CORRESPONDENCE

RE: A Randomized Phase II/III Study of Dalotuzumab in Combination With Cetuximab and Irinotecan in Chemorefractory, KRAS Wild-Type, Metastatic Colorectal Cancer

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With great interest, we read the study by Sclafani et al. about the role of dalotuzumab in KRAS wild-type metastatic colorectal cancer (mCRC) patients (1). The study ended up with a conclusion that dalotuzumab could not improve survival of KRAS wild-type mCRC patients. The authors also suggested that further biomarker-driven studies are warranted because insulin-like growth factor type 1 (IGF-1) receptor ligands are promising biomarkers.

Indeed, the development of targeted therapies is increasingly dependent on our knowledge of biomarker. We have several concerns about the biomarker analyses of Prof. Sclafani’s study. First, we would like to suggest the authors to further clarify the origin of tumor tissue used for biomarker analyses. In the past few years, more and more studies emphasized different expression of certain biomarkers between primary tumors and matched metastatic sites in various types of tumors, including colorectal cancer (2,3). The discrepancy between primary and metastatic sites may weaken the predictive value of IGF-1. We noticed that the authors mentioned that data on source of tumor were not available. As the authors claimed in the discussion, perhaps it was difficult to distinguish source of tumor between right-side colon and left-side colon or rectum, but we believe it might be feasible to clarify primary or metastatic tumor based on formalin-fixed, paraffin-embedded tissue. Second, we would like to recommend the authors discuss why they selected mRNA expression of IGF-1 as a biomarker because mRNA might be significantly affected by tissue fixation, especially in formalin fixation (4). Third, even if mRNA expression analyses of formalin-fixed, paraffin-embedded samples are acceptable, the authors need to further discuss why they chose 25% as cutoff point for IGF-1. Fourth, it is difficult to understand why the authors performed subgroup analyses only between arms A and C. Given the fact that numerically better survival was achieved in arm B than arm A, we would like to suggest the authors provide detailed overall survival and progression-free survival results in patients with IGF-1-overexpressing tumors and low IGF-1 tumors in arm B, respectively.

References