

3. RELAPSED/REFRACTORY MULTIPLE MYELOMA

IMMUNE EFFECTOR CELL COLITIS DURING TREATMENT WITH AN ANTI-BCMA BISPECIFIC ANTIBODY

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Immune effector cell (IEC) associated colitis is a rare side effect observed after both anti BCMA as well as after anti CD19 directed CAR T cell therapy. In a recent series of 14 patients, IEC colitis presented with acute-onset diarrhea and abdominal pain, starting median three months after CAR-T therapy.¹ It is less recognized that this type of colitis can also occur after bispecific antibody therapy and this may delay a timely diagnosis. We present a 61 year old female patient with Multiple Myeloma (MM) who received 4th line teclistamab (TEC) therapy and developed a more insidious start of the diarrhea, which was eventually classified as IEC- associated colitis. She received TEC monotherapy according to the standard treatment schedule with weekly dosing in cycles 1-2, developed mild grade 1 CRS during step up dosing and had local skin reactions at the administration site. From the third cycle on, she developed grade 1 diarrhea, liver enzyme elevations and reported progressive fatigue and severe muscle pain in the week after TEC administration. Because of these toxicities, the treatment interval was prolonged to biweekly in cycle 3 and quarter-weekly from cycle 4. After cycle 6, the patient had a rhinovirus upper respiratory tract infection and the diarrhea had progressed to a grade 3 with also severe cramping and abdominal pain. Subsequent microbiological evaluation was negative and she deteriorated clinically with weight loss resulting in cessation of TEC treatment. The MM was in complete remission and patient was referred to the gastroenterologist. Subsequent endoscopy demonstrated a mild ileitis terminalis, a mild antral gastritis and small erosions in the duodenum. Histology showed mild chronic inflammation with granulomas of the duodenum and ileum and focal cryptitis without granulomas in the colon, which may be compatible with Crohn's disease. MRI of the small intestine demonstrated some diffuse wall thickening of the distal jejunum and

ileum. Laboratory tests showed an elevated CRP (30-67 mg/L). Fecal calprotectin levels were high; 2200 ug/g (N < 50) indicative of intestinal inflammation. A diagnosis of an inflammatory enterocolitis was made with a discrepancy between endoscopic and radiologic findings and the clinical and biochemical parameters. Finally, three months after the last TEC administration, prednisone 40 mg was started, leading to decreased diarrhea and abdominal pain, but tapering the prednisone below 15 mg was not possible. By now, she had lost 11 kg of body weight. Ultimately, vedolizumab, an anti $\alpha\beta7$ -integrin directed antibody, was started with fast complete clinical and biochemical resolution of all complaints. Prednisone could be discontinued 3 months after start of vedolizumab. At present, more than a year after cessation of TEC, her MM remains in complete remission. IEC-like colitis may also occur following bispecific antibody therapy. Awareness of this entity in patients presenting with a microbial-negative colitis should prompt early referral to a GI specialist for further work up, including endoscopy with biopsies. The described patient had already shown local skin and systemic inflammatory reactions to TEC treatment, including elevated liver enzymes, myalgia and fatigue, possibly predisposing her to the subsequent development of colitis. Notably, the colitis persisted for several months after discontinuation of therapy. Whether this patient can safely receive bispecific or CAR T-cell therapy, in case of future MM relapse, remains uncertain.

References

1. Fortuna GG, Banerjee R, Savid-Frontera C, Song J, Moran-Segura CM, Nguyen JV, Lekakis L, Fernandez-Pol S, Samraj AN, Naresh KN, et al. Immune effector cell-associated enterocolitis following chimeric antigen receptor T-cell therapy in multiple myeloma. *Blood Cancer J.* 2024;14:180.