EXPECTATIONS AND PRIORITIES OF ELDERLY CANCER PATIENTS FOR INITIAL MEDICAL TREATMENT

PRIORITY study

Abstract

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STUDY ABSTRACT

SPONSOR	INSTITUT BERGONIE
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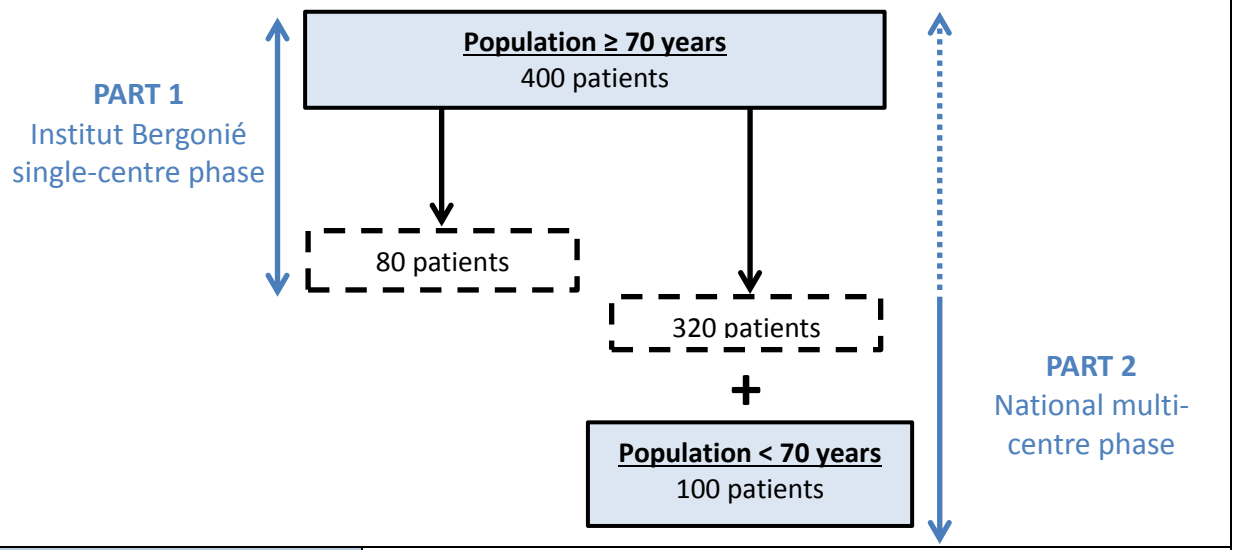
TITLE	Expectations and priorities of elderly cancer patients for initial medical treatment. PRIORITY study.
RATIONALE / BACKGROUND	Approximately 60% of cancers occur in people over 65, but these patients are proportionately under-represented in clinical trials. As a result, the impact of anti-cancer treatments on these patients is poorly taken into account, which can affect the quality of their care. The 2014-2019 Cancer Plan states that clinical research in geriatric oncology must be designed to take better account of the objectives of the proposed treatment. This requires a new definition of outcome measures, adjusted to patients' priorities. Indeed, overall survival, which represents the amount of life gained, is not sufficient to assess the expectations of elderly people, who legitimately have more qualitative expectations, such as quality of life or the impact of treatment on different areas of life (cognitive, social, functional, etc.). Apart from quality of life and improved survival, there are currently no guidelines for evaluating cancer treatments in the elderly population using more qualitative measures. Elderly patients need to be repositioned at the centre of their assessments to enable a more precise understanding of the real benefits and consequences of medical treatment. The PRIORITY study proposes to identify and evaluate changes in the expectations and priorities of these patients, when faced with first-line cancer medical treatment.
OBJECTIVES	**Primary objective** To describe the priorities of patients 70 years of age and older receiving first medical treatment for cancer, at treatment initiation and 3 months after treatment initiation. The primary outcome measure is a prioritisation of 4 items by patients, from a list of 8 expectations concerning the objectives of their treatment: efficacy of treatment, life expectancy, autonomy, daily tasks, social activities, burden of treatment, toxicity, economic aspect. **Secondary objectives** • To assess the intra-individual reproducibility of the expectations prioritisation grid concerning the initial measurement of the priorities of elderly subjects. • In patients aged 70 and over receiving initial medical treatment for cancer: – To describe patient expectations, at treatment initiation and 3 months after treatment initiation. – To describe patient priorities and expectations, 6 and 12 months after treatment initiation. – To describe, 3, 6 and 12 months after initiation of treatment, the proportion of patients whose priorities are stable compared with when treatment was initiated. – To look for associations between patients' characteristics (at

	initiation of treatment) and their priorities (at initiation of treatment and 3 months after initiation of treatment). – To describe overall survival in 2 groups of patients defined according to whether or not their priorities at 3 months were stable compared with their priorities at initiation of treatment. • For 2 groups of subjects (1- patients aged 70 and older and receiving initial medical treatment for cancer; 2- patients aged under 70 and receiving initial medical treatment for cancer): – To study the perception of the disease at initiation of treatment, – To look for an association between the perception of the disease at treatment initiation and a change in priorities between treatment initiation and 3 months after, – To look for an association between the perception of the disease at treatment initiation and the quality of life at treatment initiation, – To look for an association between the perception of the disease at treatment initiation and the change in quality of life between treatment initiation and 3 months after. • For 3 groups of subjects (1- patients aged 70 and over and receiving initial medical treatment for cancer; 2- patients aged under 70 and receiving initial medical treatment for cancer; 3- medical oncologists and oncogeriatricians): to compare subjects' priorities at initiation and 3 months after initiation of treatment.
STUDY DESIGN	This is a prospective study, for which recruitment will be conducted in two parts: – Part 1: Institut Bergonié single-centre phase (patient population aged 70 and over) – Part 2: national multi-centre phase. The main population will be patients aged 70 years and older. In parallel, a control population of patients aged 18 to 69 will be set up. The inclusion and exclusion criteria will be identical for both populations.
	
INCLUSION CRITERIA	1. Man or woman: a. Age ≥ 70 years b. 18 to 69 years of age (control population) 2. Living conditions 0-3 (WHO index). 3. First-line medical treatment for cancer (chemotherapy, targeted

	therapy, hormone therapy, combination): a. neoadjuvant b. adjuvant; prior neoadjuvant medical treatment is permitted, c. advanced/metastatic; prior neoadjuvant and/or adjuvant medical treatments are permitted. d. For prostate cancers: patients with biological relapse without metastasis present are eligible in the advanced/metastatic disease group. 4. Solid tumours (colorectal, ovarian, endometrium, lung, prostate, bladder, breast, sarcoma and kidney) and lymphoma (indolent and aggressive). 5. Life expectancy greater than 3 months. 6. Patients potentially compliant with the study follow-up rules. 7. Patients affiliated to a social security scheme. 8. Patients who have received clear information from the investigator about the study and have not refused to participate.
EXCLUSION CRITERIA	1. Treatment by exclusive surgery. 2. Radiotherapy alone or in combination with medical treatment (radio-hormone therapy or concomitant radio-chemotherapy). 3. Patient having already received a first line of medical treatment in the same indication as that at the time of patient enrolment in the trial: a. Patient in a neoadjuvant situation: having already received one or more lines of neoadjuvant medical treatment, b. Patient in an adjuvant situation: having already received one or more lines of adjuvant medical treatment, c. Patient in a metastatic situation: having already received one or more lines of metastatic medical treatment, 4. Supportive care without specific medical treatment. 5. History of another cancer being treated at the time of inclusion. 6. Patient already included in this study. 7. Patients who, for psychological, psychiatric, social, family or geographical reasons, could not be regularly monitored according to the study criteria; patients deprived of their liberty or under guardianship.
NATURE OF THE INTERVENTION ASSESSED IN THE RESEARCH	Patients' expectations and priorities will be assessed using two self-assessment questionnaires which will be carried out before the initiation of treatment and at 3, 6 and 12 months after the initiation of treatment.
OUTCOME MEASURES	**<u>Primary outcome measure</u>** • Description of the questionnaires 1. The expectations questionnaire: our questionnaire consists of 8 items, graded using an opinion scale (Not at all, Somewhat, Moderately, Fairly, Very much): - Efficacy of prescribed treatment for cancer - Life expectancy - Autonomy - Daily tasks - Social activities - Burden of treatment - Toxicity - Economic aspect 2. A prioritisation grid: comprising four choices to gather patients' priorities regarding their specific treatment, from among the eight

items in the expectations above.

- These questionnaires will be given to patients at the end of the consultation by the investigating physician, the CRA or the UCOG (oncogeriatric coordination unit) nurse. They will be given before initiation and at three, six months, and twelve months after treatment initiation.
- Primary outcome measure analysis

The ranking of priorities will be summarised by calculating the percentage of patients placing an item among their four priorities, i.e. assigning a value of 1.2, 3 or 4 to that item. Calculations will be performed separately for each item. For each item, we will describe the percentage of patients who prioritised the item concerned out of the 4 top items, then the percentage of patients who indicated the item as the 1st item to be prioritised.

Secondary outcome measures

- Each item concerning patients' expectations (treatment efficacy, life expectancy, autonomy, daily tasks, social activities, burden of treatment, toxicity, economic aspect) will be described individually at the different measurement times of interest (initiation of treatment, 3, 6 and 12 after initiation)
- Expextation stability is defined, for an item on the expectations questionnaire, by an identical response at treatment initiation and at the subsequent measurement time of interest (3, 6 and 12 months after treatment initiation)
- Priority stability is defined by identical prioritisation (the same 4 expectations selected and rated in the same order) between treatment initiation and the subsequent measurement time of interest (3, 6 and 12 months after treatment initiation)
- Associations will be sought between patient priorities at treatment initiation, then at 3 months with the following characteristics:
  - Patient's age,
  - Sex (M or F),
  - Educational level (last degree obtained),
  - Living environment (urban or rural) / Isolation (living alone yes/no),
  - Cancer location,
  - Line of treatment (neoadjuvant, adjuvant, metastatic),
  - Type of treatment (chemotherapy, hormone therapy, targeted therapy),
  - Quality of life,
  - Complete oncogeriatric assessment,
  - Co-morbidities,
  - General condition,
  - Toxicity,
  - Progression of the disease.
- Quality of life is defined by the EORTC QLQ-C30 questionnaire and by the elderly-specific module QLQ-ELD14
- Disease perception at treatment initiation will be assessed using the “Brief Disease Perception Questionnaire” (Bref Questionnaire de Perception de la Maladie - BQPM).
- A full oncogeriatric assessment will be carried out during the initial consultation and will include the systematic performance of the following tests:

	- Instrumental Activities of Daily Living (IADL, Lawton & Brody, Gerontologist 1969), and Activities in Daily Living (ADL, Katz et al. JAMA 1963), - Get up and go test (Mathias et al, Arch Phys Med Rehabil. 1986) - Mini Nutritional Assessment (MNA; Guigoz et al. FactsResGerontol 1994) - Mini Mental State Examination (MMSE; Folstein et al. J PsychiatrRes 1975), - Geriatric Depression Scale (GDS-15; Sheikh et al. Clin Gerontol 1986). - Co-morbidities will be assessed at the beginning of the study by the Cumulative Illness Rating Scale-Geriatric (CIRS-G; Extermann et al. J Clin Oncol 1998). • Overall condition will be assessed by the WHO living conditions score at the four time points of the assessment, • Toxicity will be assessed by collecting the following events at the three time points of the assessment (3, 6 and 12 months): - Unscheduled hospitalisation and cause, - Postponement of treatment due to toxicity, - Dose adjustment due to toxicity, - Treatment discontinuation due to toxicity, - Febrile neutropenia. • Disease progression will be determined at 3, 6 and 12 months of treatment according to the investigator's clinical judgement based on the standard criteria in force: - RECIST criteria (Eisenhauer et al., Eur J Cancer 2009) for solid tumours, - PSA, RECIST (visceral locations), PET Scan (bone lesions) for prostate cancers (Scher, J Clin Oncol, 2008 and 2011), - Lugano Lymphoma classification criteria (Cheson et al. J Clin Oncol 2014). • Overall survival is defined as the time between the date of inclusion and the date of death from any cause. • The repeatability of the prioritisation grid developed in this study will be assessed by administering the prioritisation grid twice to a sample of 80 patients for the initial measurement of priorities: once at the time of the initial consultation and then a second time, for example at the start of treatment visit, and within no more than 10 days. • For 3 groups of subjects (1- patients aged 70 and over and receiving initial medical treatment for cancer; 2- patients aged under 70 and receiving initial medical treatment for cancer; 3- medical oncologists and oncogeriatricians): the subjects' priorities at initiation and 3 months after initiation of treatment will be compared.
STUDY SIZE	**<u>Total (Part 1 and Part 2):</u>** 400 patients in the main population (≥ 70 years) 100 patients in the control population (aged 18 to 69). <u>Part 1</u>: 80 patients in the main population (≥ 70 years) <u>Part 2</u>: 320 patients in the main population (≥ 70 years)

	100 patients in the control population (aged 18 to 69).
EXPECTED NUMBER OF CENTRES	Part 1: Institut Bergonié single-centre study Part 2: multi-centre study (approximately 10 national centres)
STUDY DURATION	**Part 1**: - Duration of the inclusion period: 8 months - Participation time for each patient: 12 months - Total study duration: 20 months **Part 2**: - Duration of the inclusion period: 48 months - Participation time for each patient: 12 months - Total study duration: 60 months
DATA STATISTICAL ANALYSIS	**Study size** • For this descriptive study, we wish to limit the inclusion period to 24 months. • The first part, carried out at Institut Bergonié, will enable us to assess the reproducibility of the expectations questionnaire. For this part, we wish to include 80 subjects aged 70 and over. The experience of the ONCODAGE study (Soubeyran et al, Plos One 2014) (200 patients included in 20 months at the Institut Bergonié), allows us to estimate the feasibility of inclusion for this first stage, with 80 patients included in 8 months. • For the second part, we wish to include 320 patients aged 70 and over and 100 patients under 70. Based on the experience of the ONCODAGE study (Soubeyran et al, Plos One 2014) (approximately 1,600 patients included in 18 months in 20 centres at national level), we estimated the feasibility of inclusion for this second stage, with 420 patients included in 18 months. As the rate of inclusions was slower than expected, the inclusion period was extended to 48 months. **Statistical methods used** **Primary outcome measure** • The analysis of the primary outcome measure will focus on the population that is eligible and evaluable for the primary outcome measure. • Expectations: for each time point of interest, the distribution of response modalities (not at all; somewhat; moderately; fairly; very much) is plotted for each of the eight items, using frequencies and percentages. Missing values will also be reported. • Priorities: for each time point of interest, the expectations reported as priorities will be plotted, in terms of frequency and percentages. • Additional analyses will be carried out to assess any response shift (RS) phenomena. **Secondary outcome measures** • Quality-of-life questionnaires – The QLQ-C30 quality of life questionnaire (outside the three targeted sub-scales for the co-primary outcome measure) will be analysed following the guidelines in the EORTC Scoring Manual. The same applies to the QLQ-ELD14 questionnaire. – The scores will be analysed if at least half of the items on the corresponding scale have been answered. – Descriptive statistics of raw and standardised QLQ-C30 and QLQ-ELD14 scores and change from inclusion will be calculated at

	each visit time and for each arm. – A cross-sectional analysis will be carried out with a graphical representation of the scores per treatment arm at the different time points. • Disease perception (BQPM questionnaire) – The distribution of subjects by modality (pessimistic, realistic, optimistic) will be reported (frequency, proportion and 95% confidence interval) by population of interest. – Associations with quality of life and changes in priorities will be sought (chi2 test or non-parametric test depending on the distribution of the variables) • Geriatric parameters – For each of the geriatric scales, the scores will be analysed. – Quantitative analysis: Scores will be described from mean values (+/- standard deviation) if the normality assumption is satisfied, and failing that on the basis of other descriptive statistics (median, range, quartiles). The scores will be described at each time point of interest. – Qualitative analysis: the rate of subjects with an abnormal score will be reported (frequency, proportion and 95% confidence interval) at each time point of interest. • The reproducibility analysis will be carried out on the population of eligible patients who completed the expectations questionnaires and the prioritisation grid on 2 occasions before the initiation of treatment, within a period of between 3 and 10 days. The reproducibility of the expectations questionnaire will be assessed by the kappa concordance coefficient; values of the kappa coefficient above 0.75 correspond to acceptable reproducibility. • Contingency tables will be presented for the priorities of the 3 groups of subjects, and a comparison will be made using a chi-2 test (or, failing that, a Fisher test). • Associations between prioritisations and patient characteristics will be investigated using a Chi-square test (univariate analyses) and logistic modelling (multivariate analyses). • Survival data will be described using the Kaplan-Meier method (median survival, probability of survival at 1 year) and presented with their 95% confidence intervals. • Quantitative variables will be described from mean values (+/- standard deviation) if the normality assumption is satisfied, and failing that on the basis of other descriptive statistics (median, range, quartiles). • Qualitative variables will be described based on frequency, percentage and 95% confidence interval (binomial law). • Missing data will be reported (per item and per questionnaire) using frequency and percentage. • Kappa coefficients will be evaluated, along with their 95% confidence intervals, and compared using the method described by Fleiss (Third Ed. 2003). • The application conditions will be checked for all analyses that will be carried out. All tests will be carried out with a risk of error of the first kind α=5% and will be exploratory. **<u>Two interim analyses will be planned</u>**: • A first interim analysis will be planned at the end of Part 1 of the

	study, i.e. once the data of the first 80 patients enrolled at Institut Bergonié (elderly population) are available. A reproducibility analysis will be carried out on these 80 patients and the results will be discussed by the steering committee. • A second interim analysis will be planned once 250 patients have been included in the elderly population, in order to describe the inclusions according to the different cancer locations. These results will be analysed by the steering committee in order to decide on any changes to the inclusion criteria, in order to ensure the inclusion of all tumour locations.
EXPECTED BENEFITS	**For patients**: Better consideration of patient expectations with the following consequences: - direct improvement in patients' experience of treatment as a result of listening to their objectives, particularly with regard to the risk of hospitalisation and adverse effects, - better definition of the indications for cancer treatments in this population, where evidence from clinical trials is lacking, - improved quality of life. **For public health**: - Improved quality of clinical trials in oncogeriatrics in line with the guidelines of the 2014-2019 Cancer Plan, by proposing more appropriate outcome measures, - Improved recruitment and relevance of the results of these future clinical trials thanks to a more specific design, - Improved cost/effectiveness ratio of treatments prescribed in oncogeriatrics by improving patient compliance. - Possible extension of the use of composite outcome measures based on patient expectations to other serious diseases (severe heart failure, chronic respiratory failure, chronic end-stage renal failure, etc.)

Elderly patient follow-up summary table

Patient Part	Visit 1 Initial consultation	Visit 2 3 months	Visit 3 6 months	Visit 4 12 months
Information note	**X**			
History of the disease/previous treatments	**X**			
WHO general condition	**X**	**X**	**X**	**X**
Height, weight	**X**	**X**	**X**	**X**
Priorities and Expectations Questionnaire	**X**	**X**	**X**	**X**
Quality of life [1]	**X**	**X**	**X**	**X**
BQPM disease perception questionnaire [2]	**X**			
Initial geriatric assessment [3]	**X**			
Simplified geriatric assessment [4]		**X**	**X**	**X**
Treatment toxicity [5]		**X**	**X**	**X**
Tumour evaluation [6]		**X**	**X**	**X**
Concomitant oncology treatments [7]		**X**	**X**	**X**
Physician part[8]				
Priorities questionnaires	**X**	**X**	**X**	**X**

[1] EORTC QLQ-C30, QLQ-ELD14 questionnaires. To be completed for 12 months, even if the treatment line is changed and/or the disease progresses and/or specific treatments are discontinued.

[2] BQPM questionnaire, to be completed at the initial visit only.

[3] The initial geriatric assessment includes: CIRS-G (Co-morbidities and associated treatments), Socio-economic Questionnaire, ADL, IADL, MNA, MMS, GDS15, GUAGT.

[4] The simplified geriatric assessment includes: ADL, IADL and changes concerning housing/environment/family and aid (shortened socio-economic questionnaire). The geriatric assessment will be continued for 12 months, even if the treatment line is changed and/or the disease progresses and/or specific treatments are discontinued.

[5] Collection of the following information: febrile neutropenia, unscheduled hospitalisation, delayed treatment, dose adjustment, discontinuation of treatment due to toxicity.

[6] Tumour assessment planned by the referring physician as part of the patient's normal cancer follow-up, based on current standard criteria (RECIST 2009 criteria for solid tumours, Scher criteria - PSA and/or RECIST- for prostate cancer and Cheson for lymphoma).

[7] Treatment line changes must be recorded with their date and type of change (chemotherapy, hormone therapy, targeted therapy). Similarly, concomitant treatments such as surgery, radiotherapy or interventional radiology related to the cancer should be recorded, along with their date and type, throughout the patient's follow-up period. [8] Collection of some information about the physician at the start of the study (year of birth, number of years of exercise, training in oncogeriatrics).

Young patient follow-up summary table

Patient Part	**Visit 1** Initial consultation	**Visit 2** 3 months	**Visit 3** 6 months	**Visit 4** 12 months
Information note	**X**			
History of the disease	**X**			
WHO general condition	**X**	**X**	**X**	**X**
Height, weight	**X**	**X**	**X**	**X**
Priorities and Expectations Questionnaire	**X**	**X**	**X**	**X**
Quality of life [1]	**X**	**X**	**X**	**X**
BQPM disease perception questionnaire [2]	**X**			
Treatment Toxicity [3]		**X**	**X**	**X**
Tumour evaluation [4]		**X**	**X**	**X**
Concomitant oncology treatments [5]		**X**	**X**	**X**
Physician Part[6]				
Priorities questionnaires	**X**	**X**	**X**	**X**

[1] EORTC QLQ-C30 questionnaire. To be completed for 12 months, even if the treatment line is changed and/or the disease progresses and/or specific treatments are discontinued.

[2] BQPM questionnaire, to be completed at the initial visit only.

[3] Collection of the following information: febrile neutropenia, unscheduled hospitalisation, delayed treatment, dose adjustment, discontinuation of treatment for toxicity.

[4] Tumour assessment planned by the referring physician as part of the patient's normal cancer follow-up, based on current standard criteria (RECIST 2009 criteria for solid tumours, Scher criteria - PSA and/or RECIST- for prostate cancer and Cheson for lymphoma).

[5] Treatment line changes must be recorded with their date and type of change (chemotherapy, hormone therapy, targeted therapy). Similarly, concomitant treatments such as surgery, radiotherapy or interventional radiology related to the cancer should be recorded, along with their date and type, throughout the patient's follow-up period.

[6] Collection of some information about the physician at the start of the study (year of birth, number of years of exercise, training in oncogeriatrics).