CT242/1 - Phase 2b study of alloHSCT patients receiving RGI-2001, an NKT cell activator, demonstrates protection from acute GVHD, correlating with increased NKT and Treg cell number in patient blood#

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#study was funded in part by REGiMMUNE

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Abstract and Study Design

- RGI-2001 is a liposomal formulation of the CD1d ligand α-GalCer that can activate natural killer T (NKT) cells and T-regulatory cells (Tregs).
- RGI-2001 was tested in a Phase 2b study for acute graft-vs-host-disease (aGHVD) prevention with tacrolimus/methotrexate (Tac/MTX) in patients undergoing allogeneic hematopoietic stem cell transplant (alloHSCT).
- Blood samples were collected and evaluated for expansion of NKT, Tregs, and other immune cell subsets.
- Patients receiving RGI-2001 had reduced aGVHD compared to a control cohort.
- The levels of NKT and Tregs are higher in patients who do not develop aGVHD who received RGI-2001.

Introduction

- aGVHD occurs when donor-derived T cells attack the immunosuppressed recipient, leading to significant morbidity and mortality.
- NKT and Treg cells are associated with the prevention of aGVDH without compromising general immune function.
- In a previous Phase IIa study, patients received a single dose of 100 ug/kg RGI-2001 which led to an elevation in Treg counts associated with a reduction in aGVHD.
- This Phase IIb study explored the effects of repeated dosing of RGI-2001. It provides further evidence regarding RGI-2001's impact on aGVHD, Treg expansion and NKT cell populations.

Baseline characteristics

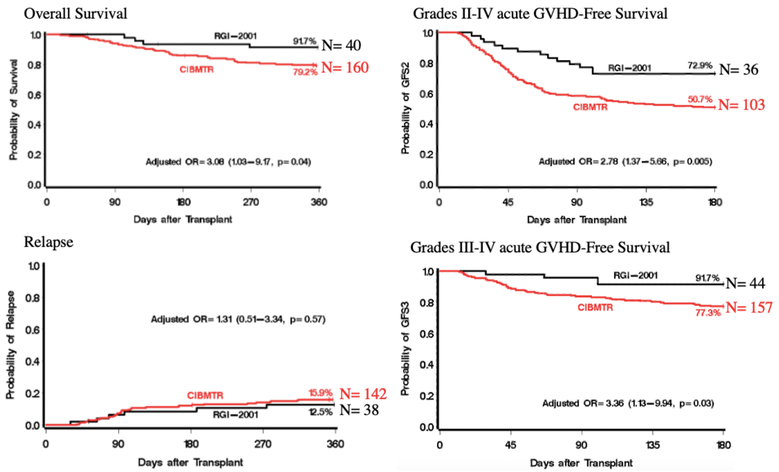
Characteristic	RGI-2001 (n=48)	CIBMTR (n=207)
Age, median (range)	52 (21-65)	50 (18-66)
Race		
White	44 (92%)	177 (86%)
African American	2 (4%)	11 (5%)
Other	2 (4%)	19 (9%)
Female Sex	21 (44%)	95 (46%)
Disease		
AML	26 (54%)	108 (52%)
MDS	7 (15%)	28 (14%)
ALL	11 (23%)	55 (27%)
CML	2 (4%)	8 (4%)
MPN	1 (2%)	8 (4%)
CMML	1 (2%)	0

Characteristic	RGI-2001 (n=48)	CIBMTR (n=207)
Donor type		
HLA-identical sibling	16 (33%)	80 (39%)
8/8 Unrelated	32 (67%)	127 (61%)
Graft source		
PBSC	39 (81%)	171 (83%)
BM	9 (19%)	36 (17%)
Conditioning Regimen	6 (13%)	31 (15%)
TBI/Cy	0	11 (5%)
TBI/VP	2 (4%)	22 (11%)
Bu/Cy	40 (83%)	143 (69%)
Flu/Bu		
GVHD Prophylaxis		
CNI + MTX	48 (100%)	206 (99.5%)*
CNI + MMF	0	1(0.5%)*

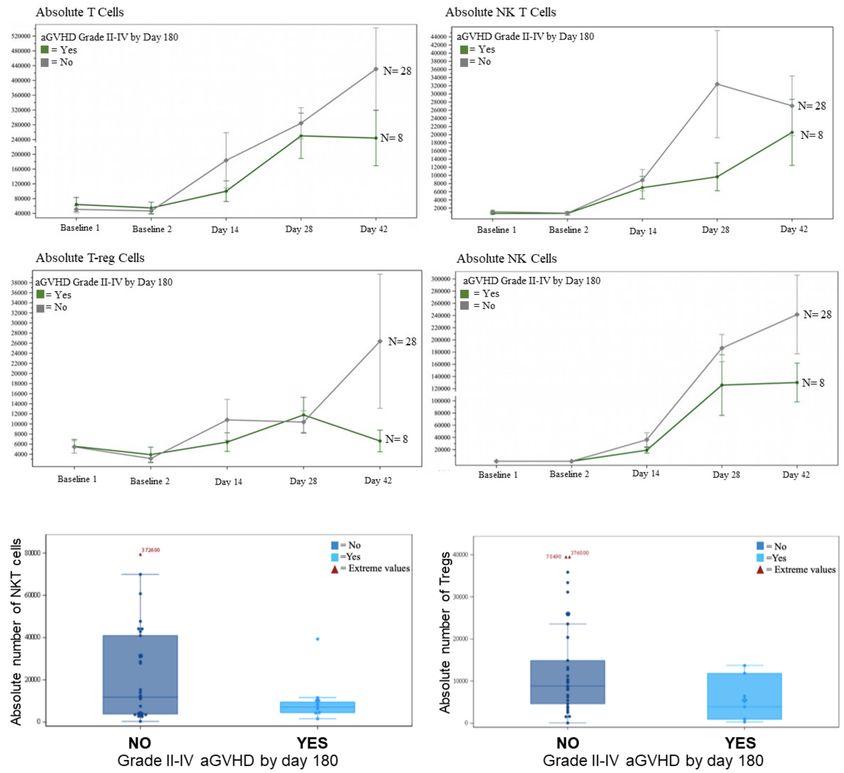
Acute and chronic GVHD outcomes

Efficacy Outcome	RGI-2001 N=48	CIBMTR N=207	Adjusted Odds ratio (95% CI) for failure	p-value
Grades II-IV acute GVHD, d100	22.9%	38.8%	2.29 (1.08-4.85)	.030
Grades II-IV acute GVHD, d180	22.9%	42.8%	2.68 (1.27-5.65)	.010
Grades III-IV acute GVHD, d100	4.2%	12.4%	3.25 (0.74-14.36)	.119
Grades III-IV acute GVHD, d180	4.2%	13.9%	3.65 (0.83-16.04)	.086
Chronic GVHD by one year, NIH (mod-severe)	33.3%	33.3%	1.02 (0.52-1.98)	.961

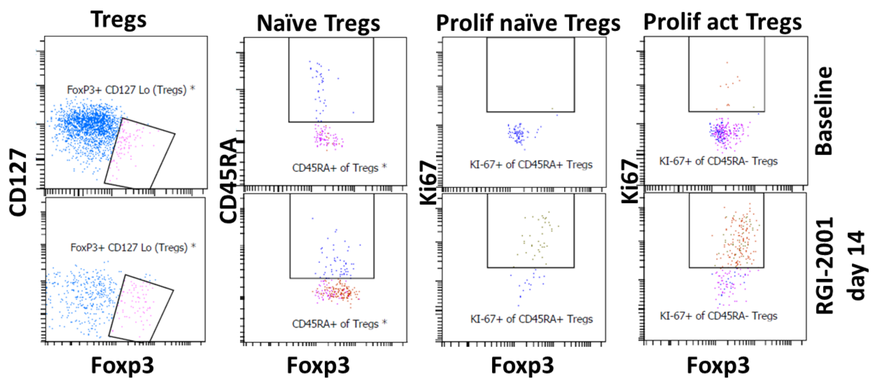
Overall survival, relapse and GVHD outcomes



Absolute T, Treg, NK T, and NK cell counts



Representative plot - exploratory Treg analysis



Summary

- Patients treated with RGI-2001 and Tac/MTX had significantly lower rates of Grade II-IV aGVHD 100 and 180 days post-alloHSCT compared to CIBMTR control. Overall survival is significantly increased while relapse is not changed for patients receiving RGI 2001.
- Flow cytometry studies indicate peripheral NKT expansion at D28 in patients receiving clinical benefit from RGI- 2001.
- The mean levels of absolute Tregs at Day 42, 1 week following the last dose of RGI-2001, was higher in subjects who were alive and had not developed Grade II-IV aGVHD by Day 180 compared with those who had died and/or did develop aGVHD.
- A large percentage of activated Tregs were proliferating, with activated Tregs proliferating to a greater extent compared with nonactivated Tregs. The proliferation was greater in after-treatment compared to baseline samples. This effect was also observed in the single-dose study (Phase 1/2a RGI-2001-002).
- The results from exploratory correlative analyses are consistent with the proposed mechanism of action of RGI-2001. RGI-2001 may induce activation and proliferation of NKT cells, leading to a reduction in aGVHD by increasing the proliferation of activated Tregs.