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Individualised physical activity programme in patients over 65 years with haematological malignancies (OCAPI): protocol for a single-arm feasibility trial

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ABSTRACT

Introduction Older adults with cancer suffer from the combined effects of ageing, cancer disease and treatment side effects. The main treatment for patients with haematological malignancies is chemotherapy, associated with significant toxicities. Chemotherapy can alter patients' physical function and quality of life which are often already diminished in older patients due to ageing and comorbidities. It therefore seems essential to develop and to evaluate interventions capable of preventing physical and psychosocial decline and its consequences. Promoting physical activity is a promising approach to improve physical function and quality of life in older adults with cancer, but there are limited data on the feasibility of such interventions among older patients with haematological malignancies, concomitant to chemotherapy.

Methods and analysis OCAPI (OnCogeriatric and Individualized Physical Activity) is a single-arm, interdisciplinary, prospective, interventional, feasibility study. It is intended to include 40 patients (20 patients with acute myeloid leukaemia and 20 patients with non-Hodgkin's lymphoma) over 65 years in an individualised 6-month physical activity programme. The programme consists of individually supervised exercise sessions with an increasing volume of physical activity either at home and/or in a laminar airflow room (depending on the disease and treatment regimen) followed by unsupervised sessions and phone follow-ups. Patients will receive an activity tracker during the 6 months of the programme. Evaluations will take place at inclusion and at 3, 6 and 12 months to assess the feasibility of the programme and to explore potential changes in physical, psychosocial and clinical outcomes. The results will generate preliminary data to implement a larger randomised controlled trial.

Ethics and dissemination The study protocol was approved by the French ethics committee (Comité de protection des personnes Est I, N°ID-RCB 2019-A01231-56, 12 July 2019). All participants will have to sign and date an informed consent form. The findings will be disseminated in peer-reviewed journals and academic conferences.

Strengths and limitations of this study

- This study will assess the feasibility of a physical activity intervention in patients over 65 years with acute myeloid leukaemia and non-Hodgkin's lymphoma.
- The feasibility of the intervention will be based on the adherence rate, the recruitment rate, the retention rate and the safety of the programme.
- The physical activity programme is composed of supervised and unsupervised sessions, performed in the laminar airflow room at the cancer care centre or at the patient's home, combined with a follow-up by phone and a monitoring with an activity tracker.
- Representatives from the targeted patient population were involved in the study by questioning their preferences for physical activity and creating with them the exercise booklet.
- Haematologists, geriatricians and certified exercise instructors contributed to the development of this study to consider the complexity and multidimensional nature of care of older patients with cancer.

Trial registration number NCT04052126.

INTRODUCTION

Cancer incidence and mortality steadily increase with age, and people over 65 years accounted for 61% and 72%, respectively, of the 4 229 662 new cancer cases and the 1 388 790 cancer deaths in Europe in 2018.[1] Also, more than half of patients diagnosed with haematological malignancies are over 65, and more than three-quarters of related deaths occurred in this age group in Europe.[1] Furthermore, the number of new cancer cases among adults aged 65 years and older is expected to increase by 47% in Europe

in 2035.[2] As a consequence, the healthcare system will have considerable and unique challenges to manage an increasing number of older patients affected by haematological malignancies.[3]

Older adults with haematological malignancies differ from younger ones due to the combined effects of functional decline, geriatric syndromes and frequent comorbidities, that might impact a treatment selection and cancer outcomes.[4] Intensive chemotherapy, the main treatment in acute myeloid leukaemia (AML) is associated with significant toxicities and a prolonged hospital stay and has been reported to impact patients' physical function and quality of life (QoL).[5] Furthermore, outpatient chemotherapy regimens, as for non-Hodgkin's lymphoma (NHL), are associated with altered QoL, both mentally and physically, compared with older patients without NHL.[6]

There is strong evidence that physical activity (PA) has numerous physical and mental health benefits in older adults.[7 8] Most international guidelines recommend a goal of 150 min/week of moderate-to-vigorous intensity PA to achieve health benefits in this population.[9 10] For older adults who cannot exercise due to health conditions, including cancer, recommendations still encourage to engage in a PA commensurate with their abilities and conditions. Furthermore, it was suggested that marked health benefits are observed with relatively minor volumes of PA.[11]

In recent years, home-based interventions have been increasingly and successfully developed to promote PA in community-dwelling older adults.[12] There are several advantages to home-based interventions, given the barriers to exercise faced by older adults.[13] It particularly removes the barrier of transportation and the limitation of community resources and makes it easier to integrate PA into daily life. A recent systematic review showed that self-control strategies using tracking monitors or daily step diaries, and setting individualised step-based goals were successful to maintain PA level in older adults, at least 6 months after the end of an exercise programme.[14]

In the context of cancer, a recent systematic review on the effectiveness of PA interventions on QoL in patients over 60 years with cancer reported that PA interventions, which were tailored to the individual capacity and preferences, as well as supervised by qualified professionals, improved the QoL.[15] Studies including phone follow-ups by professionals also found positive results. Yet, none of the 13 randomised controlled trials (RCTs) included patients with haematological malignancies.

For adults with haematological malignancies, two meta-analyses reported strong positive effects of PA interventions in patients with stem cell transplantation on physical fitness, fatigue and QoL.[16 17] Promising benefits from systematic reviews were also observed in patients with leukaemia[18 19] and lymphoma.[20 21] However, these studies did not focus specifically on interventions in older patients with haematological malignancies.

To date, only two pilot studies assessed the feasibility of a PA programme in patients ≥60 years with haematological malignancies.[22 23] Both studies enrolled 16 patients and proposed, respectively, a supervised alternating endurance and resistance workout on 6 of 7 days a week and a supervised virtual reality exercise for 20 min a day, five times a week, from the start of chemotherapy until hospital discharge. The interventions were deemed feasible (high adherence rate) and safe (no adverse events). However, in both studies, no significant improvement in physical or psychosocial outcomes was observed, while in the first study,[23] QoL significantly decreased during the study period.

While these data suggested the feasibility of a PA programme in older adults with haematological malignancies, interventions were predominantly of short duration, and neither tailored to the individual physical fitness and preferences nor integrated into the cancer care or patient lifestyle. These limits are in line with the gaps identified in recent narratives reviews that focused on PA studies in older adults with cancer.[24 25]

In this context, it appears important to develop PA programmes tailored to older patients with haematological malignancies to support a regular and sustainable PA practice. Interventions should be: (1) flexible along the cancer continuum to be adapted to the treatment plans, (2) patient-centred and personalised to be adapted to the individual situation and (3) combined with professional, tailored guidance and autonomy support to promote continued engagement and long-term PA.

The primary aim of the OnCogeriatric and Individualized Physical Activity (OCAPI) trial is to determine the feasibility (ie, recruitment, retention and adherence rates, and safety of the programme) of a 6-month individualised PA programme, concomitant with chemotherapy treatments in older patients over 65 years with AML and NHL. The secondary aim is to investigate the safety of the programme and to assess potential changes in physical, psychosocial and clinical outcomes in short and medium follow-ups.

METHODS

Study design

OCAPI is a single-arm feasibility, interdisciplinary, prospective intervention trial conducted by the haematology department of Leon Berard Comprehensive Cancer Center (CLB, Lyon, France) in patients over 65 years with AML and NHL.

Study population

Patients must meet all of the following inclusion criteria to be eligible for participation in the OCAPI trial: (1) aged 65 years or older; (2) histologically confirmed AML or NHL; (3) required first-line curative chemotherapy; (4) able to follow-up at the CLB; (5) residing in one of the following French regions: Ain, Ardèche, Drôme, Isère, Loire, Rhône, Savoie, Haute-Savoie; (6) Eastern

Cooperative Oncology Group (ECOG) performance status (PS) <3; (7) life expectancy >6 months; (8) able to engage in PA with a medical certificate issued by the investigator; (9) available and willing to participate in the study for the whole duration; (10) able to understand, read and write French language; (11) affiliated to a social security system; (12) having given written informed consent.

The exclusion criteria are: personal history or co-existence of another primary cancer (except for in situ cancer regardless of the site and/or basal cell skin cancer and/or cancer in complete remission for more than 5 years); treated by immunotherapy alone; participating in a concurrent exercise study; deprived of liberty by court or administrative decision.

Recruitment of participants

Recruitment started on November 2019. Participants will be recruited in CLB and will be screened weekly during the haematological malignancies' boards of the CLB, as described in figure 1. The study will be proposed by a haematologist to patients, prior to the treatment onset (or up to 5 days after the start of the chemotherapy if the patient's condition is not deteriorated, according to the investigator's assessment). In practice, the investigator will check patients' eligibility, and explain the study orally with a written informed consent form. After a sufficient period for reflection, the participants will provide the consent signed by themselves, which will also be signed by the investigator (original archived by the investigator and one copy returned to the patient). The end date for this study is planned in November 2022.

Intervention

The 6-month programme consists of four components: (1) individual supervised PA sessions; (2) individual unsupervised PA sessions; (3) PA follow-ups by phone; (4) PA monitoring with an activity tracker. The progressive programme is composed of an initiation period (1st month), a transition period (2nd to 3rd months) and a period of autonomy (4th to 6th months). The programme structure is detailed in table 1.

Individual supervised PA sessions

The sessions will be planned once a week during the initiation and transition phases, for a total of 12 sessions over 3 months (table 1). For patients receiving outpatient chemotherapy (mostly patients with NHL), the sessions will take place at the patient's home conducted by a subcontracted certified exercise instructor. For patients receiving intensive chemotherapy during a prolonged stay in a laminar airflow room (mainly patients with AML), the sessions will take place at the CLB by a certified exercise instructor. When the patients will return home, the sessions will be delivered by a subcontracted certified exercise instructor.

The instructor will propose resistance, balance and flexibility exercises, of low to moderate intensity, for 20–45 min per session, once a week over 3 months.

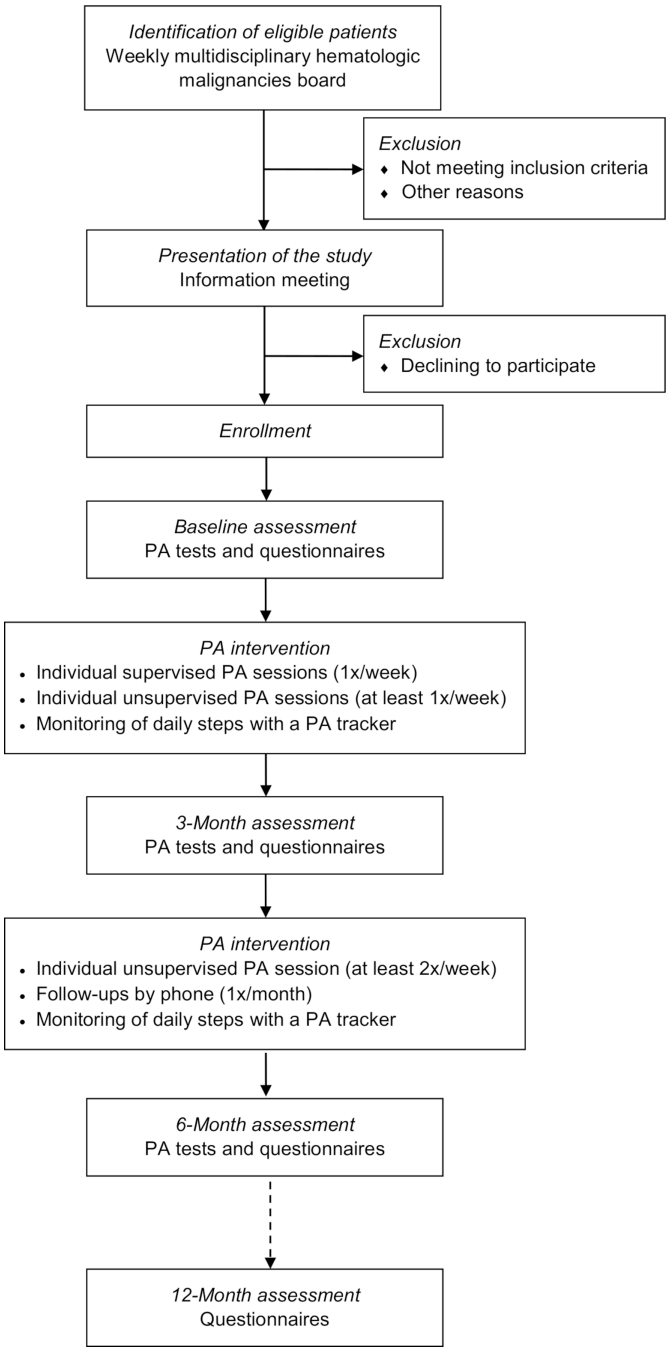

Figure 1 Flowchart of the OCAPI trial. OCAPI, OnCogeriatric and Individualized Physical Activity; PA, physical activity.

Exercises will be tailored according to the results of each patient's physical fitness assessment at baseline and then according to previous sessions.

The instructor will use a specific exercise booklet, which proposes 70 exercises that can be performed in three different body positions (lying down, sitting and standing) to adapt the difficulty to each patient's capacity. Also, patients will be provided an exercise kit (ball and elastic band) to practise and a logbook to report the type and duration of all physical activities performed during the week. During these sessions, the instructor will also select, explain and note down

Table 1 Overview of the physical activity programme

Period	Initiation (1st month)	Transition (2nd to 3rd months)	Autonomy (4th to 6th months)
Individual supervised exercise session	1×/week	1×/week	Ø
Individual unsupervised exercise session	Ø	At least 1×/week	At least 2×/week
PA follow-ups by phone	Ø	Ø	1×/month
PA monitoring with a PA tracker	Throughout the programme		

PA, physical activity.

on a dedicated sheet the exercises to be performed without supervision during the week (see below). The instructor will also motivate each participant to integrate regular PA into their living environment and condition.

Individual unsupervised PA sessions

The sessions will start during the transition phase and will be planned at least once a week during the transition phase and at least two times a week during the autonomy phase (table 1). During the unsupervised sessions, patients will perform the exercises by themselves, using the booklet that includes photos and detailed explanations for each exercise to assist themselves to perform the exercises correctly. Depending on the treatments, individual unsupervised exercise sessions will be performed in the laminar airflow room of the CLB or at the patient's home.

PA follow-ups by phone

The remote follow-ups will take place once a month during the autonomy phase and will be carried out through personalised phone calls by a certified exercise instructor. The follow-ups will aim to review the PA achievements of patients, to provide advice and to adapt the exercises if needed.

PA monitoring with an activity tracker

Patients will receive an activity tracker to wear during the day throughout the entire programme (except during treatments in the laminar airflow room), to promote regular walking. The activity tracker used in this study is the Garmin Vivofit 4 (Garmin, Olathe, Kansas, USA), appreciated by patients with cancer for the 1 year long battery life, the large screen and the clear text.[26] At the beginning of the programme, a target number of steps will be determined by the certified exercise instructor, in agreement with patients, according to their capacities. Patients will be advised to report the number of daily steps measured with the activity tracker in a paper-based logbook at the end of the day. Every week during the initiation and transition phases, the instructor will adjust individually the targeted steps based on patient feedback, to improve progressively their PA level. Patients, who own a smartphone and wish to use the Garmin application, will be able to use it in parallel to the paper-based logbook.

Outcome measurements

Primary outcome

The primary outcome is the adherence rate of the intervention, defined in this study as the ratio of supervised and unsupervised sessions performed by patients to the number of scheduled sessions, as well as the ratio of phone calls performed to the number of scheduled calls, and the percentage of days wearing the activity tracker versus days of the programme (excluding time spent in the laminar airflow room if applicable).

Secondary outcomes

The secondary outcomes (table 2) are:

- The recruitment rate of the intervention, defined as the ratio of patients included in the study out of the number of eligible patients.
- The retention rate of the intervention, defined as the percentage of patients who completed the intervention among patients included in the study.
- The safety of the intervention, defined as the number, type and duration of programme-related adverse events.
- Effects of the programme at 3 months after enrollment, on physical fitness, body mass index (BMI), PA level, self-efficacy for exercise, PA barriers, physical function, cognitive impairment, depression, nutritional status, comorbidities, fatigue, health-related QoL, social vulnerability, falls and specific cancer-related data.
- Effects at the end (6 months) and at distance from the programme (12 months).

Evaluations

Patients will benefit from three evaluations at inclusion, 3 months after inclusion (ie, mid-programme) and 6 months after inclusion (at the end of the programme). The evaluations will be composed of (1) a multidimensional PA-linked assessment performed by a certified exercise instructor, and (2) a multidimensional geriatric assessment performed by a geriatrician. Self-questionnaires included in these evaluations will be administered by a clinical research assistant. Selected questionnaires will also be sent by post to patients at 1 year after inclusion in the programme, anticipating the difficulty that patients may have in returning to the centre at this time.

Table 2 Data collection schedule

Assessments	At baseline	After 3 months	After 6 months	After 1 year
PA assessment				
Walking endurance (*6-min walk test or 2-min step in place test*)*	✓	✓	✓	
Walking speed (*10-metre walk test*)†	✓	✓	✓	
Upper body strength (*30-second arm curl test*)	✓	✓	✓	
Grip strength (*hand grip dynamometer test*)	✓	✓	✓	
Lower body strength (*30-second chair stand test*)	✓	✓	✓	
Upper body flexibility (*back scratch test*)	✓	✓	✓	
Lower body flexibility (*chair sit and reach test*)	✓	✓	✓	
Mobility (*timed up and go test)*†	✓	✓	✓	
Balance (*open-eyes unipodal test*)	✓	✓	✓	
Weight and body mass index	✓	✓	✓	
PA level (*GSLTPAQ*)	✓	✓	✓	✓
Number of steps (*activity tracker*)	Continuously in a logbook			
Self-efficacy for Exercise Score (*SEES*)	✓	✓	✓	
PA barriers (*Barriers to Being Active Quiz*)	✓	✓	✓	✓
Geriatric assessment				
Physical function (*ADL/IADL*)	✓	✓	✓	
Cognition (*MoCA*)	✓	✓	✓	
Depression (*Geriatric Depression Scale*)	✓	✓	✓	
Nutritional status (*Mini Nutritional Assessment*)	✓	✓	✓	
Comorbidities (*CIRS-G*)	✓	✓	✓	
Fatigue (*FACIT-F*)	✓	✓	✓	✓
Health-related QoL (*QLQ-C30*)	✓	✓	✓	✓
Social vulnerability (*EPICES*)	✓			✓
Falls in the past 12 months	✓			✓
Sociodemographic and clinical data				
Age, sex	✓			
Marital status	✓			
Tobacco, alcohol	✓			
Date of diagnosis	✓			
Tumour characteristics	✓			
Performance status (*ECOG*)	✓	✓	✓	
Toxicities (grade >2)		✓	✓	
Treatment response			✓	
Programme follow-up				
Programme-related adverse events	Continuously in a logbook			
Programme satisfaction (questionnaire)			✓	

*6-min walk test for patients treated in an outpatient basis and 2-min step in place test for those in a laminar airflow room.
†Only for patients treated by chemotherapy in an outpatient basis.
ADL, Activities of Daily Living; CIRS-G, Cumulative Illness Rating Scale—Geriatric; ECOG, Eastern Cooperative Oncology Group; EPICES, Evaluation of Deprivation and Inequalities in Health Examination Centres; FACIT-F, Functional Assessment of Chronic Illness Therapy—Fatigue (FACIT-F); GSLTPAQ, Godin-Shephard Leisure-Time PA Questionnaire; IADL, Instrumental Activities of Daily Living; MoCA, Montreal Cognitive Assessment; PA, physical activity; QLQ-C30, 30-item Core Quality of Life Questionnaire; QoL, quality of life.

PA assessment

Physical fitness of the study patients will be mainly measured with the Senior Fitness Test, developed and validated for American adults over 60 years[27] and also evaluated among 1237 French men and women between 60 and 89 years old.[28] It includes measures of walking endurance, upper and lower body strength, upper and lower body flexibility, mobility and BMI. This test battery will allow to evaluate each physical fitness element of each patient with three levels based on the percentiles of the scores among the total patients—below the 25th percentile (low), between the 25th and 75th percentile (intermediate) and above the 75th percentile (high). According to these results, the PA sessions during the intervention will be tailored by the certified exercise instructor. For example, if a patient has a lower level of upper body strength compared with other components, upper body strength exercises will be prioritised during the sessions.

Walking endurance will be evaluated using the 6-min walk test for patients treated with chemotherapy on an outpatient basis or using the 2-min step in place test for patients treated with chemotherapy in a laminar airflow room. The first test consists of measuring the distance of metres covered for 6 min round-trip on a 30-metre circuit, and the second one the number of knee raises completed in 2 min raising the knee at a height between the patella and the iliac crest.[27] Only for patients treated with chemotherapy on an outpatient basis, walking speed will also be assessed using the 10-metre walk test. It measures the time of seconds to walk 6 m at a comfortable and a maximal walking speeds on a 10-metre course.[29]

Upper body strength will be assessed using the 30-second arm curl test. It measures the number of flexions of the arm performed in 30 s by holding a 2 kg weight for women and 3 kg for men. In addition, grip strength will be assessed using the hand grip dynamometer test. This test measures the maximum force in kg with the elbow flexed at 90°, arm in slight abduction and the wrist and hand semi-pronated.[30]

Lower body strength will be measured using the 30-second chair stand test. It measures the number of complete raises from a sitting position in 30 s with the arms across the chest.[27]

Upper body flexibility will be assessed using the back scratch test. It measures the distance of centimetres between the tips of middle fingers (+/−) when placing one hand behind the head and back over the shoulder and the other in the middle of the back.[27]

Lower body flexibility using the chair sit and reach test. It measures the distance of centimetres between the tips of middle fingers and toes (+/−), when sitting on the edge of a chair with one leg stretched and the fingers trying to reach forwards the toes.[27]

Mobility will be assessed using the timed up and go test, only for patients treated with chemotherapy on an outpatient basis. It measures the total time of seconds to get up from a sitting position, walk 2.5 m, turn around a cone, get back and sit on the chair.[27] Balance will also be evaluated using the open-eyes unipodal test, measuring the time of seconds to stand on one leg (for a maximum of 60 s), lifting the foot of the other leg to the middle of the calf.[31]

Weight (kg) and height (cm) will be measured to calculate the BMI (kg/m^2).

The level of PA will be measured using the Godin-Shephard Leisure-Time PA Questionnaire (GSLTPAQ) with three questions on mild, moderate and strenuous leisure-time PA bouts of at least 15 min duration in a typical week.[32] Scores derived from the GSLTPAQ include total weekly leisure-time PA, in which the number of bouts at each intensity is multiplied by 3, 5 and 9 metabolic equivalents, respectively, and summed. These scores can be used for ranking individuals from the lowest to highest PA levels. The number of steps will also be recorded in a logbook.

Self-efficacy for exercise will be evaluated using the Self-Efficacy for Exercise Scale.[33] It measures patients' beliefs in their ability in the face of nine perceived barriers. Each item is measured on a 10-point Likert scale (0=not at all confident to 10=very confident). The higher the scores, the greater the confidence to be active.

PA barriers will be assessed using the Barriers to Being Active Quiz.[34] This is a 21-item questionnaire that will qualitatively assess barriers to the regular practice of PA.

Geriatric assessment

Physical function will be assessed using the Katz Index of Independence in Activities of Daily Living (ADL)[35] and the Lawton Instrumental Activities of Daily Living Scale (IADL).[36] The ADL index measures the patient's ability to perform independently six basic activities of daily living (bathing, dressing, toileting, transferring, continence and feeding). A score of 6 indicates the full function, a score ≤6 indicates dependence. The IADL index measures eight functions (ability to use a telephone, shopping, food preparation, housekeeping, laundry, mode of transportation, responsibility for own medications and ability to handle finances). The IADL score ranges from 8 (high function, independent) to 0 (low function, dependent).

Cognitive impairment will be assessed using the Montreal Cognitive Assessment.[37] This test evaluates seven different cognitive domains (visuospatial and executive functions, naming, memory, attention, language, abstraction, delayed recall and orientation). A score of 26 or above on a maximum of 30 is considered normal.

Depression will be assessed using the Geriatric Depression Scale-15.[38] It consists of 15 items inquiring about the patient's mood in the previous week. The score ranges from 0 to 15 and a score of 0–4 indicates normal status, 5–9 indicates mild depression and 10 or more indicates moderate to severe depression.

Nutritional status will be evaluated using the Mini-Nutritional Assessment (MNA). The MNA consists of anthropometric measurements (weight, height and weight loss), six questions related to lifestyle, medication and mobility, eight questions related to the number of

meals, food and fluid intake, and autonomy of feeding, and a subjective assessment of self-perception of health and nutrition. The MNA score distinguishes patients with a malnourished status (below 17), at risk of malnutrition (between 17 and 23.5) or with an adequate status (between 24 and 30).[39]

Comorbidities will be assessed using the Cumulative Illness Rating Scale—Geriatric (CIRS-G).[40] The CIRS-G is composed of 14 items, each assessing an organ system (eg, heart) by a score from 0 to 4 (0=no problem and 4=serious issue). Higher scores indicate higher severity (maximum score=56 points).

Fatigue will be assessed using the Functional Assessment of Chronic Illness Therapy—Fatigue (FACIT-F).[41] The FACIT-F is a 13-item tool that measures an individual's level of fatigue during patients' usual daily activities over the past week. The level of fatigue is rated on a five-point Likert scale (4=not at all fatigued to 0=very much fatigued) for each item. The lower the scores, the greater the fatigue.

Health-related QoL will be assessed using the European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QLQ-C30).[42] The QLQ-C30 is a 30-item questionnaire that evaluates a global QoL domain, 5 functioning domains (physical, role, emotional, cognitive and social), 3 symptom domains (pain, fatigue and nausea) and 6 single items (dyspnoea, insomnia, anorexia, diarrhoea, constipation and financial impact). Each item is associated with a score ranging from 0 to 100.

Social vulnerability will be assessed using the Evaluation of Deprivation and Inequalities in Health Examination Centres Score.[43] The score ranges from 0 to 100 with the threshold for deprivation at 30, and higher scores indicating greater deprivation levels.

Falls will be assessed by questioning the number of falls in the past 12 months.

Sociodemographic and clinical data

Sociodemographic and clinical data will be extracted from the CLB's patient record (age, sex, marital status, smoking status and alcohol habit, the ECOG PS, the date of diagnosis, tumour characteristics, chemotherapy toxicities (grade >2), treatment response).

Programme follow-up

Participation will be assessed according to the frequency of supervised and unsupervised PA sessions, phone calls and days wearing the activity tracker, as indicated in patient charts.

The number and type of adverse events attributable to the exercise programme will be collected from participants' logbooks.

Patient satisfaction will be evaluated at the end of the programme, using a programme evaluation questionnaire. Questions will be addressed each component of the programme and will be scored on a 4-point Likert scale (strongly disagree, somewhat disagree, somewhat agree, strongly agree). Additional open-ended questions will be prompted patients to reflect on self-perceived benefits, positive and negative points, and suggestions for improvement.

Sample size calculation

The sample size was defined empirically to explore the feasibility of the programme according to the enrollment potential in the study centre. Because the main objective of the OCAPI trial was to assess the programme's feasibility, without major regard for the efficacy of the trial, no formal calculation was performed. Given that approximately 60 patients over 65 years with NHL and 50 patients over 65 years with AML are treated per year at the CLB and that recruitment challenges in this type of population have been identified in past exercise studies (approximately 40% inclusion), our study aims at recruiting 20 patients with NHL and 20 patients with AML.

Data analysis

All statistical analyses will be carried out on an exploratory basis on all subjects included in the study and will allow to raise hypotheses before conducting an efficacy study. Given the limited sample size, non-parametric tests will be performed.

Continuous data will be described at baseline, 3 months, 6 months and 12 months, by the number, mean, SD, median, first and third quartile value, minimum and maximum, and the number of missing data. These data will be compared two by two between the different study times using a Wilcoxon signed-rank test.

Discrete data will be described at inclusion, at 3, 6 and 12 months, by their frequency of occurrence and their percentage. Missing data will be presented but will not be included in the calculation of the percentage. These data will be compared using a McNemar's test.

The evolution of the different repeated measures at inclusion, at 3, 6 and 12 months will be represented by graphs and compared by non-parametric analysis of variance (performed on ranks). For exploratory purposes, descriptive analyses in subgroups can also be carried out in order to differentiate patients with AML from patients with NHL.

Data management

The database for clinical data will be created using Access software and the access will be secured and limited to the professionals involved in the study (personal ID and password required). Data monitoring will be provided by the trial steering committee, including overall project supervision, progress monitoring, advice on scientific credibility and ensuring the integrity and appropriate running of the project. The clinical research assistant will verify all consent forms, compliance with established protocol and procedures, and data quality in the case report form. The research team will make quarterly reports to the trial steering committee.

Patient and public involvement

Two associations of AML and NHL patients' representatives (Fédération Leucémie Espoir, leucemie-espoir.org, France Lymphome Espoir, francelymphomeespoir.fr) were involved in preparing the conduct of the PA intervention and evaluations, in particular by considering patients' expectations and experience. The associations will be involved in plans to disseminate the study results to their members and wider patient communities concerned.

Ethics and dissemination

The study protocol was approved by the French ethics committee (Comité de protection des personnes Est I, N°ID-RCB 2019-A01231-56, 12 July 2019). The study is registered on ClinicalTrials.gov (NCT04052126). All participants will have to sign and date an informed consent form. The findings will be disseminated in peer-reviewed journals and academic conferences.

DISCUSSION

To the best of our knowledge, the OCAPI trial will be the first study to assess the feasibility and to explore the benefits of a PA programme, concomitant to chemotherapy regimens, in patients over 65 years with haematological malignancies. The OCAPI study will specifically test a PA programme in two different haemato-oncological situations, that is, patients with AML and NHL managed with distinct treatment protocols and different survival outcomes. Current PA studies target predominantly older breast and prostate cancer survivors, which limits the reproducibility of the evidence in other types of cancer such as haematological malignancies.[15 24 44]

Despite the promising health benefits of PA in various cancer situations, engaging in regular and sustainable PA can be challenging, especially for older adults with cancer presenting with geriatric syndromes and frequent comorbidities. The OCAPI trial was based on strategies, mainly derived from behavioural change theories,[45] such as providing social support from the certified exercise instructor, that were found to be effective to improved PA in older adults with or without cancer.[15 24 25 44 46 47] These strategies will be evaluated by patients from the OCAPI study, at the end of the intervention with a semi-structured questionnaire, to select the most relevant ones for future implementation on a larger scale.

Performing a geriatric assessment is of primary importance to provide a detailed evaluation of the health status of older adults with cancer at baseline.[48] In the OCAPI study, alongside with comprehensive assessment of PA level and physical fitness, we will target relevant outcomes and domains in geriatric oncology, that is, cognitive and functional status, mood, fatigue, social status and support, nutrition, comorbidities and geriatric syndromes, as recommended by the International Society of Geriatric Oncology.[49] In addition, conducting a follow-up 3 and 6 months after the start of the PA programme (concurrent with the start of treatments) will allow to assess whether the programme increases participants' PA levels and provides an understanding of the impact of exercise on elder-relevant outcomes, both in the medium term.

During the development of the OCAPI study, representatives from the targeted patient population were involved by questioning their preferences for PA and creating with them the exercise booklet, putting patients at the heart of every step of the project. In addition, the collaboration between haematologists for treatment, geriatricians for the consideration of age-related changes and certified exercise instructors for the exercise programme was conducted to consider, in an interdisciplinary manner, the complexity and multidimensional nature of care of older patients with cancer.[25] For example, it was decided in a collegial manner to start the individual unsupervised PA sessions after a certain period of supervised PA practice in order to ensure the safety of the patients. By involving many stakeholders in the OCAPI trial, there may be a potential to integrate more easily PA regimens across the cancer continuum of older adults with haematological malignancies, resulting in possible improvement in autonomy and QoL for patients and a reduction of healthcare utilisation.[24]

We recognise some limitations in the OCAPI trial. As in most feasibility studies, the sample size is small and there is no control group. However, before initiating exercise trials that have the primary objective of evaluating effects on cancer outcomes, there is a prerequisite of confirming that the exercise programme is feasible and safe for the target population.[50]

Given the paucity of data in older patients with haematological malignancies and potential health benefits of PA in this population, this trial will provide new insights on the feasibility and physical, psychosocial and clinical effects of an individualised programme in patients over 65 years with AML and NHL. The results of this trial will provide quantitative and qualitative outcomes that will help design a future RCT on a PA intervention in older patients with haematological malignancies.

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Contributors BFou, OP and BFer designed the trial. BFou elaborated the exercise booklet. BFou and OP obtained funding. EN-V and MM brought their expertise on haematological oncology aspects of the protocol; CR and EP-F on geriatrics; GYM, LD and BFou on physical activity. BFou, OP and AM fulfilled administrative procedures for this project. BFou wrote the first draft of the manuscript, which was critically reviewed by OP and BFer. BFou, EN-V, CR, OP, GYM, AM, LD, A-SM, SA, AB, LG, YG, LL, PR, CS, EP-F, CT, MM and BFer reviewed and contributed to the final version of the manuscript. The authors read and approved the final manuscript.

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