ELSEVIER

Blood 142 (2023) 7160–7161

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

803.EMERGING TOOLS, TECHNIQUES AND ARTIFICIAL INTELLIGENCE IN HEMATOLOGY

Clinical Utility of Circulating Tumor (ct)DNA Quantity and Kinetics in Patients Undergoing CAR T-Cell Therapy for Relapsed/Refractory Aggressive B-Cell Lymphoma

Imogen Caldwell, FRACP,FRCPA[1,2], Yan Zhuang Yap[1], Mark R Dowling, MBBS, PhD[3,4], Javad Saghebi[5], Aaron Jun Ning Wong[5], Roxane Legaie[1], Rainier Arnolda[1], Clarissa Wilson, MSc, BSc[1], Danielle Ignacio[3], Nicole O'Leary[3], Stephanie Yaung, PhD[6], Bowdoin Su, MD[7], Corinna Woestmann[8], Michael Dickinson, MBBS, D. MDSci, FRACP, FRCPA[3,4], Ella Thompson, PhD BSc[4,1], Piers Blombery, PhD MBBS, FRACP, FRCPA[3,4,1]

[1] Department of Pathology, Peter MacCallum Cancer Centre, Melbourne, Australia
[2] Department of Pathology and Laboratory Medicine, Auckland City Hospital, Auckland, New Zealand
[3] Department of Clinical Haematology, Peter MacCallum Cancer Centre and The Royal Melbourne Hospital, Melbourne, Australia
[4] Sir Peter MacCallum Department of Oncology, The University of Melbourne, Melbourne, Australia
[5] Department of Cancer Imaging, Peter MacCallum Cancer Centre, Melbourne, Australia
[6] Roche Diagnostics Solutions, Santa Clara, CA
[7] Roche Molecular Systems, Santa Clara, CA
[8] Signature Diagnostics GmbH, Potsdam, Germany

Background: CD19-targeted CAR T-cells are approved for relapsed and/or refractory (RR) aggressive B-cell lymphomas. While some patients experience durable remissions, others do not respond or relapse. Improved patient selection and early identification of patients who may need additional therapies are thus necessary. ctDNA is a promising biomarker for prognostication in DLBCL and has the potential to guide therapeutic decisions. We aimed to explore the possible clinical utility of ctDNA quantitation in patients with aggressive B-cell lymphomas undergoing CAR T-cell therapy.
Methods: Twenty-eight patients undergoing CAR T-cell therapy as part of standard of care pathways for RR aggressive B-cell lymphoma were included. Pre- and post-CAR T-cell infusion ctDNA samples were retrospectively analyzed with a panel of over 400 genes relevant to B-NHL using a modified version of the AVENIO ctDNA analysis workflow (Roche; Research Use Only) based on the previously described CAPP-Seq workflow (Kurtz, J Clin Oncol 2018). Peripheral blood was used as a source of germline DNA to allow selection of tumor-specific variants in the ctDNA. ctDNA levels were expressed as mean mutant molecules per mL (MMPM) and ctDNA clearance was determined using a detection cutoff of p = 0.005. ctDNA results were correlated with clinical findings and outcomes including response rate, PFS and OS.
Results: Eighteen male and 10 female patients were included in the analysis (median age 63). Sixteen (57%) patients had a diagnosis of DLBCL while the remainder had transformed FL or MZL (n=6), HGBL (n=4) and PMBL (n=2). Seventeen patients were treated with tisagenlecleucel and 11 with axicabtagene ciloleucel. Twenty-five (89%) patients had stage III or IV disease and 15 (54%) patients had ≥3 lines of prior therapy. The median number of tumor-specific variants in baseline ctDNA samples was 31 (range 1-252). ctDNA levels correlated with metabolic tumor volumes across all time points (Spearman r=0.69, p<0.0001). There was a greater reduction in ctDNA quantity observed in those who achieved CR/PR (n=21) at day 28 vs those who progressed (n=7) (median MMPM log-fold reduction 1.3 vs -0.9). Baseline ctDNA quantity was significantly higher in those with an elevated LDH pre-lymphodepletion compared to those with a normal LDH (median MMPM 228.5 vs 7.6, p = 0.0003). Survival also correlated with baseline ctDNA measurement with patients with a ctDNA quantity above the median of the cohort having a significantly shorter OS compared to those below the median (median OS 6.7 mo vs not reached, p=0.0012). Four patients had no detectable ctDNA at day 28 post CAR T-cell infusion including 1 patient with pseudoprogression on imaging (SUVMax 10) who had no evidence of lymphoma on biopsy and remained in CR. Of the 4 patients who were ctDNA negative at day 28, 3 remained in long-term remission.
In summary, measurement of ctDNA quantity and kinetics shows promising clinical utility in the context of CAR T-cell treatment for aggressive B-cell lymphoma including prediction of outcome and resolving radiological pseudoprogression. Larger prospective cohorts and standardized methodological approaches are required to optimize predictive thresholds for clinical outcomes.

Disclosures Caldwell: *Roche:* Research Funding. **Dowling:** *Gilead:* Honoraria; *Novartis:* Honoraria; *Abbvie:* Patents & Royalties. **Yaung:** *Roche:* Current Employment, Current equity holder in publicly-traded company. **Su:** *Roche:* Current Employment, Current equity holder in publicly-traded company. **Woestmann:** *Employee of Signature Diagnostics GmbH:* Current Employment. **Dickinson:** *F. Hoffmann-La Roche Ltd:* Other: travel, accommodation, expenses; *F. Hoffmann-La Roche Ltd, Amgen, MSD, Janssen, Bristol-Myers Squibb, Novartis, Gilead Sciences, Abbvie:* Honoraria; *Novartis, F. Hoffmann-La Roche Ltd, Takeda, Celgene, MSD, Abbvie, Lilly:* Research Funding; *Novartis, F. Hoffmann-La Roche Ltd, Bristol-Myers Squibb, Gilead Sciences, Janssen, Abbvie, Genmab:* Consultancy.

https://doi.org/10.1182/blood-2023-182999