Reply to the letter to the editor 'On the underreporting of health-related quality of life and regulatory approval' by Bhamidipati et al

Reply to "On the Underreporting of Health-Related Quality of Life and Regulatory Approval" by Bhamidipati and colleagues

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We are pleased that our publication [1] met the interest of Bhamidipati and colleagues. Data reported in their correspondence are based on the analysis of trials leading to FDA approval for solid or hematologic malignancies, between 2009 and 2018, which is a period of time entirely including the time-frame considered in our analysis. Their results are very similar to ours, showing sub-optimal adoption of Quality of Life (QoL) among endpoints and poor QoL reporting in publications.

We strongly believe that QoL assessment is crucial to evaluate the benefit-harm balance of new anticancer treatments. Especially when trial results show a questionable clinical relevance due to the adoption of surrogate endpoints, like progression-free survival (PFS), QoL results should be considered of paramount importance to prove the added value of a new treatment [2].

In the database we used for our published analysis [1], 87 publications of trials conducted in the advanced / metastatic setting showed a positive result based on a primary endpoint different from overall survival, mostly PFS [3]. Of these 87 publications, the majority (67) did not report positive OS results in the primary publication. Although this situation (a positive result in a surrogate endpoint, without evidence of benefit in overall survival) is exactly the situation requiring the availability of QoL data in order to judge the clinical relevance of the results, disappointingly 21 of those studies (31.3%) did not include QoL among study endpoints, and 40 publications (59.7%) did not present any QoL results.

In accordance with the analysis presented by Bhamidipati and colleagues, these results highlight the lack of QoL information for several new treatments that, on the basis of positive results, are subject to evaluation for regulatory approval.

Bhamidipati and colleagues underline the recent position of most important scientific societies, which led to the inclusion of QoL within the evaluation tools of treatment value. As a matter of fact, the attention of scientific community to these issues is recently increasing. At 2018 ESMO meeting, a whole session of oral presentations about metastatic breast cancer was dedicated to QoL results of positive and potentially practice-changing randomized trials. Dr. Leslie Fallowfield, who acted as discussant of that session, recently commented our analysis [4] highlighting that unfortunately QoL is often still considered a “Cinderella outcome”.

Also ASCO, at the end of 2018, dedicated a post to this specific topic, emphasising QoL as a key element for the assessment of new treatments, even more in those situations where the statistical significance of results conflicts with their clinical relevance [5].

As Bhamidipati and colleagues state, the burden now falls to regulatory agencies, which should make efforts to encourage the inclusion and timely reporting of QoL issues. On the other hand, we believe that also the scientific community should make efforts to pursue a more rigorous methodology in QoL assessment and reporting.

Disclosure

Massimo Di Maio received honoraria and had roles as consultant or advisor for AstraZeneca, Lilly Pharma, Bristol Myers Squibb, MSD and Janssen. Francesco Perrone received honoraria from Bayer, Daiichi Sankyo, Ipsen, AstraZeneca and Bristol Myers Squibb and received research funding from Roche and Bayer. Laura Marandino declared no conflicts of interest.

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