persons (CPP)

The research conducted in the context of this study is characterised by the following points:

- It does not pertain to the medicinal product but rather to the care strategies
- It involves medical procedures performed in the usual manner
- In light of current knowledge, the medical strategy cannot be considered as superior to the other
- The study involves special monitoring procedures, which represent negligible risks.

In this context, this research may be considered as aimed at evaluating intermediate care, as special monitoring procedures are stipulated by the protocol. The special monitoring procedures implemented represent only negligible risks and constraints for the patient. Patient information is a written document submitted to the CPP. The study does not alter the usual therapeutic management of the patients, nor does it compromise their mental or physical well-being.

In the context of the public health act (LPSP act), a dossier shall be submitted as is to the study coordinator's CPP (article L 1121-1 2° of the Public Health Code).

9.6. Good Pharmaco-epidemiology Practices

This study is a real-life study for which the guidelines for Good Clinical Practices do not apply (30). This study must be conducted in accordance with the Pfizer protocol and standard operating procedures.

The study shall conform to the Good Pharmaco-epidemiology Practices (GPP) directives issued by the International Society for Pharmaco-Epidemiology (ISPE) (31), to the 1964 Helsinki declaration (and its subsequent amendments and clarifications) (32) and to good pharmacovigilance practice (33).

By signing the agreement, the physician undertakes to observe the instructions and procedures described in these latter and, as such, to adhere to the principles.

9.7. Patient enrolment

Announcements approved by the ethics committees may be used as procedures for patient enrolment into the study.

If the enrolment aims are not met, actions such as extending the inclusion period may be considered.

9.8. Pharmacovigilance problems and protocol or good epidemiological practice violations

In the event of a ban or restriction imposed by a competent authority in any area worldwide, or if the participating physician is made aware of information that could influence the evaluation of the benefits or risks of the test product, Pfizer must be informed immediately.

Moreover, the participating physician informs Pfizer of the urgent safety measures take to protect the study patients from immediate danger, along with all serious violations of this protocol, or of good epidemiological practice, of which the participating physician is informed.

10. PHARMACOVIGILANCE OBLIGATIONS

As the amendment to the protocol involves a change of pharmacovigilance procedures, the following paragraphs should only be taken into account once approved by the regulatory authorities.

All adverse events affecting patients withdrawn from the study, whatever the cause, declared upstream of the amendment, shall be processed according to amendment no. 2.
Adverse events affecting patients being monitored and declared upstream shall be processed according to amendment no. 3.
The table below summarises the requirements for recording adverse events on the electronic case report form and for declaring adverse events to via the Non-interventional study adverse event report form (NIS AEM Report Form) to the Pfizer pharmacovigilance department. These requirements are defined for three types of events: (1) serious adverse events (SAEs), (2) non-serious adverse events (AEs) (where applicable) and (3) situations involving exposure to a Pfizer product, including exposure during pregnancy or breast feeding, medication errors, overdosage, misuse, extravasation and occupational exposure. These events are defined in the section "Definition of an adverse event".

Adverse event	**Recorded in the study electronic CRF**	**Declared by the NISAEM Report Form to the Pfizer Pharmacovigilance department within 24 h of being made aware of the event**
SAE	All	All
Non-serious AE	All	All *Missing important information (PGR SUTENT V16.0)* *Use-related information:* - *in the paediatric population* - *in patients suffering from severe liver failure* - *in patients suffering from heart failure*
Situations **involving exposure to a Pfizer medicine**, including exposure during pregnancy or breast feeding, medication errors, overdosage, misuse, extravasation, lack of efficacy, or occupational exposure	All (independently of the presence of an associates AE), **except for occupational exposure**	All (independently of the presence of an associates AE)

For each AE, the physician must identify and gather sufficient information both to determine the outcome of the adverse event and to ascertain whether it meets the criteria for classification as a SAE (see the "serious adverse events" section below).
Adverse events must be reported to Pfizer within 24 h of the physician being made aware of them, whether the participating physician considers that these events are linked to a study medicine or not.

In particular, if the serious adverse event is fatal or life-threatening, Pfizer must be immediately notified, whatever the information available concerning the adverse event. This time frame also applies to any new (follow-up) information concerning previously notified adverse events. In those rare situations where the physician is not immediately informed of the occurrence of an adverse event, this latter must declare the event within 24 hours of being made aware and must specify the moment at which he/she was first made aware of this adverse event.

For adverse events considered to be serious or identified in the right-hand column of the above table, that must be declared to Pfizer within 24 hours of being made aware, the physician must seek and provide Pfizer with all additional information within this 24-hour time frame. Moreover, Pfizer may ask a physician to urgently obtain specific additional follow-up information. This information may be more detailed than that entered into the study case report form. In general terms, this information shall include a sufficiently detailed description of the adverse event to enable a complete medical evaluation of the case, along with the independent determination of a possible causality. All relevant information concerning the event, such as concomitant treatments or diseases, must be provided. In the event of the patient's death, a summary of the available autopsy results must be sent as soon as possible to Pfizer, or to its accredited representative.

Notification period

For each patient, the adverse event notification period starts from the moment that the patient receives his/her first dose of study medicine, or from the date at which the patient provides his/her informed consent, if he/she has already been exposed to the test drug, and ends at the end of the study observation period, i.e. at least at the end of a period of 28 calendar days after the last administration of the test drug; a declaration must be sent to the Pfizer Pharmacovigilance department, or to its accredited representative, for all types of adverse events listed in the table above and occurring during this period. If the patient receives the test drug on the last day of the observation period, the notification period is extended by a further 28 calendar days after the end of the observation period. In most cases, the consent signature date corresponds to the date the patient is included in the study.

In some cases, there may be a delay between the signing of the consent form and inclusion in the study.

In cases where the patient gives his/her consent but is not included in the study (e.g.: the patient changes his/her mind concerning his/her participation; screening test failure), the notification period ends at the date of the decision not to include the patient.

If the physician is made aware of a serious adverse event occurring at any time after the end of the observation period that he/she considers may be linked to the study medicine, this serious adverse event must also be declared to the Pfizer Pharmacovigilance department.

Evaluation of causality

The physician must assess and report the causal relationship. For all adverse events, sufficient information must be obtained by the physician to determine the causality of each adverse event. The physician must monitor those AEs considered to be related to the study medicine until the resolution or stabilisation of the event and/or its sequelae, at a level deemed acceptable by the physician, and Pfizer must agree with this evaluation.

The evaluation of causality by the physician is the determination of the fact that there is a reasonable possibility that the study medicine caused or contributed to the adverse event. If the final determination of causality is "unknown" and if the physician is unable to determine whether the study medicine caused the event, then the event must be reported within 24 hours.

If the physician is unable to determine the aetiology of the event, but has determined that the study medicine is not the cause of the event, this fact must be clearly stated in the case report form and on the non-interventional study adverse event report form (NIS AEM Report Form).

DEFINITION OF AN ADVERSE EVENT

Adverse events

An adverse event is an adverse manifestation occurring in a patient two whom a medicinal product has been administered. The event does not need to present a causal relationship with the treatment or use. Some examples if adverse events include, though this list is in no way restrictive:

- Abnormal test results (see below for circumstances under which an abnormal test result constitutes an AE);
- Clinically significant symptoms and signs;
- Alteration of clinical examination results;
- Hypersensitivity;
- Lack of efficacy;
- Drug abuse;
- Drug dependence.

Moreover, for medicines, they may include signs or symptoms resulting from:

- Overdosage;
- Weaning;
- Misuse;
- Off-MA (Marketing Authorisation) use;
- Drug interactions;
- Extravasation;
- Exposure during pregnancy;
- Exposure during breast feeding;
- Medicinal error;
- Occupational exposure.

Abnormal test results

The criteria used to determine whether an abnormal result for an objective test should be reported as an adverse event are as follows:

- The test result associated with symptoms and/or
- The test result requires additional diagnostic investigations, or a medical/surgical procedure and/or
- The test result leads to a dosage change or withdrawal from the study, to the administration of a significant additional concomitant treatment, to another treatment and/or
- The test result is considered as an adverse event by the physician or sponsor.

Simply repeating an abnormal test, failing any of the above-mentioned conditions, does not constitute an adverse event. An abnormal test result arising from an error does not need to be reported as an adverse event.

Serious adverse events

A serious adverse event is defined as an adverse manifestation in a patient receiving a medicinal product or nutritional product, at any dose, or using a medical device, and:

- Causing the patient's death;
- Creating a life-threatening situation;
- Requiring the patient's hospitalisation or extension of hospitalisation (see below for circumstances under which this does not constitute an adverse event);
- Causing permanent or major invalidity or disability (significant impairment in the ability to perform tasks of everyday life);
- Leads to a congenital anomaly or malformation.

The progression of the malignant disease during the study (including signs and symptoms of progression) must not be reported as a serious adverse event, except if the outcome is death during the study, or during the adverse event notification period. Hospitalisation due to signs and symptoms of disease progression should not be reported as a serious adverse event. If the malignant disease causes the patient's death during the adverse event notification period, then the event leading to death must be recorded as an adverse event, and as a grade 5 serious adverse event.

An event shall be defined as a medically significant event based on a medical and scientific judgement. A medically significant event may not be immediately life-threatening and/or lead to death or hospitalisation. If, however, it is established that the event could represent a danger to the patient and/or require a procedure to avoid any of the aforementioned outcomes, the medically significant event must be reported as serious.
For example, this category of medically significant events includes allergic bronchospasm requiring intensive care at the A&E department or at home, blood crasis disorders, convulsions not leading to hospitalisation, or the development of drug dependence or drug abuse.
Moreover, any suspected transmission of an infectious agent, whether pathogenic or not, by a Pfizer product, is considered to be a serious adverse event. Suspicion of this event may be induced by clinical symptoms or examination results indicating infection in a patient exposed to a Pfizer product. The terms "suspected transmission" and "transmission" are considered to be synonymous.
These cases are considered to be unexpected and must be managed as serious cases by the Pfizer Pharmacovigilance department. These cases may also where applicable be reported as product defects.

Hospitalisation

Hospitalisation is defined as any initial admission (even for periods of less than 24 hours) to a healthcare establishment, or any extension of admission.
Admission also includes transfer, within the hospital, to an intensive care unit (e.g.: from the psychiatric unit to a medical unit, from the medical unit to a coronary care unit, or from the neurology unit to a tuberculosis treatment unit).

An A&E consultation does not necessarily constitute a hospitalisation; an event leading to an A&E consultation, however, must be considered as medically significant.
Hospitalisation in the absence of adverse event does not constitute an adverse event in and of itself and requires no declaration. For example, the following reasons for hospitalisation, without AE, do not need to be declared:

- Social admission (e.g.: the patient has nowhere to sleep)
- Administrative admission (e.g.: for an annual examination)
- Optional admission not associated with a triggering AE (e.g.: for a scheduled plastic surgery procedure)
- Hospitalisation for observation, with no associated AE
- Admission for the treatment of a re-existing ailment unrelated to the development of a new AE, or to aggravation of the pre-existing ailment (e.g.: for an examination following on from persistent biological anomalies pre-dating the treatment)
- Admission scheduled by the protocol during the clinical study (e.g.: for a procedure required by the study protocol)

Situations requiring declaration to the Pfizer Pharmacovigilance Department within 24 hours.

Situations involving exposure during pregnancy or breast feeding, medication error, overdosage, misuse, extravasation, lack of efficacy or occupational exposure, are described below.

Exposure during pregnancy (or exposure *in utero*)

Exposure during pregnancy occurs if:

1. A woman becomes pregnant or is found to be pregnant while receiving or exposed to a study medicine (e.g.: environmental exposure), or the woman becomes pregnant or is found to be pregnant after having interrupted and/or having been exposed to a study medicine (maternal exposure);

2. An example of environmental exposure would be a case involving direct contact with a Pfizer product by a pregnant woman (e.g.: a nurse reports that she is pregnant and has been exposed to chemotherapeutic agents).

3. A man has been exposed, in the context of a treatment or of environmental exposure, to a study medicine before or during the conception period and/or he was exposed during his partner's pregnancy (paternal exposure).

As a general rule, cases of prospective and retrospective exposure during pregnancy, whatever the source, should be declared according to the serious adverse events declaration procedure, whether an associated adverse event is observed or not.
If a female patient enrolled in the study, or the partner of a male patient in the study becomes pregnant or is found to be pregnant during the patient's treatment with the study medicine, the physician must declare this information to Pfizer, whether an adverse event is observed or not, by filling the non-interventional study adverse event report form, along with the supplemental "exposure during pregnancy" form.
Moreover, the information concerning the environmental exposure to the study medicine by a pregnant woman (e.g.: a patient reports that she is pregnant and has been exposed to a cytotoxic product by

inhalation or by accidental spillage) must be declared to Pfizer, whether an associated adverse event occurs or not, by filling the non-interventional study adverse event report form, along with the supplemental "exposure during pregnancy" form.
The information submitted must include the expected date of birth (see below for information concerning the date of birth).
A follow-up should be implemented to obtain general information concerning the pregnancy.
Moreover, a follow-up must be implemented to obtain information concerning the outcome of the pregnancy for all cases giving rise to a notification of exposure during pregnancy whose outcome is unknown.
A pregnancy must be monitored to its term, or to its termination (e.g.: elective abortion) and Pfizer must be informed of the outcome.
This information shall be provided as a follow-up to initial exposure during pregnancy report. In the case of a birth, the neonate's structural integrity can be ascertained at birth.

In the event of termination of pregnancy, the reason must be specified and, if possible, the structural integrity of the foetus should be evaluated by visual inspection (unless the results of the tests conducted before the procedure suggested a congenital abnormality and that these results were declared).

If the outcome of the pregnancy meets the criteria for an SAE (e.g.: ectopic pregnancy, spontaneous abortion, foetal death *in utero*, neonatal death, or congenital anomaly [for a living baby, an aborted foetus, foetal death *in utero*, or neonatal death]), the SAE declaration procedures must be observed.

Additional information concerning the outcomes of pregnancies declared as SAEs are as follows:

- Spontaneous abortion, including miscarriage and foetal retention;
- Neonatal deaths occurring within one month of birth must be declared as SAEs, whatever the cause of death. Moreover, the death of an infant under the age of 1 month must be declared as an SAE when the physician considers that the infant's death is connected, or potentially connected, to exposure to the study medicine.

Additional information concerning exposure during pregnancy may be requested. Follow-ups of outcomes after birth shall be dealt with on a case-by-case basis (e.g.: follow-up of premature babies to identify any development retardation).

In the case of paternal exposure, a form for communicating information for pregnant partners shall be issued to the study participant for his partner. The issuing of this document to the study participant for transmission to his partner must be documented.

Exposure during breast feeding

Exposure situations during breast feeding must be reported, irrespective of whether an associated AE is observed.
Exposure during breast feeding should not be notified when a Pfizer product specifically indicated for use in breast feeding women (e.g.: vitamins) is administered in accordance with MA.
However, if the infant presents with an AE associated with the administration of such a medicinal product, the AE must be declared along with the exposure during breast feeding.

Medication error

The term medication error refers to any unintentional error in the prescription, dispensing or administration of a medicinal product, that could cause or result in inappropriate use of a medicinal product or in harm to the patient, whereas he/she it is under the supervision of the healthcare professional, the patient or the consumer. These events may be linked to professional practice, products, procedures and systems, in particular: prescription; transmission of an order; product information, packaging and nomenclature; composition; delivery; distribution; administration; product training; surveillance and use.

Medication errors include:

- Quasi-accidents, whether directly involving a patient or not (e.g.: inadvertent/erroneous administration, which is the accidental use of a non-indicated product, or prescription by a healthcare professional or patient/consumer);
- Confusion concerning the product name (e.g.: trade name, brand name).

The participating physician must declare the following medication errors to Pfizer, irrespective of whether an associated AE/SAE is observed:

- Medication errors involving patient exposure to the product, irrespective of whether the medication error is accompanied by an adverse event or not.
- Medication errors not directly involving a patient (e.g.: potential medication errors or quasi-accidents). When a medication error does not involve patient exposure to the product, the following minimum criteria constitute a case of medication error:
    - Identifiable notifier;
    - Suspicious product;
    - Medication error.

Overdosage, Misuse, Extravasation

Cases of overdosage, misuse and extravasation associated with the use of a Pfizer product must be declared to Pfizer by the participating physician, irrespective of whether or not an associated AE/SAE is observed.

Lack of efficacy

Cases of lack of efficacy of a Pfizer product must be declared to Pfizer by the participating physician, irrespective of whether or not an associated AE/SAE is observed, whatever the indication of the Pfizer product.

Occupational exposure

Cases of occupational exposure to a Pfizer product must be declared to Pfizer by the participating physician, irrespective of whether or not an associated AE/SAE is observed.

11. PROPERTY AND COMMUNICATION OF RESULTS

Pfizer shall remain the owner of all forms of case reports, data analyses and reports resulting from this study.

Any information obtained from this study shall be considered as confidential, until the analysis and final review, by Pfizer and the members of the scientific committee, have been completed.

11.1. Communication and publication by Pfizer

Pfizer will honour its commitment to publicly disclose the results of the clinical study by publishing them on www.clinicaltrials.gov, www.pfizer.com and/or the European clinical trials database (EudraCT), and other public registers, in accordance with applicable local laws/regulations

11.2. Publication by participating physicians

Pfizer does not object to the members of the scientific committee or participating physicians publishing the results of the study. To prevent the accidental disclosure of confidential information or industrial property, however, these results can only be published following revision and consent by Pfizer. Prior to publication or presentation, a copy of the final text must be sent by the members of the scientific committee or participating physicians to Pfizer for comments. Such comments will be intended to check the scientific content of the proposed publications and/or presentations and to ensure that the data and materials relating to Pfizer's products and activities are fairly, accurately and reasonably presented.
The participating physicians will provide Pfizer with the articles, abstracts, or full text of any planned communications (posters, conference speeches, etc.) at least 30 days prior to submission for publication. If an action is required to protect intellectual property rights, the members of the scientific committee or the participating physician will accept to delay disclosure for a period not exceeding 60 additional days.
The participating physician may request the deletion of any previously undisclosed confidential information (other than the study results) before new publication.
If the study is multi-centric, the participating physician agrees that the first publication will be a joint publication covering all centres. If the document has not been submitted to all participating centres for publication 12 months after the end of the study however, the participating physician is free to publish independently, subject to the other provisions stipulated in this paragraph.
All study-related publications must conform to ethics rules concerning copyright and publication,
The publication of results shall also give rise to an article in the financial agreement between Pfizer and the participating physician and/or establishment. In this section, publication by participating physicians, the meaning of the defined terms is that specified in the agreement.

12. SCIENTIFIC COMMITTEE

12.1. Composition

The scientific committee shall consist of the following members:

PPD

PPD

12.2. Role of the Scientific Committee

The purpose of this committee is to validate the study protocol, the case report form (CRF and questionnaires), the results and analysis reports, along with all valuations (communications, publications).

It shall also take part in implementing the therapy management platform and will validate the call scenario, physician compensation and team training.

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14. ANNEXES

14.1. Appendix 1: Patient information and consent leaflet

Pfizer	**Patient information and informed consent letter**		**Page:** 1 of 5
RENACALL STUDY			
	Protocol no.: A6181213		**Date**: 09/02/2017
Room	**Language: French**	**Centre no.: All centres**	**Country: France**
Protocol title: Evaluation of the impact of a therapy management platform on the management of patients suffering from advanced/metastatic renal cell carcinoma and receiving first line treatment with sunitinib, versus standard follow-up			
Name of participating physician			Physician's phone number
Patient's name			

This document is a patient information and informed consent letter. It contains all the detailed explanations of the intermediate care study that you are invited to take part in, along with a consent form that you will be asked to sign should you agree to participate.

I NATURE AND PURPOSE OF THE STUDY

You have been invited to take part in a study on advanced/metastatic renal cell carcinoma called RENACALL "Evaluation of the impact of a therapy management platform on the management of patients suffering from advanced/metastatic renal cell carcinoma and receiving first line treatment with sunitinib" conducted by the Pfizer laboratory.

This study will evaluate the impact of a therapy management platform in conjunction with standard care for patients suffering, like you, from advanced metastatic renal cell carcinoma and receiving 1st line treatment with sunitinib.

This is multi-centre intermediate care study conducted in metropolitan France, with prospective data collection performed by the physician. All patients will be asked to fill in a compliance questionnaire and a satisfaction questionnaire concerning the therapy management platform.

II PROJECT ORGANISATION

Between 10 and 20 oncology centres, located in metropolitan France, will take part in this study.

During the consultation marking the initiation of your sunitinib treatment, your physician will invite you to take part in this study. In all, 100 patients suffering from the same disease and receiving the same treatment as you (sunitinib) will be included in the study.

This project is an intermediate care study, i.e. the patients having accepted to take part will be treated according to the physician's usual practices and, in addition, will benefit from platform-based follow-up. This latter shall consist in regular phone calls to accompany you in your real life home management of your treatment with sunitinib (prevention, advice and guidance of patients towards options).

If you accept to take part, you will be included in the study and nurses will contact you according to a schedule defined in the protocol and reviewed with you during the first call.

A STUDY PROCEDURES

The protocol for this study involves monitoring you, at the most, during the first 4 cycles (i.e. 24 weeks) of your sunitinib treatment. If your physician or yourself deem necessary to continue follow-up by the therapy management platform nurse beyond these first 4 cycles, then you will be monitored until the end of treatment.

	Patient information and informed consent letter	**Page:** 2 of 5
RENACALL STUDY		
	Protocol no.: A6181213	**Date**: 09/02/2017

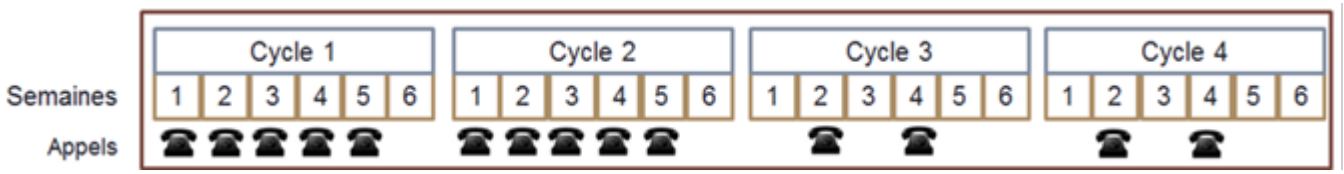
Room	**Language: French**	**Centre no.: All centres**	**Country: France**

Protocol title: Evaluation of the impact of a therapy management platform on the management of patients suffering from advanced/metastatic renal cell carcinoma and receiving first line treatment with sunitinib, versus standard follow-up

Name of participating physician	Physician's phone number
Patient's name	

Your participation in this study would consist in:

- accepting that your physician provide us with information concerning your health, without this information exceeding the scope of your health follow-up
- accepting to be contacted by a therapy management platform nurse according to the following schema:



- filling in a treatment compliance questionnaire
- filling in a call centre-related satisfaction questionnaire at the end of the study or when treatment is stopped

B EXPECTED DURATION AND EXPECTED NUMBER OF PATIENTS IN THE STUDY

If you decide to take part in this study, you will be one of the 100 patients suffering from advanced/metastatic renal cell carcinoma treated with sunitinib and included by one of the centres in metropolitan France.

The maximum duration of your participation in this study will be of 4 treatment cycles, i.e. 24 weeks. If your physician or yourself deem necessary to continue follow-up by the therapy management platform nurse beyond these first 4 cycles, then you will be monitored until the end of treatment.

This study will not in any way alter your relationship with your physician, who will be able to prescribe any procedure or treatment he/she deems necessary over the coming consultations.

C RESTRICTIONS ASSOCIATED WITH THE STUDY AND PATIENT INFORMATION

This study does not comprise any restrictions that you must observe.

Throughout the duration of the study, you will be covered by the insurance policy, taken out by the sponsor Pfizer, in accordance with current French legislation, should the study be detrimental to you.

Details of the person to contact for additional information, or in the event of damages associated with the study:

	Patient information and informed consent letter	**Page:** 3 of 5
RENACALL STUDY		
	Protocol no.: A6181213	**Date**: 09/02/2017

Room	**Language: French**	**Centre no.: All centres**	**Country: France**

Protocol title: Evaluation of the impact of a therapy management platform on the management of patients suffering from advanced/metastatic renal cell carcinoma and receiving first line treatment with sunitinib, versus standard follow-up

Name of participating physician	Physician's phone number
Patient's name	

SCIENTIFIC AND MEDICAL INFORMATION

TEL. / +33 (0)1 58 07 34 40

III RESPONSIBILITIES AND RIGHTS OF THE PATIENT AND CONFIDENTIALITY

A STUDY TERMINATION

The participating physician, i.e. the physician who has invited you to take part in this study, or the sponsor, may decide to terminate your participation in the study if:

a) You fail to observe the participating physician's instructions

b) You develop a serious ailment requiring the treatment to be stopped

c) The study is stopped by the sponsor or by the health authorities.

B RIGHTS

Your participation in this study is completely free and voluntary. Take time to read this information leaflet and discuss the matter with your physician and family if you wish. Do not hesitate to ask your physician should you require any additional information. If you decide not to take part, or to withdraw from this study, for whatever reason, this will not in any way alter your relationship with the physician following you in the context of this study, or with your attending physician. Should you change your mind and decide to no longer participate in this study, you may request the destruction of all data pertaining to yourself.

If you have any questions during the study, you should contact the physician following you in the context of this study.
In accordance with current French legislation, the protocol describing the study in which you are taking part received a favourable pronouncement from the **XXXX Committee for the Protection of Persons** (CPP) dated XX/XX/XXXX. The purpose of this committee is to ensure the scientific relevance of the study, the conditions required for your protection and the observance of your rights.

If you wish, your attending physician will be informed of your participation in this study.

After analysing all data for all patients, you will be informed of the overall results of this study via the physician who follows you in the context of this study.

C DATA CONFIDENTIALITY

All medical files and documents related to this study that identify you will be strictly confidential and will not be disclosed to third parties, to the extent permitted by current law and/or regulations. The data collected pertaining to yourself, identified by a code number, will remain anonymous for the subsequent analysis of study results. If it is decided to communicate or publish the overall results of this study in the scientific literature, only anonymised data will be presented.

Pfizer	**Patient information and informed consent letter**	**Page:** 4 of 5
RENACALL STUDY		
	Protocol no.: A6181213	**Date**: 09/02/2017

Room	**Language: French**	**Centre no.: All centres**	**Country: France**

Protocol title: Evaluation of the impact of a therapy management platform on the management of patients suffering from advanced/metastatic renal cell carcinoma and receiving first line treatment with sunitinib, versus standard follow-up

Name of participating physician	Physician's phone number
Patient's name	

In the context of this study, you accept that appointed Health Authority representatives, Pfizer representatives, other physicians, nurses and individuals taking part in this study be allowed to access your medical files. You accept that these documents be communicated, under the above-described conditions, even if you decide to withdraw from this study.

The data pertaining to yourself and recorded in the context of this study for epidemiological evaluation purposes, including those data concerning your lifestyle, will undergo computer processing by Pfizer or on its behalf. In accordance with act 78-17 of 06 January 1978 on data protection, amended by act 2004-801 of 06 August 2004 on the protection of individuals with regard to the processing of personal data, you have the right to access and correct your data. You can exercise these rights at any time with the physician following you in the context of this study.

Pfizer is the owner of the data and, as such, shall control their use and take all necessary steps to ensure their protection.

IV COMPENSATION OF THE PARTICIPATING PHYSICIAN

The participating physician, or hospital in which he/she practices, will receive financial compensation for this study from the sponsor.

	Patient information and informed consent letter	**Page:** 5 of 5
RENACALL STUDY		
	Protocol no.: A6181213	**Date**: 09/02/2017

Room	**Language: French**	**Centre no.: All centres**	**Country: France**

Protocol title: Evaluation of the impact of a therapy management platform on the management of patients suffering from advanced/metastatic renal cell carcinoma and receiving first line treatment with sunitinib, versus standard follow-up

Name of participating physician	Physician's phone number
Patient's name	

CONSENT TO PARTICIPATE IN THE STUDY

Dr. …….. invited me to take part in a study implemented by Pfizer on the treatment of metastatic renal cell carcinoma called "**Evaluation of the impact of a therapy management platform on the management of patients suffering from advanced/metastatic renal cell carcinoma and receiving first line treatment with sunitinib, versus standard follow-up**".

I confirm that I am of legal age.
I confirm that I am insured with a social security scheme, or the beneficiary of such a scheme.
I have read and perfectly understood the above information. I was given the time and opportunity to ask any questions I may have had concerning the study and this form.
I have read all the pages of this consent form and am aware of the risks and benefits described.
I have been informed that I will be covered, during this study, by the insurance taken out by Pfizer the sponsor, in accordance with current French legislation.
I have been notified that the data concerning myself will remain strictly confidential. I only allow Pfizer employees, their representatives, any service providers under contract to Pfizer, along with the various regulatory authorities to view these data, on condition that Pfizer undertakes to enforce their confidentiality, in accordance with act no. 78-17 of 06 January 1978.
I accept that the data recorded during this study may be subject to computer processing by or for Pfizer. I have noted that I can exercise my right of access and correction with Pfizer, stipulated by act no. 78-17 of 06 January 1978 on data protection, amended by act no. 2004-801 of 06 August 2004 on the protection of individuals with regard to the processing of personal data, via the physician following me for this study.
I have been informed that I am free to accept or refuse participation in this study and to withdraw from the study at any time, without this affecting my relationship with my physician. My signing of this consent does not in any way release Pfizer from its responsibilities and I retain my full rights provided under the law.
I accept that the result of the study be published and communicated to the concerned Authorities and to Pfizer.
I freely accept to take part in this study under the conditions specified in this document.
By signing this consent form, I confirm that all the information I have provided, in particular concerning my medical history, is to the best of my knowledge accurate.
I have noted that I will receive a signed copy of this consent form.

.

The patient
Patient's last name / first name in block capitals:

Date: ----------
Patient's signature:

The participating physician
Participating physician's last name / first name in block capitals:
Dr, Prof.: ----------

Date: ----------

Participating physician's signature:

Sponsor PFIZER
23-25, avenue du Dr Lannelongue
75,668 PARIS Cedex 14

14.2. Appendix 2: Contact authorisation form

Phone contact request form

for the call centre

Box to be filled in by the Physician: *Study A6181213 - RENACALL*

► Centre no.: /…/…/…/…/ - Patient no.:/…/…/

► Date of patient inclusion in the study (D0): ……

► *Physician's name:* ……..

► *Physician's phone no.:* …… ► *Physician's postal code:* ……..

Box to be filled in by the Patient:

I hereby give you my contact details, such that you can contact me in the context of this study. I have noted that you are bound by professional secrecy, that my contact details will not be provided to third parties, will not be used for purposes other than this study and will be destroyed, at the latest, at the end of this study. I authorise you to enter my contact details into a computer program to enable you to schedule and manage our contacts. In accordance with the Data Protection Act, I have the right to access and correct my contact details throughout the duration of the study. I can exercise this right via my physician. I remain free, at any time during the study, to request that you stop contacting me and to delete my contact details from your program, without having to justify myself.

M. ☐ Mrs ☐ Name: …….. First name:

…….

Address:……

……

……

……

……

Preferred **contact phone number** (1 digit per box please): _ _ _ _ _ _ _ _ _ _

Other phone no. at which I can be contacted: _ _ _ _ _ _ _ _ _ _

Hours during which you are most likely to be able to contact me from Monday to Friday (tick the time slots)**:**

8:30 to 10am ☐ 10am to 12pm ☐ 12 to 2pm ☐ 2 to 4pm ☐ 4 to 6pm ☐ 6 to 8pm ☐

Date: **Patient's signature:**

PPD

14.3. Appendix 3: ECOG

ECOG Performance Status

These scales and criteria are used by doctors and researchers to assess how a patient's disease is progressing, assess how the disease affects the daily living abilities of the patient, and determine appropriate treatment and prognosis. They are included here for health care professionals to access.

ECOG PERFORMANCE STATUS*	
Grade	**ECOG**
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

* As published in Am. J. Clin. Oncol.:
Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982.

The ECOG Performance Status is in the public domain therefore available for public use. To duplicate the scale, please cite the reference above and credit the Eastern Cooperative Oncology Group, Robert Comis M.D., Group Chair.

14.4. Appendix 4: SPC

14.5. Appendix 5: Non-Inclusion Register

Non-inclusion register

PURPOSE OF THE NON-INCLUSION REGISTER
The non-inclusion register serves to compare patients to be included in the RENACALL study with eligible patients who have not been included.
This comparison is used to evaluate inclusion biases and thus to measure their impact on the representativeness of the studied population.
Consequently, the statistical results will be fully usable and publishable.

INSTRUCTIONS FOR FILLING IN THE NON-INCLUSION REGISTER
The non-inclusion register should be filled in during the RENACALL study inclusion period, for all adult patients meeting the inclusion and non-inclusion criteria, but who did not wish to take part in the study.

We remain available to answer any questions on:
PPD

CHARACTERISTICS OF PATIENTS NOT INCLUDED IN THE STUDY

CENTRE NO. |__|__|__|__|

	Year of birth	Gender	ECOG performance status	Reason for non-inclusion
1.	__ / ____ *month year*	☐ Man ☐ Woman	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ Patient refusal ☐ Other, specify: _____
2.	__ / ____ *month year*	☐ Man ☐ Woman	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ Patient refusal ☐ Other, specify: _____
3.	__ / ____ *month year*	☐ Man ☐ Woman	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ Patient refusal ☐ Other, specify: _____
4.	__ / ____ *month year*	☐ Man ☐ Woman	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ Patient refusal ☐ Other, specify: _____
5.	__ / ____ *month year*	☐ Man ☐ Woman	☐ 0 ☐ 1 ☐ 2	☐ Patient refusal ☐ Other, specify: _____

[redacted]

	Year of birth	Gender	ECOG performance status	Reason for non-inclusion
			☐ 3 ☐ 4	
6.	__| / ____| *month year*	☐ Man ☐ Woman	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ Patient refusal ☐ Other, specify: _____
7.	__| / ____| *month year*	☐ Man ☐ Woman	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ Patient refusal ☐ Other, specify: _____
8.	__| / ____| *month year*	☐ Man ☐ Woman	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ Patient refusal ☐ Other, specify: _____
9.	__| / ____| *month year*	☐ Man ☐ Woman	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ Patient refusal ☐ Other, specify: _____
10.	__| / ____| *month year*	☐ Man ☐ Woman	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ Patient refusal ☐ Other, specify: _____

11.	__| / ____| *month year*	☐ Man ☐ Woman	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ Patient refusal ☐ Other, specify: _____
12.	__| / ____| *month year*	☐ Man ☐ Woman	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ Patient refusal ☐ Other, specify: _____
13.	__| / ____| *month year*	☐ Man ☐ Woman	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ Patient refusal ☐ Other, specify: _____
14.	__| / ____| *month year*	☐ Man ☐ Woman	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ Patient refusal ☐ Other, specify: _____
15.	__| / ____| *month year*	☐ Man ☐ Woman	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4	☐ Patient refusal ☐ Other, specify: _____

Please enter the date and electronically sign

the non-inclusion register:

Date: |___|___||___|___||**2**_|_**0**_|___|___|

14.6. Appendix 6: Case report form

A6181213

RENACALL STUDY

Pragmatic evaluation of the impact of a therapy management platform on the management of patients suffering from advanced/metastatic renal cell carcinoma and receiving first line treatment with sunitinib, versus standard follow-up

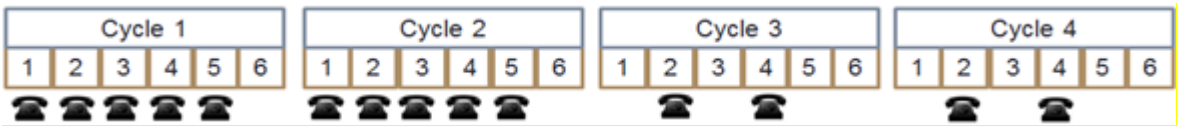
C A S E R E P O R T F O R M

Centre identifier __ __

Patient identifier __ __

1 PATIENT INCLUSION AND FOLLOW-UP SCHEMA

Verification of inclusion criteria by the investigator
Patient information/consent by patient's initials and signature on the consent form
Connection to the e-CRF module and e-CRF data input



Therapy management platform call scheme

2 INCLUSION VISIT

Inclusion visit date: __/__/ **20**__ **(DD/MM/YYYY)**

Date of consent signing: __/__/ **20**__ **(DD/MM/YYYY)**

DEMOGRAPHIC CHARACTERISTICS		
Month and year of birth	__/__/__/__ (mm/yyyy)	
Gender	❑ Male	2
	❑ Female	

2.1 Verification of eligibility criteria

INCLUSION CRITERIA		
Patient suffering from advanced/metastatic renal cell carcinoma, receiving sunitinib first-line treatment, as per SPC recommendations	❑ Yes	❑ No
Resolution (grade ≤ 1 according to CTCAE version 4.03 of June 2010) of all acute toxic effects due to radiotherapy or surgical procedure prior to initiation of sunitinib;	❑ Yes	❑ No
Man or woman aged 18 or over	❑ Yes	❑ No
Patient who can be monitored for 6 months	❑ Yes	❑ No
Female patient of child-bearing age using a form of contraception during treatment with Sunitinib and for at least 28 days after termination of treatment with Sunitinib;	❑ Yes	❑ No
Patient having signed his/her consent form;	❑ Yes	❑ No
Patient affiliated with a social security scheme.	❑ Yes	❑ No

A single "no" to one of the criteria negates the patient's eligibility for the study

NON-INCLUSION CRITERIA		
Patient participating in a clinical trial during sunitinib treatment	❑ Yes	❑ No
Patient managed by a home hospitalisation service during sunitinib treatment	❑ Yes	❑ No
Patient taking part in therapeutic education programmes, or benefiting from nursing consultation, or from any other significant treatment support and likely to impact adverse event management.	❑ Yes	❑ No
Patient untreated and/or symptomatic brain metastases prior to sunitinib initiation	❑ Yes	❑ No
Patient refusing the use of his/her personal data	❑ Yes	❑ No
Patient with an ECOG performance status upon inclusion > 2;	❑ Yes	❑ No
Serum creatinine > 1.5 times the upper normal limit	❑ Yes	❑ No
Patient presenting with a bilirubin level > 2 mg/dl, aspartate transaminase (ASAT) or alanine transaminase (ALAT) ≥2.5 times the upper limit of the normal value, or ≥5 times the upper limit of the normal value in the presence of liver metastases upon initiation of sunitinib treatment;	❑ Yes	❑ No
Patients who are staff members of a centre involved in the study, or close to one of the	❑ Yes	❑ No

staff members of a centre directly involved in conducting the study, or patients employed by Pfizer and involved in conducting the study		

A single "yes" to one of the criteria negates the patient's eligibility for the study

2.2 Contact form

Please fill in the contact form below and return it to the logistics centre.

☐ M. ☐ Mrs

Name: _____

First name: _____

Phone no. 1: _____ Phone no. 2 (optional): _____

Preferred call times: ☐ 9am-12pm ☐ 12-2pm ☐ 2-5pm ☐5-7pm

Display: Print pre-completed contact form button

2.3 Patient characteristics upon initiation of sunitinib treatment

Month and year of birth (mm/yyyy) _|_| / _|_|_|_|

Gender ❑ Male 2
❑ Female

Weight : _|_|_|,_| kg **Height:** _|_|_| cm **BMI:** _|_|,_| (auto)

ECOG: ☐ Yes ☐ No

If yes, Date: _|_| / _|_| / _|_|_|_| (DD/MM/YYYY)

If yes, score: ☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4

e-CRF instruction: a link shall be added allowing the physician to view the score variables

Karnofsky score: ☐ Yes ☐ No

If yes, Date: _|_| / _|_| / _|_|_|_| (DD/MM/YYYY)

If yes, score: ☐ 100% ☐ 90% - 80% ☐ 70% - 60% ☐ 50% - 40% ☐ 30% - 10% ☐ 0%

e-CRF instruction: a link shall be added allowing the physician to view the score variables

Risk score - Criteria of Heng *et al.*:

☐ Good ☐ Poor

☐ Intermediate ☐ Not available

Number of risk factors: 0 = Good; 1 to 2 = Intermediate; 3 to 6 = Poor.
e-CRF instruction: a link shall be added allowing the physician to view the risk score variables

2.4 History of the disease

Description of the primitive kidney cancer

Date of initial diagnosis _|_|/_|_|/_|_|_|_| (DD/MM/YYYY or MM/YYYY)
(anatomopathology report)

Histology
- ❑ Clear cell carcinoma
- ❑ Tubulopapillary carcinoma, specify:
  - ❑ Type I
  - ❑ Type II
- ❑ Chromophobe cell carcinoma
- ❑ Other, specify: _____

Mixed tumour? ☐ Yes ☐ No

➔If Yes, specify the dominant tumour: _____

Stage of the disease - TNM classification

❑ T0 ❑ T1 ❑ T2 ❑ T3 ❑ T4 ❑ Tx
❑ N0 ❑ N1 ❑ N2 ❑ Nx
❑ M0 ❑ M1 ❑ Mx

Furhman grade

❑ I ❑ II ❑ III ❑ IV

Description of the primitive kidney cancer treatment

Nephrectomy: ☐ Yes ☐ No

Radiotherapy: ☐ Yes ☐ No

Other: ☐ Yes ☐ No

If yes, specify: _____

Description of the metastatic renal cell carcinoma

Is the renal cell carcinoma metastatic? ☐ Yes ☐ No

If yes, Date of appearance first metastases: _|_|/_|_|/_|_|_|_| (DD/MM/YYYY or MM/YYYY)

Number of different metastatic sites currently affected: _|_|

Give the locations of the metastases:

Lung	☐ Yes	☐ No	☐ Blank
Bone	☐ Yes	☐ No	☐ Blank
Mediastinum	☐ Yes	☐ No	☐ Blank
Liver	☐ Yes	☐ No	☐ Blank
Retroperitoneal lymph node	☐ Yes	☐ No	☐ Blank
Subclavian lymph node	☐ Yes	☐ No	☐ Blank
Adrenal gland	☐ Yes	☐ No	☐ Blank
Nephrectomy compartment	☐ Yes	☐ No	☐ Blank
Kidney	☐ Yes	☐ No	☐ Blank
Brain	☐ Yes	☐ No	☐ Blank
Skin	☐ Yes	☐ No	☐ Blank
Peritoneum	☐ Yes	☐ No	☐ Blank
Gastrointestinal	☐ Yes	☐ No	☐ Blank

Pancreatic	☐ Yes ☐ No ☐ Blank
Skin	☐ Yes ☐ No ☐ Blank
Other 1	☐ Yes ☐ No ☐ Blank
Other 2	☐ Yes ☐ No ≤ Not specified

If yes, please specify: _____

2.5 Medical history and co-morbidities at the time of the inclusion visit

Former or current co-morbidities? ☐ Yes ☐ No

Diabetes ☐ Yes ☐ No ➔ if yes, specify current: ☐ Yes ☐ No
➔ Current treatment: ☐ Yes ☐ No

Thyroid ☐ Yes ☐ No ➔ If yes, specify ☐ Hypothyroidism ☐ Hyperthyroidism
➔ Specify current: ☐ Yes ☐ No
➔ Current treatment: ☐ Yes ☐ No

CerebroVascular Accident (stroke) ☐ Yes ☐ No ➔ if yes, year: _|_|_|_| (YYYY)
➔ Current treatment: ☐ Yes ☐ No

Hypertension ☐ Yes ☐ No ➔ if yes, specify current: ☐ Yes ☐ No
➔ Current treatment: ☐ Yes ☐ No
If yes, year initiated: _|_|_|_| (YYYY)

Myocardial infarction ☐ Yes ☐ No ➔ if yes, year: _|_|_|_| (YYYY)
➔ Current treatment: ☐ Yes ☐ No

Deep vein thrombosis ☐ Yes ☐ No ➔ if yes, specify current: ☐ Yes ☐ No
➔ Current treatment: ☐ Yes ☐ No

Angina pectoris ☐ Yes ☐ No ➔ if yes, specify current: ☐ Yes ☐ No
➔ Current treatment: ☐ Yes ☐ No

Kidney failure ☐ Yes ☐ No ➔ if yes, specify current: ☐ Yes ☐ No
➔ Current treatment: ☐ Yes ☐ No

Liver failure ☐ Yes ☐ No ➔ if yes, specify current: ☐ Yes ☐ No
➔ Current treatment: ☐ Yes ☐ No

Other ☐ Yes ☐ No ➔ if yes, specify _____
➔ specify current: ☐ Yes ☐ No
➔ Current treatment: ☐ Yes ☐ No

2.6 Haematological and biochemical profile prior to sunitinib initiation

Please fill in the following table:

Date of biological examination: ⎵⎵ / ⎵⎵ / 20⎵⎵ (DD/MM/YYYY)

Haematological profile

Parameters	Value obtained	Value	Unit
Haemoglobin	☐ Yes ☐ No ☐ Not performed		☐ g/dL ☐ Other **If other,** specify: ___
Neutrophils	☐ Yes ☐ No ☐ Not performed		☐ /mm^3 ☐ Other **If other,** specify: ___
Platelets	☐ Yes ☐ No ☐ Not performed		☐ 10^9/L ☐ Other **If other,** specify: ___

Biochemical profile

Parameters	Value obtained	Value	Unit
Creatinine	☐ Yes ☐ No ☐ Not performed		☐ mg/dL ☐ Other **If other,** specify: ___
ALAT (GPT)	☐ Yes ☐ No ☐ Not performed		☐ U/L ☐ Other **If other,** specify: ___
ASAT (GOT)	☐ Yes ☐ No ☐ Not performed		☐ U/L ☐ Other **If other,** specify: ___
Total bilirubin	☐ Yes ☐ No ☐ Not performed		☐ mg/dL ☐ Other **If other,** specify: ___
Calcium	☐ Yes ☐ No ☐ Not performed		☐ mmol/L ☐ Other **If other,** specify: ___
Albumin	☐ Yes ☐ No ☐ Not performed		☐ g/L ☐ Other **If other,** specify: ___
LDH	☐ Yes ☐ No ☐ Not performed		☐ UI/L ☐ Other **If other,** specify: ___

Were abnormal values of other biological parameters observed (last available examination)? ☐ Yes ☐ No

Parameters	Value obtained	Abnormal result	For abnormal results, value	Unit
Haematology				
Haematocrit	☐ Yes ☐ No ☐ Not performed	☐ Yes☐ No		☐ % ☐ Other **If other,** specify: ___
White blood cells	☐ Yes ☐ No ☐ Not performed	☐ Yes☐ No		☐ 10^9/L ☐ Other **If other,** specify: ___
Biochemistry				
Alkaline phosphatase	☐ Yes ☐ No ☐ Not performed	☐ Yes☐ No		☐ U/L ☐ Other **If other,** specify: ___
TSH	☐ Yes ☐ No ☐ Not performed	☐ Yes☐ No		☐ mU/L ☐ Other **If other,** specify: ___
fT3	☐ Yes ☐ No ☐ Not performed	☐ Yes☐ No		☐ pmol/L ☐ Other **If other,** specify: ___

[redacted]

fT4	☐ Yes ☐ No ☐ Not performed	☐ Yes☐ No		☐ pmol/L ☐ Other **If other,** specify: ___
Sodium	☐ Yes ☐ No ☐ Not performed	☐ Yes☐ No		☐ mmol/L ☐ Other **If other,** specify: ___
Potassium	☐ Yes ☐ No ☐ Not performed	☐ Yes☐ No		☐ mmol/L ☐ Other **If other,** specify: ___

2.7 Other examinations

Arterial blood pressure

Examination: ☐ Yes ☐ No

If yes, examination date: _|_| / _|_| / _|_|_|_| (DD/MM/YYYY)

If yes, specify values: _|_|_| / _|_|_| mmHg

syst. diast.

Electrocardiogram (ECG)

Electrocardiogram: ☐ Yes ☐ No

➔ **If yes,** Date : _|_| / _|_| / _|_|_|_| (DD/MM/YYYY)

Normal result: ☐ Yes ☐ No ➔ if abnormal, specify:

☐ Atrial fibrillation (AF)

☐ Ventricular arrhythmia

☐ Atrioventricular block (AV block)

☐ Other, specify: _____

Echocardiography

Echocardiography: ☐ Yes ☐ No

➔ **If yes,** Date: _|_| / _|_| / _|_|_|_| (DD/MM/YYYY)

Normal result: ☐ Yes ☐ No ➔ if abnormal, specify: _____

Oral examination ❑ Yes ❑ No

Oral examination: ❑ Yes ❑ No

➔ **If yes,** Date : _|_| / _|_| / _|_|_|_| (DD/MM/YYYY)

➔ **If yes,** Result: ❑ Normal ❑ Abnormal

2.8 Initiation of Sunitinib first line treatment

Initiation of sunitinib treatment

Date of first day of cycle 1: __/__/____ (DD/MM/YYYY)

Dose and dosage regimen:

☐ 50 mg/day, 4 weeks followed by a 2-week break

2.9 Symptomatic or preventive treatments

Symptomatic or preventive treatments prescribed during the initial visit

Prescription of an anti-emetic treatment: ☐ Yes ☐ No

Prescription of an anti-diarrhoeal treatment: ☐ Yes ☐ No

Initiation of anti-neutropenic treatment ☐ Yes ☐ No

Prescription of an anti-hypertensive treatment: ☐ Yes ☐ No

Prescription of mouth washes and local anaesthetics: ☐ Yes ☐ No

Prescription of emollients, moisturising creams: ☐ Yes ☐ No

Prescription of analgesics: ☐ Yes ☐ No

Prescription of an anti-gastro-oesophageal reflux treatment: ☐ Yes ☐ No

Bisphosphonate treatment: ☐ Yes ☐ No

Other anti-tumour treatment: ☐ Yes ☐ No

If yes, specify: _____

Other prescriptions: ☐ Yes ☐ No

If yes, specify: _____

e-CRF instruction: 'Please send an anonymised copy of available prescriptions issued to the patient after th inclusion visit to the logistics centre, to enable the therapy management platform nurses to advise the patien Each prescription must comprise the patient's participation no.'

2.10 Sunitinib treatment accompanying measures

The information received by the patient upon sunitinib treatment initiation (several boxes possible) was provided:

☐ by yourself

☐ by the care team. Specify the type of individuals involved (nurse, intern, etc.)

_____

☐ by means of an information leaflet or any other medium / material / document issued to the patient:

Specify the medium: _____

☐ other: _____

3 FOLLOW-UP VISIT - ROUTINE END-OF-CYCLE CONSULTATIONS

Identical follow-up data collection by the physician for all three visits: W6, W12 and W24.

Follow-up visit date: __/__/20__ (DD/MM/YYYY)

Scheduled cycle end date: __/__/20__ (DD/MM/YYYY)

3.1 Tumour evaluation

Has a tumour evaluation been carried out since the last visit dated [date of last recorded visit]: ☐ Yes ☐ No

If yes, examination date: __/__/____ (DD/MM/YYYY)

X-ray examination (several choices possible) performed to determine tumour progression:

☐ Scan ☐ MRI ☐ PET scan ☐ X-ray ☐ Echography

Response to treatment according to participating physician, according to RECIST v1.1 criteria

☐ CR (complete response)

☐ PR (partial response)

☐ SD (stable disease)

☐ PD (progressive disease)

☐ NA (not assessable) Reason: _____

3.2 Clinical parameters

ECOG: ☐ Yes ☐ No

If yes, Date: __/__/____ (DD/MM/YYYY)

If yes, Score: ☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4

e-CRF instruction: a link shall be added allowing the physician to view the score variables

Karnofsky score: ☐ Yes ☐ No

If yes, Date: __/__/____ (DD/MM/YYYY)

If yes, score: ☐ 100% ☐ 90% - 80% ☐ 70% - 60% ☐ 50% - 40% ☐ 30% - 10% ☐ 0%

e-CRF instruction: a link shall be added allowing the physician to view the score variables

Arterial blood pressure

Examination: ☐ Yes ☐ No

If yes, examination date: __/__/____ (DD/MM/YYYY)

If yes, specify values: ___/___ mmHg (syst./ diast.)

3.3 Haematological and biochemical examination since last visit

Please fill in the following table:

Date of biological examination: _|_| / _|_| / 20_|_| (DD/MM/YYYY)

Haematological profile

Parameters	Value obtained	Value	Unit
Haemoglobin	☐ Yes ☐ No ☐ Not performed		☐ g/dL ☐ Other **If other,** specify: ___
Neutrophils	☐ Yes ☐ No ☐ Not performed		☐ /mm^3 ☐ Other **If other,** specify: ___
Platelets	☐ Yes ☐ No ☐ Not performed		☐ 10^9/L ☐ Other **If other,** specify: ___

Biochemical profile

Parameters	Value obtained	Value	Unit
Creatinine	☐ Yes ☐ No ☐ Not performed		☐ mg/dL ☐ Other **If other,** specify: ___
ALAT (GPT)	☐ Yes ☐ No ☐ Not performed		☐ U/L ☐ Other **If other,** specify: ___
ASAT (GOT)	☐ Yes ☐ No ☐ Not performed		☐ U/L ☐ Other **If other,** specify: ___
Total bilirubin	☐ Yes ☐ No ☐ Not performed		☐ mg/dL ☐ Other **If other,** specify: ___
Calcium	☐ Yes ☐ No ☐ Not performed		☐ mmol/L ☐ Other **If other,** specify: ___
Albumin	☐ Yes ☐ No ☐ Not performed		☐ g/L ☐ Other **If other,** specify: ___
LDH	☐ Yes ☐ No ☐ Not performed		☐ UI/L ☐ Other **If other,** specify: ___

Were abnormal values of other biological parameters observed (last available examination)? ☐ Yes ☐ No

Parameters	Value obtained	Abnormal result	For abnormal results, value	Unit
Haematology				
Haematocrit	☐ Yes ☐ No ☐ Not performed	☐ Yes☐ No		☐ % ☐ Other **If other,** specify: ___
White blood cells	☐ Yes ☐ No ☐ Not performed	☐ Yes☐ No		☐ 10^9/L ☐ Other **If other,** specify: ___
Biochemistry				
Alkaline phosphatase	☐ Yes ☐ No ☐ Not performed	☐ Yes☐ No		☐ U/L ☐ Other **If other,** specify: ___
TSH	☐ Yes ☐ No ☐ Not performed	☐ Yes☐ No		☐ mU/L ☐ Other **If other,** specify: ___
fT3	☐ Yes ☐ No ☐ Not performed	☐ Yes☐ No		☐ pmol/L ☐ Other **If other,** specify: ___

fT4	☐ Yes ☐ No ☐ Not performed	☐ Yes☐ No		☐ pmol/L ☐ Other **If other,** specify: ___
Sodium	☐ Yes ☐ No ☐ Not performed	☐ Yes☐ No		☐ mmol/L ☐ Other **If other,** specify: ___
Potassium	☐ Yes ☐ No ☐ Not performed	☐ Yes☐ No		☐ mmol/L ☐ Other **If other,** specify: ___

3.4 Symptoms and tolerance since last visit

Since the last visit dated [date of last recorded visit]**, has the patient presented with:**

Skin reactions or disease: ☐ Yes☐ No *If yes,* how many episodes: ⌊_⌋⌊_⌋

Digestive disorders: ☐ Yes ☐ No *If yes,* how many episodes: ⌊_⌋⌊_⌋

Heart disorders: ☐ Yes ☐ No *If yes,* how many episodes: ⌊_⌋⌊_⌋

Haemorrhagic disorders: ☐ Yes☐ No *If yes,* how many episodes: ⌊_⌋⌊_⌋

Haematological disorders: ☐ Yes☐ No *If yes,* how many episodes: ⌊_⌋⌊_⌋

Infections: ☐ Yes ☐ No *If yes,* how many episodes: ⌊_⌋⌊_⌋

Pains: ☐ Yes☐ No *If yes,* how many episodes: ⌊_⌋⌊_⌋

If yes, specify the location: _____

Endocrine disorders: ☐ Yes☐ No *If yes,* how many episodes: ⌊_⌋⌊_⌋

Inflammatory disorders (mucositis, etc.) ☐ Yes☐ No *If yes,* how many episodes: ⌊_⌋⌊_⌋

General symptoms (asthenia, anorexia, etc.) ☐ Yes☐ No *If yes,* how many episodes: ⌊_⌋⌊_⌋

Occurrence of other adverse events ☐ Yes☐ No *If yes,* how many episodes: ⌊_⌋⌊_⌋

If yes, specify: _____

In the instructions for completing the AE report form, insist on:
'please give a precise description of the event, its duration, its impact on the patient's life, the corrective measures implemented and any medical procedures required: medical consultation, A&E department, hospitalisation'
'please evaluate the degree of severity of this case according to CTCAE v4.03 (June 2010)'
'please fill in the adverse event report form for all AEs, whether serious or not, whether associated with the sunitinib treatment or not'

e-CRF instruction: **Pharmacovigilance form:** ***Each time a table row is validated, the participating physician is directed to a form to be filled in.***

Description of the adverse effect:

Type of event	Description of the event	Start date	Severity	Grade (CTCAE v4.03)	Impact on activities of daily living:	Causal relationship	Change	Corrective medical action	Last action performed on Sutent® during the adverse event
Overview of all previous AEs (e-CRF + CATI) and follow-ups									

____ (auto)	....	--/--/-- (DD/MM/YYYY)	☐ Non-serious ☐ Serious If serious, severity criteria (several possible answers): ☐ Caused death If death, specify: Date of death: --/--/---- (DD/MM/YYYY) Cause of death: _____ ☐ Life-threatening ☐ Hospitalization / prolonged hospitalization ☐ Anomaly / congenital malformation ☐ Permanent or major invalidity or disability ☐ Medically significant event	☐ Grade 1 ☐ Grade 2 ☐ Grade 3 ☐ Grade 4 ☐ Grade 5	☐ Does not affect daily life ☐ Makes certain actions difficult to accomplish ☐ Affect activities of daily life	☐ Related to taking Sutent® ☐ Related to a concomitant medicine If other, specify the treatment ___	☐ Recovered If recovered, recovery date: --/--/-- (DD/MM/YYYY) ☐ Recovered with sequelae If recovered, recovery date: --/--/-- (DD/MM/YYYY) ☐ Recovering ☐ Not recovered ☐ Unknown	☐ Prescription of a treatment, specify: ☐ Medical consultation (general practitioner, specialist, emergency department) →§3.7 ☐ Hospitalisation. →§3.7 ☐ Other, specify: ☐ Not applicable	☐ Interruption (temporary, permanent, or delayed) If causality = Sutent®, →§3.5 ☐ Dose reduction If causality = Sutent®, →§3.5 ☐ Dose increase If causality = Sutent®, →§3.5 ☐ Dose unchanged ☐ Unknown ☐ Not applicable

(Dynamic table: auto-incrementation of the number of rows displayed according to the number of AEs declared above. The table is shared with that of AEs declared by the nurses using the CATI system).

3.5 Conditions of use of the sunitinib treatment

Has the sunitinib dose and/or dosage regimen been changed since the last documented visit dated [date of last recorded visit], including during the day's follow-up visit?

☐ Yes ☐ No

If yes, describe all modifications observed:

Date	**Change of dose**	**If yes, new dose (mg/day)**	**Change of dosage regimen**	**If yes, new regimen**	**Reason for the modification**
___ / ___ / _____ (DD/MM/YYYY)	☐ Yes ☐ No	☐ 25 ☐ 37.5 ☐ 50 ☐ 62.5 ☐ 75 ☐ Other: ___	☐ Yes ☐ No	: _____ ____	☐ AE; If yes, specify which one: ___ * ☐ Other, specify: _
___ / ___ / _____ (DD/MM/YYYY)	☐ Yes ☐ No	☐ 25 ☐ 37.5 ☐ 50 ☐ 62.5 ☐ 75 ☐ Other: ___	☐ Yes ☐ No	: _____ ____	☐ AE; If yes, specify which one: ___ ☐ Other, specify: _

(Dynamic table: rows can be added if more than two modifications are observed)

**: If AE ticked, the physician has already described this AE in the previous section, the e-CRF will thus display the list of AEs already filled in and the physician can simply select the relevant AE (without having to describe it again)*

Has the sunitinib treatment been temporarily interrupted since the last documented visit dated [date of last recorded visit], including during the day's follow-up visit? ☐ Yes ☐ No

If yes, describe each interruption:

Date	Duration	If yes, reason for interruption
___ / ___ / _____ (DD/MM/YYYY)	___ days ☐ Ongoing	☐ AE*; If yes, specify which one: ___ ☐ Radiotherapy ☐ Surgery ☐ Other, specify: _____
___ / ___ / _____ (DD/MM/YYYY)	___ days ☐ Ongoing	☐ AE; If yes, specify which one: ___ ☐ Radiotherapy ☐ Surgery ☐ Other, specify: _____

(Dynamic table: rows can be added if more than two modifications are observed)

**: If AE ticked, the physician has already described this AE in the previous section, the e-CRF will thus display the list of AEs already filled in and the physician can simply select the relevant AE (without having to describe it again)*

3.6 Concomitant treatments

Have any symptomatic or preventive treatments been added since the last visit dated [date of last recorded visit] (including the current visit for the next cycle)? ☐ Yes ☐ No

If yes, please specify the prescriptions:

Symptomatic or preventive treatments prescribed since the last visit

Prescription of an anti-emetic treatment: ☐ Yes ☐ No

Prescription of an anti-diarrhoeal treatment: ☐ Yes ☐ No

Initiation of anti-neutropenic treatment ☐ Yes ☐ No

Prescription of an anti-hypertensive treatment: ☐ Yes ☐ No

Prescription of mouth washes and local anaesthetics: ☐ Yes ☐ No

Prescription of emollients, moisturising creams: ☐ Yes ☐ No

Prescription of analgesics: ☐ Yes ☐ No

Prescription of an anti-gastro-oesophageal reflux treatment: ☐ Yes ☐ No

Bisphosphonate treatment: ☐ Yes ☐ No

Other anti-tumour treatment: ☐ Yes ☐ No

Specify: _____

Other prescriptions: ☐ Yes ☐ No

Specify: _____

e-CRF instruction:

'Please send an anonymised copy of the available prescriptions issued to the patient after the day's visit to t logistics centre, to enable the therapy management platform nurses to advise the patient. Each prescriptio

comprise the patient's participation no.'

3.7 Scheduled and unscheduled medical procedures

History of calls to a healthcare professional during the previous cycle

Has the patient contacted a healthcare professional since the last documented visit dated [date of last recorded visit], excluding any cases of adverse event? ☐ Yes ☐ No

If yes, please fill in the following table for each new call to a healthcare professional:

Date	Type of call	Specialist field of the healthcare professional	Reason for the call	Action implemented
___ / ___ / _____ (DD/MM/YYYY)	☐ Scheduled ☐ Unscheduled	List {General practitioner; Oncologist; Cardiologist; Nephrologist; Accident and Emergency; Nurse; Other, etc.}	☐ AE*; If yes, specify which one: ___ ☐ Other, specify: _____	☐ Temporary Sutent® interruption ☐ Treatment prescribed Specify: _____ ☐ Consultation with medical specialist ☐ Nephrologist ☐ Cardiologist ☐ Other: _____ ☐ Consultation with attending physician ☐ Emergency department. Date: _____ Location: _____ Hospitalisation: ☐Yes ☐No ☐ Hospitalisation. Date: _____ Location: _____ ☐ Hygiene and nutrition advice ☐ Other, specify: _____ ☐ Not applicable

(Dynamic table: rows can be added if more than two consultations are observed)

**: If AE ticked, the physician has already described this AE in the previous section, the e-CRF will thus display the list of AEs already filled in and the physician can simply select the relevant AE (without having to describe it again)*

History of consultations with a healthcare professional during the previous cycle

Has the patient consulted a healthcare professional since the last documented visit dated [date of last recorded visit], excluding any cases of adverse event? ☐ Yes ☐ No

If yes, please fill in the following table for each new consultation with a healthcare professional:

Date	Type of consultation	Specialist field of the healthcare professional	Reason for consultation	Action implemented
___ / ___ / _____ (DD/MM/YYYY)	☐ Scheduled ☐ Unscheduled	List {General practitioner; Oncologist; Cardiologist; Nephrologist; Accident and Emergency; Nurse; Other, etc.}	☐ AE*. If yes, specify which one: ___ ☐ Other, specify: _____	☐ Sutent® dose modification ☐ Temporary Sutent® interruption ☐ Termination of Sutent® ☐ Treatment prescribed Specify: _____ ☐ Consultation with medical specialist ☐ Nephrologist ☐ Cardiologist ☐ Other: _____ ☐ Consultation with attending physician ☐ Emergency department. Date: _____ Location: _____ Hospitalisation: ☐Yes ☐No ☐ Hospitalisation. Date: _____ Location: _____ ☐ Hygiene and nutrition advice ☐ Other, specify: _____ ☐ Not applicable

(Dynamic table: rows can be added if more than two consultations are observed)

*: *If AE ticked, the physician has already described this AE in the previous section, the e-CRF will thus display the list of AEs already filled in and the physician can simply select the relevant AE (without having to describe it again)*

History of hospitalisations during the previous cycle

Has the patient been hospitalised since the last documented visit dated [date of last recorded visit], excluding any cases of adverse event?

☐ Yes ☐ No

If yes, please fill in the following table for each new hospitalisation:

Date	Type of hospitalisation	Duration	Location	Reason	Action implemented
___ / ___ / _____ (DD/MM/YYYY)	☐ Scheduled ☐ Unscheduled	___ days ☐ Ongoing	☐ Day hospital ☐ Hospital / University Hospital ☐ CLCC ☐ Private clinic ☐ Other: ___	☐ AE*. If yes, specify which one: ___ ☐ Other, specify: ____	☐ Sutent® dose modification ☐ Temporary Sutent® interruption ☐ Termination of Sutent® ☐ Treatment prescribed Specify: _____ ☐ Consultation with medical specialist ☐ Nephrologist ☐ Cardiologist ☐ Other: _____ ☐ Consultation with attending physician ☐ Emergency department. Date: _____ Location: _____ Hospitalisation: ☐Yes ☐No ☐ Hospitalisation. Date: _____ Location: _____ ☐ Hygiene and nutrition advice ☐ Other, specify: _____ ☐ Not applicable

(Dynamic table: rows can be added if more hospitalisations are observed)

*: *If AE ticked, the physician has already described this AE in the previous section, the e-CRF will thus display the list of AEs already filled in and the physician can simply select the relevant AE (without having to describe it again)*

3.8 Decision concerning sunitinib treatment

Participating physician's decision following this follow-up visit

❑ Continue treatment, date of day 1 of next cycle: ___ / ___ / _____ (DD/MM/YYYY)

Dose and dosage regimen:

☐ 50 mg/day, 4 weeks followed by a 2-week break

☐ Other, specify: _____

❑ Termination of current treatment, date stopped:: ___ / ___ / _____ (DD/MM/YYYY)

❑ Break from therapy

❑ Change of line of therapy *(fill in the end of treatment appraisal form)*

❑ Continued break from therapy

❑ Resumed sunitinib treatment, date resumed: ___ / ___ / _____ (DD/MM/YYYY)

In the event of treatment termination, the physician is directed to the end of treatment form.

3.9 Sunitinib treatment accompanying measures if treatment continued

The patient was given information for his/her Sunitinib® treatment since the last documented visit dated [date of last recorded visit] (several boxes possible):

☐ no new information

☐ by yourself

☐ by the care team. Specify the type of individuals involved (nurse, intern, etc.)

_____

☐ by means of an information leaflet or any other medium / material / document issued to the patient:

Specify the medium: _____

☐ other: _____

4 END-OF-TREATMENT FORM

DATA CONCERNING TERMINATION OF THE FIRST LINE OF TREATMENT

Date treatment stopped _|_|_ / _|_|_ / _|_|_|_|_ (DD / MM / YYYY)

Reason for termination of Sutent®

- ❑ Disease progression
- ❑ Toxicity, specify _____
  - **has an AE report form been filled in:** ❑ Yes ❑No
  - if no, please report the AE
- ❑ Intercurrent disease, specify _____
- ❑ Patient's choice
- ❑ Physician's choice, specify _____
- ❑ Death
  - **has an AE report form been filled in:** ❑ Yes ❑No
  - if no, please report the AE
- ❑ Other, give details: _____

DISEASE OUTCOME

Best response to first line treatment with sunitinib (RECIST criteria)

- ❑ Complete response
- ❑ Stable disease
- ❑ Partial response
- ❑ Disease progression
- ☐ Not assessable **If NA,** Reason: _____

Date of first progression before initiation of a second metastatic line *(if not specified in previous tumour evaluation)*

_|_|_ / _|_|_ / _|_|_|_|_ (DD / MM / YYYY)

14.7. Appendix 7: Intervention by nurse

RENACALL STUDY

Evaluation of the impact of a therapy management platform on the management of patients suffering from advanced/metastatic renal cell carcinoma and receiving first line treatment with sunitinib, versus standard follow-up

INTERVENTION BY NURSE

A. MANAGEMENT BY THE THERAPY MANAGEMENT PLATFORM [1]

The patients will be monitored not only in the standard manner, but also via the therapy management platform.
Calls shall be made by nurses specially trained for this role, from a centralised platform based in the Paris region. If necessary, the nurses may be assisted by physicians from the therapy management platform.

The aim of these calls is to support the patients in the management of their treatment by listening to and advising them, implementing preventive measure and taking actions when deemed necessary; the purpose of these calls is to support patients in the management of their sunitinib treatment.

Call frequency is presented in the following figure:

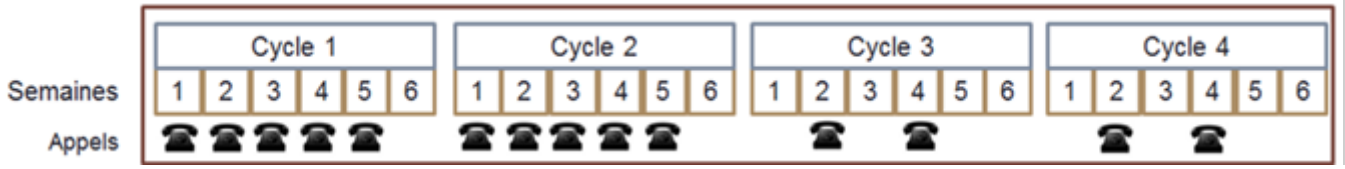


Figure 1. Call frequency for patients

The chosen rate is of:

- For the first two cycles, C1 and C2: 5 calls during the first 5 weeks of each cycle (i.e. one call per week; no call during week 6 as the patients are usually seen in consultation),
- For cycles 3 and 4: 2 calls per cycle on weeks 2 and 4.

These calls will be made for patients treated with Sutent®; in the event of termination of treatment during the follow-up period, the call following termination will close the intervention. In the event of cycle start postponement, the first call made shall be postponed to match the expected organisation (cycles 1 and 2: first call during week 1 of the cycle; cycles 3 and 4: first call during week 2 of the cycle).

[1] Information obtained from the RENACALL protocol

B. DATA COLLECTED

	1st call	Follow-up calls	Freephone number call
General information concerning the interview	X		
Patient's general condition	X	X	X
Introduction: treatment initiation	X		
Introduction: support follow-up and treatment resumption		X	X
Treatment compliance (+ Morisky at W4 cycles 1, 2 and 4)	X	X	X
Initial and support prescriptions	X		
Additional prescriptions		X	X
Care pathway (medical procedures, hospitalisation, emergencies)	X	X	X
Examination and additional tests follow-up	X	X	X
Tolerance, reported side effects	X	X	X
Monitoring of side effects and corrective actions		X	X
Setting appointments	X	X	X
Overview of advice and preventive actions covered	X	X	X
Declaration + transmission of report sheets	X	X	X

** During ad hoc calls to the freephone number, the nurse can go directly to the desired section of the questionnaire in order to meet the patient's request*

C. PRE-CALL CHECK-LIST

Instruction: Check-list pre-filled for the nurse. This sheet can be printed from the CATI system at the start of the call.
The data are obtained from the physician CRF and from previous calls. The information will also be displayed during the call in the appropriate sections, where they can be updated.

[Date - time of sheet generation]

Patient characteristics	**Physician information**
Name: _____ First name: _____ Age: _____ ECOG: _____(date) Heng criterion: _____(date) Call: Week x, Cycle x (Nth scheduled call)	Name: _____ First name: _____ Tel.: _____

Information received by the patient:

Verbal information from the oncologist; verbal information from the medical team; written information (specify medium)

Medical history and current co-morbidities

Diabetes; Hypothyroidism; Hyperthyroidism; Stroke; Hypertension; Deep vein thrombosis; Myocardial infarction; Angina pectoris; Kidney failure; Liver failure; Other: ____

Concomitant treatments

Surname	Indication	Date first taken	Status	Reason for prescription	Dosing	Recommendations
----	---	---	---	---	__	---

Adverse events (resolved and unresolved)

AE type	AE description	Start date	Severity	Grade	Causal relationship	Change	Corrective medical action	Action on suspected treatment
Overview of all previous AEs (e-CRF + CATI) and follow-ups								
---	---	---	---	---	---	---	---	---

History of calls to a healthcare professional (scheduled and unscheduled)

Date	Type of call	Specialist field of the healthcare professional	Reason for the call	Action implemented
__/__/__	---	---	---	---

History of consultations with a healthcare professional (scheduled and unscheduled)

Date	Type of consultation	Specialist field of the healthcare professional	Reason for consultation	Action implemented
__/__/__	---	---	---	---

History of hospitalisations (scheduled and unscheduled)

Date	Type of hospitalisation	Duration	Location	Reason	Action implemented
__/__/__	---	---	---	---	---

Nurse's comments:

General CATI comment: ____

Name (date): _____

Oncologist's response: _____ (*where applicable)*

Name (date): _____
Oncologist's response: _____ *(where applicable)*

D. INTERVENTION BY NURSE

Info: Depending on the type of call (1st call, cycle-start call or last call), the nurse will be automatically directed to the relevant patient questionnaire. The important data obtained from the physician CRF and from previous CATI calls will be made available to the nurse throughout the questionnaire and can be updated and completed.

D.1. Phone contact

1- Hello, I am *[Nurse's Last and First names]*, a nurse with the company PPD. I am calling in the context of the Sutent® treatment follow-up *(therapy management platform)*. Could I speak to *[Patient's Last and First names]*.
- *If Yes*, I am calling you for your support in taking the Sutent® treatment. Are you available to talk about it?
  - *If Yes, go to "Start call"*
- *If not, or not available at this time:* go to "Unsuccessful call / appointment"

Setting appointments

Info: The CATI Appointment module allows periods of unavailability to be specified, during which the patient does not wish to be called. The preferred call times are available via this module.

- If first call:
  The first interview must be held within 7 days of prescription of your Sutent® treatment, that is between *[Sutent® prescription date]* and *[date + 7 days]*. Would you be available during this period? At what time could we call you?
  ↳ *[Make an appointment]*
- Subsequent calls:
  In order to respect the call schedule, it was agreed that we would call you between *[theoretical call date -1 day]* and *[theoretical call date +1 day]*. Would you be available during this period? At what time could we call you?
  ↳ *[Make an appointment]*

D.2. Introduction and general discussion

D.2.1. General introduction to the first call:

Info: Information to present to the patient during the first call only

↳ A few days ago, your oncologist, Dr *[Doctor's Last and First names]* offered you regular telephone support to assist you in the management and tolerance of the Sutent® treatment he/she prescribed for you. I am a member of the team of nurses working in collaboration with your physician. *(Whenever possible, you will speak with me during your future calls).*

↳ I propose to call you on a regular basis to answer any questions you may have, to discuss your health and to advise you in the management of your treatment. For this, it

is agreed that i will call you once a week for the first 3 months of treatment, then once every two weeks for the following 2 cycles. *(In all, 14 calls are scheduled)*

- I would also like to point out that the purpose of these calls is not to replace Dr *[Doctor's Last and First names]* for the treatment or diagnosis of your disease. Your physician will continue to treat you as normal; We are here to assist you in managing your treatment, to advise you, to answer any questions you may have and to help you deal with any events that may occur. We are in constant connection with your physician, who will receive a report of each phone call and we can contact him/her by phone if necessary.

1- **If first call:** Did your physician clearly explain how to take the treatment?) ❑ Yes ❑ No
   - *If yes or no:* ***Advice on taking the treatment:*** Sutent® treatment takes place in cycles: it must be taken every day (50mg once per day) for 4 weeks, followed by a 2-week break without treatment. This treatment can be taken either with or without food, with a large glass of water, at any time during the date, though preferably at a set time.

2- **If first call:** Did your physician or the medical team give you a document concerning your treatment, such as an information note or follow-up notebook? Have you read it? ❑ Yes ❑ Yes, Sutent® notebook ❑ No
   - *If Yes, or Yes Notebook*, Do you have any further questions?
   - *If Yes notebook!* **Sutent® notebook advice:** In the *notebook you were given*, **you can** take notes and keep a treatment calendar, along with a schedule of appointments with your physicians, or of examinations you need to do. You can also enter any adverse events or drug reactions that may occur, along with their onset date and duration. This will enable the medical and care teams to better help you manage your treatment and your health.
     - I would ask you to have your notebook with you during the future calls so that you can readily access this information. You can also take this notebook with you during your consultations with the oncologist, in order to discuss any remarks you may have with him/her.
   - *If Not,* (check the data on the summary sheet)
     - *If the patient has received a document:* Your physician indicates that he/she issued you with [document], do you remember? Have you read it?

3- **If first call:** Did your physician explain how you should manage any treatment-related side effects that may occur? ❑ Yes ❑ No
   - *If yes or no:*
   - Over the coming months, please do not hesitate to inform us of any problems related to your general condition that you may encounter, even the mildest ones, or that do not seem serious.

- I would also like to inform you that you can contact us on the study's freephone number *[freephone number]* should you suffer any adverse event, or should you require any other advice. You can contact us during the week between *9am and 7pm*.
- In case of a serious event, however, or for any other emergency situation, you should directly call your oncologist or the emergency services (Emergency medical services: 15 or Fire brigade: 18) who can respond rapidly and thus provide better assistance.

4- **If first call**: Let's go over the treatments prescribed by your physician. Has your physician prescribed any support medicines? ❑ Yes ❑ No *If yes*, Do you have the prescriptions with you? Do you know what medicines have been prescribed for you?

- *If Yes*, Do you have the prescriptions with you? Do you know what medicines have been prescribed for you?
  - *[Check that the patient has the necessary information and that he/she is aware that he/she can act on his/her symptoms. Help him/her identify the treatments and their symptoms. Advise him/her to keep the prescriptions available.]*
- *If yes*, Do you have these medicines available at home?
  - *[Identify the systematic prescriptions to start upon initiation of Sutent® treatment, along with the supplemental prescriptions to use as and when necessary.]*
- *If not, Check the data entered*
  - *If prescriptions received:* Unless we are mistaken, the physician informed us that he/she prescribed you *[treatments]*. Do you have this prescription or treatment with you?

Table 2 + Concomitant treatments

Surname	Indication	Date first taken	Status	Reason for prescription	Dosing	Physician's advice
Overview of previous treatments						
Name : ___	□ antiemetic □ antidiarrhoeal □ anti-neutropenic □ antihypertensive □ mouthwashes and local anaesthetics □ emollients, moisturising creams □ analgesics □ anti-gastro-oesophageal reflux agents □ bisphosphonates □ Other, specify ____	□ Date first taken: __ / __ / __ (DD/MM/YYYY) □ when necessary	□ Ongoing □ Stopped, End date __ /__/__ (DD/MM/YYYY)	□ Curative □ Preventive ❑ Not available	❑ Dosage regimen: __ doses __ time(s) per day for __ weeks ❑ Not available	*Recommendations:* _____ ❑ Not available

Instruction: identifying all treatments available to the patient will allow the nurses to adapt the advice and actions to be implemented. The nurses will have received an anonymised copy of the patient's prescriptions from the physician

5- **If first call:** Could you tell me when you took Sutent® for the first time? ❑ Taken ❑ Not taken
   - *It taken,* Date first taken: __/__/____ (DD/MM/YYYY)
   - *If not taken,* Why haven't you started the Sutent® treatment?
     - ❑I forgot to start
     - ❑I am stressed / anxious at the though of taking it
     - ❑Other, specify: _____

   Do you have any questions, or topics you would like to discuss before starting to take your treatment? *[Guide and advise the patient. Notify the oncologist if major problem]*

D.2.2. Introduction of the "Regular" interview (excluding the first call of the first cycle)

Info: The introduction discussion is a 'free' discussion between the nurse and the patient, to be held during each call. It concerns the patient's overall health, in order to win his/her trust at the start of the interview. These data will not be collected, unless an AE is declared.

- How have you been since our last talk? How is it going?
  - *If resuming a cycle, a tumour evaluation should have been conducted during week 6*
    - Date of last tumour evaluation: __/__/____ (DD/MM/YYYY)
    - Response: RC / RP/ SD / PD/ NE, reason _____
      - *If answer: encourage the patient during the conversation*
      - *If disease stable: be optimistic for the remainder of the treatment*
- Are you sleeping well?
- Do you have a good appetite?
- Are you able to maintain an activity?
  - *If an AE is reported, the nurse can access the report form directly [D.5 Collecting new AEs]*

D.2.2.1. Introduction of the interview if first call of cycles 2, 3 or 4

1- **If start of cycle 2, 3 or 4**: Unless I am mistaken, you should have started a new Sutent® treatment cycle. Have you resumed your treatment? ❑ Yes ❑ No
   - *If yes,* Date resumed: __/__/____ (DD/MM/YYYY)
   - *If No,* Why haven't you resumed the Sutent® treatment?
     - ❑ I planned to resume on: date __/__/____ (DD/MM/YYYY)
     - ❑ I forgot to resume
     - ❑ I am stressed / anxious at the though of resuming
     - ❑ I suffered an adverse event *(see list of AEs for advice)*
     - ❑ My physician delayed/temporarily interrupted my treatment

- ❑ Other, specify: _____
  - ↳ *Do you have any questions, or topics you would like to discuss before resuming your treatment? (Guide and advise the patient. Notify the oncologist if problem)*

2- **If start of cycle 2, 3 or 4**: Was the dose or dosage regimen *(treatment schedule)* changed by your physician during your last follow-up visit? ❑ Yes ❑ No

- *If no*, no change, *Check the available data*
  - ↳ *If a change is specified on the e-CRF [Table 1]*: Your physician informed us that he/she changed *[dose/regimen]* for *[value]*, did he mention this to you?
- *If Yes, (corresponds to the table below)*
  - Dose changed: ❑ Yes ❑ No
    - *If yes*, what is the new prescribed dose: _ _ (mg/day)
  - Change of treatment regimen: ❑ Yes ❑ No
    - *If Yes,* what is the new regimen: __ every __ days for __ weeks, then __ weeks' rest.
  - Reason for change(s)?

    ☐ AE, specify: ____
    ☐ Other, specify: ____
    ☐ Not available

→ In the event of an additional visit to the oncologist, the e-CRF may not have been updated. If a difference arises between physician and patient data, a validation will be requested in the call overview sent to the physician.

Table 1 - Sutent® treatment changes

Date modified:	Change of dose	If yes, new dose	Change of dosage regimen	If yes, new regimen	Reason for the modification
__/__/____ (DD/MM/YYYY)	❑Yes ❑No	☐ 25 ☐ 37.5 ☐ 50 ☐ 62.5 ☐ 75 ☐ Other: _.__ ☐ Not available	☐ Yes ☐ No	☐ Regimen: _____ ☐ Not available	☐ AE; If yes, specify which one: __ ☐ Other, specify: _ ☐ Not available

3- **If start of cycle 2, 3 or 4**: Let's go over the treatments prescribed by your physician. Did your physician prescribe any support medicines? ❑ Yes ❑ No

i. *If Yes*, Do you have the prescriptions with you? Do you know what medicines have been prescribed for you?

1. [Check that the patient has the necessary information and that he/she is aware that he/she can act on his/her symptoms. Help him/her identify the treatments and their symptoms. Advise him/her to keep the prescriptions available.]

ii. *If yes*, Do you have these medicines available at home?
    1. *[Identify the systematic prescriptions to start at the beginning of the cycle, along with the supplemental prescriptions to use as and when necessary.]*

iii. *If not, Check the data entered*
    1. *If prescriptions received:* Unless we are mistaken, the physician informed us that he/she prescribed you *[treatments]*. Do you have this prescription or treatment with you?

Table 2 + Concomitant treatments

Surname	Indication	Date first taken	Status	Reason for prescription	Dosing	Physician's advice
Overview of previous treatments						
Name : ___	☐ antiemetic ☐ antidiarrhoeal ☐ anti-neutropenic ☐ antihypertensive ☐ mouthwashes and local anaesthetics ☐ emollients, moisturising creams ☐ analgesics ☐ anti-gastro-oesophageal reflux agents ☐ bisphosphonates ☐ Other, specify _____	☐ Date first taken: __ / __ / __ (DD/MM/YYYY) ☐ when necessary	☐ Ongoing ☐ Stopped, End date __ /__/__ (DD/MM/YYYY)	☐ Curative ☐ Preventive ❑ Not available	❑ Dosage regimen: __ doses __ time(s) per day for __ weeks ❑ Not available	*Recommendations: _____* ❑ Not available

<u>Instruction</u>: identifying all treatments available to the patient will allow the nurses to adapt the advice and actions to be implemented. The nurses will have received an anonymised copy of the patient's prescriptions from the physician

D.2.2.2. Introduction to the mid-cycle interviews (excluding the first call of the cycles)

4- **If mid-cycle call**: Let's go over the treatments prescribed by your physician. During our last call, you stated that you had a number of support prescriptions or treatments for managing adverse events. Have you been prescribed any additional treatments since last time? ❑ Yes ❑ No

i. *If Yes*, Do you have the prescriptions with you? Do you know what medicines have been prescribed for you?

1. (record all new prescriptions)

Table 2 + Concomitant treatments						
Surname	**Indication**	**Date first taken**	**Status**	**Reason for prescription**	**Dosing**	**Physician's advice**
Overview of previous treatments						
Name: ___	□ antiemetic □ antidiarrhoeal □ anti-neutropenic □ antihypertensive □ mouthwashes and local anaesthetics □ emollients, moisturising creams □ analgesics □ anti-gastro-oesophageal reflux agents □ bisphosphonates □ Other, specify _____	□ Date first taken: __ / __ / __ (DD/MM/YYYY) □ when necessary	□ Ongoing □ Stopped, End date __ /__/__ (DD/MM/YYYY)	□ Curative □ Preventive ❑ Not available	❑ Dosage regimen: __ doses __ time(s) per day for __ weeks ❑ Not available	*Recommendations: _____* ❑ Not available

Instruction: identifying all treatments available to the patient will allow the nurses to adapt the advice and actions to be implemented. The nurses will have received an anonymised copy of the patient's prescriptions from the physician

D.2.3. "Freephone" interview

Instruction: During calls to the freephone number, the nurse can access all of the CATI questionnaire in order to meet the patient's request. Once the patient's request has been dealt with, either the next interview can be conducted, depending on its theoretical date, or an appointment can be made

1- What is the reason for your call?
   - Answer, Advice, Action *[Provide the appropriate answer to the question, by reference to the concerned section of the questionnaire]*

2- Do you have any other questions or problems you would like to discuss?
   - If yes, *[Go to q1]*
   - If no, *[Go to q3]*

3- We had agreed to call you on [date] to go over your health and treatment management in greater detail. Would you like to talk about this now?
   - *If yes, [redirection to "Regular" questionnaire]*
   - *If no*, Could we make an appointment for this interview? *[Make an appointment]*

D.3. Compliance and care pathway

If 1st call The rest of the discussion covers the period from the last appointment with your oncologist dated *[inclusion date] (Sutent® initiation consultation) to the current date.*
If subsequent calls*:* The rest of the discussion covers the period from the last call, dated *[date of last call]* to the current date.

D.3.1. Treatment compliance

Since our last call, have you taken your treatment every day?
❑ Yes ❑ No

a) ***If yes,*** For information, if you forget to take your capsule one day, do not attempt to make up for this omission by taking 2 capsules the next day, take only the usual dose.

If W4 calls for Cycles 1, 2 or 4: ***Morisky treatment compliance questionnaire***

The following questions concern the entire current cycle, hence the past 4 weeks:

i. Did you, at any time, forget to take your treatment? ❑ Yes ❑ No
ii. Did you sometimes have trouble remembering to take your treatment? ❑ Yes ❑ No
iii. Did you ever stop taking your treatment when feeling better? ❑ Yes ❑ No
iv. If you felt worse when taking your treatment, did you at any time stop taking it? ❑ Yes ❑ No
v. When you suffered an adverse event, did you ever reduce or adapt the treatment? ❑ Yes ❑ No

→ *If at least 1 Yes:* Have you forgotten or interrupted your treatment since our last call?

b) ***If No,*** could you describe to me the periods when you did not take your treatment? What was the reason? *[Report the interruption - Table 3]*

↳ *If omission:* For information, if you forget to take your capsule one day, do not attempt to make up for this omission by taking 2 capsules the next day, take only the usual dose.

– *If W4 calls for Cycles 1, 2 or 4:* ***Morisky treatment compliance questionnaire.***

The following questions concern the entire current cycle, hence the past 4 weeks: *[qualify the question if the patient declared having forgotten or interrupted his/her treatment: "We have already discussed this, but I need to validate certain details"]*

i. Did you, at any time, forget to take your treatment?❑ Yes ❑ No
ii. Did you sometimes have trouble remembering to take your treatment?❑ Yes ❑ No
iii. Did you ever stop taking your treatment when feeling better? ❑ Yes ❑ No

iv. If you felt worse when taking your treatment, did you at any time stop taking it? ❑ Yes ❑ No

v. When you suffered an adverse event, did you ever reduce or adapt the treatment? ❑ Yes ❑ No

Table 3 - Treatment interruptions		
Date	**Duration (days)**	**Reason for interruption**
Overview of previous interruptions	_ _	-
__/__/____ (DD/MM/YYYY)	_ _ *Ongoing*	Adverse event Medical decision Omission Lack of efficacy Improved health Other: _____

Instruction: if Adverse event is ticked, the AE declaration table appears for data input. New AEs are added to the table in section D.5. AE collection

D.3.2. Scheduled and unscheduled medical procedures

↳ Have you called upon or consulted a healthcare professional since our previous interview (or since the start of treatment for the first call)? ❑ Yes ❑ No
- *If new call, [Report a new call – Table 4]*
- *If new consultation, [Report a new consultation – Table 4']*

↳ *If cycle-end call (week 4):* Are you scheduled to see your oncologist during the coming weeks? ❑ Yes ❑ No
- *If yes, [Report a new consultation]*
- *Reminder:* Before the consultation with your oncologist, do not forget to perform all the additional tests he/she asked for, to help him/her define the most appropriate treatment. If you have a follow-up notebook in which you take notes, remember to bring it with you.

Table 4 - History of calls to a healthcare professional				
Date	**Type of call**	**Specialist field of the healthcare professional**	**Reason for the call**	**Action implemented**
Overview of previous calls				
__/__/____ (DD/MM/YYYY)	☐ Scheduled ☐ Unscheduled	List {General practitioner; Oncologist; Cardiologist; Nephrologist; Accident and Emergency; Nurse; Other, etc.} If Other, specify: _____	☐ AE; *specify*: ___ ☐ Other	☐ Temporary Sutent® interruption ☐ Treatment prescribed Specify: _____ ☐ Consultation with medical specialist ☐ Nephrologist ☐ Cardiologist ☐ Other: _____ ☐ Consultation with attending physician ☐ Emergency department. Date: __/__/____ (DD/MM/YYYY) Location: _____ Hospitalisation: ☐Yes ☐No ☐ Hospitalisation. Date: __/__/____ (DD/MM/YYYY)

				Location: _____ ☐ Hygiene and nutrition advice ☐ Other, specify: _____ ☐ Not applicable

Instruction: if Adverse event is ticked, the AE declaration table appears for data input. New AEs are added to the table in section D.5. AE collection

Table 4' - History of consultations with a healthcare professional				
Date	**Type of consultation**	**Specialist field of the healthcare professional**	**Reason for consultation**	**Action implemented**
Overview of previous consultations				
__/__/__/__/__/__/__/__ (DD/MM/YYYY)	☐ Scheduled ☐ Unscheduled	List {General practitioner; Oncologist; Cardiologist; Nephrologist; Accident and Emergency; Nurse; Other, etc.} If Other, specify: _____	☐ AE; *If yes,* specify which one: ___ ☐ Scheduled examination ☐ Other	☐ Sutent® dose modification ☐ Temporary Sutent® interruption ☐ Termination of Sutent® ☐ Treatment prescribed Specify: _____ ☐ Consultation with medical specialist ☐ Nephrologist ☐ Cardiologist ☐ Other: _____ ☐ Consultation with attending physician ☐ Emergency department. Date: __/__/____ (DD/MM/YYYY) Location: _____ Hospitalisation: ☐Yes ☐No ☐ Hospitalisation. Date: __/__/____ (DD/MM/YYYY) Location: _____ ☐ Hygiene and nutrition advice ☐ Other, specify: _____ ☐ Not applicable

Instruction: if Adverse event is ticked, the AE declaration table appears for data input. New AEs are added to the table in section D.5. AE collection

D.3.3. Hospitalisations or visits to accident and emergency

- Have you been hospitalised, or have you been to accident and emergency since our previous interview (or since the start of treatment for the first call)? ❑ Yes ❑ No
  - *If Yes*, *[Report a new hospitalisation – Table 5]*
  - *If Yes,* Did the hospitalisation lead to a temporary interruption of treatment?? ❑ Yes ❑ No
    - *If Yes*, have we discussed this previously? ❑ Yes ❑ No
      - *If No, [Report a new treatment interruption – Table 3]*

Table 5 - Hospitalisations or visits to accident and emergency					
Date	**Type of hospitalisation**	**Duration (days)**	**Location**	**Reason**	**Action implemented**
Overview of previous hospitalisations					
__/__/___ (DD/MM/YYYY)	☐ Scheduled ☐ Unscheduled	_ _ day ❑ Not available	☐ Day hospital ☐ Hospital / University Hospital ☐ CLCC ☐ Private clinic ☐ Other: _____ ☐ Hospital (no details)	Adverse event Other: ____	☐ Sutent® dose modification ☐ Temporary Sutent® interruption ☐ Termination of Sutent® ☐ Treatment prescribed Specify: _____ ☐ Consultation with medical specialist ☐ Nephrologist ☐ Cardiologist ☐ Other: _____ ☐ Consultation with attending physician ☐ Emergency department. Date: __/__/____ (DD/MM/YYYY) Location: _____ Hospitalisation: ☐Yes ☐No ☐ Hospitalisation. Date: __/__/____ (DD/MM/YYYY) Location: _____ ☐ Other, specify: _____ ☐ Hygiene and nutrition advice ☐ Not applicable

Instruction: if Adverse event is ticked, the AE declaration table appears for data input. New AEs are added to the table in section D.5. AE collection

D.3.4. Monitoring additional examinations

- **If cycle-start call for cycle 1, 2, 3 or 4 (post oncologist visit)**

Did your oncologist ask you to perform additional examinations over the coming weeks of treatment? ❑ Yes ❑ No

- *If Yes,* What examinations did he/she recommend carrying out? When do you need to do them? *[Add an examination – Table 6]*
  - If you have these examinations before the next call, do not hesitate to have your results with you so we can discuss them.
- Amongst these examinations, have you already had any? Which ones?
  - *If Yes,* Are there any points you would like to talk about? *[AE report depending on results]*

- **If mid-cycle call:**
- During our previous calls, you stated having one or more additional examinations. Did you do them? ❑ Yes ❑ No

- *If Yes,* When did you have it? *[update Table 6]*
  - *If Yes,* Are there any points you would like to talk about? *[AE report depending on results]*
- *If No*, The examination results that you notify to the medical team in charge of following you may, if your physician deems necessary, lead to an adaptation of your treatment. It is thus important that you undergo the examinations requested by your physician in order to help him/her care for you.

Table 6 - Additional examinations			
Type of examination	**Recommended date**	**Status**	**Result**
Biological examination, blood sample Urine analysis Hypertension monitoring Cardiovascular profile Thyroid function profile Liver profile Oral profile Skin clinical examination Other: ….	❑Date: __/__/____ (DD/MM/YYYY) ❑Frequency: __/wk ❑ Not applicable	❑Done, date: __/__/____ (DD/MM/YYYY) ❑Appointment made, Date: __/__/____ (DD/MM/YYYY) ❑To do	❑Don't know ❑Normal ❑Abnormal: AE

D.4. Tolerance and actions implemented

Monitoring of the outcome of previously reported adverse events

- During the last call of *[date]*, we spoke of your problems concerning *[event]*.
  - What is the current situation? *[Update Table 7]*
  - We had determined that you could do *[action]* to prevent / relieve *[event]*. Did you do it? Did it provide relief? *[Update Table 7]*

Adverse event follow-up

- *If the AE is resolved and where applicable, inform the patient of actions to implement to prevent the recurrence of symptoms*
- In the event of AE progression, new estimation of grade and of medical actions to implement *[see section D.5. New AE collection]*

Table 7 - Adverse events (past and current)									
Type of event	**Description of the event**	**Start date**	**Severity**	**Grade (CTCAE v4.03)**	**Impact on activities of daily living**	**Causal relationship**	**Change**	**Corrective medical action**	**Action on suspected treatment**
Overview of all previous AEs (e-CRF + CATI) and follow-ups									
_____ (list choice)	…… …….. …… …….. …… ……..	--/--/-- (DD/MM/YYYY)	☐ Non-serious ☐ Serious If serious, severity criteria (several possible answers): ☐ Caused death If death, specify: Date of death: --/--/---- (DD/MM/YYYY) Cause of death: ___ ☐ Life-threatening ☐ Hospitalization / prolonged hospitalization ☐ Permanent or major invalidity or disability ☐ Anomaly / congenital malformation ☐ Medically significant event	☐ Grade 0 ☐ Grade 1 ☐ Grade 2 ☐ Grade 3 ☐ Grade 4	☐ Does not affect daily life ☐ Makes certain actions difficult to accomplish ☐ Affect activities of daily life	☐ Related to taking Sutent ® ☐ Related to a concomitant medicine; Specify the treatment: __	☐ Recovered If recovered, recovery date: --/--/-- (DD/MM/YYYY) ☐ Recovered with sequelae If recovered, recovery date: --/--/-- (DD/MM/YYYY) ☐ Recovering ☐ Not recovered ☐ Unknown	☐ Prescription of a treatment, specify: ☐ Medical consultation (general practitioner, specialist, emergency department) ☐ Hospitalisation. ☐ Nurse's advice, specify: _____ ☐ Other, specify: ☐ Not	☐ Interruption (temporary, permanent, or delayed) ☐ Dose reduction ☐Dose increase ☐ Dose unchanged ☐ Unknown ☐ Not applicable

								applicable	

Instruction: for all current AEs, check AE outcome. If the AE is unresolved, a new row will be generated and linked to the source row. AEs reported by the physicians via the e-CRF are distinguished from AEs reported by the nurses using CATI.

D.5. New AE collection

Intro: as the interview progresses the nurse will gain access to the various screens concerning the adverse events described by the patient at any time during the telephone conversation; moreover, at this stage of the interview, the nurse will check for any other AEs that may not have been mentioned before.

Since the last interview, since starting taking Sutent® (for the first call), have you had any discomfort, or have you experienced unexpected effects related to your Sutent® treatment other than those we have already discussed? ❑ Yes ❑ No

- *If Yes, [Go to AE information collection questionnaire]*
  - *Once the patient has finished describing the AE:* Have you experienced any other discomfort or adverse reactions?
- *If not, check for the absence of AEs:* Do not hesitate to report any problems you might encounter, even the mildest such as for example:
  - Changes to skin, nail or hair
  - Digestive disorders
  - Breathing difficulties
  - Heart disorders or change in blood pressure
  - Mouth or gum problems
  - Other adverse events such as tiredness or fever, etc.

Ongoing grade 3 / 4 AE: *Recommendation for temporary interruption of Sutent® treatment pending oncologist's medical opinion:* ❑ Yes ❑ No

- If Yes, In this situation, I recommend that you temporarily interrupt your Sutent® treatment until further notice. Your oncologist will be alerted and his/her medical opinion requested. We will contact you to inform you of his/her decision.

Activities of daily life: preparing meals, shopping, using a telephone, paying.
Major daily activity: Showering, dressing and undressing, eating, going to the toilet.

Instruction: any report of a grade 3 or 4 AE, except for a biological AE, will trigger an email alert for the oncologist + Level 3 TEC. Other alerts are generated on a case by case basis for certain grade 2 AEs.

Table 8 - AE / Grade / Action look-up table for Sutent®-related AEs		
Adverse event	**CTCAE grade estimation**	**Recommendations and Actions to implement**
Skin toxicity		
- Skin irritation - Dry skin - Cracked skin - Nail fissures - Hyperkeratosis (corn, psoriasis, warts)	- Intensity of dryness? o Asymptomatic <10% of body area and not associated with erythema or pruritus (Grade 1) o Symptomatic 10 to 30 % of body area and associated with erythema or pruritus (Grade 2) o >30% of body area and associated with erythema or pruritus (Grade 3) - Impact on daily life o Does not affect activities of daily life (Grade 1 / 2) o Affects activities of daily life (Grade 2 > Grade)	- No event / prevention: moisturising cream to prevent dryness, Dexeryl or Biafine emollient cream, pedicure and manicure at start of treatment - Grade 1: antiseptic foot bath, bepanthren / moisturising cream for relief, salicylic acid officinal formula (apply a thick layer of cream after evening ablutions, then put on socks). Use gentle and scent-free soap. - Grades 2 and 3: consultation with dermatologist or chiropodist (rapid care required as difficult to estimate / manage over the phone)
- Hand and foot syndrome	- Minor skin o Alterations or dermatitis (Grade 1) o Desquamation, blisters, haemorrhagic lesions, oedema (Grade 2) o Ulcerative lesions (Grade 3) - Sensitivity / pain / discomfort o Painless (Grade 1) o Pain with no functional impairment (Grade 2) o Functional impairment with no pain (Grade 2)	- Grade 1: urea-based daily use keratolytic emollients, e.g.: Xerial® 30 or 50 (labo SVR), Akerat S® (Avène). - Grade 2: consultation with oncologist or GP if involved in patient follow-up and good relationship with patient + alert oncologist in report. - Grade 3: patient's condition requires consultation with oncologist

	○ Pain and functional impairment (Grade 3)	
- Skin colouration - Dermal alteration	- Intensity of discolouration ○ Mild: < 10% of body area → No psychological impact. (Grade 1) ○ Pronounced: >10% of body area + psychological impact (Grade 2) - Dermal alteration ○ Mild thickening (Grade 1) ○ Leathery appearance; papillary formation (Grade 2)	- No event / prevention to grade 2: temporary non-contagious alteration, without consequences. No direct care required.
- Alopecia	- Intensity of hair loss ○ Thinning or localised <50%, wig not needed. (Grade 1) ○ Total (Grade 2)	- Grades 1 and 2: no treatment or action to implement, but reversible in most cases
Digestive disorders		
- Acid reflux - Heartburn	- Description of intensity ○ Mild (Grade 1) ○ Moderate or mild, but frequent (Grade 2) ○ Severe or moderate, but frequent (Grade 3)	- Grade 1: Gaviscon for initial reflux episodes. Avoid food causing reflux - Grade 2: continue Gaviscon + Inexium (IPP) as self-medication if reflux too frequent - Grade 3: contact oncologist
- Diarrhoea	- stool frequency ○ stools more frequent, but < 4/day compared to usual, not necessarily liquid (grade 1) ○ very frequent stools < 4-6/day, liquid (grade 2) ○ >7 stools/day, incontinence, impact on activities of daily living. - Accompanied by vomiting? ○ Yes (Grade 3)	- Grade 1: Dietary advice (drink often and in small amounts; low-fibre diet) + take antidiarrhoeal agents prescribed by physician: smecta, the imodium, then tiofan according to intensity (reassess the grade) - Grade 2: if treatments no longer sufficient, contact attending physician. - Grade 3: vomiting + diarrhoea: consult GP rapidly as need to be examined
- Nausea - Vomiting	- **Nausea:** ○ loss of appetite with no change in eating	- Grade 1: antinauseant / preventive anti-emetic; nutritional advice (eat slowly, fractionate meals,

	habits (Grade 1) ○ Reduction in food intake, without significant weight loss, dehydration or malnutrition. (Grade 2) ○ Reduced calorie intake or tube feeding (Grade 3) **Vomiting:** - Frequency / 24 hours ○ 1 to 2 episodes (at least 5 min. apart). (Grade 1) ○ 3 to 5 episodes (at least 5 min. apart) (Grade 2) ○ >6 episodes, reduced calorie intake or tube feeding - Other factors? ○ Persistence over 48h or combined with diarrhoea (Grade 1 → 2, 2 → 3)	avoid fatty or spicy meals, drink between meals) - Grade 2, 3: persistent or vomiting + diarrhoea: consult GP rapidly as need to be examined
- Abdominal pain	- Pain level ○ Mild (Grade 1) ○ Moderate + impact on activities of daily living. (Grade 2) Severe ++ major impact on activities of daily living (Grade 3) - Blood in stools (Grade 2 > 3)	- Grade 2: alert oncologist in report - Grade 3: contact oncologist by phone + alert oncologist by email
Heart disorders		
- Hypertension	- Have you measured your blood pressure, or had it measured recently? ○ 120-139 / 80-89 (Grade 1) ○ 140-159 / 90-99 (Grade 2) ○ ≥ 160 / ≥100 (Grade 3) ○ Malignant HTN, transient or permanent neurological deficit (Grade 4)	- Grade 1: Continue regular monitoring and taking treatment if prescribed. Contact oncologist preventively as nurse does not have all necessary information to determine severity - Grades 2 and 3: Contact oncologist rapidly, he/she will decide whether treatment should be initiated

	- Other concomitant symptoms?
	  o Dizziness, tiredness (Grade 1 > Grade 2)
	  o Pre-existing heart disease, kidney failure, single kidney (Grade 1> Grade 2, Grade 2 > Grade 3)	

Haemorrhagic and endocrine disorders		
- Anaemia	- STANDARD Man: 13 – 17 g/dL; Woman: 12 – 15 g/dL - Grade 1: < 10 g/dL (6.2 mmol/L or 100g/L) - Grade 2: 8 – 10 g/dL (6.2- 4.9 mmol/l or 100-80g/L) - Grade 3: <8 g/dL (≤ 4.9 mmol/L or 80 g/L)	- Grade 1: no action - Grade 2: oncologist email alert - Grade 3: patient contacts oncologist
- Haematuria		- Alert oncologist by email as soon as haematuria observed
- Neutropenia	- Grade 0: 1,8 – 7 *109/L - Grade 1: 1,5 – 1.8 *109/L - Grade 2: 1,0 – 1.5 *109/L - Grade 3: 0.5 – 1.0 *109/L (1000 mm3 + fever) - Grade 4: <0,5 *109/L Presence of fever? Yes (Grade 2 > 3, 3 > 4)	- Grade 1: no prescription of GCSF, talk to oncologist at next visit - Grade 2: alert oncologist in report - Grade 3: alert oncologist by email; if fever: Fever management advice + rapidly contact oncologist by phone - Grade 4: rapidly contact oncologist by phone
- Thrombocytopaenia	- STANDARD > 150 * 109/L - Grade 1: 75,0 – 150 *109/L - Grade 2: 50,0 – 75.0 *109/L - Grade 3: 25,0 – 50.0 *109/L	- Grade 1: no action recommended - Grade 2: oncologist email alert - Grade 3: rapidly contact oncologist + alert oncologist by email
- Increased creatininaemia	- STANDARD: 7 to 13 mg/L - Grade 1: 1 to 1.5* previous value - Grade 2: 1.5 to 3* previous value - Grade 3: 3 to 6* previous value - Grade 4: >10 * previous value	- No grade 1 event, recommend drinking to avoid dehydration. Creatinine drops during the 2 weeks of break. - Grade 2: oncologist email alert - Grade 3: rapidly contact oncologist + alert

	-	oncologist by email
- Hypothyroidism	- Grade 1: TSH 5 to 10 µU/mL - Grade 2: TSG > 10 µU/mL	- Grade 1: asymptomatic, does not require management - Grade 2: general practitioner, additional tests to implement appropriate treatment
- Hyperthyroidism	- Grade 1: TSH 0.30 to 0.10 µU/mL - Grade 2: TSH < 0.10 µU/mL	- Grade 1: asymptomatic, does not require management - Grade 2: general practitioner, additional tests to implement appropriate treatment
Infectious problems		
- Mucositis - Stomatitis - Ulcers - Infections of the oral mucosa	- Intensity and location o Asymptomatic (Grade 1) o Localised ulceration, swallowing difficulties, dry mouth (Grade 2) o Confluent ulcers, mild bleeding (Grade 3) o Tissue necrosis, significant spontaneous bleeding (Grade 4) - Diffuse pain? (Grade 2)	- No grade 2 event: systematic treatment by sodium bicarbonate mouth wash + Kéal; oral hygiene advice (regular tooth brushing with a soft toothbrush) o If ulcers present, fungal treatment and/or viscous xylocaine treatment o If pain, Efferalgan® codeine mouthwash - Grade 3: Contact oncologist / emergency department rapidly - Grade 4: Emergency department / hospitalisation
- Gingivitis	- How intense is the pain? o Mild (Grade 1) o Moderate (Grade 2): o Severe (Grade 3) - Do you experience discomfort when eating meals? o Mild (Grade 1) o Strong discomfort with oral meals (Grade 2) o Oral feeding impossible (Grade 3) - Diffuse pain? (Grade 2)	- Grade 1: treatment with pansoral, talk to oncologist at next visit - Grade 2: efferalgan codeine mouthwash for pain. Talk to oncologist at next visit. Alert oncologist by email. - Grade 3: Alert oncologist by email + call oncologist
- Diffuse oral pain	o - Moderate pain (Grade 1)	- Grade 1: treatment with pansoral, talk to

	○ - Moderate and limits activities of daily living (Grade 2) ○ - Severe + Major daily impact	oncologist at next visit - Grade 2: efferalgan codeine mouthwash for pain. Talk to oncologist at next visit. Alert oncologist by email. - Grade 3: Alert oncologist by email + call oncologist
- Fever	- Ignition ○ 38-39 °C (Grade 1) ○ 39-10 °C (Grade 2) ○ > 40 °C for less than 24 hours (Grade 3) ○ > 40 °C for more than 24 hours (Grade 4) - Other symptoms? ○ Burning sensation when urinating, cough, diarrhoea, chills, sweats (Grade 1 > 2, Grade 2 > 3)	- No event / prevention: antibiotics not systematically prescribed. - Grade 1: monitor. Paracetamol if <38.2 °C without symptoms / If persistent, change to grade 2 - Grade 2: if 38.2 °C or more after 1h, direct to physician, sign of infection. Alert oncologist by email. - Grade 3: If ~40 °C + sign of an infection, direct to oncologist + alert oncologist by email. - Grade 4: emergency department
Other symptoms		
- Headaches	- What is the intensity of your headaches? ○ Mild (Grade 1) ○ Moderate (Grade 2): ○ Severe (Grade 3) - Do your headaches impact the activities of your daily life? ○ Does not affect daily life (Grade 1) ○ Makes certain actions difficult to accomplish (Grade 2) ○ Affect activities of daily living (Grade 3) - Presence of dizziness? tinnitus? hypertension or risk of hypertension? (Grade 3)	- Grade 1: treatment with paracetamol (Efferalgan®, Doliprane®) or aspirin (Aspegic®). Reassure the patient as there is no problem of drug interaction. - Grade 2: redirect to general practitioner. Notify during next oncologist visit, particularly if several episodes. - Grade 3: contact oncologist + alert oncologist by email.
- Tiredness (asthenia,	- What is the intensity of your tiredness?	- Grades 1 and 2: try to maintain a healthy lifestyle

apathy, malaise)	○ Mild (Grade 1) ○ Moderate (Grade 2): ○ Severe (Grade 3) ○ *Totally incapacitating (Grade 4)* - Does your tiredness impact the activities of your daily life? ○ Does not affect daily life (Grade 1) ○ Makes certain actions difficult to accomplish (Grade 2) ○ Affects major daily activities (Grade 3)	(eat and drink correctly); take as many naps as necessary; exercise a little and relax as much as possible. Stop work during cycle 1 to manage cumulative fatigue over the treatment period - Grade 3: if persistent tiredness / rapid onset, alert oncologist by email.
- Weight loss	- Intensity of weight loss ○ 5 to 10% of starting weight (Grade 1) ○ 10 to 20% of starting weight (Grade 2) ○ > 20% of starting weight (Grade 3)	- Grade 1: no care required. Eliminate mucositis, heartburn, dysgeusia. - Grade 2: Implementation of nutritional support by general practitioner. Eliminate mucositis, heartburn, dysgeusia. - Grade 3: Inform oncologist rapidly, requires total secondary nutrition.
- Other	cf: CTCAE classification to estimate grade and to determine actions to implement	

D.6. Overview of advice and preventive actions to implement

Instructions: This section is an overview of the advice and preventive actions recommendations that the nurse declares to have given the patient throughout the questionnaire. The purpose of this summary is to underline the actions to implement before ending the call.

Overview of advice given during the interview:
Before finishing, I would like to go over the important points that we spoke of today:
[tick the information issued to the patient and perform a brief recap]

Treatment management advice

❑ Advice on taking Sutent® (once daily at set times, without opening the capsule. In the event of omission, do not double intake. Observe the physician's decisions in the event of interruption or termination. etc.)

❑ Advice on using the Sutent® follow-up notebook (treatment calendar, appointment management, adverse event follow-up, etc.)

❑ Report all adverse events (onset, change or increase, etc.)

General preventive advice:

❑ Advice on taking systematic preventive treatments (identification of preventive treatments to initiate rapidly)

❑ Healthy lifestyle advice (healthy eating and drinking, maintaining appropriate physical activity, sleeping and relaxing when necessary, etc.)

❑ Dietary advice (grapefruit prohibited, healthy and varied diet, etc.)

❑ Oral hygiene advice (regular mouthwashes, very gently toothbrush, avoid mint-flavoured toothpaste, etc.)

AE-specific preventive advice:

❑ Prevention of skin toxicity (gentle, fragrance-free soap, hypoallergenic moisturising cream and products, consultation with a chiropodist at the start of treatment, etc.)

❑ Prevention of digestive disorders (drink sufficiently in small amounts; low-fibre diet; avoid coffee, alcohol, greasy, spicy or acidic food, etc.)

❑ Prevention of cardiac disorders (frequent blood pressure measurements, limit salt and alcohol intake, etc.)

❑ Prevention of infectious/inflammatory problems (avoid high-risk contacts, regular hand disinfection, etc.)

❑ Other preventive advice (fatigue management, pain management, regular appropriate activity, etc.)

Actions recommended to the patient:

❑ Do not forget the scheduled consultation with the oncologist

❑ Perform the requested additional examinations (blood pressure monitoring, blood profile, additional examinations requested by the oncologist, etc.)

E. END OF INTERVIEW AND NEW APPOINTMENT

- I would like to thank you for your time and answers.
- As agreed, I would like to propose contacting you again between [theoretical date -1 day] and [theoretical date + 1 day] to go over the management of your treatment and any adverse events. Would you like to make an appointment now?
  - *Yes*: agree on an appointment between [theoretical date -1 day] and [theoretical date + 1 day]
  - *No: check the preferred call times*
  - *Note any unavailable periods*
- Have a nice day.

F. PHARMACOVIGILANCE DECLARATION

Instruction: After finishing the call with the patient, the nurse will be directed to the CATI tool Report section in order to issue any reports of adverse events (new AE or AE follow-up) identified during the call. A new sheet is generated for each AE.
At the end of the call, the sheets are sent to Pfizer's PV department and to the physician via the e-CRF for validation.

G. SUMMARY OF THE INTERVENTION AND ORGANISATION OF PHONE CALLS

Instruction: A summary note will be generated automatically and sent to the physician via the e-CRF. It shall comprise:

- *A box with the salient points to be taken into consideration by the physician*
- *The phone call details (automatic: number of attempts, date and duration of the call)*
- *A summary of events declared by the patient (new or follow-up)*
- *Actions undertaken by the patient and actions recommended to the patient.*
- *Main advice given to the patient*

Validation of any discrepancies between patient and e-CRF data will be requested.

14.8. Appendix 8: Adverse event report form

Non-interventional study: Adverse event report form

For Pfizer use

AER number	Date reported to Pfizer

Enter all dates in DD/MM/YYYY format

A	6	1	8	1	2	1	3

PROTOCOL / STUDY NUMBER

0	0		

CENTRE NO.

PATIENT ID/RANDOMISATION NUMBER

Protocol title: RENACALL STUDY: Evaluation of the impact of a therapy management platform on the management of patients suffering from advanced/metastatic renal cell carcinoma and receiving first line treatment with sunitinib, versus standard follow-up

☐ **Initial report** ☐ **Follow-up report** **Country in which the event occurred:**

Patient data Age: _____ Height: _____ cm Ethnic origin:

☐ Man ☐ Woman Weight: _____ kg ☒ Local regulations forbid asking the question

If the patient is deceased: Date of death: ___/_____/_____ Cause of death: _____ Autopsy performed ☐ YES ☐ NO ☐ UNKNOWN

If yes, what is the cause of death as determined by the autopsy: ___/_____/_____

Patient's history

☐ None ☐ Unknown

Note any relevant medical history below. Include any other diseases present at the time of the event, along with pre-existing medical conditions. If there is not enough space, use additional copies of the page..

Disease (specify)	Onset date	End date	Tick if disease is current	Relevant information *including surgical procedures and dates*
	___/___/_____	___/___/_____	☐	
	___/___/_____	___/___/_____	☐	

Test drug, Dosage form, route of administration	Tick if Pfizer product	Assay	Units	Frequency	Start date	End date	Tick if current drug
	☐				___/___/_____	___/___/_____	☐
	☐				___/___/_____	___/___/_____	☐

Concomitant drugs

☐ None ☐ Unknown

Report below any concomitant medicines taken during the 2 weeks preceding onset of the event. Exclude any medicines taken only more than 2 weeks prior to onset of the event, along with any medicines taken to treat the event, or taken after onset of the event. If you do not have enough space, use several copies of this page.

Drug name (registered trademark and INN)	Indication	Route of administration	Start date	End date	Tick if current drug
			___/___/_____	___/___/_____	☐
			___/___/_____	___/___/_____	☐

Relevant additional examinations

Note only those additional examination results that are relevant to the event(s); for example, laboratory analysis and imaging result. If you do not have enough space, use several copies of this page.

Examination	Date	Result	Units	Normal values Lower limit	Normal values Upper limit	Comments

AER number

Enter all dates in DD/MM/YYYY format

A	6	1	8	1	2	1	3

PROTOCOL / STUDY NUMBER

0	0		

CENTRE NO.

PATIENT ID/RANDOMISATION NUMBER

SERIOUS ADVERSE EVENTS (if more than 2, use additional copies of this page)
If known, specify the diagnosis rather than the signs and symptoms.

Adverse event: _____	**Adverse event:** _____
Onset date: ___/____/_____	**Onset date:** ___/____/_____
Is the event serious? : ☐ YES ☐ NO If yes, specify the seriousness criteria below:	**Is the event serious? :** ☐ YES ☐ NO If yes, specify the seriousness criteria below:
Seriousness criterion (several choices possible): ☐ Caused death ☐ Life-threatening ☐ Hospitalisation/extension of hospitalisation ☐ Permanent or major invalidity or disability ☐ Anomaly / congenital malformation ☐ Medically significant event	**Seriousness criterion (several choices possible):** ☐ Caused death ☐ Life-threatening ☐ Hospitalisation/extension of hospitalisation ☐ Permanent or major invalidity or disability ☐ Anomaly / congenital malformation ☐ Medically significant event
Progress at the time of this report, or at the time of death: ☐ Recovered Recovery date: ___/____/_____ ☐ Recovered with sequelae ☐ Recovering ☐ Not recovered ☐ Unknown **Is there a reasonable possibility that the event was linked to the test drug:** ☐ YES ☐ NO **If yes, specify the test drug:** _____ **Is there a reasonable possibility that the event was linked to a concomitant drug:** ☐ YES ☐ NO **If yes, specify the concomitant drug:** _____	**Progress at the time of this report, or at the time of death:** ☐ Recovered Recovery date: ___/____/_____ ☐ Recovered with sequelae ☐ Recovering ☐ Not recovered ☐ Unknown **Is there a reasonable possibility that the event was linked to the test drug:** ☐ YES ☐ NO **If yes, specify the test drug:** _____ **Is there a reasonable possibility that the event was linked to a concomitant drug:** ☐ YES ☐ NO **If yes, specify the concomitant drug:** _____
Last action undertaken during the event(s), specify the name of the drug: _____ ☐ Interruption (temporary, permanent, or delayed) ☐ Dose reduction ☐ Dose increase ☐ Dose unchanged ☐ Unknown ☐ Not applicable _____ ☐ Interruption (temporary, permanent, or delayed) ☐ Dose reduction ☐ Dose increase ☐ Dose unchanged ☐ Unknown ☐ Not applicable	**Last action undertaken during the event(s), specify the name of the drug:** _____ ☐ Interruption (temporary, permanent, or delayed) ☐ Dose reduction ☐ Dose increase ☐ Dose unchanged ☐ Unknown ☐ Not applicable _____ ☐ Interruption (temporary, permanent, or delayed) ☐ Dose reduction ☐ Dose increase ☐ Dose unchanged ☐ Unknown ☐ Not applicable

Did an AE/SAE re-appear during re-administration of the drug? ☐ Yes ☐ No ☐ Unknown ☐ Not applicable

If yes, which AE(s)/SAE(s):

Event history (narrative): *Please provide any relevant information concerning this event and that is not reported in another field of this form (circumstances, chronology; diagnosis and symptomatic treatment). If you do not have enough space, use several copies of this page.*

Centre employee in charge of notification for the centre:

_____ (Last and first names IN BLOCK CAPITALS) _____ (Date)

Address: _____ (Street) _____ (Town) _____ (Post code) _____ (Country)

Phone no.: _____ Fax no.: _____ Email: _____

Investigator's name if different:

Investigator's signature:

Date investigator (or notifier) informed: _____-_____-_____ (DD MMM YYYY)

[redacted]

14.9. Appendix 9: "Morisky" patient self-questionnaire (Sutent® treatment compliance)

Questionnaire concerning your treatment

(tick a single answer per question)

	Yes	No
• Do you ever forget to take your medicines?	❑	❑
• Do you even have problems remembering to take your medicines?	❑	❑
• When you feel better, do you sometimes stop taking your medicines?	❑	❑
• Sometimes, if you feel worse after taking your medicines, do you stop taking them?	❑	❑

Additional question concerning adverse events

	Yes	No
• When you suffer an adverse event, do you ever reduce or adapt the treatment?	❑	❑

14.10. Appendix 10: "Physician" call centre satisfaction evaluation questionnaire

- Collected via the e-CRF at the end of the last follow-up visit (end-of-study visit)
  - 3 dimensions evaluated

	Very satisfied	Satisfied	Not very satisfied	Not satisfied	No opinion
Satisfaction concerning advice					
▪ Do you consider that your patient's support by a call centre helped reduce the number and/or frequency of grade 3 and 4 AEs thanks to the advice provided?					
▪ Do you consider that your patient's support by a call centre helped improve treatment compliance?					
▪ How satisfied or dissatisfied are you with your patient's change in quality of life thanks to the advice provided by the call centre?					
Satisfaction concerning management					
▪ Do you consider that your patient's support by a call centre helped reduce your workload?					
Overall satisfaction					
▪ Overall, how satisfied or dissatisfied are you with the management of your patient by the call centre?					

Do you have any comment to make
□1 Yes □0 No

Where possible, would you wish to continue this type of support?
□1 yes, absolutely
□2 maybe
□3 not really
□4 not at all
□5 no opinion

14.11. Appendix 11: "Patient" call centre satisfaction evaluation questionnaire

- Collected via a self-questionnaire at the end of the last follow-up visit (end-of-study visit)
- 4 dimensions evaluated

	Very satisfied	Satisfied	Not very satisfied	Not satisfied	No opinion

[redacted]

Satisfaction concerning advice
▪ How satisfied or dissatisfied were you with the prevention advice you received from the call centre to avoid serious adverse events associated with your Sutent® treatment? ▪ How satisfied or dissatisfied were you with the treatments recommended by the call centre to reduce / limit the side effects associated with your Sutent® treatment? ▪ How satisfied or dissatisfied were you with the call centre's ability to direct you to a general practitioner / oncologist when your situation required it?
Satisfaction concerning management
▪ How satisfied or dissatisfied were you with the explanations given by the call centre concerning your disease, your treatment and/or their side effects?
Satisfaction concerning the service
▪ Were you satisfied or dissatisfied with the interest shown by the call centre nurses in what you were saying, in your problems and in yourself? ▪ Do you consider that the frequency, duration and number of follow-up calls that you received from the call centre were adapted to your situation? ▪ How satisfied or dissatisfied were you with the availability of the call centre nurses via the freephone number provided - ease of contacting the freephone number, answer speed, recall if message on voice mail, wait time, etc.?
Overall satisfaction
▪ Overall, how satisfied or dissatisfied are you with the support you received by the call centre supporting you in management of your Sutent® treatment?

Do you have any comment to make
□$_1$ Yes □$_0$ No

Where possible, would you wish to continue this type of support?

□$_1$ yes, absolutely

□2 maybe
□3 not really
□4 not at all
□5 no opinion

Would you recommend this type of follow-up to a friend or family member?

□1 yes, absolutely
□2 maybe
□3 not really
□4 not at all
□5 no opinion

Do you consider that you needed the advice and actions proposed by the call centre throughout the duration of your participation in this study?

❑ Yes ❑No

If not: When do you think you became independent concerning management of your treatment and its side effects? _____