WECAN SmartStart in Cancer Patient Advocacy

WECAN MASTERCLASS in Cancer Patient Advocacy

HRQOL: Are we talking about the same thing?

Challenges in interpreting HRQOL findings across trials

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Randomised Controlled Trial (Example)

	Trial 1	Trial 2
Population	Same population of cancer patients	
Treatment	Placebo vs new treatment	
Sample size	Similar sample size	
Overall survival (OS)	No benefit in OS	No benefit in OS
Progression Free Survival (PFS)	Benefit in PFS	Benefit in PFS
Health-related quality of life (HRQOL)	Worsening in HRQOL	Benefit in HRQOL

Why were there conflicting HRQOL conclusions?

It starts with the **research question**:

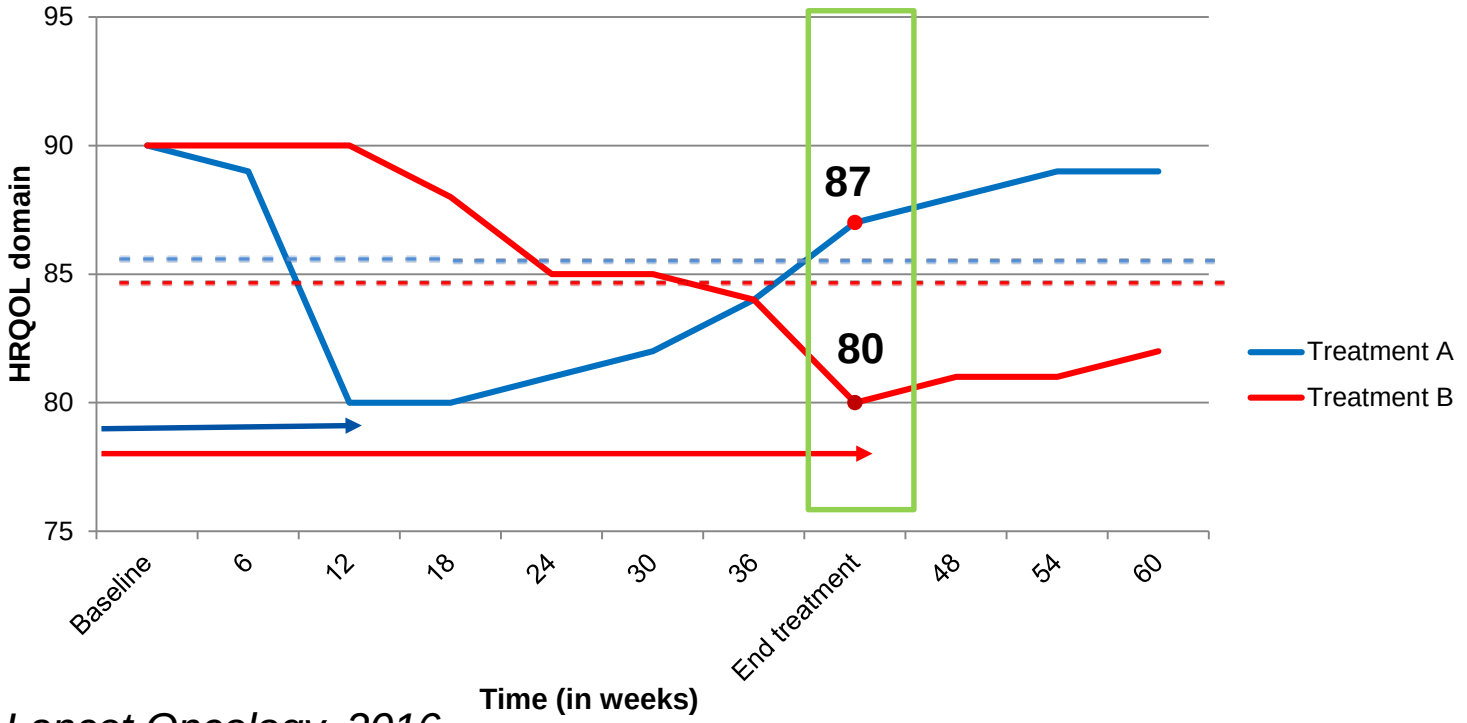
	Trial 1	Trial 2
Research question	To compare HRQOL between treatment arms	

Which statistical method would be appropriate to test this question?

t-test, linear regression, ANOVA, repeated measures ANOVA, Mann-Whitney, linear mixed model, generalised estimating equation, joint longitudinal model, pattern mixture model, log-rank test, Cox proportional hazards, Chi-square test, Fisher's exact test, Cochran-Mantel Haenszel test, logistic mixed model, area under the curve… and many more…

A hypothetical example (not based on real data)

S1	Time to first worsening	Treatment A is **worse** than Treatment B
S2	“Global picture”: Overall means across time	**No difference** between treatments
S3	Specific time point: end of treatment	Treatment A is **better** than Treatment B



SISAQOL Consortium, The Lancet Oncology, 2016

A need for more well-defined HRQOL questions

- Each statistical method focuses on a different aspect of the data and responds to a different research question.
- The conclusions are different because the interpretations of the research question varied.
- There is a need to ask more well-defined questions to allow for better communication of HRQOL findings.

Randomised Controlled Trial (Example)

	Trial 1	Trial 2
Population	Similar group of cancer patients	
Treatment	Placebo vs new treatment	
Sample size	Similar sample size	
Health-related quality of life (HRQOL)	**Worsening in HRQOL**	**Benefit in HRQOL**

"What questions were these two trials asking – were they <u>really</u> the same?"

Unpacking the research question

- Were they assessing the same **HRQOL areas**?
- Were they assessing the same **endpoints?**
- Were the same **population of patients** included in the analysis?

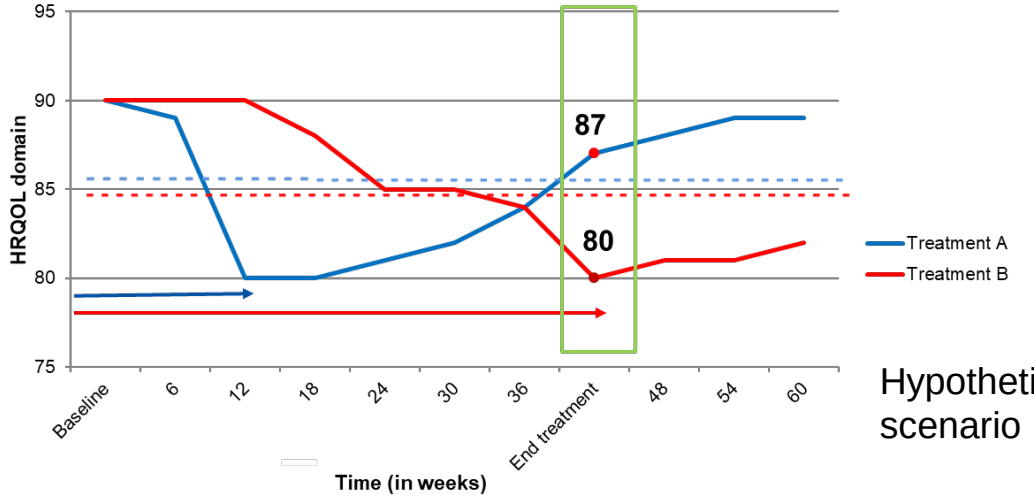
Were they assessing the same HRQOL areas?

	Trial 1	Trial 2
HRQOL measure	EORTC QLQ-C30	
HRQOL areas	Cognitive functioning	Global health status, physical functioning, social functioning,

- Conclusions about HRQOL were not necessarily based on the same HRQOL areas.

Were they assessing the same endpoints?

	Trial 1	Trial 2
Endpoints	Change in HRQOL scores at 46 weeks *(~10 months)*	Time to >/10 point HRQOL worsening from baseline… *(Result: ~4 months to ~8 months)*



Hypothetical scenario

- Conclusions about HRQOL were not based on the same endpoint.
- The two trials were responding to different aspects of the data.

Were they assessing the same endpoints?

	Trial 1	Trial 2
Endpoints	Change in HRQOL scores at 46 weeks *(~10 months)*	Time to >/10 point HRQOL worsening from baseline… *(Result: ~4 months to ~8 months)*
	What if a patient's **disease progresses** and does not respond to the questionnaire at week 46?	What if a patient's **disease progresses** and dropped out of treatment before a >/10 point worsening is recorded?
	Ignored = not included in the analyses*	disease progression = >/10 point worsening of HRQOL scores

Missing data

Handling of missing data

- Handling of missing data differed between the two trials.

Were the same population of patients included in the analysis?

	Trial 1	Trial 2
Analysis population	Only patients alive and free of disease at 46 weeks	All patients included in the trial

- The patient population included in the analyses differed between the two trials.

Unpacking the research question

- Because of the vagueness of the research question on HRQOL, the interpretation of the research question differed between the two trials affecting design and analysis decisions.

- The two trials did not answer the same question.
  - Different HRQOL areas
  - Different endpoint
  - Different handling of missing data
  - Different analysis population

- The HRQOL results of the two trials are not directly comparable… but they looked like they were…

How can we make things better?

How can we make things better?

- Many decisions need to be made when assessing HRQOL in cancer clinical trials, and **these decisions impact the conclusions about patients' HRQOL.**
- With the many decisions, there are so **many ways to do things differently**.
- There is **a need to agree on a set of standards** on how to design, analyse and interpret HRQOL data in cancer clinical trials.
- We **need to do this with patients (and their representatives)** because patients are the experts of their own HRQOL, and they provide valuable insights on what matters to them.

A need for international multi-stakeholder collaboration

- SISAQOL initiative: set international standards for the analyses of HRQOL data in cancer clinical trials
- Setting standards for HRQOL analyses is a challenge. The topic is multi-faceted and complex. Nobody is an expert on all issues related to HRQOL analyses in cancer clinical trials!
- International multi-stakeholder collaboration: regulators, payers, academics, industry, clinicians, biostatisticians, patient representatives, and HRQOL experts

Special thanks to Kathy Oliver and IBTA
for their insightful contributions since the very start of SISAQOL

Stakeholders are interested in improving how we assess HRQOL in cancer clinical trials

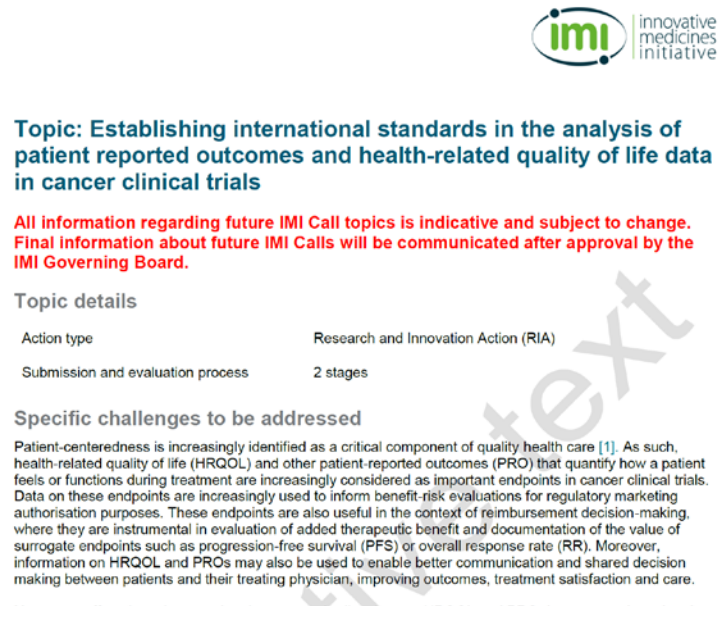
- FDA-ASCO Public Workshop: 2019 Clinical Outcome Assessments in Cancer Clinical Trials
- July 12 2019
- Meeting outcome: To explore the use of **physical function** as an **outcome measure** and advance the **standardization** of data collection, COA tools, endpoints, analysis, and visualization of physical function in oncology for **regulatory decision-making**.

Sessions
Exploring the value of electronic PRO assessments to facilitate learning health care systems
Systematically defining research objectives and framing questions using the estimand framework
Using a standardized estimand framework for medical product review and labeling: a case study
Seeing the Forest Through the Trees – Where do we go from here?

Webcast Link: https://collaboration.fda.gov/coacct

Collaborate with us?

- Statistics are just tools to answer research questions.
- **Well-defined research questions** and **well-informed decisions** on various aspects on the design, analysis and interpretation of HRQOL are needed to make things better.



imi innovative medicines initiative

Topic: Establishing international standards in the analysis of patient reported outcomes and health-related quality of life data in cancer clinical trials

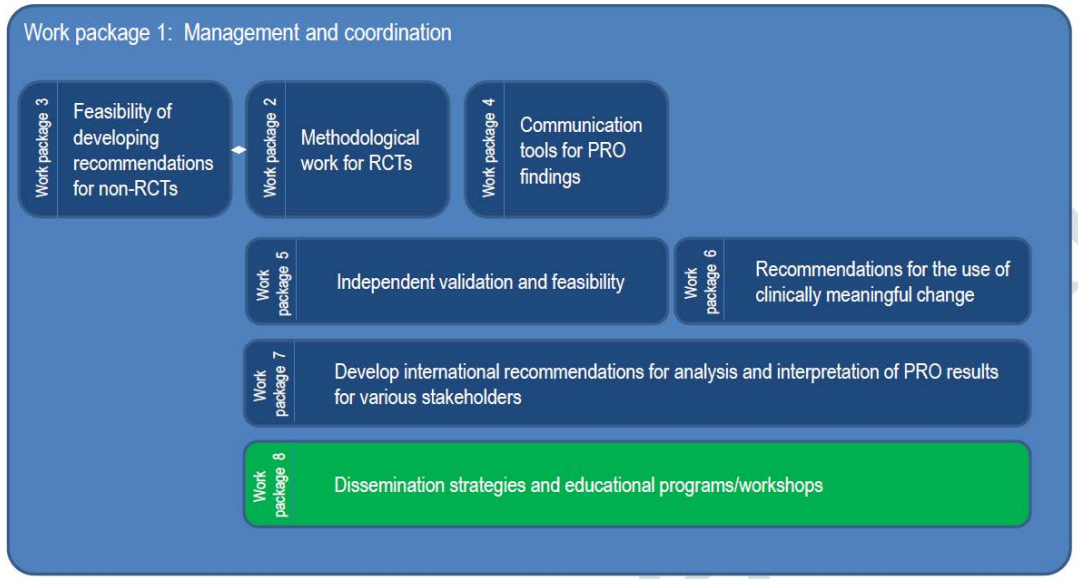
All information regarding future IMI Call topics is indicative and subject to change. Final information about future IMI Calls will be communicated after approval by the IMI Governing Board.

Topic details

Action type	Research and Innovation Action (RIA)
Submission and evaluation process	2 stages

Specific challenges to be addressed

Patient-centeredness is increasingly identified as a critical component of quality health care [1]. As such, health-related quality of life (HRQOL) and other patient-reported outcomes (PRO) that quantify how a patient feels or functions during treatment are increasingly considered as important endpoints in cancer clinical trials. Data on these endpoints are increasingly used to inform benefit-risk evaluations for regulatory marketing authorisation purposes. These endpoints are also useful in the context of reimbursement decision-making, where they are instrumental in evaluation of added therapeutic benefit and documentation of the value of surrogate endpoints such as progression-free survival (PFS) or overall response rate (RR). Moreover, information on HRQOL and PROs may also be used to enable better communication and shared decision making between patients and their treating physician, improving outcomes, treatment satisfaction and care.



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