Letters to the editor

Reporting of HRQoL results from the PALOMA-2 trial: Relevant data are still missing

Rugo et al. [1] report results on health-related quality of life (HRQoL) from the PALOMA-2 trial, in which palbociclib plus letrozole was compared with letrozole plus placebo. Key conclusions include:

1. a positive trend (HR <1) favouring the palbociclib arm for time to deterioration (TTD) in HRQoL;
2. a significantly greater improvement in pain scores in the palbociclib plus letrozole arm;
3. the value of radiological assessments in estimating treatment effects on HRQoL.

These conclusions are not supported by the PALOMA-2 trial data, but result from highly biased post hoc analyses and assumptions on treatment effects based on observed correlations.

Ad (1): the authors define deterioration in the FACT-B total score as a decrease of ≥7 points with no subsequent <7-point decrease. However, according to the statistical analysis plan the predefined response criterion was the established minimally important difference of a decrease by ≥7 points alone [2]. In 2016 Pfizer, the manufacturer of palbociclib, submitted HRQoL data for benefit assessment in Germany using the predefined response criterion [3, 4]. Using this criterion, the 'positive trend' in favour of palbociclib is reversed (HR 1.06, 95% CI 0.85–1.31).

Ad (2): the authors report a significantly greater improvement in pain scores in the palbociclib group. This conclusion is based on a selective analysis of a single item in the Breast Cancer Subscale. Such an analysis was neither predefined in the study protocol [2, 4], nor is it recommended in the FACT-B scoring guidelines [5]. Moreover, the results are incomprehensible, as the effect size and confidence interval are not reported. Regardless of the invalidity of the analysis, another subscale of the FACT-B (physical well-being) also includes a single item on pain, but the authors do not report the results.

Ad (3): the authors' data show significant differences in (post hoc) TTD between patient cohorts with and without tumour response (Figures 2B-D in [1]) or progression (Figures S2A-C in [1]). However, these analyses do not support their conclusion that 'these data emphasize the value of radiological assessment on treatment effect'. The different findings on HRQoL between patients with and without response/progression cannot be attributed to an effect of palbociclib. The between-treatment comparison among all patients (Figure 2A in [1]) clearly shows no difference between treatment groups, despite a substantial difference in response/progression. Therefore, the observed correlation between response/progression and HRQoL probably just indicates different baseline risks for deterioration of HRQoL between patients with response/progression and those without. By no means do these data support any conclusion on the value of radiological assessment in estimating treatment effects on HRQoL.

We also wonder why the authors do not report the full HRQoL data collected in the PALOMA-2 trial. According to the protocol (and in contrast to the methods section of Rugo et al. [1]), HRQoL data were also collected after progression [2]. These data are of paramount importance to patients and clinicians.

In conclusion, we strongly recommend following general principles of evidence-based medicine for the reporting of results on HRQoL. This includes both the unbiased and full reporting of relevant data.

T. Kaiser*, M. Köhler & B. Wieseler
Institute for Quality and Efficiency in Health Care (IQWiG), Drug Assessment, Cologne, Germany
(*E-mail: thomas.kaiser@iqwig.de)

Funding

None declared.

Disclosure

The authors have declared no conflicts of interest.

References

1. Rugo HS, Diéras V, Gelmon KA et al. Impact of palbociclib plus letrozole on patient-reported health-related quality of life: results from the PALOMA-2 trial. Ann Oncol 2018; 29(4): 888–894.
2. Finn RS, Martin M, Rugo HS et al. Palbociclib and letrozole in advanced breast cancer. N Engl J Med 2016; 375(20): 1925–1963.
3. Pfizer Pharma GmbH. Dossier zur Nutzenbewertung gemäss § 35a SGB V: Palbociclib (Ibrance®); Modul 4A: Medizinischer Nutzen und medizinischer Zusatznutzen, Patientengruppen mit therapeutisch bedeutsamem Zusatznutzen. Stand: 22.11.2016. https://www.g-ba.de/downloads/92-975-1744/2016-11-22_Palbociclib_Modul4A.pdf (20 March 2018, date last accessed).
4. Institute for Quality and Efficiency in Health Care. Palbociclib (breast cancer) – benefit assessment according to §35a Social Code Book V. Published online 1 March 2017. https://www.iqwig.de/en/projects-results/projects/drug-assessment/a16-74-palbociclib-breast-cancer-benefit-assessment-according-to-35a-social-code-book-v.7749.html (20 March 2018, date last accessed).
5. FACIT. FACT-B Scoring & Interpretation Materials. http://www.facit.org/FACITOrg/Questionnaires (20 March 2018, date last accessed).

doi:10.1093/annonc/mdy204
Published online 4 June 2018