REMOTE MONITORING FOR AMBULATORY CARE OF ELDERLY PATIENTS WITH CANCER

TS-PAC STUDY

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Interventional research protocol involving human participants - Category 2 with minimal risks and constraints

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SUMMARY

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PRINCIPAL INVESTIGATOR / COORDINATOR	Dr Mathilde CABART
RESEARCH LEAD	Prof Pierre-Louis SOUBEYRAN
ACRONYM	TS-PAC
TITLE	Remote monitoring for ambulatory care of elderly patients with cancer. The TS-PAC study
RATIONALE / CONTEXT	In France, more than half of patients with cancer are over 65 years old. The majority of these elderly patients have geriatric fragilities (Caillet et al., 2014; Mohile et al., 2011), exposing them to increased risks of toxicity from cancer treatments (Extermann et al., 2012; Ruiz et al., 2019), but also to undesirable reactions to complications or unscheduled hospitalizations. Elderly patients also have different expectations to younger patients regarding the goals and consequences of cancer treatments, emphasizing the maintenance of quality of life and independence, at the expense of quantity of life (Fried et al. al., 2002). To provide better care for these patients, it is therefore important to diagnose toxicities and treatment complications as early as possible and to respond to these better, anticipating possible hospitalizations. Further, there is a need to identify tumor events (progression, relapses) early and to treat patients before their general condition deteriorates. We must fully appreciate the benefits of treatments for patients, not only on tumor control but also on quality of life and autonomy. Telemedicine and connected health tools seem to be able to improve the care of these patients. In the STAR (Basch et al., 2016, 2017) and SENTINEL (Denis et al., 2017) studies patients undergoing chemotherapy or having completed their treatment received weekly remote monitoring via an online questionnaire concerning 12 symptoms. This helped improve quality of life, reduce emergency department visits and unscheduled hospitalizations, detect tumor progression earlier, start treatment in patients in better general condition, and thus lengthened overall survival. In addition, patient-reported outcomes (PRO) have been shown to be useful to tailor medical management and assess prognosis. PRO collection enables better detection of symptoms by the doctor (Detmar et al., 2002; Montemurro et al., 2016) and a more accurate estimate of their severity (Novello et al., 2014), especially for subjective symptoms (Basch et al., 2006). This leads to therapeutic adaptations, reduces subsequent

	undesirable effects and improves quality of life. In addition, a patient's subjective assessment of his/her quality of life and state of health at the start of treatment (for example with the QLQ-C30 questionnaire) is correlated with overall survival (Gotay et al., 2008; Lee et al., 2018; Maione et al., 2005; Quinten et al., 2009; Sloan et al., 2012). Improvement in or deterioration of quality of life during treatment is also correlated with survival (Eton et al., 2003; Vickers et al., 2016), probably due to the direct effect of treatment on cancer symptoms. However, this is also likely to be due to the supportive care that improves both quality of life and overall survival (Temel et al., 2010), irrespective of treatment efficacy. The TS-PAC study therefore aims to develop a remote monitoring tool enabling the weekly collection of symptoms reported by elderly patients during cancer treatment, to detect early any toxicities and unfavorable changes which might require specific management. This tool will also make it possible to collect patient self-reports of perceived benefits observed following treatment in addition to the clinical parameters usually assessed (e.g. tumor control, progression-free survival and overall survival).
OBJECTIVES	**Primary objective** To assess the feasibility of using an online remote monitoring tool during the care of patients over the age of 65 who are receiving medical treatment for cancer. **Secondary objectives** • To evaluate and describe the responses to the self-questionnaires available on the remote monitoring tool: o Number of toxicities and clinical symptoms reported by patients triggering a "red" alert. o Compliance (for patients on oral therapy). o Subjective evaluation of the benefit provided by the treatment. o Satisfaction with the use of the remote monitoring tool. o Quality of life relative to patient health (EORTC QLQ-C30 and QLQ-ELD14). o Depression and anxiety in patients (HAD scale). • To evaluate and describe the other parameters collected by the coordinating nurse during telephone and / or clinical follow-up: o Risk of drug-related iatrogenesis. o Autonomy for activities of daily living using the ADL and IADL scales. o Geriatric frailty of patients using the G8 score and, if necessary, an onco-geriatric assessment. o Precariousness of patients with the EPICES score. o Distance and travel time to the care facility. o Computer experience. o Number of unscheduled hospitalizations and reasons. • To describe the feasibility of using the tool at the different evaluation points according to patient characteristics at inclusion: o Risk of drug-related iatrogenesis. o Autonomy for activities of daily living. o Geriatric fragility of patients. o Precariousness of patients with the EPICES score. o Distance and travel time to the care facility. o Computer experience.

	• To evaluate technical procedures for the remote monitoring tool. • Describe the remote monitoring process (number or rate of alerts by level of severity, patient management following alerts triggered by the tool, number of telephone reminders made by the Coordinating Nurse to the patient).
ENDPOINTS	**Primary endpoint**: The primary endpoint is the proportion of patients who completed at least all of the following questionnaires at 3 months (9 questionnaires in total): • Six weekly questionnaires on toxicities and clinical symptoms completed within 3 months of the start of treatment: o Toxicities and clinical symptoms will be assessed through 20 questions selected and adapted from the French version of the PRO (patient-reported outcomes) of the CTCAE (Common Terminology Criteria for Adverse Events) (Basch et al., 2014; National Cancer Institute, 2017). o A weekly questionnaire on toxicities and clinical symptoms will be considered complete if the patient has answered the first 7 mandatory questions (out of the 20 items). • Two questionnaires assessing the health-related quality of life, completed before the start of treatment and at 3 months: o Quality of life (QOL) will be assessed using the EORTC QLQ-C30 questionnaire (Aaronson et al., JNCI 1993) comprising 30 items. The targeted dimensions of the QLQ-C30 will be the five functional scales (physical, daily activity, emotional, cognitive and social) and the overall quality of life scale. o A QOL questionnaire will be considered complete if the scores of the 5 functional scales and the overall QOL score are calculable (more than 50% of the items of each sub-scale answered) according to the EORTC scoring manual. • The questionnaire evaluating the perceived benefit of the treatment at 3 months. The questionnaire will be considered as complete if the patient has answered the first question: "How effective do you find your cancer treatment?" **Secondary endpoints:** <u>Answers to the self-questionnaires available on the remote monitoring tool</u> • Toxicities and symptoms will be assessed weekly using 20 questions selected and adapted from the French version of the CTCAE PRO (Basch et al., 2014; National Cancer Institute, 2017). For each question, predetermined response thresholds have been established, triggering "orange" (to watch) or "red" alerts (intervention by the healthcare team required). The number of red alerts will be collected for each patient. • The subjective evaluation of the perceived benefit of treatment will be evaluated at 3 and 6 months by a questionnaire developed specifically for this project. • Patient satisfaction with the use of the remote monitoring tool will be evaluated at 3 and 6 months by a questionnaire developed specifically for this project. • Quality of life will be assessed at inclusion, 3 months and 6 months using the EORTC QLQ-C30 questionnaire (Aaronson et al., JNCI 1993) and, for people over 70 years old, using the QLQ-ELD14 module specifically for the elderly (Wheelwright et al., 2013). The targeted dimensions of the QLQ-C30

	will be the 5 functional scales (physical, daily life, emotional, cognitive, and social) and the overall quality of life scale. • Depression and anxiety will be assessed at baseline, 3 months and 6 months, using the HAD questionnaire (Zigmond and Snaith, 1983). <u>Parameters collected by the Coordinating Nurse during telephone and / or clinical follow-up</u> At inclusion: • The risk of drug-related iatrogenesis will be assessed by collecting the number of different drugs taken by the patient (Queneau et al., 2007). • Patient autonomy for activities of daily living will be assessed using two scales: the ADL scale (Katz et al., 1963) and the IADL scale (Lawton and Brody, 1969). • The geriatric frailty of patients will be assessed using the G8 score for patients aged 70 and over (Soubeyran et al., 2014), and if necessary, using a standardized geriatric assessment (EGS). Geriatric interventions will be described by domain. Patients will be separated and described according to 3 groups reflecting their frailty: (1) patients under 70 years old and over 70 years old with a G8 score> 14, (2) patients over 70 years old with a G8 score ≤ 14 having had an EGS without intervention, and (3) patients over 70 years of age with a G8 score ≤ 14 having had an EGS with geriatric intervention. • Patient precariousness will be assessed using the EPICES (Evaluation of Deprivation and Inequalities in Health Examination Centres) score (Labbé et al., 2007). • The distance between the place of residence and facility where the care is delivered, as well as the average time required for this journey, will be evaluated (collection of the place of residence). • Patients' computer experience will be evaluated (regular access to a computer, tablet or smartphone, to send emails and / or use applications and / or search the Internet). At 3 months and 6 months: • The number of unscheduled hospitalizations> 24 hours and the number of emergency room visits, as well as their reason, will be assessed. <u>Feasibility of using the tool at different evaluation times depending on the characteristics of the patients at inclusion</u> The feasibility of using the tool is defined as for the primary endpoint. The completion rates of the online questionnaires will be described at 3 months and 6 months according to the following parameters at inclusion: • Risk of drug-related iatrogenesis. • Autonomy for activities of daily living. • Geriatric frailty of patients. • EPICES precariousness score. • Distance and travel time to the care facility. • Computer experience. <u>Technical details when using the remote monitoring tool.</u> The technical procedures when using the remote monitoring tool will be assessed by collecting the following parameters: • Type of device on which the application is used (e.g. smartphone, tablet, or computer). • Number of times the software bugs or crashes • Management of the failure by Coordinating Nurse or by the supplier.

	<u>Description of the monitoring process</u> The remote monitoring process will be described by: • The number and / or rate of alerts generated by the tool depending on the severity level of the alert. • The nature and number of actions implemented and interventions carried out.
RESEARCH DESIGN	Single-center, prospective cohort pilot study evaluating the feasibility of a online remote monitoring tool during the care of patients over 65 years of age being medically treated for cancer.
INCLUSION CRITERIA	1. Patients 65 years of age and over. 2. Histologically proven cancer: breast, lung, ovary, prostate, bladder, kidney, ENT, colon-rectum, melanoma, sarcoma, lymphoma, myeloma, or myelodysplastic syndrome. 3. Included before starting medical treatment (chemotherapy, hormone therapy, targeted therapy, immunotherapy or combination). 4. Informed consent dated and signed. 5. Patients affiliated with a French social security scheme in accordance with the French law on biomedical research (Article 1121-11 of the French Code of Public Health).
NON INCLUSION CRITERIA	1. Life expectancy less than 12 months. 2. Patient declining to use a tablet, computer, smartphone or the Internet. 3. Patient not knowing how to read and understand French. 4. Technical impossibility of connecting to the Internet in the patient's living area. 5. Patient already included in this study or in another study evaluating a remote monitoring system.

STUDY PROCEDURE	Each patient will have to answer the remote monitoring questionnaires on a mobile phone, tablet or computer via the Internet. Responses will be sent to the referring oncologist and team (Coordinating Nurse). For each question, predetermined response thresholds have been established, triggering "orange" (to watch) or "red" alerts (intervention by the healthcare team required. Follow-up by self-questionnaire is as follows: • Weekly: toxicity and clinical symptom assessment questionnaire. • Every 3 months: QLQ-C30 +/- ELD14 quality of life questionnaires, HAD anxiety and depression assessment questionnaire, questionnaire for the subjective assessment of perceived benefit of treatment, and client satisfaction with use of the tool questionnaire. If a "red" alert is triggered, the team will decide on the type of intervention which can be: • A phone call to the patient • A change in treatment • Prescription of supportive oncological care • A consultation. • Hospitalization. • The intervention of a local health professional (attending physician, nurse). • The transmission of potentially useful information to the patient's pharmacist. Alerts will be raised by the Coordinating Nurse within 24 hours during the week, Monday to Friday, 9 a.m. to 5 p.m. excluding public holidays. The Nurse will be available and contactable directly if necessary during these hours. This is not 24 hour surveillance. Patients will be warned that in an emergency, they should systematically contact their attending physician or the ambulance (SAMU) outside of these time slots. In parallel, patient will continue standard follow-up with their referring oncologist and, if necessary (age ≥ 70 years and G8 score ≤ 14), will benefit from an onco-geriatric evaluation at inclusion then at 3 and 6 months. At the end of 6 months of remote monitoring, the Coordinating Nurse will inform the patient of the end of study participation. Within one month of the end of the remote monitoring, the nurse will also proceed to the remote uninstallation of the application and will organize the return of the equipment (tablet and/or 3/4G key) if these were lent for the study.
SIZE OF STUDY	The primary endpoint is the proportion of patients who completed at least 9 questionnaires at 3 months: 6 weekly toxicities / clinical symptoms questionnaires (20 items including 7 mandatory) + 2 EORTC QLQ-C30 quality of life questionnaires (30 items, mandatory scores for the 5 functional scales + the overall QOL) + 1 questionnaire evaluating the benefit of the treatment perceived by the patient (3 items, 1st question mandatory). Based on the results of other feasibility studies on remote monitoring in oncology (SENTINEL (Denis et al., 2014), STAR (Judson et al., 2013) and e-DomSanté1 (Quénel-Tueux et al., 2018)), we will consider the use of our online tool for the remote monitoring of elderly patients with cancer as feasible if 75% of the patients included and having started medical

	treatment against cancer answer all the questionnaires defined in the primary endpoint criterion. The inclusion of 30 eligible and evaluable patients will allow us to estimate this rate of 75% of patients who answered all the questionnaires (9 in total) with a 95% confidence interval on a bilateral basis of (55.6% - 88.2%). The confidence interval was calculated using Wilson's method with continuity correction. Estimating that 10% of patients will not be eligible / evaluable, we estimate that 33 patients should be included.
RESEARCH DURATION	Duration of the inclusion period: 24 months Duration of participation of each participant: 6 months Total duration of research: 30 months
STATISTICAL ANALYSIS	Analysis populations • Eligible population: all patients included with no major deviations from the eligibility criteria. • Eligible and assessable population: eligible patients who started medical treatment (chemotherapy, hormone therapy, targeted therapy, immunotherapy or combination). Statistical analyses: • The primary endpoint will be calculated from the eligible and assessable population. • The proportion of patients who completed 9 questionnaires at three months will be calculated as follows: number of eligible and assessable patients who completed the 9 questionnaires at 3 months divided by the number of eligible and assessable patients. The proportion will be reported with its 95% confidence interval (binomial law). • The secondary endpoints will be calculated from the eligible and assessable population as for the primary endpoint. • The scores of the questionnaires (continuous variables) will be described on the basis of means (+/- standard deviation) if the normality hypothesis is satisfied, and failing that, on the basis of other descriptive statistics (median, range, quartiles). • The scores can be categorized according to the thresholds described in the literature. For each questionnaire, the proportion of patients with a score above or below the predefined threshold will then be reported with its 95% confidence interval (binomial law). • The quantitative variables will be described from the mean and the standard deviation if the assumption of normality is respected, failing other descriptive statistics will be used (minimum, maximum, median and quartiles). • The qualitative variables will be described on the basis of the numbers and associated frequencies, expressed as a percentage (%). For each variable, the number of missing data will be described. Whenever possible, the reasons will be documented to assist the interpretation of results.

EXPECTED OUTCOMES	**To assess the feasibility** of using an online tool for elderly patients. **Improve the coordination** of care between hospital and home health professionals. **Create a new strategy** for monitoring patients undergoing treatment for cancer, to optimize their care pathway, and to reduce health inequalities that may affect elderly patients at risk due to their geriatric fragility. **Introduce patient-reported outcomes** into standard care which will thus be more centered around the patient, empowering the patient. PRO collected from elderly patients can also be used routinely, to educate caregivers to take into account the most frequent symptoms, but also in future therapeutic trials on elderly cancer patients.