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Treatment of squamous cell carcinoma of the anal canal (SCCA): a new era?

There are no therapies available after progression on cisplatin and 5-FU that can improve survival for patients with squamous cell carcinoma of the anal canal (SCCA). Recently, two studies have been published [1, 2] that open the era of checkpoint inhibitors in SCCA.

The use of anti-PD-1 therapy in SCCA is possible because the human papillomavirus (HPV) plays a primary role in SCCA tumorigenesis. The risk of this malignancy is increased in patients suffering from disorders associated with immunosuppression [3], because this predisposes the anal epithelium to HPV infection.

In patients with SCCA, HPV is present in ~90% of patients with metastatic anal cancer. Furthermore, HPV is associated with an increased risk of cancer of the head and neck, cervix and penis. Cancerogenesis mediated by HPV infection is related to the viral oncoproteins and these oncoproteins may have implications for the rational design of immunotherapy trials in SCCA [4].

Ott et al. [1] have recently published data concerning pembrolizumab in patients with SCCA. In this group of patients, pembrolizumab showed an overall response rate of 17% with 42% of stable disease and a disease control rate of 58% with a median duration of 3.6 months. Median progression free survival was 3.0 months and median OS was 9.3.

Data have also been reported on nivolumab in SCCA: Morris et al. [2] reported a median progression-free survival of 4.1 months and median overall survival of 11.5 months with a durable response of 78% in SCCA patients treated with nivolumab, with few side-effects reported. Interestingly, pre-treatment expression of PD-1, CD-8, LAG-3 and TIM-3 showed a correlation with response to nivolumab [2].

These trials open the era of checkpoint inhibitors in SCCA. Furthermore, several studies have demonstrated that NRAS and KRAS genes are wild-type in patients with squamous cell anal carcinoma [5, 6]. This suggests that cetuximab or panitumumab could be a valid treatment strategy for these patients. Cetuximab or panitumumab may have an effect on the immune response by two mechanisms: complement-dependent cytotoxicity and complement-dependent cell-mediated cytotoxicity.

It will be very interesting to demonstrate in future studies whether there is an association between immunotherapy and anti-EGFR therapy in SCCA.

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Including Lynch syndrome in personalized prognostication and follow-up of stage II and III colon cancer

We read with interest the paper by Dienstmann et al. [1], in which the authors found that incorporating microsatellite instability (MSI), *BRAF* and *KRAS* mutational status to overall

survival models with TNM staging increases prognostic accuracy in stage II and III colorectal cancer (CRC) patients.

The data presented prompts some considerations on the identification of Lynch syndrome (LS) in CRC patients. As LS is known to account for ~3.3% of all CRCs [2] and approximately 1 in 5 CRC patients with high MSI, a conservative estimate of the number of LS CRC patients in this study is 220 (3% of 7326 CRC