IMPROVE-BMT: a protocol for a pilot randomised controlled trial of prehabilitation exercise for adult haematopoietic stem cell transplant recipients

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ABSTRACT

Introduction Haematopoietic stem cell transplant (HSCT) in adults is an intensive medical procedure for a variety of haematological malignancies. Although there is a large body of evidence demonstrating the negative effects of HSCT on physical function and psychosocial parameters, there is limited evidence on the impact of HSCT on body composition and bone health. Further, aerobic and resistance-training exercise interventions aimed at improving physical function and patient-reported outcomes largely take place during the peri-transplant and post-transplant period. Prehabilitative exercise, or exercise prior to medical treatment, has been successfully deployed in presurgical candidates and other tumour sites, yet there is a paucity of evidence on the effect of prehabilitation in HSCT patients. The aim of this study is to investigate the feasibility, acceptability and safety of a resistance training exercise programme in patients with haematological malignancies prior to HSCT.

Methods and analysis Impact of Prehabilitation in Oncology Via Exercise-Bone Marrow Transplant is a single-site, pilot randomised controlled trial of an exercise intervention compared with usual care. The primary aim is to assess the feasibility, acceptability and safety of the resistance-training exercise intervention prior to HSCT. Secondary aims include evaluating the differences in physical function, body composition, bone mineral density and patient-reported outcomes between the exercise group and usual care control group. Outcome measurements will be assessed: prior to HSCT, on/around day of HSCT admission, +30 days post-HSCT and +100 days post-HSCT. The exercise intervention is a home-based resistance training exercise programme that incorporates resistance band and body weight exercises. The primary outcomes will be reported as percentages and/or mean values. The secondary outcomes will be analysed using appropriate statistical methods to portray within-group and between-group differences.

Ethics and dissemination The study has Penn State College of Medicine approval. Results will be disseminated through scientific publication and presentation at exercise-related and oncology-related scientific meetings.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study includes a pragmatic trial design that uses a personalised home-based exercise programme during the pretransplant phase in adults receiving an autologous or allogeneic stem cell transplant.

⇒ It is the first study to include body composition and bone density as important outcomes that may be affected by the prehabilitation exercise intervention.

⇒ This study does not provide a multimodal prehabilitation intervention (eg, dietary, psychosocial).

⇒ As a single-site pilot trial, this study is not statistically powered.

Trial registration number NCT03866909.

INTRODUCTION

Haematopoietic stem cell transplant (HSCT) is a potentially curative yet intensive and high-risk medical treatment option for patients with haematopoietic disorders. The two major forms of HSCT include: autologous (AUTO) and allogeneic transplantation (ALLO). In 2020, a number of AUTO and ALLO HSCTs performed in the USA were 11557 and 8326, respectively, demonstrating a 44% and 34% increase in the past 10 years.1 Mortality rates post-HSCT are dependent on a number of factors including remission status at the time of transplant, donor stem cell source and compatibility, and frequency and severity HSCT-related complications.2 3 Medical approaches to improve clinical and functional outcomes post-HSCT include reduced-intensity ablative chemotherapy, measures to reduce the incidence and severity of graft-versus-host disease and
initiation of prophylactic regimens during immunosuppressive therapy administration.

The number of AUTO and ALLO survivors in the USA is projected to grow to 29,1000 and 234,000, respectively, by 2030. HSCT involves periods of prolonged reduced physical activity, which combined with HSCT therapy-related toxicity and symptoms, places survivors at a higher risk of developing longstanding physical, psychological and psychosocial issues. These may include lower levels of physical function, declines in quality of life (QoL), reduced levels of physical activity and ongoing negative changes to body composition and bone health.

Although there is a large body of evidence documenting the negative effects of HSCT on physical function and various psychosocial parameters, less is known about the impact of haematological malignancies and HSCT on changes in body composition and bone health. Sarcopenia is defined as a generalised, progressive musculoskeletal disorder that affects muscle function, muscle mass and muscle quality. Sarcopenia is associated with an increased risk of falls and fractures, reduced ability to perform activities of daily living, risk of developing cardiovascular and respiratory diseases, and overall survival. Retrospective studies report that 34%–55% of prospective AUTO and ALLO recipients present with sarcopenia.

In a prospective cohort study by Morishita et al, 51% of patients who experienced sarcopenia exhibited significant decreases in muscle strength, lower scores in physical functioning, pain and health-related QoL compared with patients without pre-HSCT sarcopenia. The presence of sarcopenia prior to HSCT also carries increased risk of longer hospitalisations, worse 2-year overall survival and increased risk of death due to infection or organ failure. Further, the incidence of sarcopenia increases over time post-HSCT with studies reporting sarcopenia in 64% and 75% of patients at 1 year and 2.5 years, respectively.

Bone density loss is a well-recognised complication in HSCT-recipients. In addition to disease-related bone abnormalities, prolonged administration of high-dose chemotherapy and long-term corticosteroid use interfere with the bone turnover and formation. Several studies report that 25% of HSCT survivors present with osteoporosis and 50% present with osteopenia. While bone loss does not currently carry the strong survival implications associated with sarcopenia, it is a serious preventable comorbidity that affects a large majority of HSCT-survivors. Currently, clinical guidelines for bone health in HSCT-recipients recommend vitamin supplementation and bisphosphonate therapy, and only briefly mention lifestyle changes, including promotion exercise, diet changes, tobacco cessation and reduced alcohol intake.

The current evidence suggests that aerobic and resistance-training exercise in HSCT patients during the peritransplant and post-transplant period is safe and effective at improving cardiorespiratory function, muscle strength, physical function, fatigue, anxiety and a variety of other treatment-related side effects. Randomised controlled trials have also shown that exercise has a positive impact on total and non-relapse mortality, haematological reconstitution, immunological capacity and stem cell survival. However, exercise during these time periods does not address the possibility of preventing HSCT-related muscular, functional and psychosocial declines.

Prehabilitation, or prehab, takes place between cancer diagnosis and the beginning of treatment and aims to intervene and improve on physical and psychological health to reduce the incidence and severity of possible future treatment-related and disease-related impairments. Prehab has been investigated in other cancer sites such as breast, lung and gastrointestinal cancer with positive changes seen in physical function, QoL, surgical outcomes, and overall morbidity and mortality. Despite the growing evidence of exercise during and after HSCT treatment, there is a paucity of evidence focusing on the feasibility and efficacy of prehabilitative exercise prior to HSCT. To our knowledge, there are only a few completed or currently active trials that include exercise during the pre-HSCT phase. The trials by van Haren et al and Rupnik et al are non-randomised feasibility trials, which do not allow for comparison to a non-exercising group. In addition, the PREeMPT trial, the PERCEPT trial and the feasibility trial by Mawson et al focus on patients diagnosed with multiple myeloma who are receiving an AUTO transplant, while Wood et al used only aerobic exercise for ALLO patients. Finally, the trials completed by Wiskemann et al and Santa Mina et al included exercise for ALLO patients during multiple phases of the transplant process, making it more difficult to discern the impact of the pretransplant exercise intervention. Further, Santa Mina et al reported a low 20% recruitment rate and a 70% attrition rate, making it difficult to draw conclusions from this small study.

Given the demonstrated deficits that HSCT patients experience before, during and after transplantation, and the growing evidence of pretreatment exercise in other cancer entities, including HSCT, we planned a randomised controlled two-arm exercise intervention trial prior to HSCT: IMPact of PRehabilitation in Oncology Via Exercise-Bone Marrow Transplant (IMPROVE-BMT)—to evaluate the feasibility, acceptability and safety of an exercise prehabilitation programme in HSCT patients (NCT03886909). IMPROVE-BMT has the potential to elucidate how exercise can act as a preventative intervention to improve functional, physical and psychosocial outcomes while addressing changes in body composition and bone health, all of which contribute to improving and prolonging survival in HSCT-recipients.

Objectives
The primary aims of this single-centre, randomised controlled trial is to determine the feasibility, acceptability and safety of a prehabilitative (pretreatment) exercise programme in adults receiving an AUTO or ALLO HSCT. The secondary aims are to compare changes in physical function, QoL, fatigue, transplant-related...
symptoms, patient-reported outcomes, body composition and bone density within-group and between-group. These secondary outcomes will provide the necessary data to calculate the sample size necessary for a larger, fully powered trial.

**METHODS AND ANALYSIS**
This manuscript adheres to the Standard Protocol Items: Recommendations for Intervention Trials checklist.35

**Study design**
The IMPROVE-BMT study is a single-site pilot feasibility randomised controlled trial.

**Participants**
Adults receiving medical care at the Penn State Cancer Institute (PSCI) are eligible for participation based on the following inclusion and exclusion criteria:

**Inclusion criteria**
- Haematological malignancies (eg, acute myeloid leukaemia, chronic lymphocytic leukaemia, multiple myeloma, non-Hodgkin’s lymphoma) in partial or complete remission.
- Females and males ≥18 years of age.
- Fluent in written and spoken English.
- Must be able to provide and understand informed consent.
- Must have an ECOG score of ≤2.
- Scheduled for an inpatient AUTO or ALLO stem cell transplant at PSCI.
- ≥2 weeks until scheduled transplant.
- Primary attending physician approval.

**Exclusion criteria**
- Haematological cancer not in remission.
- Evidence of an absolute contraindication (eg, heart insufficiency >NYHAIII or uncertain arrhythmia; uncontrolled hypertension; reduced standing or walking ability36 for exercise).
- Other comorbidities or musculoskeletal complications that preclude participation in the exercise programmes as deemed by the exercise interventionist.
- Receiving non-transplant related chemotherapy and/or radiotherapy.
- Not fluent in written and spoken English.
- Active infections, haemorrhages and cytopenias that could place transplant patients at risk for further adverse events, deemed by the exercise interventionist, physician and/or nurse.

**Recruitment procedures**
Research staff will prescreen the electronic medical records of patients placed on the HSCT list by nurse coordinators. Research staff will contact the patient’s physician for medical clearance and approval to approach the patient for study presentation. Physicians will also refer qualified patients to research staff. Additionally, research staff will attend the weekly bone marrow transplant team meeting where all potential transplant patients and updates on scheduled transplant dates are discussed. All eligible and approved patients will be approached and consented for the study by an approved study team member.

**Randomisation and blinding**
Patients will be stratified based on transplant type (AUTO or ALLO) then randomised to the Home-Based exercise group (EX) or the Usual Care+Educational Programme group (UC). Randomisation will use block randomisation and the allocation scheme will be made with a computerised random number generator by a researcher not involved in study-related activities. Patient allocation will be placed in sealed envelopes and not opened until baseline assessments are completed. Patients will not be blinded to their group assignment. Study team members involved in patient-facing activities are also not blinded to group assignment.

**Exercise intervention**
The pretransplant exercise intervention duration will last at least 2 weeks and a maximum of 24 weeks (until the day of transplant hospital admission). This is dependent on when the study participant is identified, approved for consent, completes baseline assessments and undergoes randomisation. The IMPROVE-BMT exercise intervention is based on previous prehabilitation trials in other cancer types and follows the frequency, intensity, time and type (FITI) principle on prescribing exercise (table 1).33,37,38

Following baseline assessments, patients will be prescribed resistance training exercises to complete at least five times per week at home, unsupervised. An exercise and cancer specialist, certified by the American College of Sports Medicine with multiple years of experience working with patient living with and beyond cancer, builds the resistance training programme by selecting exercises from a catalogue of preselected exercises that include modifications of each exercise to target varying levels of physical function. Based on the patient’s clinico-pathological history, the exercise and cancer specialist will select exercises that can be safely performed yet effectively target upper-body and lower-body strength development. Each exercise session takes approximately 30–45 min to complete. Each patient in the exercise group will receive a study manual containing study information, guidelines for safe exercise and exercise logs to complete for each exercise session. The exercise and cancer specialist will review and collect the exercise logs at clinic visits with patients. If patients have large gaps (ie, greater than 3 weeks) between scheduled clinical visits, the exercise and cancer specialist will review the exercise logs with the patient over the phone and provide new exercise logs via mail. The exercise logs will be used to track completion and adherence of the prescribed exercise programme. Each resistance training session consists of 1–2 warmup sessions, followed by 4–5 resistance training exercises. Each exercise session takes approximately 30–45 min to complete.
exercises, 4–6 upper-body and lower-body strength exercises, followed by 2 cool down stretches. All resistance exercises will be completed using a combination of the patient’s body weight and resistance bands. Training intensity will be adapted using the rating of perceived exertion (RPE) scale (target scores 14–16 out of 20 for resistance exercises). Patients will also be encouraged to walk at least 15 min every day at an intensity of 12–14 on the RPE scale and will be increased or 5–10 min per session if possible until patients are achieving a minimum of 15 min of walking per session.

The exercise and cancer specialist will progress the exercise sessions if the patient does not report any new or worsening side effects or symptoms. Incremental progression of the exercise sessions will entail modifying one or more of the FITT principles on prescribing exercise, specifically, increasing or decreasing sets, repetitions, weight, and/or the number of exercises prescribed. Patients may be withdrawn from the intervention if the patient requests to discontinue the study, the treating physician and/or exercise and cancer specialist deems it is unsafe for the patient to exercise, or if the patient meets any of the exclusion criteria. In addition to the structured intervention, patients will receive an educational counselling session from the exercise and cancer specialist which will include information on HSCT-related effects and transplant precautions and expectations.

Adapted inpatient exercise

Participants in both groups will be given educational information on exercising during their inpatient transplant treatment at PSCI. The information will consist of current exercise guidelines and recommendations for cancer patients actively receiving treatment. The exercise intervention will not be supervised. Participation is not required.

Usual care

After baseline testing and randomisation, patients in the UC group will receive an educational counselling session from the exercise and cancer specialist which will include information on HSCT options, transplant precautions and expectations, and initial and post-transplant exercise recommendations. The session also goes over common potential effects of having HSCT and how to incorporate physical activity into their care routine. Patients in the UC group will not receive any formal instruction to perform exercise. Participants in the UC group are presented with the option to meet with an exercise and cancer specialist at the final study visit for a no cost exercise counselling session.

Outcome assessments

Table 2 presents each outcome assessment for each assessment time point. Briefly, outcome measurements will be assessed at four time points: prior to HSCT, on/around day of HSCT admission, +30 days post-HSCT and +100 days post-HSCT.

Isometric handgrip strength

Isometric strength testing will be done using handheld dynamometry for handgrip strength. Isometric grip strength has shown strong relationships with muscle mass, function and health status. Reliability and validity of isometric hand-held dynamometry have been previously reported. Measurements will be repeated three times and the average reading of the dominant hand will be reported.

Aerobic capacity

Submaximal endurance performance will be assessed with the 6 min walk test (6MWT). Patients will be advised to walk as fast as possible on a hallway for 6 min according to the American Thoracic Society Guidelines. The covered distance will be measured. The distance walked during the 6MWT is significantly correlated with VO2 peak (r=0.67, p<0.001) and perceived physical function (r=0.55) and has high reliability (r=0.93, p<0.001).

Physical functioning

30 s Chair Stand Test (30CST): Lower extremity strength will be measured using the 30CST. The participant is instructed to complete as many full sit to stands as possible within 30 s. The 30CST is highly correlated as a surrogate to leg-press performance (r=0.71–0.78) and is valid in detecting decreasing lower body strength.

Timed Up-and-Go Test (TUG): The TUG requires participants to rise from a chair, walk 3 m around an
obstacle, and walk back to the chair and sit down and measures physical mobility and agility.44 Participants will be given two trials, with the fastest time used. The TUG is strongly correlated to the Berg balance score (r=0.81), gait speed (r=0.60), and the Barthel index of ADL’s (r=0.78).44

Short Physical Performance Battery (SPPB): The SPPB is a short battery of performance tests of lower extremity functioning.45 The tests measure gait speed, standing balance and lower extremity strength and power. To test gait speed, patients are instructed to walk 4 m at their usual pace with assistive devices if needed. Four progressively more challenging positions are used to test balance (bipedal, semi tandem, full tandem and unipedal stance). To test lower extremity strength, patients are asked to stand up and sit down five times as quickly as possible. The SPPB has been established as a valid and reliable test of physical performance and has been shown to be associated with muscle mass, risk of falls and mortality.46

Berg Balance Scale (BBS): The BBS is a used as a clinical measure of functional balance in older adults.47 It consists of 14 items performed by the patient and scored by the tester. The battery requires patients to perform various physical tasks such as sitting to standing, standing and sitting unsupported, rotating, retrieving objects from the floor and a unipedal stance. The validity and reliability of the BBS has been well established, in addition to its use to predict future fall risk.47–49

Fried Frailty Index: The Fried Frailty Index is a short battery of physical performance tests and observational assessments that evaluates phenotypic frailty. The index is a validated tool in defining and identifying those at high risk of frailty. The index evaluates weight loss in
the past year, weakness via grip strength, self-reported fatigue, gait speed and self-reported physical activity levels.50

SARC-F: The SARC-F questionnaire is a short five-item battery containing observational assessments that is a rapid diagnostic test for sarcopenia and poor outcomes. There are five SARC-F (Strength, Assistance in Walking, Rising from a chair, Climbing stairs, History of Falls) components: strength (S), assistance with walking (A), rising from a chair (R), climbing Stairs (C), and history of falls (F).51

Total body lean mass, appendicular lean mass, body fat and bone mineral content will be assessed by whole-body dual-energy X-ray absorptiometry (DXA) scans (GE Lunar iDXA, Boston, Massachusetts, USA). Patients will receive DXA scans prior to the start of the prehabilitation period (T0) and at the conclusion of the study (T3). DXA scans provide valid and reliable measurements of body composition and bone density with large reference data sets.52

Quality of life

QoL will be assessed with the validated 30-item self-assessment questionnaire of the European Organisation for Research and Treatment of Cancer, Core Quality of Life Questionnaire, Cancer, 30 items (EORTC QLQ-C30 (Quality of Life Questionnaire- Cancer 30 items), version 3.0). It includes five multi-item functional scales (physical, role, emotional, cognitive and social function), three multi-item symptom scales (fatigue, pain, nausea/vomiting) and six single items assessing further symptoms (dyspnoea, insomnia, appetite loss, constipation, diarrhoea) and financial difficulties.53 Scores will be calculated according to the EORTC scoring manual and the clinical relevance of changes will be interpreted using evidence-based guidelines.54 HSCT-specific QoL will be assessed using the 29-item high-dose chemotherapy module (EORTC QLQ-HDC-29) which will focus on common HSCT-related issues.55

Fatigue

Fatigue will be assessed with the Multidimensional Fatigue Inventory (MFI). The MFI is 20-item validated questionnaire with good internal consistency (α=0.84) that covers general, physical and mental fatigue, and reduced activity and motivation56 and is recommended for use in cancer patients.57

Pain

The Brief Pain Inventory- Short Form (BPI) is a validated nine-item, self-assessment questionnaire that measures the intensity of pain (sensory dimension) and interference of pain in the patient’s life (reactive dimension).58 The BPI also asks the patient about pain relief, pain quality, and patient perception of the cause of pain. The BPI has demonstrated good test–retest reliability of the BPI is 0.78–0.93.58

Adverse events (Patient-Reported Outcomes--Common Terminology Criteria for Adverse Events)

The PROs-Common Terminology Criteria for Adverse Events (PRO-CTCAE) is a patient-reported outcome measure developed to evaluate symptomatic toxicity in patients on cancer clinical trials.59 The PRO-CTCAE item library contains 124 items representing 78 symptomatic toxicities. Specific items addressing exercise and HSCT-related toxicities were selected to create an individualised form to capture adverse and serious adverse events. The PRO-CTCAE is individualised but still demonstrates a high test–retest reliability (>0.70) and high correlation with the QLQ-C30.59

Sleep questionnaire

Sleep quality and sleep problems will be assessed with the validated and frequently used Pittsburgh Sleep Quality Index (PSQI).60 The PSQI has an 89.6% diagnostic sensitivity and 86.5% specificity in distinguishing good and poor sleepers.60

Depression

Depressive symptoms will be assessed with the 20-item Centre for Epidemiological Studies Depression Scale (CES-D), which has shown high internal consistency (α=0.85).61 The CES-D scale is a widely used validated self-report instrument to measure current depressive symptomatology and to identify possible cases of depressive disorders, both in the general population and in patients with cancer.62

Patient-reported physical activity

Physical activity behaviour in the domains of commuting activity, leisure time activities such as cycling, walking and sports, household and occupational activity will be assessed via the Short QUestionnaire to ASsess Health-enhancing Physical Activity (SQUASH).63 64 The SQUASH has been reported to be reliable (r=0.45–0.90) and correlated with free-living actigraphy readings.64

Leisure-time exercise

Physical activity patterns during a patient’s leisure time will be assessed using the Godin Leisure-Time Exercise questionnaire. The questionnaire asks patients to recall, during a 7-day period, the frequency to which they participated in strenuous, moderate and mild exercise and has high reliability in classifying maximum oxygen intake (α=0.83).65

Exercise counselling and programming preferences

No specific survey has been produced to measure exercise programming and counselling preferences. However, Karvinen et al66 provided 3 closed-ended items about exercise counselling preferences, 10 closed-ended items asking about exercise programming preferences, 3 open-ended items on preferred exercises and 2 items asking about personal exercise equipment and current fitness centre memberships. These questions have been used in
previous studies evaluating exercise programming preferences in patients with cancer and survivors.67 68

**Statistical analysis and sample size calculations**

Our primary outcomes are descriptive. Acceptability will be defined by the proportion of approached patients who agree to participate and complete at least the prehab counselling session. Our a priori threshold is 50%. We will consider the intervention feasible if 50% of included patients complete at least one third of the prescribed exercise sessions for 2 weeks or more. Safety will be reported by the number of exercise-associated events. Exercise adherence during the prehabilitation period will be calculated as the proportion of completed exercise sessions over the number of prescribed exercise sessions. Summary statistics including mean and SD for continuous variables and frequency with percentage for categorical variables will be reported. We will examine differences within-group and between-group using linear mixed-effects models for physical performance measures, patient-reported outcomes and body composition. A two-sided significance level of 0.05 will be used for all statistical tests. Various clinical covariates including transplant type, prehabilitation duration and baseline differences will be included as statistical covariates to address heterogeneity. Evaluation of missing data will occur at the time of analysis in order to select the best method to evaluate and analyse missing data. This study will provide estimates of mean and SD to support a sample size calculation for a larger, fully powered trial. The anticipated sample size for this pilot trial is 84 participants—42 in each intervention arm—based on the PSCI HSCT programme annual enrolment and projected withdrawal rate from similar previous trials within our working group. All data will be entered and stored on secure servers at PSCI. Regular data range checks will be performed to promote data quality.

**Ethics and dissemination**

This trial will be carried out in accordance with the latest version of the Declaration of Helsinki. The study protocol was approved by the Penn State University Institutional Review Board (Study00010914). All participants will provide written informed consent prior to the initiation of any study-related activities. Participants will have the option to withdraw consent at any point in the study. Important protocol modifications will be communicated to all necessary parties. The results of this study will be reported and disseminated through publication in peer-reviewed journals, presentations at haematology and exercise-related meetings, and HSCT education and support groups.

**Patient and public involvement**

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research. After completion of the study, a lay summary will be available for study participants who request one.

Adverse and serious adverse events are assessed at each follow-up visit using the National Institute of Heath developed PRO-CTCAE measure. In the unlikely event an unanticipated adverse event were deemed to be definitely related to the study occurred, the relative merits and risks of continuing the research would be discussed with the treating physician. IMPROVE-BMT is also audited semi-annually by the Data Safety Monitoring Committee of PSCI, where review of all adverse and serious adverse events will be reviewed and continuation of the trial is determined. A Research Quality Assurance audit, conducted by the Clinical Trials Office at the PSCI, is performed on an annual basis to ensure all regulatory processes are followed.

**DISCUSSION**

This study will evaluate the feasibility, acceptability and safety of a pre-HSCT exercise intervention. Given the intensity of HSCT and the long-standing toxicities many recipients experience, additional supportive care methods must be explored. Currently, there is limited evidence on how prehabilitative exercise prior to HSCT affects physical function, QoL, body composition and bone density. This study uses a home-based, pragmatic and personalised exercise programme to enhance feasibility and adherence and to address barriers such as distance, transportation, access to equipment and avoidance of public spaces. It is anticipated that the results from this study will largely contribute to the foundational knowledge of how prehabilitative exercise affects the preparation and recovery process of HSCT-recipients. Further, results from this pilot feasibility trial will provide data to calculate effect sizes and sample size for a larger, fully powered multicentre trial. Pilot results will potentially demonstrate that exercise given in a clinical setting is something that patients may want and can change the way oncology standard of care uses the time prior to HSCT. Recruitment started in June 2019. Due to the COVID-19 pandemic, an institution-wide hold was put on all in-person clinical trial recruitment and face-to-face study-related activities from March 2020 to July 2020 and again from September 2020 to March 2021. The pandemic-related pauses in research did not affect the home-based exercise sessions for enrolled participants, however, DXA scans for patients enrolled during restricted periods were not collected. The estimated completion date for recruitment is October 2022 and study-related follow-ups will be completed in early 2023.
REFERENCES

38. Wiseman M, Kuehl R, Dregger P, et al. Physical exercise training versus relaxation in autologous hematopoietic stem cell transplantation (PETRA study)-rationale and design of a randomized trial to evaluate a yearlong exercise intervention on overall survival and side-