Response from Drs. Formica/Zaniboni to Dr. Milano

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We would like to thank Dr. Milano et al. for the point they made on the possible role of drug-induced immune response occurring during treatment with either anti-VEGF or anti-EGFR agents [1].

We acknowledge the increasing importance that immune checkpoint inhibitors are gaining in the therapeutic armamentarium in oncology [2].

However, the impact of antitumor immunity, and in particular of PD-1/PD-L1-modulated immune response, is far to be fully elucidated in colorectal cancer.

Initial clinical data demonstrated no response with anti-PD-1 or anti-PD-L1 drugs in colorectal cancer [3, 4]. Subsequently, the clinical ‘niche’ (5–10 %) of microsatellite instable tumors was suggested to be sensitive to PD-1/PD-L1 targeting agents for this disease [5].

Moreover, the different biologic drugs in use for CRC patients may have different power in triggering an immune reaction, such as the NK-related antibody-dependent cellular cytotoxicity (ADCC), which is higher for the IgG2 cetuximab and lower for the IgG1 panitumumab, and this should be further taken into consideration [6].

We do strongly agree that combination regimens of anti-VEGF or anti-EGFR therapies with immunotherapies represent an extremely attractive new frontier; however, the molecular basis of such a treatment approach still needs to be accurately defined.

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