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CORRESPONDENCE

Bevacizumab in advanced cervical cancer

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Angiogenesis and hypoxia have been proven to be the established players in cervical cancer progression, and relevant markers, including vascular endothelial growth factor, carbonic anhydrase 9 and hypoxia-inducible factor-1α was proven to be associated with poor prognosis in cervical cancer patients primarily treated with chemoradiation [1].

GOG 240 was the first study involving an agent targeting angiogenesis, bevacizumab, which demonstrated a significant prolongation of survival in advanced, recurrent or persistent cervical cancer [2]. Tewari et al. [2] reported a 3.7-month improvement in median overall survival (OS) of patients with recurrent, persistent, or metastatic cervical cancer when treated with systemic chemotherapy and bevacizumab, compared to chemotherapy alone. Previous radiation therapy (RT) was associated with better outcomes in the experimental arm compared to the control arm [2]. However, definitions of persistent and refractory disease were not provided. It would be interesting to know the cut-off point in dimensions of the tumors or relapse-free time after radical treatment. In addition, no information was provided about the median clinical target volume of irradiated tumors as well as median time from completion of RT to study enrollment. It is highly relevant to ensure that both arms were balanced with regards to these two clinical parameters, as they consist important predictors of response [3]. An unrecognized role of previous RT, the biological effect of which has a long duration of up to 6–12 months, on OS cannot be excluded. This is particularly relevant not only for the interpretation of the study results, but also for the elucidation of underlying biology. Despite the gross amount of translational data, the molecular response of the tumors after chemoradiation in terms of angiogenesis markers remains elusive. Definitive chemoradiation might result in neovascular depletion of tumors, thus the timepoint and sequence of bevacizumab administration emerges as an important factor for predicting responses.

Finally, all data from trials using bevacizumab, including GOG 240 [2], RTOG 0417 [4], and the study of Zighelboim et al. [5] are consistent with significant toxicities, particularly grade 3–4 bleeding, thromboembolic events, and GI fistulas as well as unanticipated hospital admissions for supportive care. This raises concerns about the anticipated goals of care, also given the absence of change in quality of life [2] particularly in heavily pretreated patients with residual toxicities.

Conflict of interest There is no conflict of interest relevant to this letter.

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