A CASE SERIES OF NEOADJUVANT IPILIMUMAB AND NIVOLUMAB IN 2 PATIENTS WITH LOCOREGIONAL MUCOSAL MELANOMA

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**Background** The standard of care for locoregional mucosal melanoma is wide local surgical resection. However, these surgeries are often in anatomically challenging areas, can be highly morbid, and tumors often recur despite negative margins.

**Methods** We report two cases of patients (labeled as UCM1 and UCM2) with locoregional mucosal melanoma from two different primary sites (vulvovaginal and sinonasal) who were not candidates for surgical resection at time of diagnosis. Patients underwent up to a total of 4 cycles of combination ipilimumab and nivolumab and, if treatment efficacy was demonstrated, continued on maintenance nivolumab. Pre-treatment biopsies were analyzed with bulk RNA-sequencing to identify the relationship of a T-cell inflamed microenvironment as well as the presence of different checkpoint inhibitor receptors with treatment response to immunotherapy.

**Results** One patient (UCM2) had a partial response to upfront immunotherapy and did not require surgical resection, whereas another patient (UCM1) initially responded but then progressed on treatment. UCM1 had a higher T-cell inflamed signature score compared to UCM2, however, also had higher levels of alternative checkpoint inhibitor receptors, including HAVCR2 (encoding TIM-3) and TIGIT. UCM1 also highly expressed LILRB4, which is a receptor expressed on a variety of immune cell types (notably macrophages) that negatively regulates tumor immunity and has been postulated to be a target for immunotherapy. Treatments were overall well tolerated with grade I/II dermatitis developing in both patients.

**Conclusions** These cases provide support that a subset of patients with locoregional mucosal melanoma may benefit from neoadjuvant immunotherapy. Further prospective studies should be done to compare outcomes, including rates of tumor recurrence, between neoadjuvant immunotherapy and conventional wide local surgical resection.

**REFERENCES**


**Ethics Approval** This study was obtained with IRB approval with informed consent obtained from participants: IRB15–0837

Abstract 563 Figure 1

Canonical markers are shown for cytotoxic, NK, and inhibitor cells obtained from bulk RNA-sequencing of tumor samples (obtained at initial biopsy) from two patients, UCM1 and UCM2. UCM1 initially responded to immunotherapy but then relapsed after 4 cycles and ultimately required surgical resection, despite UCM1’s tumor having a higher T cell inflamed score (using a T cell inflamed signature score from Gajewski et al. Cancer J 2010; 16: 399-403).While UCM2 had a relatively lower T-cell inflamed score, the patient also had lower levels of other checkpoint receptors (such as HAVCR2, encoding TIM-3, and TIGIT) and had an excellent response to immunotherapy and did not require surgical resection.

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