POST MARKETING SURVEILLANCE STUDY TO OBSERVE SAFETY AND EFFICACY OF INLYTA®

Sponsor : Pfizer Pharmaceuticals Korea Ltd

Protocol No. : A4061075

Product Name : INLYTA® capsules 1mg, 5mg (Axitinib)

Version No. : V2.2

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Amendment Log

Version	Date	Updated by	Reason
Ver.1.0	03/May/2018	SYMYOO (CRO)	Initial version
Ver.2.0	26/Aug/2019	PPD	Newly created version in MEDIHELPLINE CO.,LTD. by CRO change
Ver.2.1	28/Jan/2021	PPD	Adding analysis for occurrence status of unexpected serious adverse events and unexpected serious adverse drug reactions
Ver.2.2	21/Jul/2021	PPD	- Update the medical coding dictionary for medical history and adverse events - Added categorical analysis to perform univariate analysis (Chi-square test) - Changed order of safety exclusion reasons

CONTENTS

1. Rationale and Background

Renal cell carcinoma (RCC) accounts for 85% of kidney cancers, and is a collection of different types of tumors that arise from the renal epithelium. Renal cell carcinoma (RCC) is diagnosed in approximately 170,000 patients worldwide annually, resulting in 82,000 deaths.
Early stage disease does not typically produce significant clinical signs or symptoms, consequently 25-30% of newly diagnosed patients present with advanced (including locally invasive or advanced) or unresectable disease. The 5-year survival rate for advanced RCC is estimated to be ≤10%.

Most RCCs are highly vascularised tumors that over-express a number of growth factors, including VEGF (Vascular endothelial growth factor), PDGF (Platelet-derived growth factor) and fibroblast growth factor (FGF). The clear cell RCC subtype represents approximately 85% of the RCC population and frequently displays allelic loss on chromosome 3p, accompanied by mutational inactivation of the von Hippel-Lindau (VHL) tumor suppressor gene. VHL-associated RCC are known for their vascularity and these tumors produce high levels of vascular endothelial growth factor (VEGF). In addition, recent studies suggest that in sporadic clear cell RCC, increased expression of VEGF is closely correlated with neovascularization, which is a prerequisite of tumor growth and metastasis.

INLYTA®, a substituted indazole derivative, is an oral, potent, and selective inhibitor that blocks signal transmission via vascular endothelial growth factor receptor (VEGFR-1, -2 and -3) which is related to vascularization of tumors and tumor proliferation.

INLYTA® was first approved as new medicine on 22 Aug 2012. As required for any new medication approved by Ministry of Food and Drug Safety (MFDS), safety and efficacy information of new medication should be provided at minimum 3,000 subjects administered in the setting of routine practice during the initial 6 years after the approval. However, based on MFDS's review upon Pfizer Korea's request, additional 3 years of study period has been granted to collect safety and efficacy information of minimum of 100 subjects.

2. Study Objective(s) and Others

2.1. Objectives

The objective of this study is to monitor usage of INLYTA® in real practice including adverse events on INLYTA®.

2.2. Study Design

Observational, non-interventional drug and multi-center study in which subjects will be administered as

part of routine practice at Korean health care centers by accredited physicians. At least 3,000 subjects should be enrolled in this study based on the Article 6 of "Basic Standards for the Re-examination of New Medicines" notified by MFDS. However, with additional 3 years of study period, at least 100 subjects who are being treated with INLYTA® within the approved indication will be studied for total of 9 years according to the review result by the MFDS per Pfizer's request to adjust the number of subjects. The study can be performed in Korean health care centers where INLYTA® is prescribed for advanced renal cell carcinoma (aRCC) after failure of one prior systemic therapy which is the indication for INLYTA® and where post-marketing study is allowed by institutions.

To achieve the target sample size, the study is being conducted in prospective study design and retrospective study design.

Patients to whom INLYTA® is first administered or patients who are already on INLYTA® during the study period should be enrolled in the study. Observation should be done from treatment initiation of INLYTA® for at least 28 calendar days. There are no visits or activities mandated by this study and routine observation will be done during INLYTA® treatment.

2.3. Study Population

All subjects enrolled should meet the usual prescribing criteria for INLYTA® as per the Local Product Document (LPD) and should be entered into the study at the physician's discretion.

2.3.1. Inclusion Criteria

Subjects must meet all of the following inclusion criteria to be eligible for inclusion in the study:

1. Patients diagnosed as advanced renal cell carcinoma (aRCC) after failure of one prior systemic therapy.
2. Patients to whom INLYTA® is first administered or patients who are already on INLYTA® during the study period
3. Evidence of a personally signed and dated informed consent document indicating that the patient (or a legally acceptable representative) has been informed of all pertinent aspects of the study.

2.3.2. Exclusion Criteria

Subjects meeting any of the following criteria will not be included in the study:

1. Any patient who does not agree that Pfizer and companies working with Pfizer use his/her information
2. Patients with hypersensitivity to axitinib or to any other component of INLYTA®
3. Patients under 18
4. Pregnant women

2.4. Sample size Considerations

Per MFDS regulation, at least 3,000 subjects were required for the study initially. However, based on the decision from MFDS on April 26, 2018, at least 100 subjects who are eligible according to '2.3 Study Population' will be observed for total of 9 years.

3. Analysis Populations

3.1. Safety Analysis Set

Safety analysis set will be included all subjects who have been administered INLYTA® at least once and evaluated with safety-related endpoints at least once.

The case below shall be excluded from the safety analysis set in the following order:

1) Subjects who have been already completed for INLYTA® prior to the contract date.
2) Subjects who have not been administered INLYTA®.
3) Subjects who have not met the inclusion/exclusion criterion.
4) Subjects who have not been evaluated for any safety-related endpoints.
5) Subjects who have any significant protocol violation.

3.2. Efficacy Analysis Set

Efficacy analysis set will be included subjects to whom INLYTA® is administered INLYTA® at least once. Subjects who are excluded from the safety analysis set shall be excluded from the efficacy analysis set.

3.3. Special Patient Population

As required by MFDS guidelines, if any of the following special patient population is identified, sub-group analysis will be conducted for:

- Pediatric subjects (aged < 19 years)
- Geriatric subjects (aged ≥ 65 years)
- Subjects with renal impairment
- Subjects with hepatic impairment

3.4. Sub-Group Analysis Set

Sub-group analysis will be conducted for safety analysis set and efficacy analysis set for:

- Sub-group 1: Subjects who are first administered INLYTA® during the study period
- Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

3.5. Population excluded from Safety Analysis

Population excluded from safety analysis will be reported separately with descriptive analysis only (number, percentage of subjects with adverse events and number of adverse events). However, subjects who have not been administered for INLYTA® will be excluded from this analysis set.

4. Study Endpoints

4.1. Safety Endpoints

The clinical nature, incidence, duration, and severity of adverse events; discontinuation due to adverse events; outcome and possible causality will be monitored in this study.

4.2. Efficacy Endpoints

- Tumor response based on RECIST 1.1
- Objective Response Rate (ORR)
  ORR will be defined as the number of subjects who achieve a best overall response of complete response (CR) or partial response (PR), divided by the total number of subjects in efficacy analysis set.
- Progression-free survival (PFS)
  PFS is defined as the time from first dose of study medication to first documentation of objective tumor progression, or to death due to any cause, whichever occurs first.
- Time to progression (TTP)
  TTP is defined as the time from the first dose of study medication to objective tumor progression excluding death.

5. General Consideration

5.1. Analysis Principles

Statistical analysis will be conducted after database is locked and performed using SAS software version 9.4 or higher according to this statistical analysis plan (SAP). If statistical analysis methods are changed, it will be described in the final clinical study report.

Continuous variables will be summarized by the descriptive statistics (number (n), mean, standard deviation (SD), median, minimum and maximum). Categorical variables will be presented in frequency and percentage (with the percentage excluding the number missing in the denominator).

In case of statistical hypothesis testing, two-sided tests will be conducted at a 5% significance level and the p-value of each test result will be presented in the summary table.

5.2. Handling of Missing and Incomplete data

5.2.1. Handling of Missing data

If data are missing or if a subject decides to discontinue from the study, there will be no imputation applied except as specified in section 5.2.2. The impact of missing data will be evaluated as appropriate.

5.2.2. Handling of Missing and Incomplete dates

Missing or incomplete dates will be handled by following rule:

	Missing	Imputation
Date of initial diagnosis	DD	01
	MM/DD	01/01
	YYYY/MM/DD	No imputation
End date of administration for study drug	'Ongoing'	Date of final follow-up

6. Statistical Analyses

6.1. Demographic and Other Baseline Characteristics

Demographic and baseline characteristics, concomitant medications and administrative status for study drug will be summarized with descriptive statistics. Continuous variables will be summarized with n, mean, SD, median, minimum and maximum. Categorical variables will be summarized with frequency (number of subjects and/or number of events) and percentage.

6.1.1. Demographic and Baseline Characteristics

1) Sex will be presented in frequency and percentage.
2) Age (year) will be presented in n, mean, SD, median, minimum and maximum, and frequency and percentage of categorized age groups.

$$Age\ (year) = \frac{(Start\ date\ of\ first\ administration) - (Date\ of\ birth)}{365.25}$$

3) Pediatric subjects will be presented in frequency and percentage.
4) Geriatric subjects will be presented in frequency and percentage.
5) Classification (inpatient/outpatient status) will be presented in frequency and percentage.
6) Height (cm) will be presented in n, mean, SD, median, minimum and maximum.
7) Weight (kg) will be presented in n, mean, SD, median, minimum and maximum.

6.1.2. Diagnosis of advanced renal cell carcinoma (aRCC)

1) Duration of aRCC (month) will be presented in n, mean, SD, median, minimum and maximum. Also, frequency and percentage of each group categorized according to the distribution of duration of aRCC will be presented.

$$Duration\ of\ aRCC\ (\text{month}) = \frac{(Start\ date\ of\ first\ administration) - (Date\ of\ initial\ diagnosis) + 1}{30.4375}$$

2) Cell component of aRCC will be presented in frequency and percentage.
3) Metastasis will be presented in frequency and percentage. In case of 'yes', categorized metastasis site will be presented in frequency and percentage.
4) Primary lesion surgery will be presented in frequency and percentage.

6.1.3. Medical History

1) Medical history
   - Medical history will be presented in frequency and percentage.
   - Medical history classified by System Organ Class (SOC) and Preferred Term (PT) according to the latest version of Medical Dictionary for Regulatory Activities (MedDRA) in detail will be presented in each frequency and percentage.
   - Renal impairment will be presented in frequency and percentage.
   - Hepatic impairment will be presented in frequency and percentage.
2) Allergic history will be presented in frequency and percentage.

6.1.4. Prior Chemotherapy/Immunotherapy and Radiation Therapy

1) Prior chemotherapy/immunotherapy
   - Prior chemotherapy will be presented in frequency and percentage.
   - Prior chemotherapy classified by Level 1 and Level 2 according to the latest version of Anatomical Therapeutic Chemical (ATC) classification system in detail will be presented in each frequency and percentage.
   - Prior immunotherapy will be presented in frequency and percentage.
   - Prior immunotherapy classified by Level 1 and Level 2 according to the latest version of ATC classification system in detail will be presented in each frequency and percentage.
2) Prior radiation therapy will be presented in frequency and percentage.

6.1.5. Concomitant Medication

1) Concomitant medication will be presented in frequency and percentage.

2) Concomitant medication classified by Level 1 and Level 2 according to the latest version of ATC classification system in detail will be presented in each frequency and percentage.

6.1.6. Administrative Status for INLYTA®

1) Period of first administration* will be presented in frequency and percentage.

*Sub-group 1: Subjects who are first administered INLYTA® during the study period

Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

2) Duration of administration (day) will be presented in n, mean, SD, median, minimum and maximum. Also, frequency and percentage of each group categorized according to the distribution of duration of administration will be presented.

$$Duration\ of\ administration\ (day) = \sum_{First}^{Last} \{(End\ date) - (Start\ date) + 1\}$$

3) Total dose (mg) will be presented in n, mean, SD, median, minimum and maximum.

$$Total\ dose\ (mg) = \sum_{First}^{Last} \{(Single\ dose \times Daily\ dosing\ frequency)\} \times \{(End\ date) - (Start\ date) + 1\}$$

4) Daily average dose (mg/day) will be presented in n, mean, SD, median, minimum and maximum. Also, frequency and percentage of each group categorized according to the distribution of duration of daily average dose will be presented.

$$Daily\ average\ dose\ (mg/day) = \frac{Total\ dose}{Duration\ of\ administration}$$

6.2. Safety Analyses

Safety analyses will be performed based on data of safety analysis set. All adverse events in CRF will be classified by System Organ Class (SOC) and Preferred Term (PT) according to the latest version of Medical Dictionary for Regulatory Activities (MedDRA).

1) All adverse events investigated after administration of INLYTA® will be summarized with the number of subjects having adverse events, incidence of adverse events with 95% confidence interval (CI) and the number of adverse events by categorizing as follows.
   - Serious adverse events and serious adverse drug reactions
   - Unexpected serious adverse events and unexpected serious adverse drug reactions
   - Unexpected adverse events and unexpected adverse drug reactions
   - Adverse events and adverse drug reactions
2) All adverse events investigated after administration of INLYTA® will be summarized with the frequency and percentage of adverse events by categorizing as follows.

- Occurrence status of adverse events by their severity
  - Grade 1 (Mild)
  - Grade 2 (Moderate)
  - Grade 3 (Severe or medically significant)
  - Grade 4 (Life-threatening consequences)
  - Grade 5 (Death related to AE)
- Occurrence status of adverse events by their outcome
  - Recovered
  - Recovered with sequelae
  - Recovering
  - Not recovered
  - Unknown
- Occurrence status of adverse events by their seriousness
  - SAE
    - Results in death
    - Is life-threatening
    - Requires inpatient hospitalization or prolongation of hospitalization
    - Results in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions)
    - Results in congenital anomaly/birth defect
    - Other important medical event: if it is determined that the event may jeopardize the subject or may require intervention to prevent one of the other outcomes listed in the definition above
  - Non-SAE
- Occurrence status of adverse events by their causality to INLYTA®
  - Related to INLYTA®: ① Certain
    ② Probable/likely
    ③ Possible
    ⑤ Conditional/unclassified
    ⑥ Unaccessible/unclassifiable
    ⑦ Not applicable
  - Not related to INLYTA®: ④ Unlikely
- Occurrence status of adverse events by their other causality (In case of 'not related to INLYTA®')
  - Disease under the study
  - Other diseases
  - Concomitant treatment drug or non-drug

- Others

- Occurrence status of adverse events by action
  - Discontinuation (permanently, temporarily or delayed)
  - Dosage reduced
  - Dosage increased
  - No change
  - Unknown
  - Not applicable

3) Occurrence status of adverse events by demographic and other baseline characteristics
   - The incidence of adverse events and 95% CI will be presented by categorical variables of demographic and other baseline characteristics.
   - To identify statistically significant difference in incidence of adverse events by categorical variables of demographic and other baseline characteristics, Chi-square test (X^2 test) or Fisher's exact test (if the expected frequency for each cell under 5 is more than 20%) will be performed.
4) Analysis of factors that affect the safety
   - In the re-examination report, logistic regression of multivariate analysis will be performed and an odds ratio with 95% CI and p-value will be presented to identify the factors that affect incidence of adverse events in demographic and other baseline characteristics.
5) Analysis for special patient populations [pediatric subjects (aged < 19 years), geriatric subjects (aged ≥ 65 years), subjects with renal impairment, subjects with hepatic impairment]
   - Adverse events and adverse drug reactions collected in each special patient population will be presented the number of subjects having adverse events, incidence of adverse events and the number of adverse events for each SOC and PT.
6) Analysis for population except from safety analysis
   - Adverse events and adverse drug reactions collected in population except from safety analysis will be presented the number of subjects having adverse events, incidence of adverse events and the number of adverse events for each SOC and PT.

6.3. Efficacy Analyses

Efficacy analyses will be performed based on data of efficacy analysis set.

1) Best overall response [Complete response (CR), Partial response (PR), Stable disease (SD), Progressive disease (PD), Not evaluable (NE)] will be presented in frequency and percentage.
2) Objective response rate (ORR) will be presented in frequency and percentage.

$$Objective\ response\ rate\ (ORR) = \frac{Number\ of\ subjects\ who\ achieves\ a\ best\ overall\ response\ of\ CR\ or\ PR}{Number\ of\ subjects\ in\ the\ efficacy\ analysis\ set}$$

3) Kaplan-Meier curve for time-to-event endpoints will be generated and presented quartiles with 95% CI, event rates and censor rates. Date of death is date of resolution of serious adverse event in which the category of seriousness is 'Results in death'. In case subjects do not have an event, censor of time-to-event is performed at the date of final follow-up.
   - Progression-free survival (PFS)
   - Time to progression (TTP)
4) Objective response rate (ORR) by demographic and other baseline characteristics
   - Objective response rate and 95% CI will be presented by categorical variables of demographic and other baseline characteristics.
   - To identify statistically significant difference in objective response rate by categorical variables of demographic and other baseline characteristics, Chi-square test (X^2 test) or Fisher's exact test (if the expected frequency for each cell under 5 is more than 20%) will be performed.
5) Analysis of factors that affect the efficacy
   - In the re-examination report, logistic regression of multivariate analysis will be performed and an odds ratio with 95% CI and p-value will be presented to identify the factors that affect objective response rate in demographic and other baseline characteristics.

6.4. Sub-Group Analyses

The following analyses will be performed for subjects who are prescribed with INLYTA® for the first time and for subjects who are already on INLYTA®, separately.

1) [6.2. Safety Analyses] - 1) ~ 4)
2) [6.3. Efficacy Analyses] - 1) ~ 5)

7. Reporting Conventions

Continuous variables will be summarized by descriptive statistics including n, mean, SD, SE, median, minimum and maximum, and categorical variables will be presented in frequency and percentage. Summary statistics including mean, SD, SE, median, minimum and maximum, etc. will be reported to two decimal places using rounding off.

The p-values through the statistical test will be reported to four decimal place and if p-values smaller than 0.0001 will be written as '<0.0001'.

8. Attachments

8.1. Attachment 1: Dummy table

POST MARKETING SURVEILLANCE STUDY TO OBSERVE SAFETY AND EFFICACY OF INLYTA®

Sponsor : Pfizer Pharmaceuticals Korea Ltd

Protocol No. : A4061075

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Version No. : V1.2

Dummy Table

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PPD	PPD	PPD

Dummy Table

Amendment Log

Version	Date	Updated by	Reason
Ver.1.0	26/Aug/2019	PPD	Initial version
Ver.1.1	28/Jan/2021	PPD	Adding analysis for occurrence status of unexpected serious adverse events and unexpected serious adverse drug reactions
Ver.1.2	21/Jul/2021	PPD	- Update the medical coding dictionary for medical history and adverse events - Added categorical analysis to perform univariate analysis (Chi-square test) - Added table for 'Reasons for excluding safety evaluation' - Indicates the number of subjects in the table titles corresponding to special population and the subjects excluded from safety evaluation

LIST OF TABLES

LIST OF FIGURE

Dummy Table

[Table 1] Demographic characteristics

Factor	Classification	Number of subjects n(%)
Sex	Male	xxx(xx.xx)
	Female	xxx(xx.xx)
	Total	xxx(xx.xx)
Age (year)	n	xxx
	Mean±SD	xx.xx±xx.xx
	Median	xx.xx
	Min~Max	xx.xx~xx.xx
	Category 1	xxx(xx.xx)
	Category 2	xxx(xx.xx)
	Category 3	xxx(xx.xx)
	…	xxx(xx.xx)
	Total	xxx(xx.xx)
Pediatric	< 19 years	xxx(xx.xx)
	≥ 19 years	xxx(xx.xx)
	Total	xxx(xx.xx)
Geriatric	≥ 65 years	xxx(xx.xx)
	< 65 years	xxx(xx.xx)
	Total	xxx(xx.xx)
Classification	Outpatient	xxx(xx.xx)
	Inpatient	xxx(xx.xx)
	Total	xxx(xx.xx)
Height (cm)	n	xxx
	Mean±SD	xx.xx±xx.xx
	Median	xx.xx
	Min~Max	xx.xx~xx.xx
Weight (kg)	n	xxx
	Mean±SD	xx.xx±xx.xx
	Median	xx.xx
	Min~Max	xx.xx~xx.xx

†Number of missing

Programming note: The categories of age will be set considering distribution of data.

[Table 2] Other baseline characteristics

Factor	Classification	Number of subjects n(%)
Duration of aRCC (month)	n	xxx
	Mean±SD	xx.xx±xx.xx
	Median	xx.xx
	Min~Max	xx.xx~xx.xx
	Category 1	xxx(xx.xx)
	Category 2	xxx(xx.xx)
	Category 3	xxx(xx.xx)
	…	xxx(xx.xx)
	Total	xxx(xx.xx)
Cell component of aRCC	Clear cell	xxx(xx.xx)
	Other	xxx(xx.xx)
	Total	xxx(xx.xx)
Metastasis	Yes§	xxx(xx.xx)

Dummy Table

Factor	Classification	Number of subjects n(%)
	Liver	xxx(xx.xx)
	Lung	xxx(xx.xx)
	Bone	xxx(xx.xx)
	Brain	xxx(xx.xx)
	Skin	xxx(xx.xx)
	Lymph nodes	xxx(xx.xx)
	Other	xxx(xx.xx)
	No	xxx(xx.xx)
	Total	xxx(xx.xx)
Primary lesion surgery	Done	xxx(xx.xx)
	Not done	xxx(xx.xx)
	Total	xxx(xx.xx)
Medical history	Yes	xxx(xx.xx)
	No	xxx(xx.xx)
	Total	xxx(xx.xx)
Renal impairment	Yes	xxx(xx.xx)
	No	xxx(xx.xx)
	Total	xxx(xx.xx)
Hepatic impairment	Yes	xxx(xx.xx)
	No	xxx(xx.xx)
	Total	xxx(xx.xx)
Allergic history	Yes	xxx(xx.xx)
	No	xxx(xx.xx)
	Total	xxx(xx.xx)
Prior chemotherapy	Yes	xxx(xx.xx)
	No	xxx(xx.xx)
	Unknown	xxx(xx.xx)
	Total	xxx(xx.xx)
Prior immunotherapy	Yes	xxx(xx.xx)
	No	xxx(xx.xx)
	Unknown	xxx(xx.xx)
	Total	xxx(xx.xx)
Prior radiation therapy	Yes	xxx(xx.xx)
	No	xxx(xx.xx)
	Unknown	xxx(xx.xx)
	Total	xxx(xx.xx)
Concomitant medication	Yes	xxx(xx.xx)
	No	xxx(xx.xx)
	Total	xxx(xx.xx)

†Number of missing
§Overlapped

Dummy Table

[Table 3] Medical history

Medical history	**n(%), [E]**
Yes	xxx(xx.xx), [xxx]
No	xxx(xx.xx)
Total	**xxx(xx.xx)**
System Organ Class[§]	
Preferred Term	**n(%), [E]**
System Organ Class	**xxx(xx.xx), [xxx]**
Preferred Term	xxx(xx.xx), [xxx]
…	xxx(xx.xx), [xxx]

[§]Overlapped, MedDRA *latest version*

E: Number of events

[1)]Renal impairment (xxx subjects (xx.xx%), xxx events)

[2)]Hepatic impairment (xxx subjects (xx.xx%), xxx events)

[Table 4] Prior chemotherapy

Prior chemotherapy	**n(%), [E]**
Yes	xxx(xx.xx), [xxx]
No	xxx(xx.xx)
Unknown	xxx(xx.xx)
Total	**xxx(xx.xx)**
Level 1[§]	
Level 2	**n(%), [E]**
Level 1	**xxx(xx.xx), [xxx]**
Level 2	xxx(xx.xx), [xxx]
…	xxx(xx.xx), [xxx]

[§]Overlapped, *ATC Classification System latest version*

E: Number of events

[Table 5] Prior immunotherapy

Prior immunotherapy	**n(%), [E]**
Yes	xxx(xx.xx), [xxx]
No	xxx(xx.xx)
Unknown	xxx(xx.xx)
Total	**xxx(xx.xx)**
Level 1[§]	
Level 2	**n(%), [E]**
Level 1	**xxx(xx.xx), [xxx]**
Level 2	xxx(xx.xx), [xxx]
…	xxx(xx.xx), [xxx]

[§]Overlapped, *ATC Classification System latest version*

E: Number of events

[Table 6] Concomitant medication

Concomitant medication	**n(%), [E]**
Yes	xxx(xx.xx), [xxx]
No	xxx(xx.xx)
Total	**xxx(xx.xx)**
Level 1§	**n(%), [E]**
Level 2	
Level 1	**xxx(xx.xx), [xxx]**
Level 2	xxx(xx.xx), [xxx]
…	xxx(xx.xx), [xxx]

§Overlapped, *ATC Classification System latest version*
E: Number of events

[Table 7] Administrative status for INLYTA®

Factor	**Classification**	**Number of subjects n(%)**
Period of first administration†	Sub-group 1	xxx(xx.xx)
	Sub-group 2	xxx(xx.xx)
	Total	xxx(xx.xx)
Duration of administration (day)	n	xxx
	Mean±SD	xx.xx±xx.xx
	Median	xx.xx
	Min~Max	xx.xx~xx.xx
	Category 1	xxx(xx.xx)
	Category 2	xxx(xx.xx)
	Category 3	xxx(xx.xx)
	…	xxx(xx.xx)
	Total	xxx(xx.xx)
Total dose (mg)	n	xxx
	Mean±SD	xx.xx±xx.xx
	Median	xx.xx
	Min~Max	xx.xx~xx.xx
Daily average dose (mg/day)	n	xxx
	Mean±SD	xx.xx±xx.xx
	Median	xx.xx
	Min~Max	xx.xx~xx.xx
	Category 1	xxx(xx.xx)
	Category 2	xxx(xx.xx)
	Category 3	xxx(xx.xx)
	…	xxx(xx.xx)
	Total	xxx(xx.xx)

†Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

Dummy Table

[Table 8] Summary of incidence of adverse events

Adverse Events	**Sub-group 1 (N=xxx) n(%), [E]**	**Sub-group 2 (N=xxx) n(%), [E]**	**Total (N=xxx) n(%), [E]**
Serious adverse events	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]
Serious adverse drug reactions	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]
Unexpected serious adverse events	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]
Unexpected serious adverse drug reactions	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]
Unexpected adverse events	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]
Unexpected adverse drug reactions	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]
Adverse events	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]
Adverse drug reactions	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]

Sub-group 1: Subjects who are first administered INLYTA® during the study period

Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

E: number of adverse events

Dummy Table

[Table 9] Serious adverse events and serious adverse drug reactions

System Organ Class§ Preferred Term	**Serious adverse events**		**Serious adverse drug reactions**	
	n(%), [E]	**[95% CI]**	**n(%), [E]**	**[95% CI]**
System Organ Class	**xxx(xx.xx), [xxx]**	**[xx.xx, xx.xx]**	**xxx(xx.xx), [xxx]**	**[xx.xx, xx.xx]**
Preferred Term	xxx(xx.xx), [xxx]	[xx,xx, xx.xx]	xxx(xx.xx), [xxx]	[xx,xx, xx.xx]
…	xxx(xx.xx), [xxx]	[xx,xx, xx.xx]	xxx(xx.xx), [xxx]	[xx,xx, xx.xx]
Total	**xxx(xx.xx), [xxx]**	**[xx.xx, xx.xx]**	**xxx(xx.xx), [xxx]**	**[xx.xx, xx.xx]**

§Overlapped, MedDRA *latest version*
E: Number of adverse events

Programming note: This table is repeated for each sub-group with the following table title and footnote.
Title : [Table 9-x] Serious adverse events and serious adverse drug reactions (sub-group x: N=xxx)
Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

[Table 10] Details of serious adverse events

Subject No.	**Sub-group†**	**System Organ Class§**	**Preferred Term§**	**Date of onset**	**Date of resolution**	**Severity**	**Outcome**	**Seriousness**	**Causality of adverse event to INLYTA®**	**Other causality of adverse event**	**Action**	**Expected ness**
Sxxx-xxx	Sub-group x	*System Organ Class*	*Preferred Term*	YYYY-MM-DD	YYYY-MM-DD	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Sxxx-xxx	Sub-group x	*System Organ Class*	*Preferred Term*	YYYY-MM-DD	YYYY-MM-DD	xxx	xxx	xxx	xxx	xxx	xxx	xxx

†Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date
§MedDRA *latest version*

Programming note: This analysis will be performed in the re-examination report only.

Dummy Table

[Table 11] Unexpected serious adverse events and unexpected serious adverse drug reactions

System Organ Class[§] Preferred Term	**Unexpected serious adverse events**		**Unexpected serious adverse drug reactions**	
	n(%), [E]	**[95% CI]**	**n(%), [E]**	**[95% CI]**
System Organ Class	**xxx(xx.xx), [xxx]**	**[xx.xx, xx.xx]**	**xxx(xx.xx), [xxx]**	**[xx.xx, xx.xx]**
Preferred Term	xxx(xx.xx), [xxx]	[xx,xx, xx.xx]	xxx(xx.xx), [xxx]	[xx,xx, xx.xx]
…	xxx(xx.xx), [xxx]	[xx,xx, xx.xx]	xxx(xx.xx), [xxx]	[xx,xx, xx.xx]
Total	**xxx(xx.xx), [xxx]**	**[xx.xx, xx.xx]**	**xxx(xx.xx), [xxx]**	**[xx.xx, xx.xx]**

[§]Overlapped, MedDRA *latest version*
E: Number of adverse events

Programming note: This table is repeated for each sub-group with the following table title and footnote.
Title : [Table 11-x] Unexpected serious adverse events and unexpected serious adverse drug reactions (sub-group x: N=xxx)
Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

[Table 12] Details of unexpected serious adverse events

Subject No.	**Sub-group**[†]	**System Organ Class**[§]	**Preferred Term**[§]	**Date of onset**	**Date of resolution**	**Severity**	**Outcome**	**Seriousness**	**Causality of adverse event to INLYTA®**	**Other causality of adverse event**	**Action**
Sxxx-xxx	Sub-group x	*System Organ Class*	*Preferred Term*	YYYY-MM-DD	YYYY-MM-DD	xxx	xxx	xxx	xxx	xxx	xxx
Sxxx-xxx	Sub-group x	*System Organ Class*	*Preferred Term*	YYYY-MM-DD	YYYY-MM-DD	xxx	xxx	xxx	xxx	xxx	xxx

[†]Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date
[§]MedDRA *latest version*

Programming note: This analysis will be performed in the re-examination report only.

Dummy Table

[Table 13] Unexpected adverse events and unexpected adverse drug reactions

System Organ Class§ Preferred Term	**Unexpected adverse events**		**Unexpected adverse drug reactions**	
	n(%), [E]	**[95% CI]**	**n(%), [E]**	**[95% CI]**
System Organ Class	**xxx(xx.xx), [xxx]**	**[xx.xx, xx.xx]**	**xxx(xx.xx), [xxx]**	**[xx.xx, xx.xx]**
Preferred Term	xxx(xx.xx), [xxx]	[xx,xx, xx.xx]	xxx(xx.xx), [xxx]	[xx,xx, xx.xx]
…	xxx(xx.xx), [xxx]	[xx,xx, xx.xx]	xxx(xx.xx), [xxx]	[xx,xx, xx.xx]
Total	**xxx(xx.xx), [xxx]**	**[xx.xx, xx.xx]**	**xxx(xx.xx), [xxx]**	**[xx.xx, xx.xx]**

§Overlapped, MedDRA *latest version*
E: Number of adverse events

Programming note: This table is repeated for each sub-group with the following table title and footnote.
Title : [Table 13-x] Unexpected adverse events and unexpected adverse drug reactions (sub-group x: N=xxx)
Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

[Table 14] Details of unexpected adverse events

Subject No.	**Sub-group†**	**System Organ Class§**	**Preferred Term§**	**Date of onset**	**Date of resolution**	**Severity**	**Outcome**	**Seriousness**	**Causality of adverse event to INLYTA®**	**Other causality of adverse event**	**Action**
Sxxx-xxx	Sub-group x	*System Organ Class*	*Preferred Term*	YYYY-MM-DD	YYYY-MM-DD	xxx	xxx	xxx	xxx	xxx	xxx
Sxxx-xxx	Sub-group x	*System Organ Class*	*Preferred Term*	YYYY-MM-DD	YYYY-MM-DD	xxx	xxx	xxx	xxx	xxx	xxx

†Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date
§MedDRA *latest version*

Programming note: This analysis will be performed in the re-examination report only.

Dummy Table

[Table 15] Adverse events and adverse drug reactions

System Organ Class§ Preferred Term	**Adverse events**		**Adverse drug reactions**	
	n(%), [E]	**[95% CI]**	**n(%), [E]**	**[95% CI]**
System Organ Class	**xxx(xx.xx), [xxx]**	**[xx.xx, xx.xx]**	**xxx(xx.xx), [xxx]**	**[xx.xx, xx.xx]**
Preferred Term	xxx(xx.xx), [xxx]	[xx,xx, xx.xx]	xxx(xx.xx), [xxx]	[xx,xx, xx.xx]
…	xxx(xx.xx), [xxx]	[xx,xx, xx.xx]	xxx(xx.xx), [xxx]	[xx,xx, xx.xx]
Total	**xxx(xx.xx), [xxx]**	**[xx.xx, xx.xx]**	**xxx(xx.xx), [xxx]**	**[xx.xx, xx.xx]**

§Overlapped, MedDRA *latest version*

E: Number of adverse events

Programming note: This table is repeated for each sub-group with the following table title and footnote.

Title : [Table 15-x] Adverse events and adverse drug reactions (sub-group x: N=xxx)

Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period

Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

[Table 16] Adverse events by their severity

System Organ Class§ Preferred Term	**Number of adverse events by their severity†(%)**					
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**	**Total**
System Organ Class	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**
Preferred Term	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)
…	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)
Total	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**

§MedDRA *latest version*

†Severity evaluation of adverse event must be done according to the *NCI CTC grade*

Programming note: This table is repeated for each sub-group with the following table title and footnote.

Title : [Table 16-x] Adverse events by their severity (sub-group x: N=xxx)

Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period

Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

Dummy Table

[Table 17] Adverse events by their outcome

System Organ Class[§] Preferred Term	**Number of adverse events by their outcome (%)**					
	Recovered	**Recovered with sequelae**	**Recovering**	**Not recovered**	**Unknown**	**Total**
System Organ Class	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**
Preferred Term	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)
…	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)
Total	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**

[§]MedDRA *latest version*

Programming note: This table is repeated for each sub-group with the following table title and footnote.
Title : [Table 17-x] Adverse events by their outcome (sub-group x: N=xxx)
Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

Dummy Table

[Table 18] Adverse events by their seriousness

System Organ Class[§] Preferred Term	Number of adverse events by their seriousness (%)							
	Results in death	**Is life-threatening**	**Requires inpatient hospitalization or prolongation of hospitalization**	**Results in persistent or significant disability /incapacity**	**Results in congenital anomaly /birth defect**	**Other important medical event**	**Non-SAE**	**Total**
System Organ Class	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**
Preferred Term	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)
…	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)
Total	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**

[§]Overlapped, MedDRA *latest version*

Programming note: This table is repeated for each sub-group with the following table title and footnote.
Title : [Table 18-x] Adverse events by their seriousness (sub-group x: N=xxx)
Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

[Table 19] Relation of adverse event to INLYTA®

Relation of adverse event to INLYTA®	Number of adverse events (%)
Related to INLYTA®	xxx(xx.xx)
Not related to INLYTA®	xxx(xx.xx)
Total	**xxx(xx.xx)**

Programming note: This table is repeated for each sub-group with the following table title and footnote.
Title : [Table 19-x] Relation of adverse event to INLYTA® (sub-group x: N=xxx)
Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

[Table 20] Adverse events by their causality to INLYTA®

System Organ Class§ Preferred Term	Number of adverse events by their causality to INLYTA® (%)							
	Certain	Probable /likely	Possible	Unlikely	Conditional/ unclassified	Unaccessible/ unclassifiable	Not applicable	Total
System Organ Class	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**
Preferred Term	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)
…	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)
Total	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**

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Programming note: This table is repeated for each sub-group with the following table title and footnote.
Title : [Table 20-x] Adverse events by their causality to INLYTA® (sub-group x: N=xxx)
Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

[Table 21] Adverse events by their other causality

System Organ Class§ Preferred Term	Number of adverse events by their other causality (%)				
	Disease under the study	Other disease	Concomitant treatment drug or non-drug	Others	Total
System Organ Class	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**
Preferred Term	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)
…	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)
Total	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**

§MedDRA *latest version*

Programming note: This table is repeated for each sub-group with the following table title and footnote.
Title : [Table 21-x] Adverse events by their other causality (sub-group x: N=xxx)
Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

[Table 22] Adverse events by action

System Organ Class§ Preferred Term	Number of adverse events by action (%)						
	Discontinuation	Dosage reduced	Dosage increased	No change	Unknown	Not applicable	Total
System Organ Class	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**
Preferred Term	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)
…	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)
Total	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**	**xxx(xx.xx)**

§MedDRA *latest version*

Programming note: This table is repeated for each sub-group with the following table title and footnote.
Title : [Table 22-x] Adverse events by action (sub-group x: N=xxx)
Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

[Table 23] Occurrence status of adverse events by demographic characteristics

Factor	Classification	No. of Subjects	Incidence of AE n(%)	[95% CI]	p-value[1)2)]
Sex	Male	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	Female	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Age	*Category 1*	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	Category 2	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Category 3	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	…	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Pediatric	< 19 years	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	≥ 19 years	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Geriatric	≥ 65 years	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	< 65 years	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Classification	Outpatient	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	Inpatient	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	

[1)]Chi-square Test
[2)]Fisher's Exact Test
*Statistically significant

Programming note: This table is repeated for each sub-group with the following table title and footnote.
Title : [Table 23-x] Occurrence status of adverse events by demographic characteristics (sub-group x: N=xxx)
Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

[Table 24] Occurrence status of adverse events by other baseline characteristics

Factor	Classification	No. of Subjects	Incidence of AE n(%)	[95% CI]	p-value[1)2)]
Duration of aRCC	*Category 1*	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	Category 2	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Category 3	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	…	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Cell component of aRCC	Clear cell	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	Other	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Metastasis	Yes[§]	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	Liver	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Lung	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Bone	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Brain	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Skin	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Lymph nodes	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Other	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	No	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Primary lesion surgery	Done	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	Not done	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	

Dummy Table

Factor	Classification	No. of Subjects	Incidence of AE n(%)	[95% CI]	p-value[1)2)]
	Total	xxx	xxx(xx.xx)	-	
Medical history	Yes	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	No	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Renal impairment	Yes	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	No	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Hepatic impairment	Yes	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	No	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Allergic history	Yes	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	No	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Prior chemotherapy	Yes	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	No	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Unknown	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Prior immunotherapy	Yes	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	No	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Unknown	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Prior radiation therapy	Yes	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	No	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Unknown	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Concomitant medication	Yes	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	No	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Duration of administration	*Category 1*	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	Category 2	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Category 3	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	…	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Daily average dose	*Category 1*	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	Category 2	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Category 3	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	…	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	

§Overlapped
1)Chi-square Test
2)Fisher's Exact Test
*Statistically significant

Programming note: This table is repeated for each sub-group with the following table title and footnote.
Title : [Table 24-x] Occurrence status of adverse events by other baseline characteristics (sub-group x: N=xxx)
Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

[Table 25] Multivariate logistic regression for occurrence status of adverse events

Factor	Classification	Estimate	Standard Error	p-value	Odds Ratio	[95% CI]
Intercept		xx.xx	xx.xx	x.xxxx		
Factor 1	*Yes*	xx.xx	xx.xx	x.xxxx	xx.xx	[xx.xx, xx.xx]
	No	Reference				
Factor 2	*Category 1*	Reference				
	Category 2	xx.xx	xx.xx	x.xxxx	xx.xx	[xx.xx, xx.xx]
	…					
…	…					

Response variable: occurrence status of adverse events
*Statistically significant

Programming note1: This analysis will be performed in the re-examination report only.
Programming note2: This table is repeated for each sub-group with the following table title and footnote.
Title : [Table 25-x] Multivariate logistic regression for occurrence status of adverse events (sub-group x: N=xxx)
Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

[Table 26] Best overall response and objective response rate

Factor	Classification	Sub-group 1 (N=xxx) n(%)	Sub-group 2 (N=xxx) n(%)	Total (N=xxx) n(%)
Best overall response	Objective response rate (ORR)†	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)
	Complete response (CR)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)
	Partial response (PR)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)
	Stable disease (SD)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)
	Progressive disease (PD)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)
	Not evaluable (NE)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)
	Not done (ND)	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)
	Total	xxx(xx.xx)	xxx(xx.xx)	xxx(xx.xx)

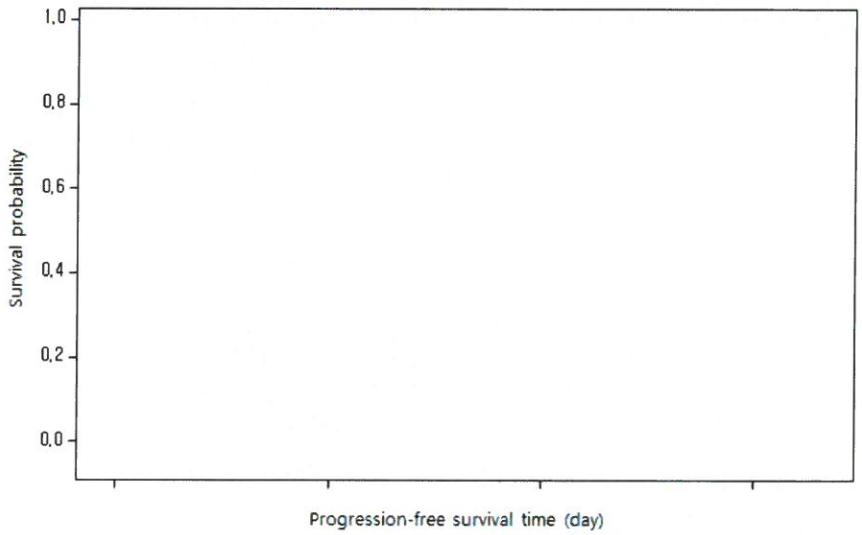
Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date
†ORR: The numerator is: number of subjects who achieves a best overall response of CR or PR
The denominator is: number of subjects in the efficacy analysis set

[Table 27] Summary statistics for progression-free survival

Factor	Classification	Number of subjects n(%)
Event rate	Event	xxx(xx.xx)
	Progressive disease	xxx(xx.xx)
	Death	xxx(xx.xx)
Censored rate	Censored	xxx(xx.xx)
PFS time (day)	75th percentile [95% CI)	xx.xx[xx.xx, xx.xx)
	50th percentile [95% CI)	xx.xx[xx.xx, xx.xx)
	25th percentile [95% CI)	xx.xx[xx.xx, xx.xx)

Programming note: This table is repeated for each sub-group with the following table title and footnote.
Title : [Table 27-x] Summary statistics for progression-free survival (sub-group x: N=xxx)
Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

[Figure 1] Kaplan-Meier curve for progression-free survival



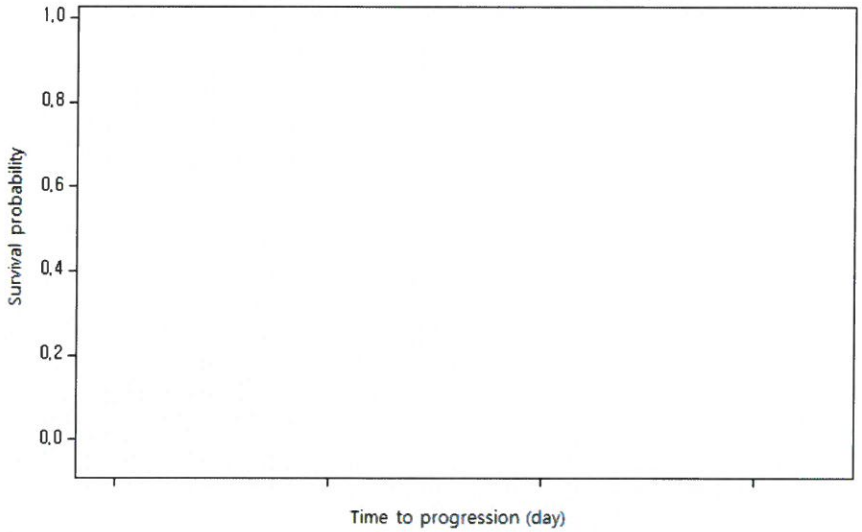
Programming note: This table is repeated for each sub-group with the following table title and footnote.
Title : [Figure 1-x] Kaplan-Meier curve for progression-free survival (sub-group x: N=xxx)
Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

[Table 28] Summary statistics for time to progression

Factor	Classification	Number of subjects n(%)
Event rate	Progressive disease	xxx(xx.xx)
Censored rate	Censored	xxx(xx.xx)
TTP time (day)	75th percentile [95% CI)	xx.xx[xx.xx, xx.xx)
	50th percentile [95% CI)	xx.xx[xx.xx, xx.xx)
	25th percentile [95% CI)	xx.xx[xx.xx, xx.xx)

Programming note: This table is repeated for each sub-group with the following table title and footnote.
Title : [Table 28-x] Summary statistics for time to progression (sub-group x: N=xxx)
Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

[Figure 2] Kaplan-Meier curve for time to progression



Programming note: This table is repeated for each sub-group with the following table title and footnote.
Title : [Figure 2-x] Kaplan-Meier curve for time to progression (sub-group x: N=xxx)
Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

[Table 29] Objective response rate by demographic characteristics

Factor	Classification	No. of Subjects	Objective Response Rate n(%)	[95% CI]	p-value[1)2)]
Sex	Male	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	Female	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Age	*Category 1*	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	Category 2	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Category 3	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	…	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Pediatric	< 19 years	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	≥ 19 years	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Geriatric	≥ 65 years	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	< 65 years	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Classification	Outpatient	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	Inpatient	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	

[1)]Chi-square Test
[2)]Fisher's Exact Test
*Statistically significant

Programming note: This table is repeated for each sub-group with the following table title and footnote.
Title : [Table 29-x] Objective response rate by demographic characteristics (sub-group x: N=xxx)
Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

[Table 30] Objective response rate by demographic and other baseline characteristics

Factor	Classification	No. of Subjects	Objective Response Rate n(%)	[95% CI]	p-value[1)2)]
Duration of aRCC	*Category 1*	xxx	xxx(xx.xx)	[xx.xx	x.xxxx
	Category 2	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Category 3	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	…	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Cell component of aRCC	Clear cell	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	Other	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Metastasis	Yes[§]	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	Liver	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Lung	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Bone	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Brain	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Skin	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Lymph nodes	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Other	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	No	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	

Dummy Table

Factor	Classification	No. of Subjects	Objective Response Rate n(%)	[95% CI]	p-value[1)2)]
	Total	xxx	xxx(xx.xx)	-	
Primary lesion surgery	Done	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	Not done	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Medical history	Yes	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	No	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Renal impairment	Yes	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	No	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Hepatic impairment	Yes	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	No	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Allergic history	Yes	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	No	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Prior chemotherapy	Yes	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	No	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Unknown	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Prior immunotherapy	Yes	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	No	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Unknown	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Prior radiation therapy	Yes	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	No	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Unknown	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Concomitant medication	Yes	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	No	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Duration of administration	*Category 1*	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	Category 2	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Category 3	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	…	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	
Daily average dose	*Category 1*	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	x.xxxx
	Category 2	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Category 3	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	…	xxx	xxx(xx.xx)	[xx.xx, xx.xx]	
	Total	xxx	xxx(xx.xx)	-	

§Overlapped
1)Chi-square Test
2)Fisher's Exact Test
*Statistically significant

Programming note: This table is repeated for each sub-group with the following table title and footnote.
Title : [Table 30-x] Objective response rate by other baseline characteristics (sub-group x: N=xxx)
Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

Dummy Table

[Table 31] Multivariate logistic regression for objective response rate

Factor	Classification	Estimate	Standard Error	p-value	Odds Ratio	[95% CI]
Intercept		xx.xx	xx.xx	x.xxxx		
Factor 1	*Yes*	xx.xx	xx.xx	x.xxxx	xx.xx	[xx.xx, xx.xx]
	No	Reference				
Factor 2	*Category 1*	Reference				
	Category 2	xx.xx	xx.xx	x.xxxx	xx.xx	[xx.xx, xx.xx]
	...					
...	...					

Response variable: objective response
*Statistically significant

Programming note1: This analysis will be performed in the re-examination report only.
Programming note2: This table is repeated for each sub-group with the following table title and footnote.
Title : [Table 31-x] Multivariate logistic regression for objective response rate (sub-group x: N=xxx)
Footnote: Sub-group 1: Subjects who are first administered INLYTA® during the study period
Sub-group 2: Subjects who has continued administration of INLYTA® since the time prior to the contract date

Dummy Table

[Table 32] Adverse events and adverse drug reactions of pediatric subjects (aged < 19) (N=xxx)

System Organ Class§ Preferred Term	**Adverse events** **n(%), [E]**	**Adverse drug reactions** **n(%), [E]**
System Organ Class	**xxx(xx.xx), [xxx]**	**xxx(xx.xx), [xxx]**
Preferred Term	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]
…	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]
Total	**xxx(xx.xx), [xxx]**	**xxx(xx.xx), [xxx]**

§Overlapped, MedDRA *latest version*

E: Number of adverse events

[Table 33] Adverse events and adverse drug reactions of geriatric subjects (aged ≥ 65) (N=xxx)

System Organ Class§ Preferred Term	**Adverse events** **n(%), [E]**	**Adverse drug reactions** **n(%), [E]**
System Organ Class	**xxx(xx.xx), [xxx]**	**xxx(xx.xx), [xxx]**
Preferred Term	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]
…	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]
Total	**xxx(xx.xx), [xxx]**	**xxx(xx.xx), [xxx]**

§Overlapped, MedDRA *latest version*

E: Number of adverse events

[Table 34] Adverse events and adverse drug reactions in the subjects with renal impairment (N=xxx)

System Organ Class§ Preferred Term	**Adverse events** **n(%), [E]**	**Adverse drug reactions** **n(%), [E]**
System Organ Class	**xxx(xx.xx), [xxx]**	**xxx(xx.xx), [xxx]**
Preferred Term	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]
…	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]
Total	**xxx(xx.xx), [xxx]**	**xxx(xx.xx), [xxx]**

§Overlapped, MedDRA *latest version*

E: Number of adverse events

[Table 35] Adverse events and adverse drug reactions in the subjects with hepatic impairment (N=xxx)

System Organ Class§ Preferred Term	**Adverse events** **n(%), [E]**	**Adverse drug reactions** **n(%), [E]**
System Organ Class	**xxx(xx.xx), [xxx]**	**xxx(xx.xx), [xxx]**
Preferred Term	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]
…	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]
Total	**xxx(xx.xx), [xxx]**	**xxx(xx.xx), [xxx]**

§Overlapped, MedDRA *latest version*

E: Number of adverse events

[Table 36] Reasons for excluding safety evaluation (N=xxx)

Reasons for excluding safety evaluation	**No. of subjects n(%)**	**Incidence of AE n(%)**
Reasons for excluding safety evaluation 1)	xxx(xx.xx)	xxx(xx.xx)
Reasons for excluding safety evaluation 2)	xxx(xx.xx)	xxx(xx.xx)
Total	**xxx(xx.xx)**	**xxx(xx.xx)**

[Table 37] Adverse events and adverse drug reactions in the subjects excluded from safety analysis (N=xxx)

System Organ Class§	**Adverse events**	**Adverse drug reactions**
Preferred Term	**n(%), [E]**	**n(%), [E]**
System Organ Class	**xxx(xx.xx), [xxx]**	**xxx(xx.xx), [xxx]**
Preferred Term	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]
…	xxx(xx.xx), [xxx]	xxx(xx.xx), [xxx]
Total	**xxx(xx.xx), [xxx]**	**xxx(xx.xx), [xxx]**

§Overlapped, MedDRA *latest version*

E: Number of adverse events