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| Protocol Section | SPIRIT-PRO  Item | Recommended Content | Page Addressed |
| **Administrative Information** | | | |
| Roles and responsibilities | SPIRIT-5a-PRO  Elaboration | Specify the individual(s) responsible for the PRO content of the trial protocol. | 3- 5 |
| **Introduction** | | | |
| Background and rationale | SPIRIT-6a-PRO  Extension | Describe the PRO-specific research question and rationale for PRO assessment  and summarize PRO findings in relevant studies. | 1 - 2 |
| Objectives | SPIRIT-7-PRO  Extension | State specific PRO objectives or hypotheses (including relevant PRO concepts/domains). | 2 |
| **Methods: Participants, Interventions, and Outcomes** | | | |
| Eligibility criteria | SPIRIT-10-PRO  Extension | Specify any PRO-specific eligibility criteria (eg, language/reading requirements or pre-randomization completion of PRO). If PROs will not be collected from the entire study sample, provide a rationale and describe the method for obtaining the  PRO subsample. | 3 |
| Outcomes | SPIRIT-12-PRO  Extension | Specify the PRO concepts/domains used to evaluate the intervention (eg, overall health-related quality of life, specific domain, specific symptom) and, for each one, the analysis metric (eg, change from baseline, final value, time to event) and the principal time point or period of interest. | 4 - 5 |
| Participant timeline | SPIRIT-13-PRO  Extension | Include a schedule of PRO assessments, providing a rationale for the time points, and justifying if the initial assessment is not pre-randomization. Specify time windows, whether PRO collection is prior to clinical assessments, and, if using  multiple questionnaires, whether order of administration will be standardized. | 4 |
| Sample size | SPIRIT-14-PRO  Extension | When a PRO is the primary end point, state the required sample size (and how it was determined) and recruitment target (accounting for expected loss to follow- up). If sample size is not established based on the PRO end point, then discuss the power of the principal PRO analyses. | 7 |

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| Protocol Section | SPIRIT-PRO  Item | Recommended Content | Page Addressed |
| **Methods: Data Collection, Management, and Analysis** | | | |
| Data collection methods | SPIRIT-18a(i)-  PRO Extension | Justify the PRO instrument to be used and describe domains, number of items, recall period, and instrument scaling and scoring (eg, range and direction of scores indicating a good or poor outcome). Evidence of PRO instrument measurement properties, interpretation guidelines, and patient acceptability and burden should be provided or cited if available, ideally in the population of interest. State whether the measure will be used in accordance with any user  manual and specify and justify deviations if planned. | 1, -5 |
| SPIRIT-18a(ii)-  PRO Extension | Include a data collection plan outlining permitted mode(s) of administration (eg, paper, telephone, electronic, other) and setting (eg, clinic, home, other). | 4 |
| SPIRIT-18a(iii)-  PRO Extension | Specify whether more than 1 language version will be used and state whether  translated versions have been developed using currently recommended methods. | 3 |
| SPIRIT-18a(iv)-  PRO Extension | When the trial context requires someone other than a trial participant to answer on his or her behalf (a proxy-reported outcome), state and justify the use of a proxy respondent. Provide or cite evidence of the validity of proxy assessment if available. | 5 |
| SPIRIT-18b(i)-  PRO Extension | Specify PRO data collection and management strategies for minimizing avoidable missing data. | 3 - 4 |
| SPIRIT-18b(ii)-  PRO Elaboration | Describe the process of PRO assessment for participants who discontinue or  deviate from the assigned intervention protocol. | 4 |
| Statistical methods | SPIRIT-20a-PRO  Elaboration | State PRO analysis methods, including any plans for addressing multiplicity/ type I (α) error. | 7 |
| SPIRIT-20c-PRO  Elaboration | State how missing data will be described and outline the methods for handling missing items or entire assessments (eg, approach to imputation and sensitivity  analyses). | 8 |
| **Methods: Monitoring** | | | |
| Harms | SPIRIT-22-PRO  Extension | State whether or not PRO data will be monitored during the study to inform the clinical care of individual trial participants and, if so, how this will be managed in a standardized way. Describe how this process will be explained to participants; eg,  in the participant information sheet and consent form. | 5 |