VEDOLIZUMAB PLUS ANTI-PD1 ANTIBODY IN ADVANCED MELANOMA PATIENTS WITH INFLAMMATORY ENTEROCOLITIS

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Background Use of immune checkpoint inhibitors in advanced melanoma is challenging in patients with a history of immune therapy related colitis or pre-existing inflammatory bowel disease (Crohn’s disease or ulcerative colitis).1 Vedolizumab is a gut-selective, anti-integrin antibody that binds to the α4β7 integrin on circulating leukocytes and inhibits their trafficking into the intestinal epithelium (figure 1).2 There is limited clinical experience of using Vedolizumab in combination with anti-PD1 antibody in melanoma patients with inflammatory enterocolitis.3 We present outcomes of a cohort of advanced melanoma patients with inflammatory enterocolitis who concurrently received Vedolizumab and anti-PD1 antibody.

Methods In this retrospective single-institution study, records of advanced melanoma patients with a history of inflammatory enterocolitis were reviewed. Patients who received anti-PD1 antibody (Pembrolizumab, Nivolumab), concurrently with Vedolizumab were selected for analysis.

Results Nine patients with stage III/IV cutaneous melanoma and pre-existing enterocolitis received Vedolizumab plus anti-PD1 antibody (table 1). A total of 96 doses of anti-PD1 antibody were administered concurrently with Vedolizumab (56 doses), with each patient receiving at least 7 doses of anti-PD1 antibody. Vedolizumab was administered intravenously (300 mg at weeks 0, 2 and 6 weeks and then every 8 weeks) along with Pembrolizumab (200 mg every 3 weeks) or Nivolumab (240 mg every 2 weeks or 480 mg every 4 weeks). Patients had a history of grade 3-4 colitis from prior checkpoint inhibitor therapy (n=4), Crohn’s disease (n= 4), and ulcerative colitis (n= 1). Seven patients were negative for BRAF V600 mutation. Six patients had no recurrence of colitis symptoms while on anti-PD1 antibody therapy. Three patients with recurrence of colitis had a prior history of Crohn’s disease (n=2), and grade 3 check-point inhibitor related colitis (n= 1). All patients with recurrence of colitis symptoms did not have melanoma progression while receiving Vedolizumab plus anti-PD1 antibody. Overall, seven patients did not experience melanoma progression on therapy. One patient had a complete response. Two patients were able to complete adjuvant treatment with anti-PD1 antibody, without melanoma recurrence on follow-up. Vedolizumab infusions were well tolerated, and no treatment related side effects were noted.

Conclusions Concurrent Vedolizumab appears to allow treatment with anti-PD1 antibody in advanced melanoma patients with pre-existing inflammatory enterocolitis. Prospective studies are needed to definitively determine the safety and anti-melanoma efficacy of this combination.

REFERENCES

Ethics Approval This study was reviewed and approved by the University of Iowa Institutional Review Board IRB 01, under IRB# 202202583. A waiver of informed consent was granted by the IRB per 45 CFR 46.116 (f)(3)