Evaluating the Prognostic Utility of the Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI) in Children and Young Adults with Relapsed Refractory B-Cell Acute Lymphoblastic Leukemia (r/r B-ALL) Prior to CAR T-Cell Therapy

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Introduction

- CAR T-Cells have demonstrated remarkable efficacy at inducing remission in children and young adults with B-cell malignancies
- While remission rates are high, most experience CRS and ≥50% will ultimately relapse
- Tools to prognosticate individual risks of post-CAR T-cell morbidity and mortality are limited
- In the allogeneic hematopoietic stem cell transplant setting, the Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI) has been validated in adult and pediatric patients to predict both overall and event free survival
- The utility of the HCT-CI in predicting post CAR T-cell outcomes remains unknown

Aims

1. To calculate at HCT-CI score for a cohort of children and young adult patients receiving CAR T-Cell Therapy
2. To determine if the HCT-CI is able to predict post-CAR outcomes including:
   - CRS
   - CRS Maximum Grade
   - Complete Response
   - Median Overall Survival
   - 2-year Cumulative Incidence of Relapse

Methods

- HCT-CI score was retrospectively calculated for 119 children and young adults with r/r B-ALL
- All patients were treated on 1 of 3 Phase I CAR trials at the National Cancer Institute (NCT01593696,NCT02315612, NCT0344839) through 12/31/2020 (Table 1)
- Scores were calculated using data collected prior to initiation of lymphodepleting chemotherapy
- Scores were analyzed with respect to outcome measures including cytokine release syndrome (CRS), complete response (CR), median overall survival (OS) and cumulative incidence of relapse (CIR)

Table 1. HCT-CI

Comorbidities	HCT-CI scores
Arrhythmia	1
Cardiovascular comorbidity	1
Inflammatory bowel disease	1
Diabetes or steroid-induced hyperglycemia	1
Cerebrovascular disease	1
Psychiatric disorder	1
Mild hepatic comorbidity	1
Obesity	1
Infection	1
Rheumatologic comorbidity	2
Peptic ulcer	2
Renal comorbidity	2
Moderate pulmonary comorbidity	2
Prior malignancy	3
Heart valve disease	3
Moderate/severe hepatic comorbidity	3
Severe pulmonary comorbidity	3
	Total score = _____

Results

- Of 119 patients, median age was 15.4 (range 4.4-30.7) and median number of prior cycles of therapy (excluding HCT) was 5 (range 1-14).
- Median HCT-CI was 2 (range 0-7); 49.6% of patients had a score ≥ 3
- Each patient had a median of 1 comorbidity (range 1-3)
- Hepatic and pulmonary systems were the predominant contributors to HCT-CI scores (Figure 1)
- There was no association between HCT-CI and CRS incidence, CRS maximum grade, CR, median OS (Figure 2), nor 2-year CIR (Figure 3)

Figure 1: System Contribution to HCT-CI Score

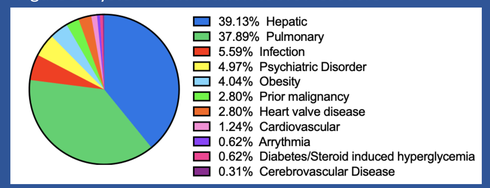


Table 1: HCT-CI in Relation to Outcomes

		All Patients (n=119)	HCT-CI 0 (n=20)	HCT-CI 1-2 (n=40)	HCT-CI 3+ (n=59)	P
Any CRS	Yes	96	15	31	50	0.28
	No	23	5	9	9	
CRS by Max Grade	0	23	5	9	9	0.37
	1	45	8	13	24	
	2	30	5	10	15	
	3	17	2	6	9	
	4	4	0	2	2	
Complete Response	Yes	82	16	27	39	0.29
	No	36	4	12	20	
Median OS			14.6 mos (9.9-38.7)	18.8 mos (7.3-27.4)	12.2 mos (7.9-14.9)	0.39
2yr CIR			49.3% (95% CI: 19.9-73.4%)	64.6% (95% CI: 41.9-80.3%)	61.6% (95% CI 42.2-76.2%)	0.36

Figure 2: Overall Survival by HCT-CI

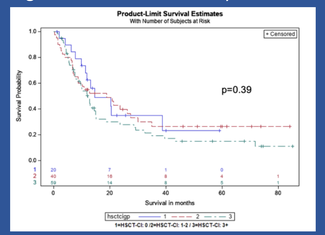
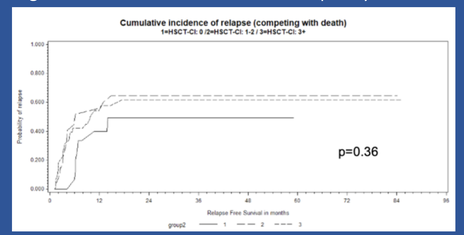


Figure 3: Cumulative Incidence of Relapse by HCT-CI



Conclusions

- The HCT-CI lacks prognostic utility in predicting post CAR T-Cell outcomes in children and young adults with r/r B-ALL
- A different set of comorbidities, alongside known determinants of response and toxicities (ie. disease burden) may be important in predicting outcomes

Future Steps

- Generation and validation of a CAR-CI that uses a combination of CAR specific comorbidities with biomarker and disease-based risk factors to predict post-CAR morbidity and mortality

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