PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Sarcoma patient willingness to participate in cancer surveillance research: a cross-sectional patient survey
AUTHORS	Schneider, Patricia; Giglio, Victoria; Ghanem, Dana; Wilson, David; Turcotte, Robert; Isler, Marc; Mottard, Sophie; Miller, Benjamin; Hayden, James; Doung, Yee-Cheen; Gundle, Kenneth; Randall, R. Lor; Jones, Kevin; Vélez, Roberto; Ghert, Michelle

VERSION 1 – REVIEW

REVIEWER	Christina Roland The University of Texas MD Anderson Cancer Center
REVIEW RETURNED	23-Oct-2020

GENERAL COMMENTS	This is a well designed, well executed survey study that will support a very important study in surveillance in extremity sarcoma patients. My only comment is the reference 18 needs reformatting in the bibliography.

REVIEWER	Riha Vaidya Fred Hutchinson Cancer Research Center, USA.
REVIEW RETURNED	04-Nov-2020

GENERAL COMMENTS	This manuscript examines the willingness of extremity soft-tissue sarcoma patients to participate in a clinical trial for post-operative surveillance regimes using a prospective, cross-sectional patient survey. The study also assesses patients' perceptions and attitudes towards clinical research. Overall, this is a well written article. It fills a gap in the literature by assessing willingness to participate in research for a patient population that has not been studied in this context. The design of this study as a feasibility assessment for a future RCT in sarcoma is a good step to ensure successful accrual for the planned clinical trial. However, there are limitations that need to be addressed to make this work more rigorous. 1. Article Summary – Strength and limitations – This section should summarize key limitations along with the strengths. 2. Introduction – This section focuses mainly on the treatment of and long-term surveillance for sarcoma and the need for an RCT for surveillance options. While this is important information, it would also be helpful to note why this willingness to participate study was necessary. There is a very brief mention of the rarity of the disease but more information on the implications of this for clinical trials and the necessity of this study would help.

	3. Methods a. What motivated the selection of the countries included in the study? Will these countries be the only ones where the SAFETY study will be opened or are these a subset? b. The last sentence in the Survey Description subsection (p. 8) is redundant given the immediately preceding paragraph. c. How were patients approached for the study? Was it in person during a post-operative follow-up visit? It is not clear if the study design allowed for patients to be recruited other than during visits. d. "We approached all new post-operative…" – please clarify if new means newly diagnosed or something else. e. It is not clear what the approach used to determine an appropriate sample size for this study was. This needs to be explained. 4. Results - Do the 142 patients approached represent all eligible patients at the study sites during the study period or a sample? 5. Other items a. One limitation of the study is that the questions about financial burden do not appear to address the direct medical cost of surveillance/ trial participation. While this will vary by country, insurance coverage and direct medical cost would be important considerations for trial participation in the US setting. This should be addressed. b. The authors correctly note the limitation of the lack of diversity with respect to race/ethnicity. While this is not uncommon in clinical trials, it would be interesting to examine study participant demographics in the context of sarcoma incidence rates by race. There has been some work done that shows higher incidence of sarcoma among African Americans. Addressing this further is also important for potentially identifying avenues to increase diversity of participants in the SAFETY study.

VERSION 1 – AUTHOR RESPONSE

▪ REVIEWER ONE ▪

Comment #1: This is a well-designed, well executed survey study that will support a very important study in extremity sarcoma patients. My only comment is that reference 18 needs reformatting in the bibliography.

Response to Reviewer: Thank you for your careful review of our manuscript. We have corrected reference 18 in the bibliography, which should now properly list the author's name.

▪ REVIEWER TWO ▪

Comment #1: Article Summary – Strength and limitations – This section should summarize key limitations along with the strengths.

Response to Reviewer: Thank you for this comment. We have revised the Strengths and Limitations section to include an important limitation of the study. Please see the Article Summary > Strengths and Limitations of This Study section (Page 3) of the revised manuscript.

Comment #2: Introduction – This section focuses mainly on the treatment of and long-term

surveillance for sarcoma and the need for an RCT for surveillance options. While this is important information, it would also be helpful to note why this willingness to participate study was necessary. There is a very brief mention of the rarity of the disease but more information on the implications of this for clinical trials and the necessity of this study would help.

Response to Reviewer: Thank you for allowing us to elaborate on this important point. We have clarified by making the following changes in the Introduction section (Page 4) of the revised manuscript:

Given the rarity of sarcoma, possible patient anxiety related to both less- and more-intensive sarcoma surveillance and the fact that clinical trial recruitment is often slower than anticipated, such a RCT will require extensive international collaboration and patient willingness to be randomly allocated to varying surveillance regimens. Patient perceptions of surveillance and of participation in a surveillance RCT are required in order to develop a study protocol that is patient-centered, compelling and feasible, and is capable of answering this high priority clinical question in a reasonable timeframe.

Comment #3A: Methods – What motivated the selection of the countries included in the study? Will these countries be the only ones where the SAFETY study will be opened or are these a subset?

Response to Reviewer: Thank you for providing us with the opportunity to clarify this point. Clinical sites from our international orthopaedic oncology research network that met the following eligibility criteria were invited to participate in this cross-sectional study: 1) sufficiently high sarcoma volume defined as greater than or equal to 20 participants per year; 2) adequate research personnel and infrastructure to manage the study; and 3) an interest in participating in the Surveillance AFter Extremity Tumor surgerY (SAFETY) trial. Please see the clarifications in the Methods > Participants > Clinical Sites section (Page 5) of the revised manuscript.

Comment #3B: Methods – The last sentence in the Survey Description subsection (p. 8) is redundant given the immediately preceding paragraph.

Response to Reviewer: We agree with this point and have since removed this sentence from the manuscript.

Comment #3C: Methods – How were patients approached for the study? Was it in person during a post-operative follow-up visit? It is not clear if the study design allowed for patients to be recruited other than during visits.

Response to Reviewer: Thank you for allowing us to expand on recruitment for our study. We have included the following additional details in the Methods > Survey Administration and Data Collection section (Page 7) of the revised manuscript:

Initially, we approached all extremity sarcoma patients in person that had consented for sarcoma surgery. However, after consulting with the SAFETY trial's Steering Committee members on the study's protocol in May 2018, we determined that patients would be approached, consented and randomized into the SAFETY trial after definitive treatment for their extremity sarcoma, as it was deemed a less stressful time for patients to make an informed decision, as well as a time point closer to the initiation of surveillance. After this decision was made, we began approaching all new recent post-operative extremity sarcoma patients for participation in this survey study, either at a post-operative clinical appointment or via telephone in this patient survey.

Comment #3D: Methods – "We approached all new post-operative…" – please clarify if new means newly diagnosed or something else.

Response to Reviewer: Thank you for your comment. We have changed this sentence from “all new post-operative …” to now state “all recent post-operative …”. Please see the Methods > Survey Administration and Data Collection section (Page 7) of the revised manuscript.

Comment #3E: Methods – It is not clear what the approach used to determine an appropriate sample size for this study was. This needs to be explained.

Response to Reviewer: Thank you for identifying this important point and providing us the opportunity to clarify. A convenience sample of one hundred thirty patients was utilized, which represents a robust sample in the study of rare diseases. Please see this addition in the Methods > Sample Size section (Page 6) of the revised manuscript.

Comment #4: Results – Do the 142 patients approached represent all eligible patients at the study sites during the study period or a sample?

Response to Reviewer: Thank you. To the best of our knowledge, the 142 patients that were approached to participate in the study represents all consecutive and potentially eligible patients that presented to one of the participating clinical sites during the study period. We have clarified this in both the Methods > Sample Size and Results > Characteristics of Respondents sections (Pages 7 and 8, respectively) of the revised manuscript.

Comment #5A: Other Items – One limitation of the study is that the questions about financial burden do not appear to address the direct medical cost of surveillance/ trial participation. While this will vary by country, insurance coverage and direct medical cost would be important considerations for trial participation in the US setting. This should be addressed.

Response to Reviewer: Thank you for identifying this and providing us with the opportunity to expand on this important point. We do agree that another limitation of our study is that while the survey addressed indirect costs associated with sarcoma surveillance, it did not address the direct costs of surveillance. However, considering that post-operative sarcoma surveillance is standard practice, this should not apply to most patients as surveillance care should be covered by the patients’ federal, provincial/state or private health insurance. Nevertheless, this cost data would likely prove valuable when considering trial participation of patients without private health insurance in countries without socialized health care such as in the USA. We have addressed this limitation in the Discussion > Strengths and Limitations section (Pages 11 and 12) of the revised manuscript.

Comment #5B: Other Items – The authors correctly note the limitation of the lack of diversity with respect to race/ethnicity. While this is not uncommon in clinical trials, it would be interesting to examine study participant demographics in the context of sarcoma incidence rates by race. There has been some work done that shows higher incidence of sarcoma among African Americans. Addressing this further is also important for potentially identifying avenues to increase diversity of participants in the SAFETY study.

Response to Reviewer: Thank you for identifying this and providing us with the opportunity to expand on this important point. As per the most recent data in the Surveillance, Epidemiology and End Results (SEER) database of the National Cancer Institute, white and black populations have similar incidence rates for soft-tissue sarcomas. However, we do recognize that our survey does not reflect these similar incidence rates. In addition, the demographic data is inconsistent with the overall North American demographic data, as black individuals comprise almost 13% of the North American population. These limitations have highlighted an important gap to address in our recruitment strategy for the SAFETY trial. Please see the Discussion > Strengths and Limitations section (Page 11) of the

revised manuscript.

Once again, thank you for your time and energy dedicated to the consideration of this work.

VERSION 2 – REVIEW

REVIEWER	Riha Vaidya Fred Hutchinson Cancer Research Center, USA
REVIEW RETURNED	06-Feb-2021

GENERAL COMMENTS	The authors have presented a well-conducted, timely, and well-written research study. All comments on the prior version of this article have been satisfactorily addressed.