SISAQOL-IMI educational workshop at WECAN academy

SISAQOL-IMI stands for Setting International Standards in Analysing Patient-Reported Outcomes and Quality of Life endpoints and is funded under the Innovative Health Initiative. This 4-year project aims to generate recommendations on how to standardise the use, analysis, and interpretation of patient-reported outcome (PRO) data in cancer clinical trials. Myeloma Patients Europe on behalf of WECAN leads patient engagement throughout the project consortium.

Background: Why was the SISAQOL-IMI project started?

PRO's: A patient-reported outcome, also known as a PRO, is a health outcome that is directly reported by the participant who experienced it, without interpretation by a clinician or anyone else. PROs may include patient assessments of health status, quality of life, or symptoms.

HRQOL: Health-related quality of life (HRQOL) is a multi-dimensional construct reflecting an individual's perceived physical, psychological, and social well-being, including the impact of disease symptoms and treatment side effects.

When investigating PROs in two very similar cancer clinical trials (e.g. same treatment, same PROs, similar patient demographics, etc.), research has shown that the results of PROs can have opposing conclusions, depending on how 1. you design the trial, 2. you analyse the PRO data, and 3. you report the PRO data.

Example: Randomised Controlled Clinical Trials in Glioblastoma

In 2014, two clinical trials comparing a new treatment vs a placebo treatment had similar results on overall survival (OS) and progression free survival (PFS) but had opposing results on health-related quality of life (HRQOL). One trial suggested there was worsening in HRQOL and the other suggested there was a benefit in HRQOL.

	RTOG 0825 (Gilbert et al NEJM, 2014)	**AVAglio (Chinot et al NEJM, 2014)**
Population	Newly diagnosed glioblastoma with central histological confirmation	
Treatment	TMZ+RT+Placebo vs TMZ+RT+BEV (new treatment)	
Sample size	309 vs 312	463 vs 458
Overall survival (OS)	**No benefit in OS** 16.1 vs 15.7 months (HR=1.13 [0.93-1.37]; p=0.11)	**No benefit in OS** 16.7 vs 16.8 months (HR=0.88 [0.76-1.02]; p=0.10)
Progression Free Survival (PFS)	**Benefit in PFS** 7.3 vs 10.7 mths (HR=0.79 [0.66-0.94]; p=0.004)	**Benefit in PFS** 6.2 vs 10.6 mths (HR=0.64 [0.55-0.74]; p<0.001)
Health-related quality of life (HRQOL)	**Worsening in HRQOL** "Longitudinal evaluation also revealed *greater deterioration* in the bevacizumab group [new treatment]…"	**Benefit in HRQOL** "In the prescribed primary analysis, *deterioration-free survival was significantly longer among patients* in the [new treatment] than among those in the placebo group …"

To identify where these differences in HRQOL came from, researchers assessed the following:

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

In this case, researchers concluded that the HRQOL outcomes were not based on the same HRQOL domains, as seen in the table. Researchers also found that two trials were not based on the same HRQOL endpoints. Trial A used the data at month 10, whereas Trial B used the data when there was a 10-point worsening from the pre-treatment score. Additionally, these two trials handled missing data (when a patient progressed and didn't respond to the questionnaire) differently. Trial A did not include any missing data in the analyses, whereas Trial B considered all patients who did not complete the questionnaire as having a 10-point worsening from the pre-treatment score. Lastly, across both clinical trials, the patient population included in the analysis was different. Trial A only included patients alive and disease free at 46 weeks, whereas Trial B included all patients.

	Trial A	Trial B
HRQOL	Cognitive functioning, motor dysfunction, communication deficit	Global health status, physical functioning, social functioning, motor dysfunction, and communication deficit
Endpoints	Change in HRQOL scores at 46 weeks *(~10 months)*	Time to >/10-point worsening from pre-treatment scores without improvement OR disease progression OR death *(Result: ~4 months to ~8 months)*
	Missing data: Ignored = not included in the analyses	Missing data: disease progression = >/10-point worsening of HRQOL scores
Population	Only patients alive and free of disease at 46 weeks	All patients included in the trials

This example shows the need for standardisation on how we design, analyse and report data in cancer clinical trials, which is the aim of the SISAQOL-IMI project. Better standardisation is important for patients taking part in cancer clinical trials as the impact that treatment has on their quality of life will be better captured, understood, and presented. This project and its generated standards are also of importance to organizations like the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA), as PRO data presented in the same way across trials and cancer diagnoses will facilitate implementation in clinical practice and inform regulatory decision making.

2023 WECAN academy session

An educational workshop was organised for patient advocacy groups at the WECAN academy 2023, one of Europe's leading training programs for cancer patient advocates. The session led by WP8 and WP1, included a presentation on the challenges with PRO data, introducing the SISAQOL-IMI project and an interactive session where audience members were asked to interpret results from two hypothetical treatments depending on how they were analysed, showcasing the need for the recommendations. A summary of the workshop was published here.

Given the target audience was patient advocates, the aim of the workshop was to give background information on the challenges with QOL research highlighting the need for the SISAQOL-IMI project. The estimand framework itself was not mentioned throughout the workshop but its main principles were highlighted with examples.

A section was also dedicated to explaining intercurrent events for a lay audience and breakdown the key things patient advocates need to look out for in a clinical trial protocol or helping in the design of a clinical trial. Intercurrent events are events that alter the anticipated course of treatment for a patient in a clinical trial. Incorporating the data from these patients wrongly in trial and PRO analysis can affect the interpretation of the gathered data. Patient advocates should know about intercurrent events to help them feedback back to pharmaceutical companies on the design of their clinical trials. We need to know how companies plan to deal with events such as treatment discontinuation or "rescue" treatment to ensure (1) patient experience is handled correctly and (2) the data generated from PROs gathered and handled correctly and consistently in their analysis and (3) data generated from patients is not wasted.

An interactive session where audience members were asked to interpret results from two hypothetical treatments depending on how they were analysed, showcasing the need for the recommendations.

Why was this session relevant to WECAN and patient advocates?

Many patients and advocates have been involved with reviewing clinical trial protocols, and the value of this is being recognised more broadly by industry, researchers, and other stakeholders. As the advocacy community continues to push for earlier involvement, you may be involved in the design of clinical trials during their initial development. Therefore, it is important to understand topics like intercurrent events, how differences in clinical trial design can result in different outcomes (e.g. the Glioblastoma trials) and how to provide constructive feedback. Ensuring PRO data is used, designed and reported consistently across cancer clinical trials means that the impact that treatment has on a patient's quality of life will be better captured, and standardized PRO data across trials and cancers will help support fair and informed decision making.

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