Rapid Increase in Blood CD19 CAR-T Vector Load during the First five Days Post Infusion Is Associated with Severe ICANS

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Introduction

- Quantifying chimeric antigen receptor T cell (CART) vector load in peripheral blood may predict outcomes and help manage toxicity in patients receiving axicabtagene ciloleucel (axi-cel) treatment for R/R Large B cell lymphoma (LBCL).
- High concordance of the Idylla™ Platform, a point-of-need, real-time assessment of CART vector load from peripheral blood, with standard droplet digital polymerase chain reaction (ddPCR) method was previously reported (98.6%).
- Here, we correlate CART vector load measurements with toxicities and clinical outcomes.

Methods

- 100 subjects at Stanford, Mayo Clinic, and Vanderbilt receiving axi-cel for LBCL were enrolled.
- Blood samples were collected for ddPCR (copies per cells) and Idylla (estimated copies per uL) vector load measurement to derive pharmacokinetics at pre-lymphodepletion and on days 1, 3, 5, 7, 14, and 28 post-infusion.
- CART vector load was log-transformed, and data points from days 1 to 5 were linearly interpolated.
- Patients with fewer than three measurements were excluded.
- A slope, representing CART vector load change from Day 0 to Day 5, was calculated with the intercept set to zero using linear models.
- Predictive analysis used LASSO to assess severe toxicity risk and identify associated key features. Toxicities were graded using ASTCT consensus grading.
- Progression-free survival (PFS) was analyzed using Kaplan-Meier methods, stratifying patients into high and low groups based on median slope during the first five days post-infusion, with log-rank tests comparing PFS.

Results

Demographics	Study Participants (n=100)
Age at Apheresis (median [IQR])	68 [58.75, 74]
Sex (%)	
Female	38 (38)
Male	62 (62)
Prior Lines of therapy (%)	
1	52(52)
>2	48(48)
GCB Cell of Origin (%)	56 (56)
ECOG (%)	
0	13 (13)
1	78 (78)
2+	9 (9)
Stage at Apheresis	
1	5 (5)
2	9 (9)
3	14 (14)
	69 (69)
Disease Type (%)	
DLBCL	94 (94)
HGBCL	4 (4)
Other	2 (2)
Treatment Location (%)	
Stanford	77 (77)
Mayo Clinic	13 (13)
Vanderbilt	10 (10)
Best Response at 6 months (%)	
CR	77 (77)
PR	14 (14)
SD	1 (1)
PD	7 (7)
Length Hospital Stay (median [IQR]) days	14 [11, 17]
Median Follow-up (median [IQR]) days	259 [114, 380]

Table 1.Baseline characteristics of the study participants.

Figure 1A: The Idylla™ System, consisting of the console, the instrument, and a cartridge.

Figure 1B: The Idylla™ system cartridge.

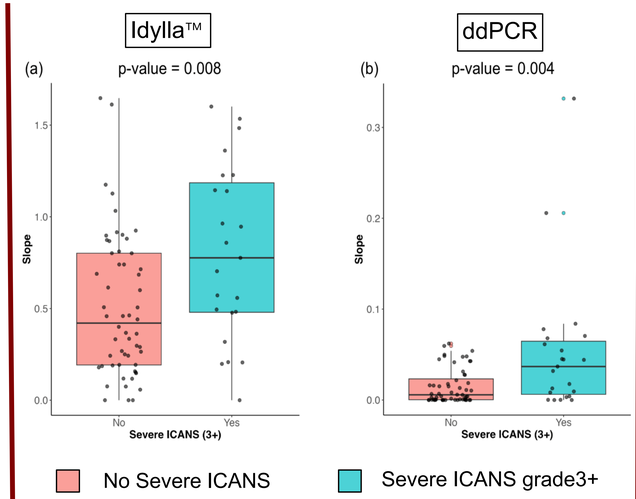

Figure 2: The change in CART vector load represented by the slopes representing CART vector load change from Day 0 to Day 5 as measured by (a) Idylla™ (log estimated copies/µL) and (b) ddPCR (log copies per cell) over first five days after axi-cel infusion for each patient, stratified by ICANS (Grade3+)

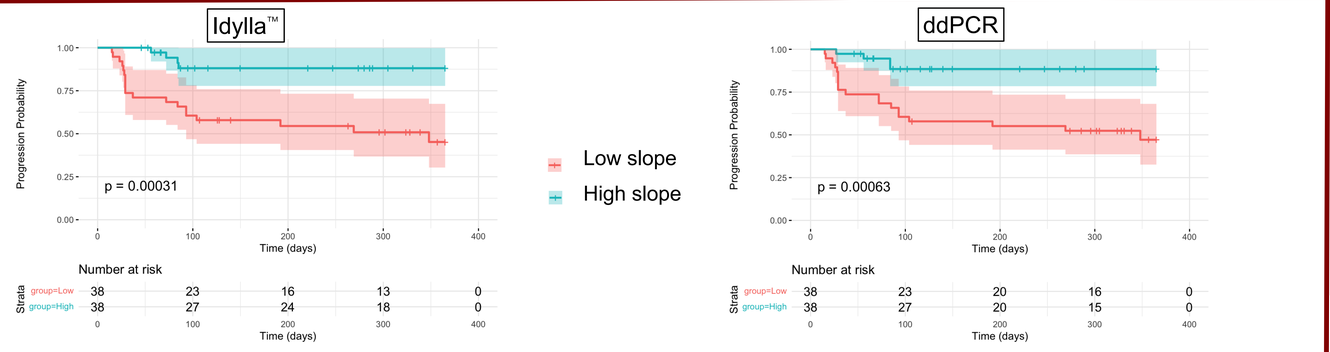

Figure 3: Kaplan-Meier curves showing progression-free survival (PFS) stratified by the median value of rate of change in CART vector load, represented by the slopes as measured by (a) Idylla™ (log estimated copies/µL) and (b) ddPCR (log copies per cell) during the first five days after axi-cel infusion. Patients were categorized into high and low groups based on the median slope value. The p-values from log-rank tests are shown, indicating statistically significant differences in PFS between the high and low groups for both measurement methods.

Conclusions

- The Idylla™ Platform is highly concordant with a validated ddPCR assay and offers rapid, automated CART vector load detection in approximately 90 minutes with only two minutes of hands-on time from blood sample to result.
- The rapid increase in blood CD19 CART vector load during the first five days is associated with severe ICANS.
- Predictive modeling for ICANS severity using LASSO shows Day 3 point-of-need CART vector load using Idylla™ measurement predicts risk of severe ICANS with average AUROC of 0.709. Other key features selected by LASSO are number of prior lines of therapy, pre lymphodepletion Ferritin levels and LDH elevation.
- The change in expansion between Days 0 and 5 as measured by either Idylla™ or ddPCR significantly stratify PFS.
- Point-of- need pharmacokinetic measurements with the Idylla Platform may serve as a complimentary tool to improve toxicity management and survival outcomes in CART therapy.

Support

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