

Letters

COMMENT & RESPONSE

Beyond Citation Counts: Measuring the Real Clinical Impact of Randomized Clinical Trials in Oncology

To the Editor We read with interest the original investigation by Unger and colleagues,¹ comparing the scientific impact, in terms of citation counts, of positive randomized clinical trials (RCTs) vs RCTs producing negative results, in the field of oncology. The amount of citations is a reasonable, “objective” measure to evaluate the impact of an RCT. However, we suggest that the real impact for clinical practice of both positive and negative trials could be better measured by their specific inclusion in clinical practice guidelines. Even limiting the discussion to the list of RCTs performed by an academic cooperative group such as the Southwest Oncology Group (SWOG), the meaning of a formally negative result can be very different among trials. For instance, the SWOG S0421 trial was conducted to evaluate the efficacy of adding atrasentan hydrochloride to docetaxel in patients with metastatic castration-resistant prostate cancer.² Single-agent docetaxel was the standard of care when the study was designed, and so it remained following the negative result: the trial did not support approval of atrasentan and had no impact on clinical practice. Conversely, when a trial compares therapeutic options already available in clinical practice, results could have a relevant clinical impact, even if negative. A negative result could imply the withdrawal of a therapy, or it could even support a treatment that, although not formally proven superior, could be considered a reasonable alternative when the whole body of results is examined in terms of efficacy, toxicity, and quality of life. For instance, the SWOG S0124 trial was designed to test the superiority of cisplatin plus irinotecan hydrochloride in patients with extensive-stage small-cell lung cancer,³ after a Japanese trial had suggested a better efficacy for this treatment compared with cisplatin plus etoposide. Despite a formally negative result, S0124 showed a substantially similar efficacy of the 2 combinations, being cited in both American Society of Clinical Oncology recommendations⁴ and European Society of Medical Oncology clinical practice guidelines.⁵

Even among formally positive trials (defined by Unger et al¹ as those showing a statistically significant difference in primary end point), we believe that the clinical relevance of the result will—or at least should—influence guidelines. Even in terms of the parameters adopted by Unger et al,¹ it would be interesting to know whether, among positive trials, the number of citations or the impact factor of the publication is significantly influenced by the magnitude of the benefit (in terms of hazard ratio and/or absolute gain).

Massimo Di Maio, MD
Chiara Baratelli, MD
Marco Tampellini, MD

Author Affiliations: Division of Oncology, Department of Oncology, University of Turin, A.O. Ordine Mauriziano, Umberto I Hospital, Torino, Italy (Di Maio); Division of Medical Oncology, Department of Oncology, University of Turin, San Luigi Gonzaga Hospital, Orbassano, Italy (Baratelli, Tampellini).

Corresponding Author: Chiara Baratelli, MD, Division of Medical Oncology, Department of Oncology, University of Turin, AOU San Luigi Gonzaga, Regione Gonzole 10, Orbassano, 10043, Italy (chiara.baratelli@gmail.com).

Published Online: June 23, 2016. doi:10.1001/jamaoncol.2016.1779.

Conflict of Interest Disclosures: None reported.

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