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### CORRESPONDENCE

# RE: Regorafenib Also Can Cause Osteonecrosis of the Jaw

# Vittorio Fusco, Giuseppina Campisi, Gianmauro Numico, Cesar A. Migliorati, Daniele Santini, Alberto Bedogni

Affiliations of authors: Oncology Unit, SS Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy (VF, GN); Department of Surgical, Oncology and Oral Sciences, Sector of Oral Medicine, Palermo University, Palermo, Italy (GC); University of Tennessee Health Science Center, College of Dentistry, Memphis, TN (CM); DH Oncology, Università Campus Bio-Medico, Rome, Italy (DS); Department of Neurosciences (DNS), University of Padua, Padua, Italy (AB)

Correspondence to: Vittorio Fusco, MD, Oncology Unit - SS Antonio e Biagio e Cesare Arrigo Hospital, Via Venezia 16, I-15121 Alessandria, Italy (e-mail: vittoriofusco1@tin.it).

We acknowledge Antonuzzo and colleagues for their correspondence in the Journal (1), reporting for the first time a case of osteonecrosis of jaw (ONJ) after regorafenib treatment: Their report is robust and adds to the growing knowledge about this serious complication. However, in our opinion, some details are missing in order to establish a clear relationship between ONJ and regorafenib exposure.

Previous anticancer treatment should be reported. Regorafenib is usually prescribed as third or further line treatment of metastatic colorectal cancer after standard therapy, including chemotherapy (oxaliplatin- and irinotecan-based schemes) and biologicals (bevacizumab or aflibercept, and/or anti-epidermal growth factor receptor [EGFR] agents in case of all-RAS wild-type status). Readers should be informed if the patient received an antiangiogenic agent such as bevacizumab or aflibercept previously. These drugs have been associated with ONJ (2–4). Therefore, it is important to know whether the patient has been exposed to bevacizumab or aflibercept. If this is the case, important information such as exposure time prior to regorafenib, time on the medication, dosing schedule, and cumulative dose are needed.

Furthermore, dental history and the presence of dental disease are important risk factors for ONJ (2). Thus, the report should provide a detailed history about oral health and dental disease such as endodontic or periodontal infections and the presence of ill-fitting dentures prior to regorafenib treatment. Did the patient receive routine dental evaluation and x-rays before or during the therapy with regorafenib, and/or any previous antiangiogenic drug treatment? It is also very interesting to know whether any dentoalveolar surgical procedure (eg, tooth

extraction, implants) was performed before, during, or after regorafenib administration.

Because medication-related ONJ is still highly debated, even in the definition and frequency estimations (5), well-documented case reports of ONJ after nonantiresorptive drugs, including clinical history and imaging, are welcome in the absence of large and prospective studies in this setting.

#### **Notes**

Cesar Migliorati is consultant for Amgen and Colgate. The other authors have no conflicts of interest to disclose.

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