Large Unstained Cell (LUC) Fraction as an Effective Monitoring Tool for CAR T-Cell Expansion in R/R B-Lymphoid Malignancies

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Introduction

Chimeric antigen receptor T-cell (CAR-T) therapy has emerged as novel therapeutic agent for the treatment of R/r B-Lymphoid malignancies. The Landscape of dysfunctional immune mechanism in peripheral blood Large unstained cell (LUC) fraction post CAR-T remains largely unclear. Knowledge regarding kinetics of CAR-T cells post-infusion is limited and whether these features might have any predictive value in the long term has not been clearly elucidated

Aim

Herein, we describe heterogeneous lymphoid population with unusual morphology, designated as Large Unstained Cell (LUC) fraction as substantial evidence of CAR-T cell expansion in peripheral blood post-infusion especially at the time of peak expansion.

Methods

We studied CAR-T cell expansion post infusion in a total of ten diffuse large B-cell Lymphoma (DLBCL; n= 05) & B-acute lymphoblastic leukemia (B-ALL; n= 05) patients receiving CAR-T cell therapy at our center over a period of twenty-one months (July 2023 – April 2025).

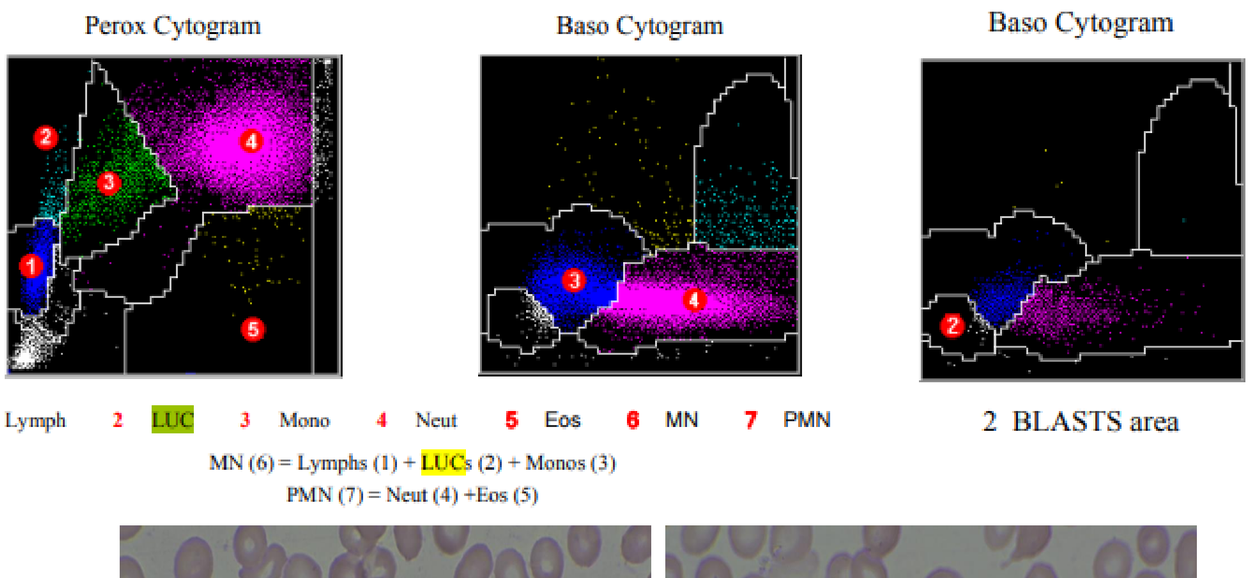
All patients received CAR-T therapy post Fludarabine–Cyclophosphamide conditioning as per protocol.

Peripheral blood parameters monitoring was done on day 0,7, 14 & 28.

Detailed morphological features of the CAR-T cell product as well as CAR-T expansion and persistence after infusion were analysed using following methods:

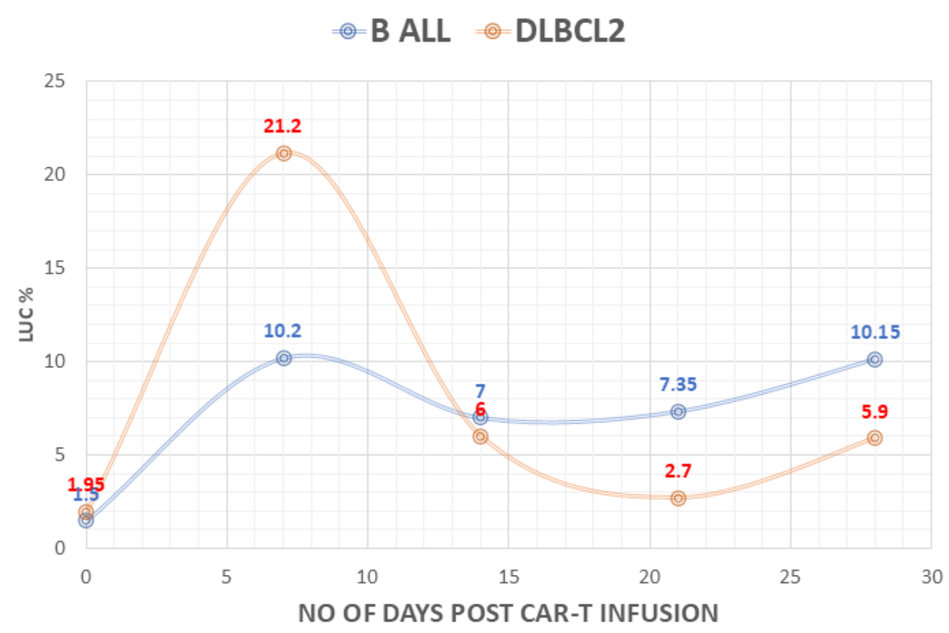
- light microscopy
- complete blood count (CBC)

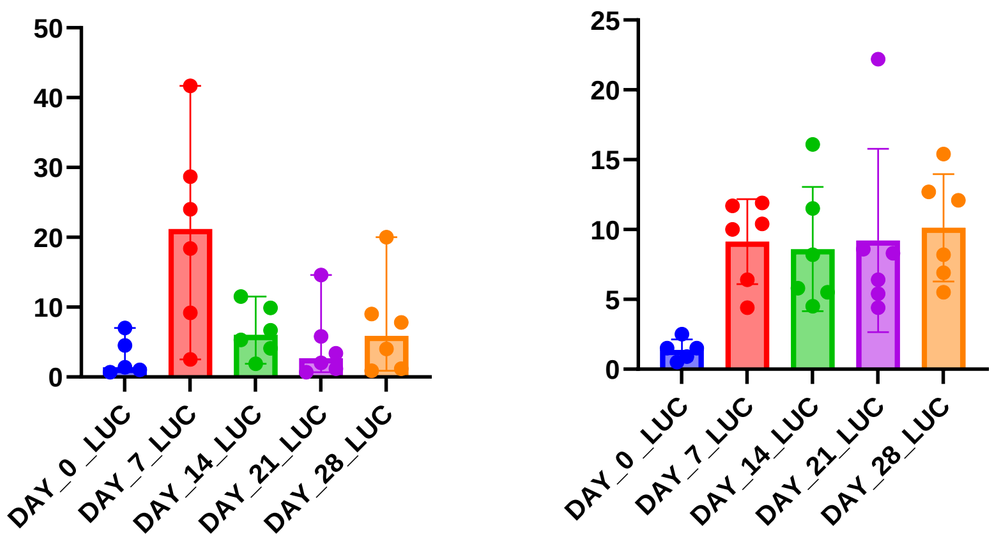
Large Unstained Cell (LUC) parameter was recorded on automated cell counter (Advia 2120i). LUC value on the Perox cytogram may be due to the presence of large atypical lymphocytes, blasts, and/or other large abnormal cells that are peroxidase-negative.



Results

CBC showed a progressive increase of total leukocytes count (TLC), lymphocyte count and LUC fraction with a median peak of day 28 (10-28), day 25 (5-28) and day 14 (5-28) in DLBCL and day 18 (14-28), day 14 (14-22) and day 7 (07-11) in B-ALL respectively. LUC showed a progressive increase from 0.9 – 2.5% at day 1 to a median peak of 14.45% (10-31.7 %) in DLBCL correlating with peak lymphocyte expansion of 24.1-71.9 %. Likewise, B-ALL also demonstrated progressive increase of LUC from 0.7-2.5% to a median peak of 26.35% (17.7-41.7 %) coinciding with median peak lymphocyte % of 73.6% (50.4-98.3 %). Morphological evaluation also showed a gradual increase in heterogenous lymphoid population at the time of peak LUC fraction as well as lymphocyte proliferation.





Conclusion

A careful analysis of lymphocyte trend, LUC fraction and peripheral blood morphology may thus be utilized as simple, cost-effective monitoring tool for proliferation and expansion of CAR-T cells. Furthermore, on comparing the DLBCL to B-ALL; B-ALL shows early proliferation and expansion of CAR-T cells, thus can be explored as early predictor of immune cell related toxicity. LUC fraction emerged as a novel and effective monitoring tool for CAR-T cell expansion post-infusion.

References

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