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Rapid Communication Open Access

Oral Toxicity: the Unsought/Unthought in the Treatment for Head and Neck Cancer with Cetuximab plus Radiotherapy

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Rapid Communication

I read with great interest the recently published article by Dr. Musio and colleges [1], stating that Cetuimab-induced mucositis might differ from that caused by other drugs and would further discuss this very issue. Although the only one randomized phase III study compared patients treated with Cetuximab plus radiation therapy versus radiation therapy alone did not show significant difference regarding oral toxicity [2-4] between the two treatment groups, there is now a growing body of evidence in the clinical practice and in the literature as well that Cetuximab may raise the risk of developing severe oral toxicity when combined with radiotherapy.

Shortly after the publication of this randomized trial, reports describing severe dermatologic and oral toxicity after treatment with Cetuximab plus radiotherapy began to appear, suggesting that Cetuximab might be more toxic than as reported in the Bonnerian trial [5-7]. It is difficult to precisely delineate the oral toxicity of Cetuximab, inasmuch as there is only one randomized trial. In spite of the fact that the evidence of oral toxicity caused by Cetuximab comes in large part from retrospective studies and case series and from commonsense in the clinical practice, underreporting in the randomized trial could not be rule out.

Although conducting a second randomized trial is now not any more possible, as radiation therapy alone is no longer the standard care of head and neck cancer, oral toxicity of Cetuximab could be delineated from other randomized trials. The addition of Cetuximab to Cisplatin-based chemoradaition in the RTOG 0522 phase III study [8] did not result in improved clinical outcomes, but in higher rates of grade 3-4 mucositis (45% vs. 35%, P=0.003) and skin reactions (40% vs. 17%, P<0.0001). In a prospective community-based study, higher incidences of skin and oral toxicities have been also reported [9].

Obviously, it would be never possible to accurately delineate the oral toxicity caused by Cetuximab in the context of multimodal therapy, inasmuch as there is overlap of toxicities. However, some morphological characters of mucositis [10] could be helpful to distinguish Cetuximab-induced mucositis from that typically associated with chemotherapy and radiation therapy. Time to manifest might also partially help to differentiate Cetuximab-induced oral toxicity. Late manifestation of toxicities does not exclude the cumulative synergistic toxicity of the drug.

In the general oncological practice, poor prognostic factors such as advanced age, poor performance status, and several co-morbidities corresponds with the preference to use Cetuximab as alternative to conventional chemotherapy [11]. However, this clinical practice might run a special risk. On the one hand, the benefit from adding Cetuximab to radiotherapy [4] evaporates in this subgroup of patients. On the other hand, comprehensive data on interaction between radiation and targeted therapy in general and particularly in those patients are lacking. Using Cetuximab in a group of patients with poor prognosis, where the balance between efficacy and toxicity is less favorable, remains also the paradoxical practice of current head and neck oncology.

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