4CPS-067

DEVELOPMENT AND MANAGEMENT OF ICANS: RISK FACTORS FOLLOWING CD19 CAR-T THERAPY IN LYMPHOPROLIFERATIVE DISORDERS

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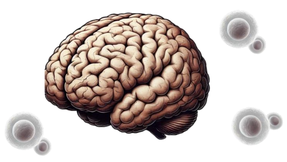
BACKGROUND AND IMPORTANCE



Immune Effector Cell-associated Neurotoxicity (ICANS)

- 1/3 of infused patients.
- Treatment of refractory cases remains unclear.
- Reliable predictive factors are limited.

AIM AND OBJECTIVE

To identify **potential risk factors** in patients treated with **anti-CD19 CAR-T** therapy for developing:

- **Any-grade-ICANS.**
- **Significant-grade-ICANS**.

MATERIALS AND METHODS

Ambispective (retrospective + prospective), single-center observational

Observational.

Patients with *hematological diseases* treated with *commercial anti-CD19 CAR-T.*

Sample size: Estimated 100 patients.

Definitions

"Ani-grade toxicity": grades 1-4.

"Relevant toxicity" grades 2-4 (requires specific treatment)

"Severe toxicity" grades 3-4.

Univariate. Two-tailed t-tests (continuous variables); Pearson's chi-squared or Fisher's exact tests (categorical variables).

Multivariate. Step-wise method based on variables that were significant in the univariate analysis.

RESULTS

101 **Patients, final analysis**

35.6 % **$ICANS_{1-4}$**

19.8 % **$ICANS_{2-4}$**

11.9 % **$ICANS_{3-4}$**

83.3 % **$ICANS_{3-4}$**

Univariate analysis

	$ICANS_{1-4}$	p	$ICANS_{2-4}$	p
Risk factors and predictive biomarkers related to ICANS				
Autoimmune condition				
No	31.9%	0.02	16.5%	0.01
Yes	70,0%		50,0%	
CAR-T therapy				
Tisa-cel	21.4%	0.02	11.9%	0.09
Axi-cel	45.7%		25.4%	
CRS grade 2-4				
No	21.3%	<0.01	9.8%	<0.01
Yes	57.5%		35,0%	
CRS grade 3-4				
No	33,0%	0.03	17.7%	0.02
Yes	80,0%		60,0%	

Treatment association to ICANS				
Number of tocilizumab doses	Positive lineal trend	<0.01	Positive lineal trend	0.03
Number of previous lines	Positive lineal trend	0.05	Positive lineal trend	0.04

Multivariate analysis (p<0.05)

$ICANS_{1-4}$ AUC=0,84 — Type of CAR-T, time infusion-CRS onset, D-dimer day 0 and IL-6 day +3.

$ICANS_{2-4}$ AUC=0,81 — Autoimmune comorbidity, number of prior lines, ≥2 CRS, IL-15 and GM-CSF day 0.

Univariate analysis

	$ICANS_{1-4}$	p	$ICANS_{2-4}$	p
Risk factors and predictive biomarkers related to ICANS				
Age (years)				
No ICANS	57.9	0.05	55.7	0.86
ICANS	51.38		55	
CRS duration (days)				
No ICANS	4.4	0.01	4.7	0.02
ICANS	6.7		7.3	
Infusion to CRS (days)				
No ICANS	2.7	<0.01	2.5	<0.01
ICANS	1.4		1.2	
LDH day 0 (UI/L)				
No ICANS	278.3	<0.01	281.2	<0.01
ICANS	415.8		514.6	
Pre-infusion MTV (mL)				
No ICANS	231.2	0.02	258.6	<0.01
ICANS	574.0		678.9	
IL-1 day 0 (pg/ml)				
No ICANS	0.3	0.63	0.3	<0.05
ICANS	0.3		0.4	
IL-6 day 0 (pg/mL)				
No ICANS	12.5	0.02	13.9	<0.01
ICANS	34.7		46.7	
D-Dimer day 0 (ng/ml)				
No ICANS	545	<0.01	728	0.21
ICANS	1,241		1,075	

Univariate analysis

	$ICANS_{1-4}$	p	$ICANS_{2-4}$	p
Risk factors and predictive biomarkers related to ICANS				
CRP day 0 (mg/dl)				
No ICANS	41.1	0.05	39.7	<0.01
ICANS	72.85		105.6	
IL-15 day 0 (pg/ml)				
No ICANS	34.0	0.01	35.3	<0.01
ICANS	38.5		54.9	
GM-CSF day 0 (pg/ml)				
No ICANS	2.3	0.3	2.2	<0.01
ICANS	2.6		3.2	
Ferritin day 0 (ng/mL)				
No ICANS	1,738.6	0.33	1,620.1	0.04
ICANS	2,566.8		3,736.9	
LDH day 3 (UI/L)				
No ICANS	216,0	<0.01	219.4	<0.01
ICANS	333.6		414.7	
IL-6 day 3 (pg/mL)				
No ICANS	355.7	<0.01	810.6	<0.01
ICANS	3,168.5		3481.3	
IL-15 day 3 (pg/ml)				
No ICANS	35.7	<0.01	40.0	<0.01
ICANS	79.4		94.9	
D-Dimer day 3 (ng/ml)				
No ICANS	741.5	<0.01	960.0	<0.05
ICANS	1,713.1		1,616.3	

CONCLUSION AND RELEVANCE

- ICANS development appears to be linked to **baseline patient characteristics, CAR-T product**, **tumor burden**, **CRS development** (including **tocilizumab** doses), and **pro-inflammatory markers** before and after infusion.
- A deeper understanding of these factors may help anticipate earlier treatment interventions to **improve patient outcomes.**

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