Validated PET-CT Metabolic Tumor Volume (MTV) Threshold Identifies High-Risk Relapsed/Refractory LBCL and Predicts 12-Month Toxicity-Free Progression-Free Survival Post–CAR T Therapy

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Introduction

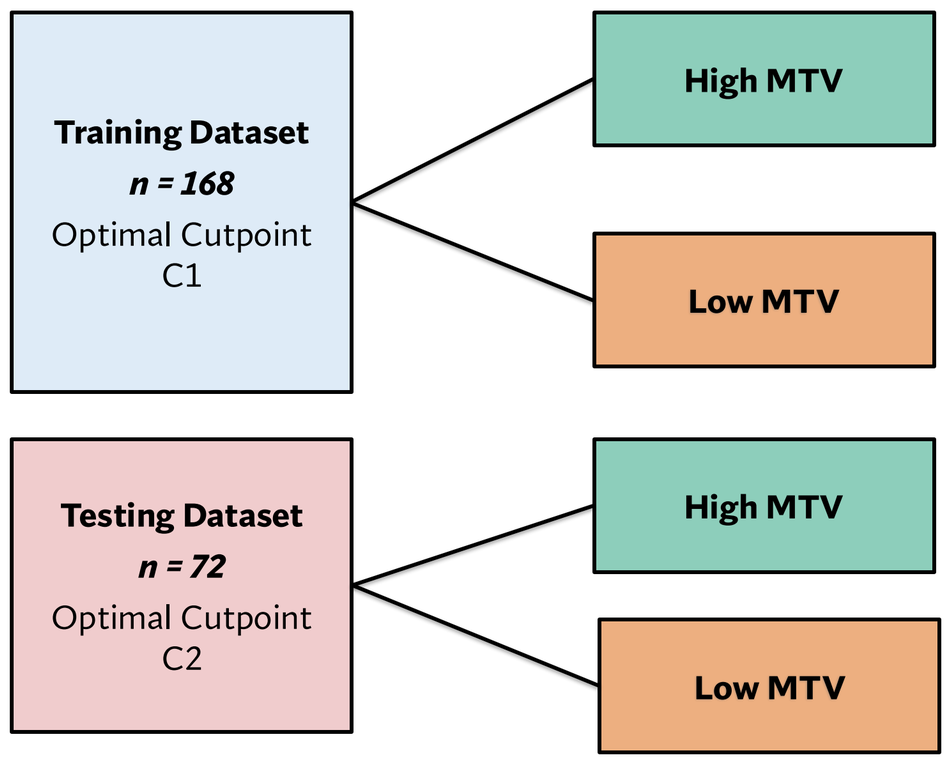
- We aimed to establish a **risk stratification cutpoint for baseline MTV** and applied findings from a training cohort to an independent validation cohort in patients (pts) receiving **CAR-T for R/R LBCL.**
- We also propose **12-month toxicity-free progression-free survival (TFPFS12)** as a composite endpoint.

Methods

- Pts who received **CD19 directed CAR-T** therapy for **R/R LBCL between 2017-2024** with evaluable PET scan (*n=240)*

Stratified random sampling by year of CAR-T infusion (70:30 split)

Compare C1 and C2 with two-sample test statistic



- **TFPFS-12:** no Grade 3 > CRS/ICANS, progressive or stable disease, or non-relapse mortality at **month 12 after CAR-T infusion**

Results

- We identified 239 pts (92% (n=220) axi-cel, 7% (n=17) liso-cel, and 1% (n=2) tisa-cel) with R/R LBCL. A data-driven cutpoint of 125.5 mL was identified in the training cohort (n=167) and was independently validated in the testing cohort (n=72) {McNemar's test: p=0.5} **(Figure 1).**
- Median follow-up = 29.5 months ([IQR]: 18.0, 53.3). Baseline characteristics were similar between MTV groups.

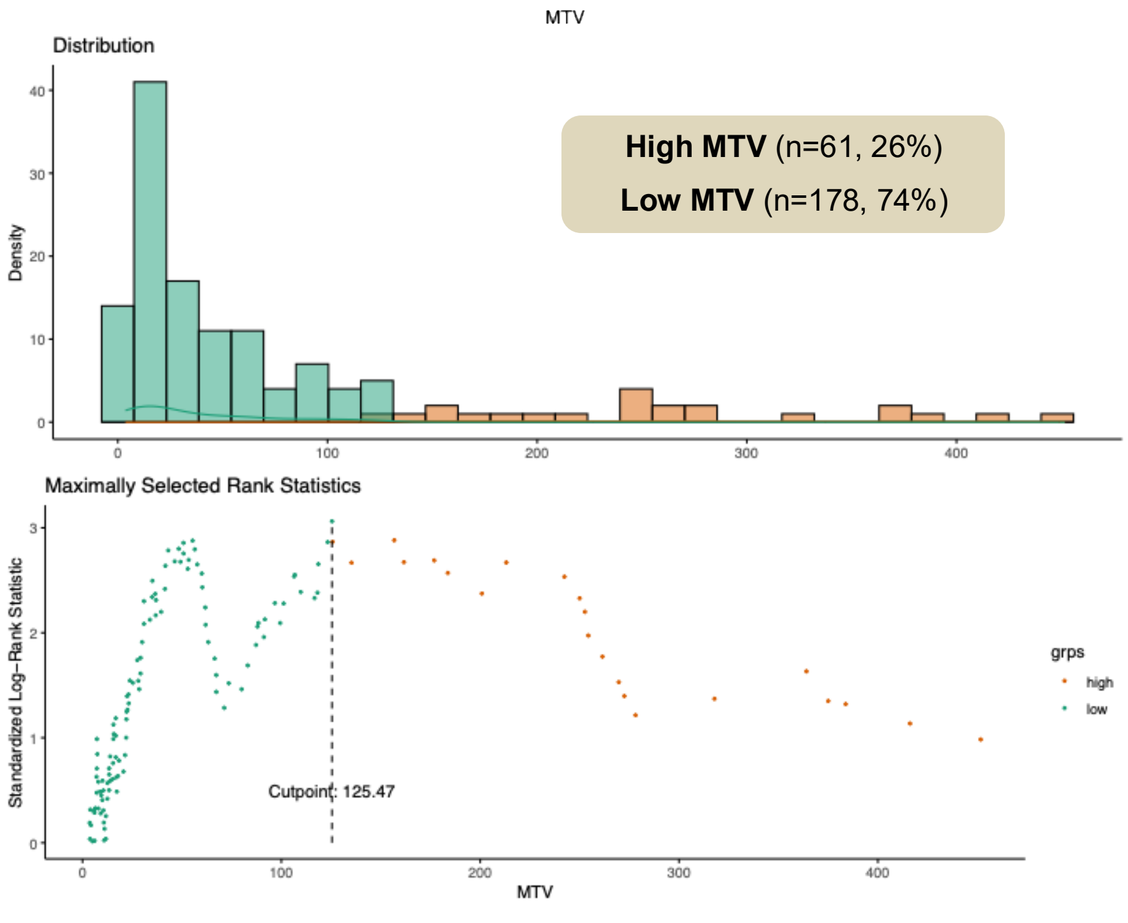


Figure 1: *Optimal cutpoint determination of training dataset, stratifying high vs. low MTV*

- Pre-apheresis LDH had a positive correlation with baseline MTV (r=0.41; p<0.01).
- TFPFS12 rate was 54% (high MTV: 30%, n=18 vs. low MTV: 52, n=91). High MTV was independently associated with worse TFPFS12 on multivariable analysis (OR 0.36, 95% CI 0.17–0.76, p=0.01), adjusted for relevant clinical covariates (**Figure 2).**

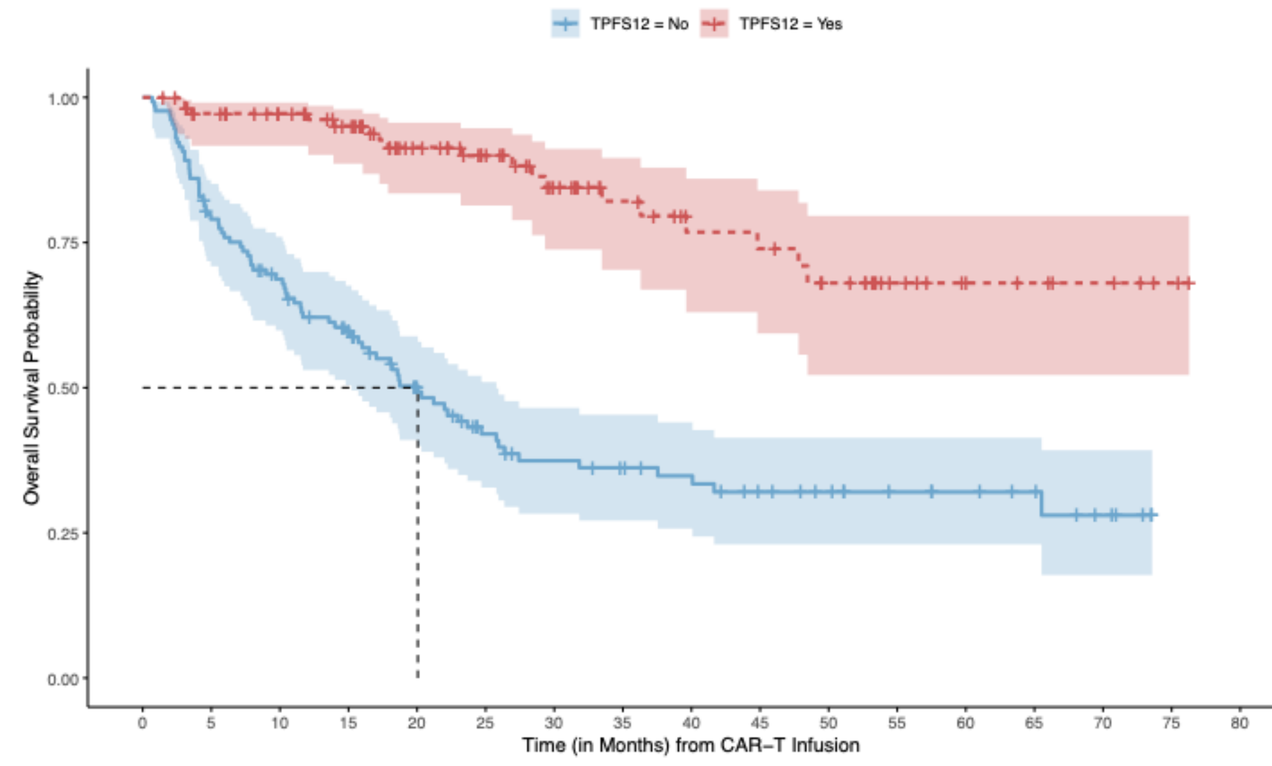


Figure 2: *Overall Survival stratified by TFPRS12 status*

- There were no differences in day 7 and day 14 CART expansion (*P* = 0.2 and *P* = 0.3) **(Figure 3).**
- Multivariable linear regression fit for log-10 transformed median area-under-the-curve over 28 days (AUC-28), MTV group, and relevant clinical covariates showed no significant association between baseline MTV peak expansion and AUC (*P* = 0.3 and P = 0.2).

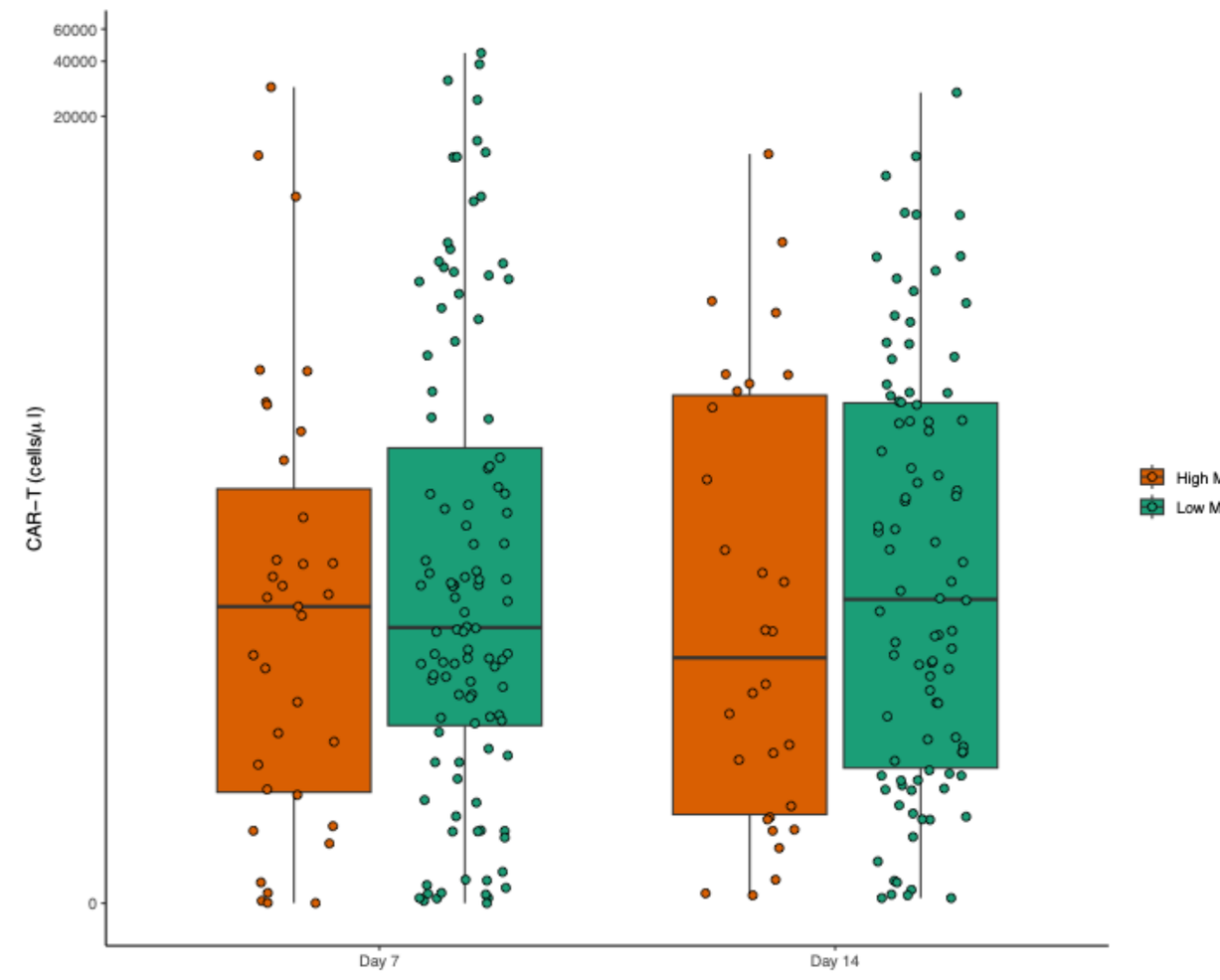


Figure 3: *Boxplot of CAR-T expansion at Day 7 and 14, stratified by MTV category*

Discussion

- This is the largest study to identify through validation that a **baseline MTV cutpoint of >125 mL independently predicts PFS and OS in R/R LBCL** treated with CAR-T, defining a high-risk subgroup with unmet therapeutic need.
- These findings support using MTV for risk-stratification in clinical trials and integrating MTV-guided risk groups with composite endpoints like **TFPFS-12 could refine efficacy and safety assessments.**

The authors have no financial relationships to disclose

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