Response to: Effect of dose reductions on clinical outcomes, or of outcomes on dose reductions?

Dear Editor,

We want to thank dr. Regan for reading and commenting on our manuscript "Palbociclib dose reductions and the effect on clinical outcomes in patients with advanced breast cancer". We would like to mention that this study was hypothesis-generating. We were aware of the limitations of this type of observational data used in this study, as described in the manuscript. To limit immortal time bias, we described an additional survival analysis in the manuscript, excluding the patients that stopped treatment (presumably due to early progression) within the first three months of treatment. Furthermore, most dose reductions occurred early during treatment, and from a clinical point of view a substantial part of the patients stopping treatment because of AEs, will have experienced a dose reduction before stopping treatment.

However, we considered the suggestion for the landmark analysis and performed this in-depth analysis on the dataset. The landmark analysis did not lead to different conclusions for this study. The overall survival between patients with a dose reduction was significantly higher compared to patients without a dose reduction (p = 0.019). We agree with dr. Regan that this analysis is the most suitable to limit immortal time bias, and we will use this in comparable future research.

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