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POSTER ABSTRACTS

614.ACUTE LYMPHOBLASTIC LEUKEMIAS: THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

Impact of Treatment with Inotuzumab Ozogamicin before or after Chimeric Antigen Receptor T-Cell Therapy in Children with Relapsed/Refractory Acute Lymphoblastic Leukemia

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Background: Inotuzumab (InO), a monoclonal antibody targeting CD22 conjugated to calicheamicin, is widely used for relapsed/refractory B-cell acute lymphoblastic leukemia (ALL) with good salvage rates (O'Brien, JCO 2022, Bhojwani, Leukemia 2019). Feasibility data on its use as a bridge to Chimeric Antigen Receptor T-cell therapy (CART) or as salvage therapy post CART is limited. Concern has been raised that InO given prior to leukapheresis might impact the quality of T-cell collection and, when used for bridging therapy prior to CART, could result in insufficient B-cell antigen load at the time of CART infusion, therefore reducing efficacy.
Methods: Data of patients who received InO monotherapy on Children's Oncology Group study AALL1621 Cohort 1 and who received any form of CART prior to study enrollment or within 1 year of coming off protocol therapy, irrespective of other anti-leukemic treatments, were collected retrospectively using a standardized Case Report Form.
Results: Forty-eight patients received InO on AALL1621; 3-year overall survival (OS) rate was 35.4±6.9%. Thirteen received InO prior to CART and thirteen received InO post CART including 1 patient who received CD19 CART prior to InO and CD22 CART post InO (Table 1).
InO prior to CART (11 CD19 CART, 1 CD22 CART, 1 unknown): Seven patients went directly to CART post InO, 5 received intervening chemotherapy, and 1 had an intervening transplant with relapse post. Nine patients received tisagenlecleucel and 3 received an investigational CART. Patients were infused CART 1-150 days (median 45 days) after coming off protocol therapy. At CART infusion, 10 patients had detectable ALL, only 2 had no CD19 expressing cells at infusion (ALL or normal B-cells) and 1 unknown. At post CART bone marrow evaluation on day 28, 7/12 (58.3%) were in a minimal residual disease (MRD) negative (<0.01%) remission, 1 had MRD=0.021%, 1 had unknown response. Three had residual disease including the single patient who received CD22-targeted CART. Four MRD negative patients who received CART post-InO are alive without relapse at a median of 3.8 years post CART and 1 is alive with a subsequent relapse. At 3 years post CART infusion OS is 53.9±13.8%.
T-cells were collected immediately following 3-9 doses of InO in 8/13 (61.5%) patients (1-6 months from date of enrollment on the study), 2 were collected prior to InO and three had unknown collection dates. All had a CART product manufactured successfully. Post CART 7/13 patients did not develop thrombocytopenia (< 50,000/uL); 5 who developed thrombocytopenia had measurable ALL at day 28 post CART or soon after. One other patient went to planned transplant post CART and remained with low platelets and ANC. Almost all patients (11/13) had ANC < 500/uL post CART, of whom 3 did not recover including two with persistent ALL.
InO Post CART (11 CD19-targeted CART, 2 CD22-targeted CART): Of the 13 patients who received InO post CART therapy, 7/13 (53.8%) achieved an MRD-negative complete remission (CR) to CART but then developed detectable disease 2-36 months post CART. Five did not have a CR post-CART, 4 of whom enrolled on AALL1621 within one month; 1 received inter-

vening chemotherapy. One had an unknown response. On univariate analysis CR rate with InO therapy was no different for those who received CART prior to InO than those who did not. As well, risk of a dose limiting toxicity event (DLT) or developing sinusoidal obstructive syndrome (SOS) during InO therapy or during subsequent transplant after InO was not different in patients with CART exposure prior to AALL1621 enrollment.

Conclusion: The ability to collect and manufacture CART cells was feasible within weeks of receiving InO. Response to CART post InO was lower than retrospective cohorts (Ceolin, Leukemia 2022) but 3-year OS post CART was consistent with published CD19-targeted CART trials at 53.9% (Maude, NEJM 2018; Pasquini, Blood Adv 2020). InO did not appear to impact durability of remission in those who attained an MRD negative remission with CART. Given most patients had a CD19 target due to disease presence at the time of CART infusion, differential response to CART based upon antigen could not be analyzed. Prior InO exposure did not appear to worsen cytopenias post CART when compared to published CART trials and was associated with a comparable 3-year OS. As well, CART exposure prior to InO did not appear to effect response or increase the risk of DLT or SOS during subsequent InO therapy.

Disclosures Rheingold: *Abbvie:* Other: Trial Steering Committee. **Ji:** *Pfizer:* Other: DSMC for International Trial. **Gore:** *Amgen:* Consultancy; *Novartis:* Consultancy; *Roche:* Consultancy. **Shah:** *CARGO:* Consultancy; *VOR:* Consultancy, Research Funding; *Lentigen:* Research Funding; *Immunoadoptive Cell Therapy Private Limited:* Consultancy, Other: Scientific Advisory Board. **Raetz:** *Pfizer:* Research Funding; *Bristol Myer Squibb:* Other: DSMC. **O'Brien:** *Pfizer:* Honoraria, Research Funding.

OffLabel Disclosure: Inotuzumab is not yet approved for pediatric patients with ALL. Use of investigational CAR T-cell therapy is also discussed

Table 1: AALL1621 Cohort 1 patients with CART prior to enrollment or post InO treatment

Variables	CART prior to InO	CART post InO
	n=13	n=13
Age at Enrollment (years)		
0-6	4	5
7-12	5	3
13+	4	5
Sex		
Female	4	9
Male	9	4
Race/ethnicity		
Hispanic of all races	2	2
Non-Hispanic White	3	7
Non-Hispanic Black	1	3
Non-Hispanic Asian	2	0
Other/Unknown	5	1
Disease status at Enrollment		
Primary refractory ALL (≥2 prior induction attempts)	1	0
First relapse refractory to ≥1 prior re-induction	0	3
Second or greater relapse	10	9
Any relapse after HSCT	2	1
Prior HSCT (prior to enrollment)		
No	10	8
Yes	3	5
Prior Blinatumomab/CART (prior to enrollment)		
Prior Blinatumomab+CART	3	0
Prior Blinatumomab only	0	4
Prior CART only	10	1
No prior Blinatumomab or CART	0	8
Baseline Bone Marrow Status (at AALL1621 enrollment)		
M2 (5%-25%)	2	5
M3 (>25%)	11	8
Cytogenetics/FISH reported		
ETV6-RUNX1	2	1
iAMP21	0	1
KMT2A-rearranged	1	4
BCR-ABL1	0	1
Other	2	3
Not reported	2	1
MRD-negative Response in Cycle 1		
MRD-negative CR/CRi	4	5
Non MRD-negative CR/CRi	3	3
Non CR/CRi	6	5
Best response with Cycles 1 and/or 2		
CR/CRi	8	8
Non CR/CRi	5	5
DLT in AALL1621 Cycle 1		
No	10	11
Yes	3	2
Duration between patients off protocol vs. date of CART		
<3 months	N/A	11
3-6 months	N/A	2
Manufacture of CART product		
Commercial Kymriah	6	9
Investigational	7	3
Unknown	0	1
Leukemia directed therapies prior to CART therapy		
Chemotherapy	N/A	5
HSCT	N/A	1
None	N/A	7
HSCT post CART?		
No	9	11
Yes	4	2

Abbreviations: CART, chimeric antigen receptor T-cell therapy; CR, complete response; CRi, complete response with incomplete count recovery; DLT, dose limiting toxicity; HSCT, hematopoietic stem cell transplantation; InO, inotuzumab ozogamicin;

Figure 1

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