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POSTER ABSTRACTS

905.OUTCOMES RESEARCH-LYMPHOID MALIGNANCIES

Frailty Impact on Outcomes of Patients Undergoing Chimeric Antigen Receptor T-Cell (CAR T) Therapy at Princess Margaret Cancer Centre: A Prospective Pilot Study

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Introduction
Princess Margaret Cancer Centre is 1 of 3 adult centres in Ontario, Canada providing Chimeric Antigen Receptor T-Cell (CAR T) therapy as a standard of care treatment for adult patients with relapsed and refractory B-cell lymphomas. There is no upper age limit for treatment consideration, and frailty may be an important factor in assessing fitness for treatment. This study aims to determine if frailty assessments pre-CAR T can predict those at higher risk for acute toxicities, PFS, and OS, as well as evaluate changes in frailty over time.
Methods
We performed a cohort study of consecutive patients with lymphoma undergoing CAR T cell therapy at our institution, from April 2021 to date. Frailty was evaluated using the Clinical Frailty Scale (CFS), Grip Strength, Gait Speed, Mini-Cog, Edmonton Symptom Assessment System (ESAS) and Patient Health Questionnaire (PHQ-2 and PHQ-9) at 5 time points: baseline (clearance visit), and 1, 3, 6 and 12 months post-CAR T. At baseline, additional assessments were completed to further characterize frailty including the Vulnerable Elders Survey (VES-13), Hematopoietic Cell Transplantation-specific Comorbidity Index (HCT-CI) and Cumulative Illness Rating Scale (CIRS). We present data on patients enrolled to date.
Results
Fifty-two patients have had their data analyzed thus far. Mean age is 57.9 ± 12.7 years and 54% are male. 50% have de novo diffuse large B-cell lymphoma, 24% transformation from follicular lymphoma,14% HGBCL, 6% PMBCL and 6% FL. Most patients (83%) received axi-cel. Median follow-up is 3.80 months (IQR 0.56-24.7 mo). All 52 patients completed assessments at baseline, 44 completed 1 month, 25 completed 3 month, 12 completed 6 month and 11 completed 12 month assessments. Median scores (and IQR) for the HCT-CI, CIRS, VES-13 and CFS at baseline were 1.5 (0-5), 3.0 (0-13), 1.0 (0-7), and 3.0 (1-7) respectively. There were clinically significant changes observed in CFS over time (p=<0.001), with mean scores of 3.3 at baseline, 3.7 at 1 month, 2.8 at 3 months and 2.1 at 12 months. There were no significant changes (p=0.051; p=0.078) between timepoints for either of the physical assessments of grip strength or gait speed.
Sixteen patients (31%) experienced immune effector cell neurotoxicity syndrome (ICANS) (4% Grade 4, 4% Grade 3, 8% Grade 2, 15% Grade 1) and forty-nine patients (94%) experienced cytokine release syndrome (CRS) (2% Grade 3, 65% Grade 2, 27% Grade 1), during the 30 days following cell re-infusion. Seven patients (13%) were admitted to the ICU, with a median in-hospital length of stay for all 52 patients of 12.5 days (IQR 7.0, 99.0). None of the variables tested (age, sex, bridging therapy, LDH, CRP and frailty assessments) were significantly associated with the development or grade of CRS or ICANS.
There have been 21 progression events and 18 deaths (6 without progression); 9 pts remain alive post-progression (Figure 1). On univariable analysis of baseline data, ECOG performance status, LDH level, and the VES-13 score were predictive of PFS, while ECOG, LDH, CRP, VES-13 score, CFS and the time to walk 4m were predictive of OS. The HCT-CI and CIRS score were not significantly associated with outcomes. On multivariable analysis of PFS, baseline VES-13 score (HR 1.17, p=0.04) and LDH (HR 1.002, p=0.05) remained significant. Multivariable analysis for OS was not performed due to insufficient number of events.

Analyses incorporating repeated measures were performed, and on univariable analysis, the CFS, 4m walk test (s), LDH, VES-13 were significantly associated with PFS and the same variables and CRP were associated with OS (Table 1). On multivariable repeated measurements analyses, only the CFS was still associated with PFS, and CFS and LDH with OS (Table 1).

Conclusions

Conducting serial frailty assessments in patients undergoing CAR T therapy is feasible. The only longitudinal measurement of frailty found to have clinically significant changes between timepoints was the CFS, suggesting an element of reversible functional impairment related to patients' lymphoma. Within the limits of our sample size, baseline measures of frailty were not predictive of CRS or ICANS; the relationship of CFS change over time with PFS and OS may be indicative of lymphoma response. Enrollment is ongoing and data on larger number of patients with longer term follow-up are needed.

Disclosures Prica: *Kite-Gilead:* Honoraria; *Astra-Zeneca:* Honoraria. **Kuruvilla:** *Karyopharm:* Other: DSMB; *Abbvie, Amgen, Astra Zeneca, BMS, Genmab, Gilead, Incyte, Janssen, Merck, Novartis, Pfizer, Roche, Seattle Genetics:* Honoraria; *Roche, Astra Zeneca, Merck:* Research Funding; *Abbvie, BMS, Gilead, Merck, Roche, Seattle Genetics:* Consultancy. **Bhella:** *Sanofi:* Consultancy; *Novartis:* Consultancy; *Gilead:* Consultancy. **Kukreti:** *Eusa pharmaceuticals:* Honoraria; *kyowa kirin pharmaceuticals:* Honoraria. **Chen:** *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; *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; *Bristol Myers Squibb:* 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; *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.

Table 1. Cox regression analysis of overall and progression free survival with repeated frailty assessments in Chimeric Antigen Receptor T-cell therapy patient's at Princess Margaret Cancer Centre

	Univariable Cox Regression				Multivariable Cox Regression			
	Overall Survival		Progression Free Survival		Overall Survival		Progression Free Survival	
	HR	p	HR	p	HR	p	HR	p
Clinical Frailty Scale	**1.61 (1.28, 2.02)**	**<0.001**	**1.38 (1.14, 1.67)**	**0.001**	**1.44 (1.08, 1.90)**	**0.012**	**1.40 (1.01, 1.96)**	**0.045**
Grip strength (kg)	0.99 (0.94, 1.03)	0.518	0.99 (0.96, 1.04)	0.862				
4m Walk Test (s)	**1.31 (1.14, 1.51)**	**0.0002**	**1.28 (1.09, 1.52)**	**0.002**			0.99 (0.74, 1.33)	0.958
Gait Speed (m/s)	0.18 (0.03, 1.08)	0.060	0.26 (0.05, 1.24)	0.092				
LDH	**1.004 (1.002, 1.006)**	**<0.001**	**1.003 (1.001, 1.004)**	**0.003**	**1.003 (1.001, 1.006)**	**0.027**	**1.002 (1.00, 1.003)**	**0.075**
CRP	**1.004 (1.002, 1.006)**	**<0.001**						
VES-13	**1.31 (1.08, 1.58)**	**0.005**	**1.22 (1.03, 1.45)**	**0.018**	1.11 (0.89, 1.37)	0.359	1.04 (0.83, 1.32)	0.717
ECOG Performance Status		0.056		0.075				
0/1	Reference		Reference					
2/3	3.06 (0.97, 9.66)		2.45 (0.91, 6.57)					

HR, hazard ratio; kg, kilograms; s, seconds; m/s, meters per second; EGOG, Eastern Cooperative Oncology Group; LDH, Lactate dehydrogenase; CRP, C-reactive protein; VES-13, Vulnerable Elders Survey.

Hazard Ratio is reported with a 95% CI.

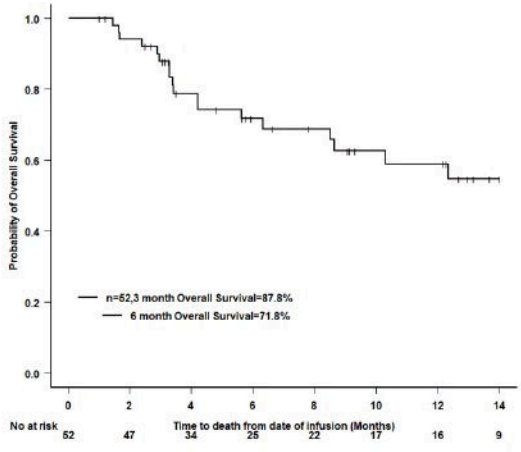

Figure 1. Overall survival of patients receiving Chimeric Antigen Receptor T-cell therapy at Princess Margaret Cancer Centre

Figure 1

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