Supplement 1

Protocol evidence per final SPIRIT-PRO item.

SPIRIT PRO Item number and description	SPIRIT-PRO wording prior to finalisation	% HTA protocols including item	% EPiC protocols including item	% international ovarian cancer protocols including item
(5a) Specify the individual(s) responsible for the PRO content of the trial protocol		6.67%	22.78%	23.1%
(6a) Describe the PRO-specific research question and rationale for PRO assessment and summarise PRO findings in relevant studies	Describe what is currently known about PROs in this area and explain the gaps in the literature	49.33%	32.91%	42.3%
	Provide a rationale for the inclusion of PROs as appropriate to the study population, intervention, context, objectives and setting	8.00%	33.54%	57.7%
(7) State specific PRO objectives or hypotheses (including relevant PRO concepts/domains	State the PRO study objective in relation to PRO domain/s, patient population and timeframe	77.33%	73.42% (17.09% in relation to dimension, population or timeframe)	30.8%
	State the PRO hypothesis and corresponding null hypothesis and to which outcome(s) the hypothesis relates	18.67%	-	PRO hypothesis provided 19.2%
(10) Specify any PRO-specific eligibility criteria (e.g. language/reading requirements or prerandomisation completion of PRO). If PROs will not be collected from the entire study sample, provide a rationale and describe the methods for obtaining the PRO subsample	If PROs will be collected in a subset of the study population or in specific centres, include a description/rationale for the sampling method	0.00%	10.76%	11.5%
	State the inclusion/exclusion criteria for PRO endpoint(s) (e.g., language/reading requirements)	45.33%	50.00%	7.7%

	Specify if PRO completion is pre-randomisation eligibility requirement	-	-	7.7%
(12) Specify the PRO concepts/domains used to evaluate the intervention (e.g. overall health-related quality of life, specific domain, specific symptom) and for each one, the analysis metric (e.g. change from baseline, final value, time to event) and the principal time point or period of interest	Describe the PRO constructs used to evaluate the intervention e.g. overall QOL, specific domain, specific symptom	-	-	73.1%
(13) Include a schedule of PRO assessments, providing a rationale for the time points, and justifying if the initial assessment is not prerandomisation. Specify time windows, whether PRO collection is prior to clinical assessments, and, if using multiple questionnaires, whether order of administration will be standardised	Specify the timepoint(s) for PRO analysis (including the principle timepoint of interest) and provide the rationale for these	Timing specified 97.33%	Timing specified 83.54%	42.3%
	Include PRO assessments in the main protocol schedule of assessments, specifying which PRO measures (PROMs) will be used at each assessment	-	-	96.2%
	Specify if baseline PRO assessment should be completed before randomisation	-	-	53.8%
	Specify the targeted time and acceptable time windows for each PRO assessment	-	-	26.9%
	If PROs are to be completed in the clinic: specify timing of PROM delivery in relation to clinical assessments (e.g. before/whilst/after seeing clinician and/or clinical assessments)	-	-	54%
	Justify the timing of PRO assessments. Scheduled	Timing justified 6.67%	Timing justified 12.03%	23.1%

	PRO assessments should link to research questions, hypotheses, length of recall, disease/treatment natural history, planned analysis and time of comparison must be comparable for both arms			
(14) 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	If PRO is the primary endpoint, state the required PRO sample size, otherwise discuss the power of the PRO analysis	50.67%	25.95%	30.8%
(18a i) Justify the PRO instrument to be used and describe the domains, number of items, recall period, and instrument scaling and scoring (e.g. 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	Describe the PROMs including, number of items/domains, instrument scaling/scoring, reliability, content and construct validity, responsiveness, sensitivity, acceptability, recall period. Provide references as appropriate	PROM identified 100%; Justification in relation to study hypotheses 41.33%; Justified in relation to measurement properties 37.33%; Justified in relation to acceptability/patient burden 14.67%	PROM identified 63.29%; Justification in relation to study hypotheses 36.71%; Justified in relation to measurement properties 46.84%; Justified in relation to acceptability/patient burden 29.11%	Justification for measure used 84.6%
(18a ii) Include a data collection plan outlining the permitted mode(s) of administration (e.g. paper, telephone, electronic, other)	Include a pre-specified data collection plan	84.00% included brief details of PRO data collection procedures but often omitted information surrounding mode of administration,	57.59%	46.2%

and setting (e.g. clinic, home, other)		setting and proxy reporting: 8.00% included PRO data collection guidelines/training information for trial personnel.		
(18a iii) Specify whether more than one language version will be used and state whether translated versions have been developed using currently recommended methods	Provide evidence of measurement equivalence across modes (i.e., when mixing modes of PRO data collection) and/or of cross cultural validity where different language versions of questionnaires are used	-	-	7.7%
(18a iv) 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		-	-	0.0%
(18b i) Specify PRO data collection and management strategies for minimising avoidable missing data	Specify procedures for data collection and management methods to minimise missing data. E.g. checking completed PROMs (including who will check forms and how will they deal with missing PROMs or missing items).	-	-	38.5%
(18b ii) Describe the process of PRO assessment for participants who discontinue or deviate from the assigned intervention protocol	Establish process for PRO assessment at (and beyond) withdrawal for patients who withdraw early from a study or who go 'off-study'/'off treatment'	-	-	34.6%
(20a) State PRO analysis methods, including any plans for addressing multiplicity/type I (a) error	Include an a priori description of all planned PRO analyses pertaining to the study hypotheses	PRO statistical analysis plan provided? 96.00%	PRO statistical analysis plan provided? 53.16%	61.5%

	Pre-specify sequence of testing/exploratory analyses to control for multiplicity or pre-specify domains (e.g. in a regulatory trial/labelling claim) (Common in pharma trials. Involves pre-specifying domains that alpha would be spent on, or ordering the domains in priority & alpha would be spent down the list)	Plans to address multiplicity of PRO data provided? 1.33%	10.13%	7.7%
(20c) State how missing data will be described and outline the methods for handling missing items or entire assessments (e.g. approach to imputation and sensitivity analyses)	State how missing data will be described	45.33%	30.38%	-
	Describe method for handling missing assessments (e.g. approach to imputation and sensitivity analyses)	45.33%	30.38%	-
	Describe methods for scoring endpoints. Where possible, reference scoring manuals for summated scales from PROM (domain-specific &/or total) & methods for handling missing items, and methodological papers for composite endpoints (e.g. QTWiST)	-	-	53.8%
(22) 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 standardised way. Describe how this process will be explained to participants; e.g. in the participant information sheet and consent form	Include an a priori plan for consistent/standardised management of PRO alerts (symptoms reported by patients that exceed a pre-defined level of severity) to be clearly communicated to all appropriate trial staff	10.67%	0.63%	0.0%
	Specify whether PRO forms will be used to	4.00%	3.80%	7.7%

	influence therapy or patient management (i.e. will the clinician use PRO responses to inform the patient's care?)			