ELSEVIER

Blood 142 (2023) 3128–3130

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Neurocognitive Outcomes over the First 3 Months after Chimeric Antigen Receptor T-Cell (CAR T) Therapy: Preliminary Findings from a Longitudinal Study

Samantha J Mayo, PhD RN[1,2], Kim Edelstein, PhD CPsych[2], Lori Bernstein, PhD CPsych[2], Tiana Coley, BS[3], Stacey Morrison, MSc[2], Abi Vijenthira, MDMS[3], Manjula Maganti[4], John Kuruvilla, MD FRCPC[3], Michael Crump, MD[3], Sita D. Bhella, MD[3], Robert Kridel[3], Vishal Kukreti, MDFRCP,MSc[3], Chloe Yang, MD[3], Shabbir MH Alibhai, MD MSc[2], Christine Chen, MHPE, MD FRCPC[3], Anca Prica, MDMSc[3]

[1] Lawrence S. Bloomberg Faculty of Nursing, University of Toronto, Toronto, Canada
[2] Department of Supportive Care, Princess Margaret Cancer Centre - University Health Network, Toronto, Canada
[3] Division of Medical Oncology and Hematology, Princess Margaret Cancer Centre - University Health Network, Toronto, Canada
[4] Department of Biostatistics, Princess Margaret Cancer Centre - University Health Network, Toronto, Canada

Introduction

People treated with systemic therapies for cancer may exhibit changes in neurocognitive functioning over time, affecting domains such as memory, processing speed, and executive functioning. There is a need for prospective data regarding neurocognitive outcomes among patients treated with Chimeric Antigen Receptor T-Cell (CAR T) therapy. The purpose of this study was to investigate the trajectory of neurocognitive performance and self-reported cognitive functioning over the first 3 months of CAR T therapy.

Methods

As part of a larger cohort study of patients treated with CAR T, neurocognitive outcomes were assessed prior to starting CAR T and again at 1- and 3- months post-CAR T. Neurocognitive performance was measured using standardized neuropsychological tests including measures of verbal memory (Hopkins Verbal Learning Test-Revised (HVLT-R) - immediate recall, delayed recall, retention), processing speed (Trail-making Test - Part A (TMT-A)) and executive functioning (Trail-making Test Part B (TMT-B), Controlled Oral Word Association Test (COWAT)). Raw test scores were converted to z-scores (Mean 0, SD 1) based on norms adjusted for age, sex, and education, where applicable. Impairment on individual tests was defined by a z score $\leq$ -1.64. Participants were categorized as showing overall impairment if they had at least two tests with a z-score of $\leq$ -1.5 or a z-score $\leq$ -2.0 on one test. Self-reported cognitive functioning was measured using the Functional Assessment of Cancer Therapy - Cognition, Perceived Cognitive Impairment score (FACT-Cog3 PCI) and the European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire C-30, Cognitive Functioning scale (EORTC QLQ-C30 CF). Demographic and clinical data were collected through self-report and patient records. Frequencies of impairment were determined at each time point, with clinically significant changes on individual test scores in the first month determined based on z-score changes of $\geq$1.0 or minimal clinically important differences for self-report questionnaires. Linear mixed models were generated to estimate the trajectory of neurocognitive performance and self-reported cognitive functioning over time from baseline to 3 months.

Results

Neurocognitive outcomes were available for 37 participants at baseline, with follow-up data available for 29 patients at 1 month and 17 patients at 3 months. Participants were 54% male, had a mean age 58.4 years (sd 11.3) and a mean 15.5 years (sd 3.2) education. All patients had a diagnosis of non-Hodgkin lymphoma (53% diffuse large B-cell lymphoma (DLBCL), 31% transformed DLBCL from follicular lymphoma). Immune effector cell-associated neurotoxicity syndrome (ICANS) affected 32% of patients (5% Grade 4, 3% Grade 3, 8% Grade 2, 16% Grade 1). Cytokine release syndrome (CRS) affected 97% of patients (3% Grade 3, 76% Grade 2, 19% Grade 1).

Frequency of overall impairment at each time point was 10/37 (27%) at baseline, 12/29 (41.4%) at 1 month, and 3/17 (17.6%) at 3 months. At each time point, impairment was most common on tests of executive functioning and memory. Based on individual test score changes between baseline and 1 month, rates of decline on individual tests of neurocognitive performance ranged

from 11.5% (TMT-A) to 34.6% (COWAT). Decline on self-reported cognitive functioning was observed for 14.3% (FACT-Cog PCI) and 28.6% (EORTC QLQ-C30 CF) of participants.

Based on mixed models (Table 1), there was a statistically significant decline in estimated mean z-scores on a test of executive function (COWAT: -0.52, 95% CI -0.89-(-0.16), p=0.007) at 1-month compared to baseline. At three months, there was a statistically significant improvement in estimated mean z-scores on memory (HVLT-R immediate recall: 0.56, 95% CI 0.11-1.01, p=0.017) and executive functioning (TMT-B: 0.87, 95% CI 0.17-1.57, p=0.019; COWAT: 0.68, 95% CI 0.19-1.16, p=0.009) compared to baseline.

Conclusions

Impairment is present in a subgroup of patients prior to starting CAR T therapy. Patients may demonstrate declines on performance-based measures and report worsening cognitive symptoms in the first month after CAR T therapy, but also improved performance in some domains by three months. Enrollment and long-term follow-up of patients in this study is ongoing. Future analyses will explore differences in trajectories among subgroups, such as those who have experienced ICANS and CRS.

Disclosures Kuruvilla: *Roche, Astra Zeneca, Merck:* Research Funding; *Abbvie, Amgen, Astra Zeneca, BMS, Genmab, Gilead, Incyte, Janssen, Merck, Novartis, Pfizer, Roche, Seattle Genetics:* Honoraria; *Abbvie, BMS, Gilead, Merck, Roche, Seattle Genetics:* Consultancy; *Karyopharm:* Other: DSMB. **Bhella:** *Sanofi:* Consultancy; *Novartis:* Consultancy; *Gilead:* Consultancy. **Chen:** *AstraZeneca:* Membership on an entity's Board of Directors or advisory committees, Other: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events; *Novartis:* Membership on an entity's Board of Directors or advisory committees, Other: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events; *Beigene:* Membership on an entity's Board of Directors or advisory committees, Other: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events; *Abbvie:* Membership on an entity's Board of Directors or advisory committees, Other: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events; *Bristol Myers Squibb:* Other: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events; *Janssen:* Membership on an entity's Board of Directors or advisory committees, Other: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events, Research Funding; *Gilead Sciences, Inc.:* Membership on an entity's Board of Directors or advisory committees, Other: Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events, Research Funding. **Prica:** *Abbvie:* Honoraria; *Astra-Zeneca:* Honoraria; *Kite Gilead:* Honoraria.

Table 1. Estimates of neurocognitive outcomes over time from linear mixed models (LMM)

Outcome Measure	Time Point	Mean (SE)	Difference in the Estimates (95% CI)	p-value
HVLT-R immediate	*T0	-0.29(0.18)	-	-
	T1	-0.35(0.22)	-0.06(-0.51-0.39)	0.796
	T2	0.26(0.27)	0.56(0.11-1.01)	**0.017**
HVLT-R delayed	T0	-0.25(0.19)	-	-
	T1	-0.65(0.30)	-0.39(-0.94-0.15)	0.152
	T2	-0.04(0.27)	0.21(-0.21-0.64)	0.293
HVLT-R retention	T0	-0.22(0.19)		-
	T1	-0.53(0.34)	-0.31(-0.97-0.36)	0.938
	T2	-0.20(0.30)	0.02(-0.57-0.62)	0.349
TMT-A	T0	0.17(0.18)	-	-
	T1	-0.07(0.38)	-0.24(-0.78-0.29)	0.364
	T2	0.58(0.20)	0.41(-0.06-0.87)	0.086
TMT-B	T0	-0.95(0.42)	-	-
	T1	-1.83(1.05)	-0.88(-2.77-1.01)	0.351
	T2	-0.08(0.37)	0.87(0.17-1.57)	**0.019**
COWAT	T0	-0.27(0.19)	-	-
	T1	-0.79(0.19)	-0.52(-0.89-(-0.16))	**0.007**
	T2	0.41(0.27)	0.68(0.19-1.16)	**0.009**
FACT-Cog PCI	T0	62.6(1.37)	-	
	T1	63.2(2.01)	0.56(-2.95-4.07)	0.746
	T2	64.9(1.73)	2.25(-1.05-5.55)	0.169
EORTC QLQ-C30	T0	82.9(2.40)	-	-
	T1	81.9(3.16)	-1.06(-8.67-6.53)	0.776
	T2	84.6(3.16)	1.64(-4.98-8.26)	0.612

*T0: Baseline (N=37), T1-1-month (N=29), T2-3 months (N=17)

Note: Means are estimated means from linear mixed models. Statistical significance is considered as $p<0.05$. *HVLT-R*, Hopkins Verbal Learning Test-Revised, *TMT-A*, Trail-making Test - Part A; *TMT-B*, Trail-making Test-Part B; *COWAT*, Controlled Oral Word Association Test; *FACT-Cog PCI*, Functional Assessment of Cancer Therapy – Cognition, version 3, Perceived Cognitive Impairment; *EORTC QLQ-C30 CF*, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C-30, Cognitive Functioning scale.

Figure 1

https://doi.org/10.1182/blood-2023-190650