

INTESTINAL PERFORATION AFTER CRS AND ICANS IN A CAR-T TREATED PATIENT: A CLINICAL CASE REPORT

G. MENARDI¹, G. TARASCO¹, A. CASTELLINO², M. VIGLIONE³, M.E. BERSIA³,
M. ALLIONE¹, D. DEGIOANNI¹, S. GASTALDI¹, L. INFANTE³, E. GRANDE³,
C. FRUTTERO⁴

1-SSFO, University of Turin; 2- Haematology department of Santa Croce e Carle Hospital Cuneo; 3-Hospital Pharmacy of Santa Croce e Carle Hospital Cuneo;
4-Director of Hospital Pharmacy of Santa Croce e Carle Hospital Cuneo



A relapsed-refractory mantle cell lymphoma patient treated with brexucabtagene autoleucel developed Cytokine Release Syndrome (CRS), Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS). Since day+3 he has been administered 4 doses of tocilizumab 8mg/kg, followed by subsequent administration of dexamethasone 10mg every 6 hours. On day +34 he developed intestinal perforation.

1
On day 34, the patient complained about acute abdominal pain. Imaging revealed acute diverticulitis complicated by perforation and perivisceral collection

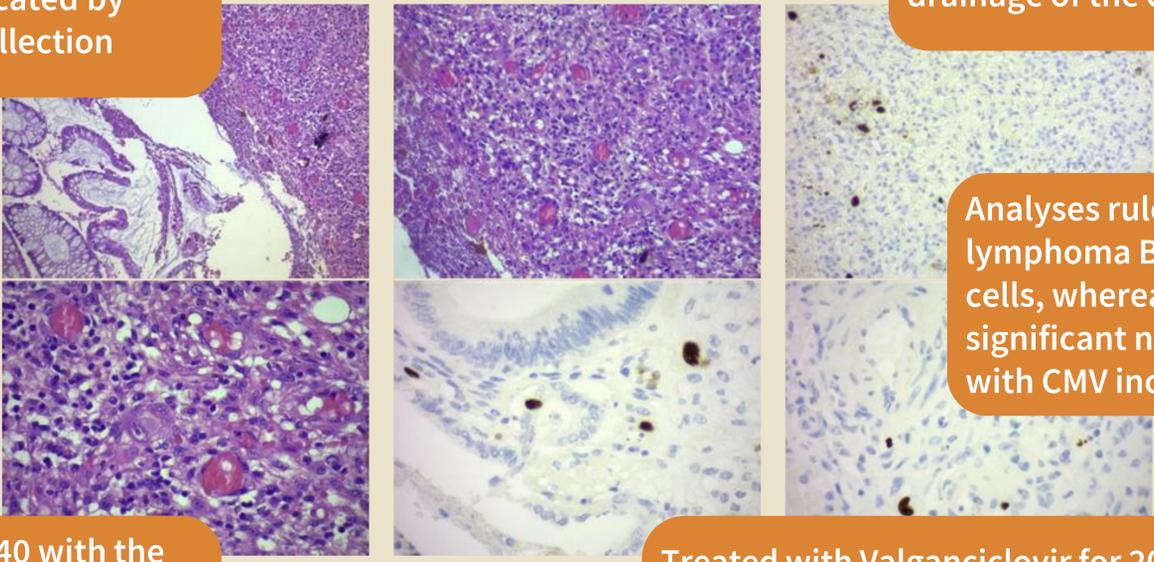


Figure-Histopathological slide from surgery material: diverticulosis with focal acute diverticulitis with suppurative inflammation and adiponecrosis

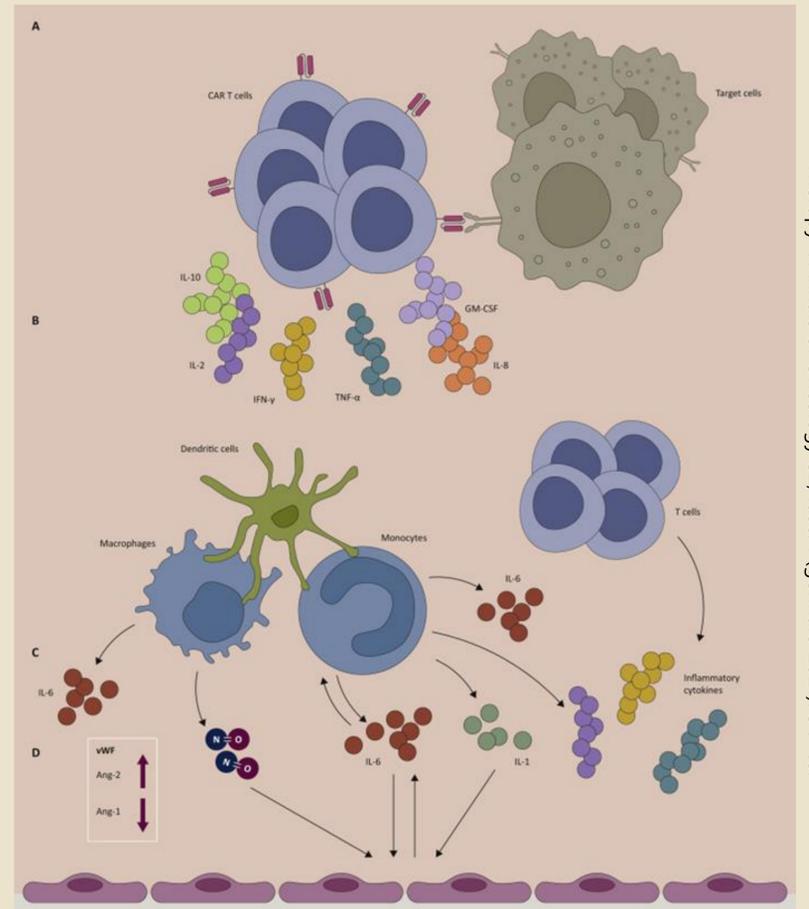
2
The patient had to undergo urgent exploratory laparotomy and colic resection with colostomy packing, lavage and drainage of the cavity

3
Analyses ruled out the presence of lymphoma B cells and infiltrating CAR-T cells, whereas it was clearly evident a significant neutrophil infiltration associated with CMV inclusion.

5
The patient discharged on day 40 with the indication to maintain oral prednisone, interrupted on day 56 without ICANS recurrence. Anti-CMV therapy was suspended on day +59.

4
Treated with Valganciclovir for 20 days with occasional neutrophil support with G-CSF. IGIV supplementation was done on day + 39 according to CAR-T management indications and to minimized the infection risk.

No brexucabtagene autoleucel related intestinal perforation were reported, and **this was the first signalling about this type of reaction in the Italian pharmacovigilance authority** (1-4 on the Naranjo's scale). Intestinal perforation in CAR-T-treated patients is mentioned in the ESMO-guidelines for the management of Immune Effector Cell-Associated Hypersensitivity(ICAH) and a correlation between tocilizumab and intestinal perforations has been suggested(5-8 Naranjo's scale score), as observed in clinical trials and post-marketing analysis among patients with rheumatoid arthritis. **This case underscores the importance of meticulous monitoring and understanding CAR-T therapy intricacies and toxicity management.**



Schubert, M.-L., M. Schmitt, L. Wang, C.A. Ramos, K. Jordan, C. Müller-Tidow, e P. Dreger. «Side-Effect Management of Chimeric Antigen Receptor (CAR) T-Cell Therapy». Annals of Oncology 32, fasc. 1 (gennaio 2021): 34-48.

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