OXFORD

JNCI J Natl Cancer Inst (2016) 108(9): djw156

doi: 10.1093/jnci/djw156
Response

RESPONSE

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We appreciated the interest of Fusco et al. in our correspondence, "Regorafenib also can cause osteonecrosis of the jaw" (1), because it allowed us to examine in depth our patient's history and underline the importance of our findings. Previous anticancer treatment for metastatic colorectal cancer included bevacizumab. The antiangiogenic treatment was started in March 2008 as standard dose (5 mg/kg dose every 2 weeks) in combination with 5-fluorouracil and irinotecan (FOLFIRI schedule) for a total of six months, followed by 12 months of bevacizumab maintenance therapy as 7.5 mg/kg dose every three weeks. Therefore, bevacizumab therapy lasted about 18 months, and it was stopped in 2009 because of surgical resection of lung metastases.

Based on the available evidence, it seems possible that bevacizumab use confers a low risk for osteonecrosis of the jaw (ONJ) development, and this risk is amplified if bevacizumab is added to bisphosphonates therapy (2). As previously reported, it is very important to underline that our patient never received bisphosphonates during her medical history. We believe that previous bevacizumab exposure cannot justify the ONJ development in our patient because of the long interval between the treatment and ONJ appearance.

In terms of her dental history, the patient had a high socioeconomic status, she received routine dental evaluation, and she had good oral health as certified by her odontologist. No dentoalveolar procedure was performed before or during regorafenib treatment. However, the patient didn't receive any oral screening, for example, dental radiography, before or during the treatment. There aren't, in fact, recommendations about ONJ-preventive protocols in patients undergoing anti-angiogenic therapy. Nevertheless, the Agenzia Italiana del Farmaco (AIFA) has recently suggested an oral health evaluation prior to the start of the anti-angiogenic drug aflibercept (3). In the future, this kind of attention should probably also be extended to patients treated with other anti-angiogenics and with known risk factors.

After ONJ diagnosis, the patient suspended regorafenib therapy, and she was entrusted to an odontologist specialized in the treatment of ONJ. The patient underwent resection of necrotic bone fragments in combination with an antibiotic therapy and oral hygiene sessions. ONJ was recovered in two weeks, so the patient had the possibility of resuming regorafenib therapy.

The patient is still on regorafenib treatment, and her oncologic disease is still in partial response from about 26 months, whereas in the last four months we didn't find any signs of ONJ relapse. In consideration of successful management of the case of our patient, we want to emphasize the importance of a multidisciplinary collaboration between oncologist, specialized odontologist, and radiologist in ONJ prevention and treatment.

We can conclude that, in our patient, the anti-angiogenic activity of regorafenib therapy was probably the major cause of ONJ development. We also believe that, as reported in literature about bisphosphonates-related ONJ (4), the long regorafenib exposure was related to ONJ appearance in our case.

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Received: May 14, 2016; **Accepted:** May 20, 2016

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CORRESPONDENCE

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