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

<sup>1</sup>Lawrence S. Bloomberg Faculty of Nursing, University of Toronto, Toronto, Canada

<sup>2</sup>Department of Supportive Care, Princess Margaret Cancer Centre - University Health Network, Toronto, Canada <sup>3</sup>Division of Medical Oncology and Hematology, Princess Margaret Cancer Centre - University Health Network, Toronto, Canada

<sup>4</sup>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

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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 on-going. Future analyses will explore differences in trajectories among subgroups, such as those who have experienced ICANS and CRS.

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Table	1. Estimates	of neurocognitive	outcomes over time	from linear mixed	models (LMM)
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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	TO	-0.25(0.19)	1.42	-
	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	TO	-0.22(0.19)		2-1
	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	TO	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)	121	12
	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	TO	-0.27(0.19)	Sector Sector	-
	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	TO	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)	120	1
	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

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

<u>Note</u>: 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

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