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Treatment of Acute Myeloid Leukemia with Orca-T

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BACKGROUND & AIM

- Allogeneic hematopoietic stem cell transplant (alloHSCT) offers a potential curative treatment for many hematological cancers.[1] However, it is associated with high mortality from complications including infection, graft versus host disease (GvHD) and relapse.
- Orca-T is an investigational allogeneic T-cell immunotherapy that includes stem and immune cells, derived from allogeneic donors, that leverages highly purified, polyclonal donor regulatory T cells to control alloreactive immune responses (**Figure 1**).
- In this sub-group analysis, we evaluated the safety and efficacy of patients with acute myeloid leukemia (AML) who were treated with Orca-T.

METHODS

- 37 adults with AML in CR/CRi (complete remission with incomplete count recovery) who received myeloablative conditioning with busulfan, fludarabine, and thiotepa (BFT) followed by Orca -T, as part of a multicenter phase 1b single-arm trial (NCT04013685) are reported here.
- Eligibility criteria included HCT-CI ≤4 and availability of 8/8 match related or unrelated North American donor.
- Patients received BFT prior to Orca-T, followed by single-agent GvHD prophylaxis with tacrolimus.
- Donors were matched via DNA-based high-resolution typing of HLA-A, -B, -C, and -DRB1.
- The median duration of follow-up was 14 months.

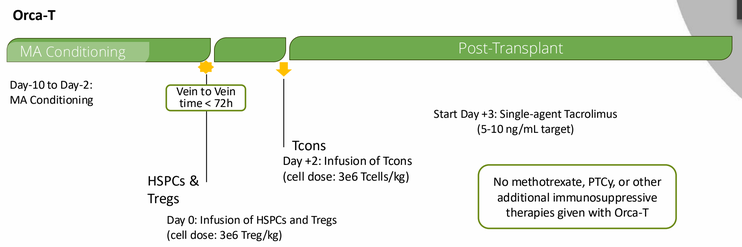


Figure 1. Orca-T treatment consisted of myeloablative conditioning with single agent prophylaxis using tacrolimus.[2]

RESULTS

AML Patients (n=37)	
Age	
Median (range)	51.0 (20-64)
Sex (female n and %)	18 (48.7)
Ethnicity, n (%)	
Hispanic or Latino	6 (16.2)
Non-Hispanic or Latino	30 (81.1)
Unknown	1 (2.7)
Race	
Asian	4 (10.8)
White/Caucasian	26 (70.3)
Other/Not reported	6 (16.2)
Missing	1 (2.7)
Donor Type, n (%)	
Matched related	23 (62.2)
Matched unrelated	14 (37.8)
Baseline HCT-CI Score, n (%)	
0	17 (45.9)
1	2 (5.4)
2	5 (13.5)
3	10 (27.0)
4	3 (8.1)
Disease status at alloHSCT, n (%)	
CR	2 (5.4)
CR1	28 (75.7)
CR2	7 (18.9)
MRD positive at alloHSCT, n (%)	15 (40.5)
DRI risk score, n (%)	
Low	0
Intermediate	33 (89.2)
High	4 (10.8)

- Orca-T was successfully manufactured at a centralized GMP facility, distributed, and infused at study sites throughout the U.S.
- Vein-to-vein time was < 72 hours for all patients, with the majority < 60 hours.
- Most had intermediate DRI scores (89%) and 41% were MRD positive at baseline.
- Relapse-free survival at 12 months was 82.5% (95% CI: 65, 91.7) (**Figure 2**).
- Non-relapse mortality and overall survival were 0% and 100% at 12 months, respectively (**Figure 3**).
- No occurrence of post-transplant lymphoproliferative disorder, cytokine release syndrome, transplant-associated thrombotic microangiopathy, and veno-occlusive disease was reported.

	AML (n=37)
Death without evidence of disease recurrence, n (%)	0
Relapse, n (%)	6 (16.2)
Censored, n (%)	31 (83.8)

Table 2. Table shows non-relapse mortality and rate of relapse for 37 AML patients at 12 months post Orca-T treatment.

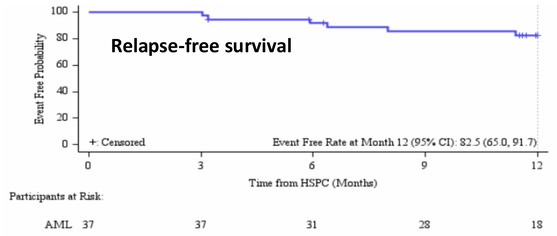


Figure 2

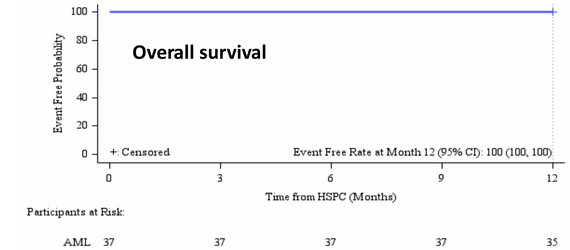


Figure 3

CONCLUSIONS

- Orca-T represents a potential reduced toxicity alternative to conventional alloHSCT.
- Combination of Orca-T with myeloablative BFT led to > 80% RFS without treatment-related mortality, and 100% overall survival in these AML patients.
- These outcomes were accomplished with consistent and reliable cell manufacturing and distribution of Orca-T at a national scale.
- A multi-center randomized controlled phase 3 trial comparing Orca-T to SOC, utilizing BFT or TBI-based conditioning, will complete enrollment during the first half of 2024 (NCT05316701).

REFERENCES

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