

Author's reply to comments to: Italian Medicines Agency's reform and time until pricing and reimbursement decisions: a time-to-event analysis

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We appreciate the comments made by Traversa and Addis, and we are aware of the limitations of our study. A more appropriate analysis should have considered for the post-reform period only those medicines which received an EU authorisation after the separation date (i.e., from March 2024 onwards). This would more clearly separate the two periods: the first period (pre-reform) would count EU authorisation and AIFA reclassification events before March 2024, while the second period (post-reform) would count EU authorisation and AIFA reclassification events after March 2024. However, at the time of the study conception, such data were not available, since the database we relied on “followed up” in time only those medicines approved at the EU level by the end of December 2023.

Traversa and Addis correctly suggest that in our analyses the post-reform period may take advantage of the negotiation work carried out in the pre-reform period, thus inflating the effect of the new AIFA committee (if any). We acknowledged this limitation in the Discussion and tried to counteract this bias by performing sensitivity analyses S1 and S4: the first one moves up the separation date by 1 month, while the second analysis removes both time at risk and reclassification events 4 months before and 4 months after the separation date. In both cases, the findings were in line with the

base-case analysis. Nonetheless, in the paper, we state that “this bias cannot be fully eliminated”.

Regarding sensitivity analysis S3, the choice of P&R presentation dossier as the start date instead of EU approval can, in principle, better isolate AIFA efficiency, since the time from EU approval to P&R presentation is up to the pharmaceutical company and not to the regulatory authority. If we compare Table 1 with Table S3.1, more than 20% of medicines approved at the EU level did not present the dossier to AIFA, and thus they were considered as censored observations in the main analysis. These observations were instead excluded in sensitivity analysis S3. This led to a moderate reduction in the proportion of censored observations in the pre-reform period (i.e., medicines not reclassified by March 2024), whereas there was a large change in the post-reform period: in the main analysis, about 40% of medicines “surviving” March 2024 were censored at the end of the follow-up, while all (100%) were reclassified in sensitivity analysis S3. This can explain the larger difference in median times and HR compared to the base-case analysis.

We remark our gratitude to Traversa and Addis for their careful and well-informed comments, as well as to the anonymous referees who evaluated our manuscript. Identifying and correcting biases in study design or data analysis is of paramount importance for any policy evaluation.

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