



Background and importance



Our university hospital is involved as a investigator of clinical trials on both CAR-T cell therapies and bispecific antibodies (BsAbs), actively contributing to the development and evaluation of these innovations for the benefit of patients. Both BsAbs and CAR-T cells can trigger CRS through T-cell activation, but comparative data remain scarce.

A bispecific antibody is an engineered antibody designed to simultaneously bind two different antigens or two distinct epitopes. By targeting two molecules at once, it can bring cells into close proximity or modulate multiple biological pathways, enhancing therapeutic efficacy, particularly in oncology and immunotherapy.



A CAR-T cell is a genetically engineered T lymphocyte that expresses a chimeric antigen receptor (CAR) on its surface, enabling it to specifically recognize and kill target cells, such as cancer cells, in an MHC-independent manner. CAR-T cell therapy harnesses and redirects the patient's immune system for targeted immunotherapy.

Cytokine Release Syndrome (CRS) is one of the most common and serious complications of CAR-T and BsAbs therapy. It occurs when:

- CAR-T cells and BsAbs trigger massive immune activation
- The body releases excessive cytokines, especially interleukin-6 (IL-6)
- This inflammatory response can rapidly lead to multiorgan failure
- Early recognition and urgent treatment are essential



Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) is a potentially severe neurological toxicity associated with immune effector cell therapies, particularly CAR-T cells and some bispecific antibodies. It manifests with symptoms ranging from mild confusion and language disturbances to seizures, cerebral edema, and coma, and is thought to result from immune-mediated inflammation affecting the central nervous system.

Materials and methods



Retrospective single-center study



All patients who received CAR-T and bispecific antibodies therapy in clinical trials



01 January, 2018 and 01 July, 2025



Demographics
 CRS's grades using ASTCT criteria
 ICANS's grade using ASTCT criteria
 Treatment with tocilizumab



University hospital of Rennes (France)

Aim and objectives

To assess frequency, timing, and management of CRS and ICANS associated with BsAbs versus CAR-T therapy in clinical trials at our center.

Results



Demographics

	BsAbs population (n = 51)	CAR-T cell population (n = 40)
Sexe		
- Male	34	27
- Female	17	13
Age (in years)		
- Median	67,0	59,1
- Standard deviation	9,0	13,6
Weight (in kg)		
- Median	69,5	77,2
- Standard deviation	16,7	24,7
Recovery	9	20
Death	0	0



CRS and ICANS

CRS	BsAbs population (n = 51)	CAR-T cell population (n = 40)
Yes	9	20
- Grade 1	2	13
- Grade 2	7	5
- Grade 3	0	2
No	42	20
ICANS	BsAbs population (n = 51)	CAR-T cell population (n = 40)
Yes		
-Grade 1	4	8
-Grade 2	4	4
-Grade 3	0	2
-Grade 4	0	2
Not applicable	-	-
No	47	32



Treatment with tocilizumab

	BsAbs population (n = 51)	CAR-T cell population (n = 40)
Total number of patients who received tocilizumab	9	20
Average dose (in mg)	531,1	581,3
Time to administration from the start of CRS (in days)	1,4	3,7
Number of injections per patient	1,2	2,5
Concomitant use of corticosteroids	44,0%	65,0%

Discussion et conclusion

CRS was more frequent with CAR-T cells than with BsAbs in clinical trials, but onset occurred earlier with BsAbs. The CRS grade appeared to be more severe with BsAbs.