Effect of Time Windows in Analysis of Health-Related Quality of Life (HRQOL) Outcomes


Aim
Patient reported HRQOL collection in randomized controlled trials (RTC) requires questionnaire completion at specific time points. Our aim was to assess whether HRQOL scores differ depending on the relative timing of completion.

Patients and Methods
In a retrospective analysis of an EORTC 3-arm RCT of 498 colon or rectum cancer patients comparing 5-FU 24 continuous infusion (Arm A), 5-FU 24 continuous plus leucovorin (LV) (Arm B) and 5-FU bolus plus LV (Arm C), HRQOL was measured as a secondary endpoint at baseline and on each of the 12 scheduled chemotherapy cycle dates using the EORTC QLQ-C30 questionnaire. A ‘time window’ variable was created to indicate when the questionnaire was completed relative to scheduled date and defined as ‘before’ (up to 10 days), ‘on’ (on cycle date), and ‘after’ (up to 10 days). Sensitivity analyses were performed extending the time window to 20 to 30 days. HRQOL mean scores were calculated using a linear mixed model including treatment, cycle number, treatment-by-cycle interaction, and the time window variable.

Results
Patient baseline characteristics were balanced across the three treatment arms. The analysis was limited to the first five cycles yielding a total of 753 questionnaires. Only for Arm C were significant (p<0.05) HRQOL mean score differences reported. Compared to HRQOL mean scores ‘on’ the scheduled cycle data, the ‘before’ HRQOL mean scores were worse for physical functioning (3.05; p=0.0003) and fatigue (5.85; p=0.0055) and the ‘after’ HRQOL mean scores were worse for nausea and vomiting (2.45; p=0.0326) and physical functioning (2.33; p=0.0110). Similar
results were reported during the sensitivity analysis. HRQOL mean score differences were well below the 10 points seen as clinically meaningful. The treatment arm comparisons between arms did not significantly change by the inclusion of the time window variable.

**Conclusion**

These results suggest that HRQOL mean scores may differ depending on the relative timing of the questionnaire completion and may vary depending on the treatment arm. In our study HRQOL scores specifically differed, with regard to relative timing, for cancer patients receiving 5-FU bolus infusion. Our findings however should be further explored in settings.