



Letter to the editor

Dramatic response under combination of immune-oncology in head & neck cancer included in the Condor study: A case report



Immune checkpoint inhibitors have changed the outcome of several tumours. Immune checkpoint inhibitors including anti-programmed cell death-1 (PD-1) monoclonal antibodies (mAb), have demonstrated efficacy in head and neck squamous cell carcinoma (HNSCC). Siu et al. reported the clinical benefit of durvalumab (an anti-programmed cell death ligand-1 (PD-L1)mAb), and durvalumab combined with tremelimumab (a selective human IgG2 mAb against anti-cytotoxic T-lymphocyte associated antigen-4 (CTLA-4)) in recurrent or metastatic (R/

M) HNSCC with low/negative PD-L1 expression (tumor cells [TCs] > 25%) [1]. This phase 2 trial evaluated durvalumab, durvalumab plus tremelimumab and tremelimumab alone for patients with R/M HNSCC. Durvalumab alone or in combination, showed clinical benefit with an objective response rate of 9.2% and 7.8% respectively.

Here, we report a dramatic response for a patient included in the Condor study.

This was a 42 year old man with no past history of tobacco or

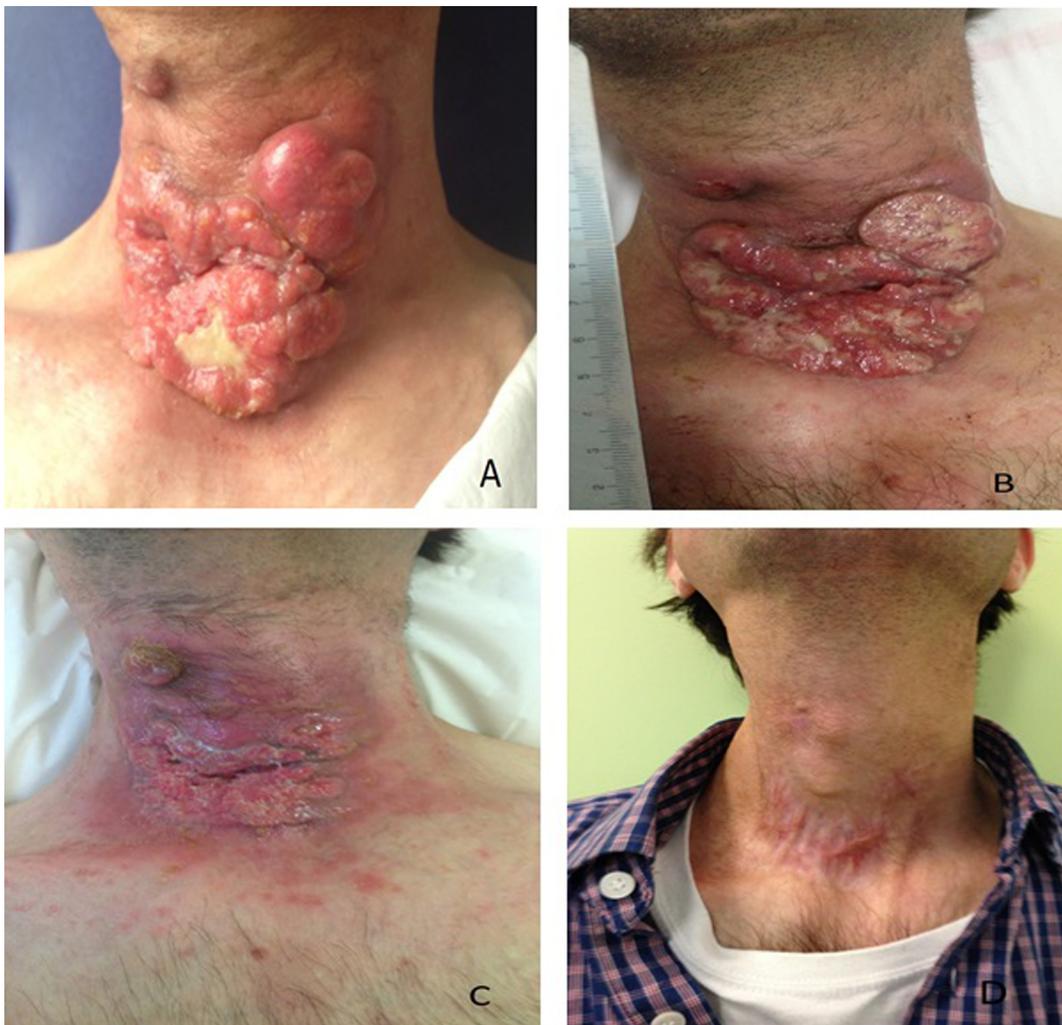


Photo 1. (A–D) Photo of the neck cutaneous tumours at baseline (A), after 15 days (B) at first evaluation – 2 months (C) and one year later (D).

<https://doi.org/10.1016/j.oraloncology.2019.01.002>

Received 20 December 2018; Received in revised form 29 December 2018; Accepted 5 January 2019

Available online 11 January 2019

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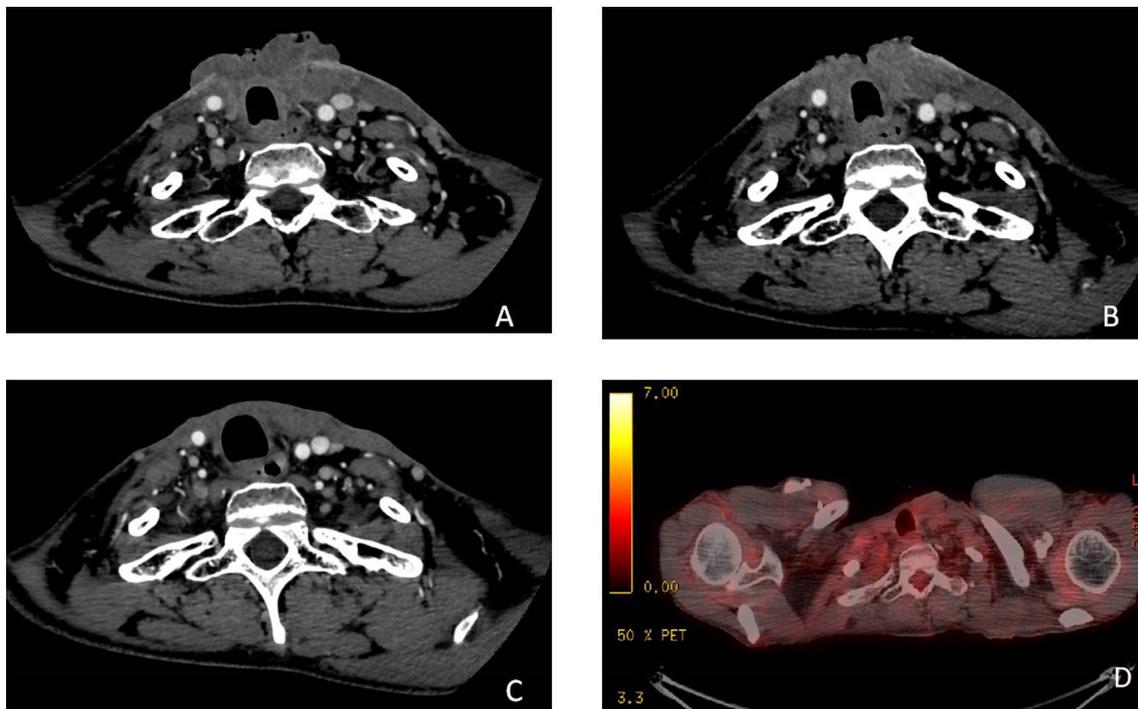


Fig. 2. (A–C) CT scan at baseline, 2 months, 1 years; (D) pet scan at 1 years.

alcohol use. In June 2012 he presented a locally advanced squamous cell carcinoma of the hypopharynx, P16 positive, treated with 6 courses of Docetaxel, platinum, 5FU (TPF) in a neoadjuvant setting. Evaluation showed a complete response on the primary tumour and partial responses (PR) on cervical lymph nodes. He underwent a surgical dissection in October 2013 followed by definitive radiation therapy associated with cetuximab ending in February 2014. Eight months later, he had a relapse with new metastatic thyroid lesions. He was treated by thyroidectomy. A few months later he relapsed with multiple cervical cutaneous metastases. In June 2015 chemotherapy with platinum, 5FU and cetuximab was started and continued until October 2015, obtaining stable disease as best response. Due to progression, he was addressed to our institution to be considered for the Condor study.

At the screening visit he presented several cervical lymph nodes, neck cutaneous infiltration of all the anterior neck (Photo 1A – Fig. 2A) and lung metastases.

He started on a combination of durvalumab and tremelimumab on December 23rd 2015. Fifteen days after starting treatment he presented a significant clinical change in tumours with a decrease in size associated with inflammatory process (Photo 1B). At first evaluation, the CT scan confirmed the partial response (PR) (Fig. 2B) given the benefit in symptoms (Photo 1C). One year later, the patient was still in PR with persistence of lymph nodes associated with a dramatic cutaneous control with no evidence of cancer (Photo 1D, Fig. 2C). A PET scanner was realized and no cutaneous hypermetabolism was found (Fig. 2D).

During treatment he did not experience any toxicity due to the experimental treatment.

According to the protocol, treatment was stopped after 12 months. He presented with new pleural lesions three months later and the combination was re-started with stable disease as best response. Two years later the patient is still alive.

Discussion

Here, we present a response with durvalumab and tremelimumab in a patient with hypopharynx squamous cell carcinoma. Immune check point inhibitors have demonstrated efficacy in R/M HNSCC [2,3]. Siu et al. reported that in patients with R/M HNSCC and low or no PD-L1 tumor cell

expression, durvalumab and durvalumab + tremelimumab resulted in clinical benefit with minimal difference between the two arms [1]. This case report shows benefit with the combination of durvalumab and tremelimumab. Siu et al. reported a median time to response of 2.0 months, 4.1 months for the combination and durvalumab monotherapy arms, respectively. This case report demonstrated an improvement in response, which occurred in less than 15 days. In addition, this case showed, an inflammatory phenomenon at the lesion site which occurred in the first fifteen days. This phenomenon should be monitored for patients with HNSCC due to the risk of dyspnea.

In second line with cytotoxic treatment, the median duration of response has been reported at 4 months for cetuximab and 7 months for paclitaxel [4]. The median OS was limited with historical treatments quite the contrary to immune check point inhibitor notably for some patients with long OS as described by Ferris et al. [5]. As our case report, some patients have presented a prolonged outcome with an estimated OS rates at 24 months at 16.9%. This prolonged outcome was irrespective of PDL-1 or HPV status.

In conclusion, in this case report the combination of durvalumab and tremelimumab showed antitumor activity in the treatment of a patient with R/M HNSCC. Further investigation is required.

Conflict of interest statement

Ravaud is member of Global, European and/or French advisory board in RCC for Pfizer, Novartis, BMS, received institutional grant support by Pfizer and Novartis and housing and travelling support for meeting by Pfizer, Novartis and BMS. Daste received housing and travelling support for meeting by BMS and Merck.

Acknowledgement

The CONDOR study was sponsored by AstraZeneca.

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