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Assessing Patient-reported & Patient-related Outcomes in Randomized Cancer Trials for Older Adults

Study Protocol and SAP
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1. Rational

More than half of patients diagnosed with cancer are aged 65 and over and this trend is going to increase as the world population ages. However, there is limited evidence on which to base treatment decisions for older adults with cancer, mainly because they are underrepresented in the randomized clinical trials (RCTs) that set the standards for cancer treatments. Although the proportion of older adults included in RCT remains lower than the proportion they represent in the general population, this proportion as well as the number of trials dedicated to older adults has been increasing over the last years.

Literature reviews on endpoints in cancer RCTs dedicated to older adults have highlighted the lack of consideration of patient-reported outcomes (PROs). A PRO is an outcome directly reported by the patient without interpretation of the patient's response by a clinician or anyone else, and pertains to the patient's health, quality of life (QoL), or functional status associated with health care or treatment. A typical PRO example is the European Organisation for Research and Treatment of Cancer (EORTC) Core Quality of Life questionnaire (QLQ-C30), a self-reported questionnaire aimed at assessing health-related quality of life (HRQoL) of patients with cancer.

Following the Clinical Outcome Assessment (COA) framework of the Food and Drug Administration (FDA), PROs are considered as part of the family of COA measures, defined as measures that describe or reflect how a patient feels, functions, or survives. COAs include PRO measures, observer-reported outcome (ObsRO) measures, clinician-reported outcome (ClinRO) measures, as well as performance outcome (PerfO) measures. An ObsRO is a measurement based on a report of observable signs, events, or behaviors related to a patient's health condition by someone other than the patient or a health professional. Generally, ObsROs are reported by a parent, caregiver, or someone who observes the patient in daily life. They do not rely on medical judgment or interpretation and include rating scales such as the Instrumental Activities of Daily Living (IADL). On the other hand, a ClinRO is a measurement based on a report that comes from a trained health-care professional after observation of a patient's health condition. Most ClinRO measures involve a clinical judgment or interpretation of the observable signs, behaviors, or other manifestations related to a disease or condition. ClinRO include reports of particular clinical findings or clinical events, as well as rating scales such as the Geriatric Depression Scale - 15-item (GDS-15). Finally, PerfO are measurements based on standardized tasks actively undertaken by a patient according to a set of instructions. Examples of PerfO assessments include measures of gait speed or memory (e.g., word recall test).

Although PROs and patient-related outcomes are more frequently used in RCTs dedicated to older adults than in RCTs including all patients with cancer, they still represent a small proportion of efficacy endpoints, in particular primary endpoints. Studies have reported that PROs represent <10% of primary endpoints and near 40% of secondary endpoints. In order to increase the use of PROs and patient-related outcomes and properly assess treatment outcomes in RCTs including older adults, one must first identify the appropriate geriatric domains and the relevant tools for the assessment of each of these domains.

2. Objective

We aim to assess the geriatric domains that should be assessed using PROs and patient-related outcomes and provide an extensive review of available tools related to these domains, bringing clear elements to guide the choice of researchers coordinating cancer RCTs involving older patients

3. Methods

The DATECAN-ELDERLY project was launched following the international DATECAN initiative that was initiated in 2009 with the objective of elaborating standardized definitions for survival endpoints in RCTs, based on a rigorous and validated consensus methodology. This collaborative work involved the network of statisticians from French Regional Comprehensive Cancer Centers, the network of the Cancer Data Centers, as well as the EORTC. After properly defining the methodology, guidelines for the definition of time-to-event endpoints to be used in randomized trials for specific cancer sites were developed, and are ongoing for additional cancer sites. These guidelines reported on tumor-centered endpoints (e.g., disease-free survival, time-to-treatment failure). Recommendations as to which clinical event(s) to include for each time-to-event endpoint were produced. One can thus refer to these guidelines when designing an RCT for the older population with tumor-centered outcomes. Patient-centered outcomes, on the other hand, had not been addressed up to date.

The DATECAN-Elderly project was thus launched to provide guidelines on geriatric domains, as well as PROs and patient-related outcomes to be considered when designing RCTs for older adults with cancer. In this population, it is relevant to go beyond the question of which event to include as endpoint. Indeed, it is necessary at first to define which domains to consider when assessing treatment benefit, and then to retrieve available relevant tools. The present work is thus aimed at identifying relevant domains of interest and providing an overview of PRO and patient-related outcome tools, to guide researchers when conducting clinical trials in older adults with cancer.

A working group made up of an international multidisciplinary panel will be set up, involving experts in medical oncology (PS, EB, RK, SM, HW), geriatrics (MH, SR), nursing (MP), surgery (KLC, IM), epidemiology (AG, SMP), and biostatistics (CB, MM), as well as representatives of the DATECAN-initiative (CB, SMP). The discussion content will be separated in two parts: (i) selection of the relevant domains to consider when assessing treatment benefit in older adults with cancer and (ii) identification of available tools to assess these domains.

As regards to domains of relevance, a review will be conducted (AG, CB) focusing of guidelines from international societies and regulatory authorities as well as minimum datasets recommended to collect in RCT including older adults with cancer. A summary of this review will be presented and discussed with all the experts. The experts will have the opportunity to comment and enrich this review, and then provide recommendations.

As regards to available tools, a narrative review will be first conducted (AG, CB) and relevant criteria to guide the choice of one tool over another will be discussed with the experts. Investigated criteria include: objective of the tool, number of items, interpretation of the score, initial target population and subsequent populations, validation available for older adults and/or adults with cancer and/or older adults with cancer, available translations, minimum clinically important differences (MCIDs), fees, and copyright. A draft document listing these characteristics for all available tools will be circulated to the experts who will enrich and comment the document. The final draft document will have to be approved by all experts.