RGI-2001 with CNI-Based Prophylaxis Demonstrates Better Acute GVHD-Free Survival Following Myeloablative Allo-HCT without Increased Relapse: Comparison of a Multi-Center Phase 2b Study with a Contemporaneous CIBMTR Cohort

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Disclosures

The presenting author has the following to disclose regarding relevant financial or personal relationships with commercial entities or competitors that may be referenced in this presentation:

Zachariah DeFilipp

Consultant:
Sanofi, Incyte, Corp., MorphoSys AG, Inhibrx, PharmaBiome AG, and Ono Pharmaceutical.

Research support:
Incyte, Corp., Regimmune, Corp., and Taiho Oncology, Inc.

Background

- Severe acute graft-versus-host disease is a major cause of morbidity and mortality after allogeneic hematopoietic cell transplantation.
- Acute GVHD is primarily mediated by effector T-lymphocytes, and prophylactic strategies have traditionally focused on T-cell suppression.
- RG1-2001 contains the active moiety α-GalCer, which binds the CD1d receptor of antigen-presenting cells resulting in activation of invariant natural killer cells, resulting in a cytokine-dependent Treg proliferation.
- RGI-2001 is being evaluated for the potential to reduce or prevent acute GVHD through Treg expansion.

Study Design

- RGI-2001-003 was an open-label, non-randomized multicenter phase 2b, study to evaluate the safety and efficacy of RGI-2001 for the prevention of acute GVHD when used in combination with tacrolimus-based GVHD prophylaxis.

- Interim results have been previously reported (ASH 2022):
  - *Grade II-IV acute GVHD by Day 100*: **20.4%**
  - *Grade III-IV acute GVHD by Day 100*: **4.1%**

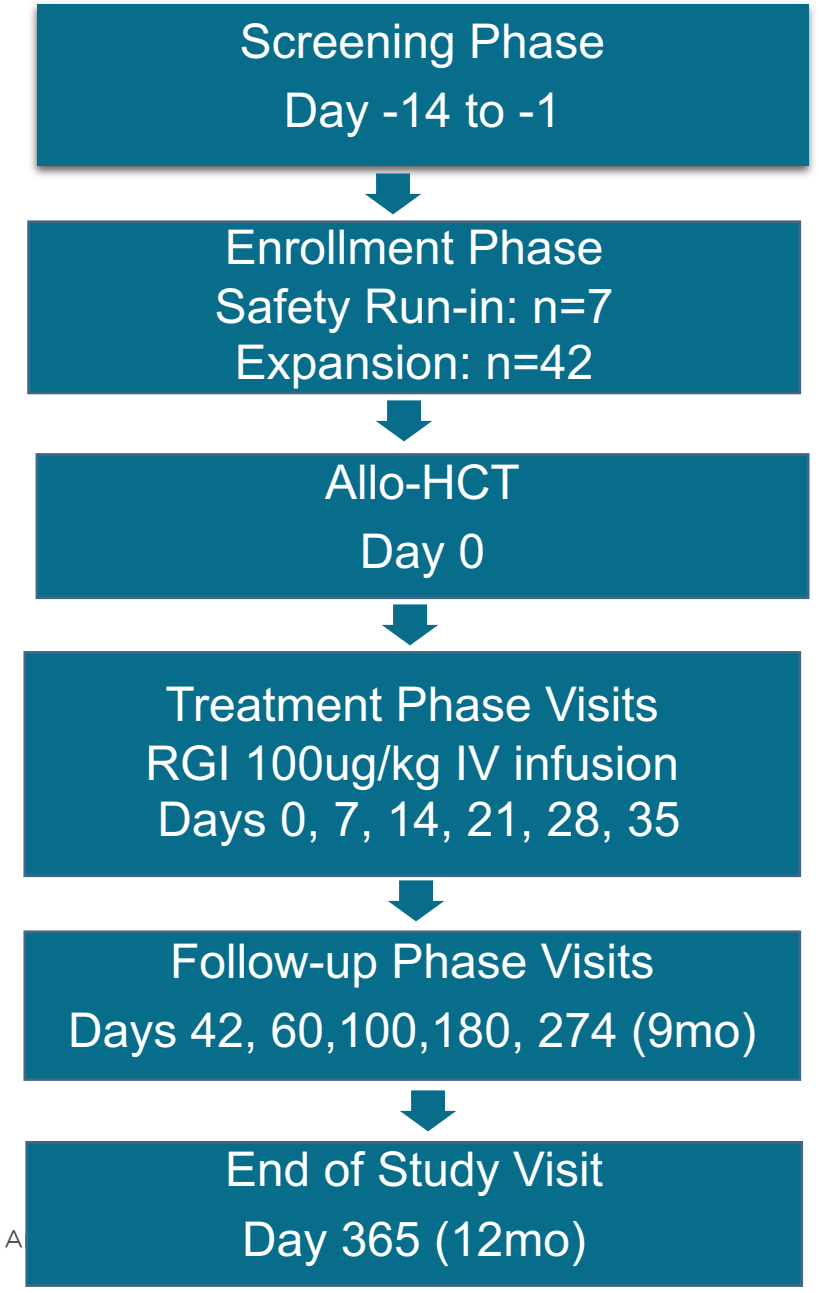
- Today, we will present:
  - Updated clinical data from the 49 participants treated on RGI-2001-003
  - A comparison to a contemporaneous control group of subjects from CIBMTR with SOC GVHD prophylaxis (CNI based regimen)

RGI-2001 Treatment Group

Forty-nine (n=49) participants were enrolled between 2019-2022 across 7 study centers in the US. 48 subjects included for efficacy analysis with CIBMTR data, 1 mismatch unrelated subject excluded.

Key eligibility criteria included:

- Age 18-65 years
- Hematologic malignancy
  - AML, ALL, in first or subsequent CR
  - MDS, CMML, MPN <10% blasts
  - CML
- HLA-identical sibling, 8/8 URD, 7/8 URD
- Myeloablative conditioning
- Bone marrow or PBSC as graft source
- GVHD prophylaxis: CNI + MTX or MMF
- No use of any additional or alternative drug(s) for GVHD prophylaxis



CIBMTR Contemporaneous Control Group

Key eligibility criteria for CIBMTR subjects (n=207):

- Study center participation in RGI-2001-003 study
- Year of allo-HCT: 2018-2019
- Eligibility criteria consistent with RGI-2001-003 study criteria:
    - Age, diagnosis, donor type, conditioning intensity, graft source, and GVHD prophylaxis regimen
- Alemtuzamab, ATG, and PT cyclophosphamide use excluded
- Clinical trial participants were excluded

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		
TBI/Cy	6 (13%)	31 (15%)
TBI/VP	0	11 (5%)
Bu/Cy	2 (4%)	22 (11%)
Flu/Bu	40 (83%)	143 (69%)
GVHD Prophylaxis		
CNI + MTX	48 (100%)	206 (99.5%)*
CNI + MMF	0	1(0.5%)*

*CIBMTR group - Tac/MTX n=205, Tac/CSA n=1, Tac/MMF n=1

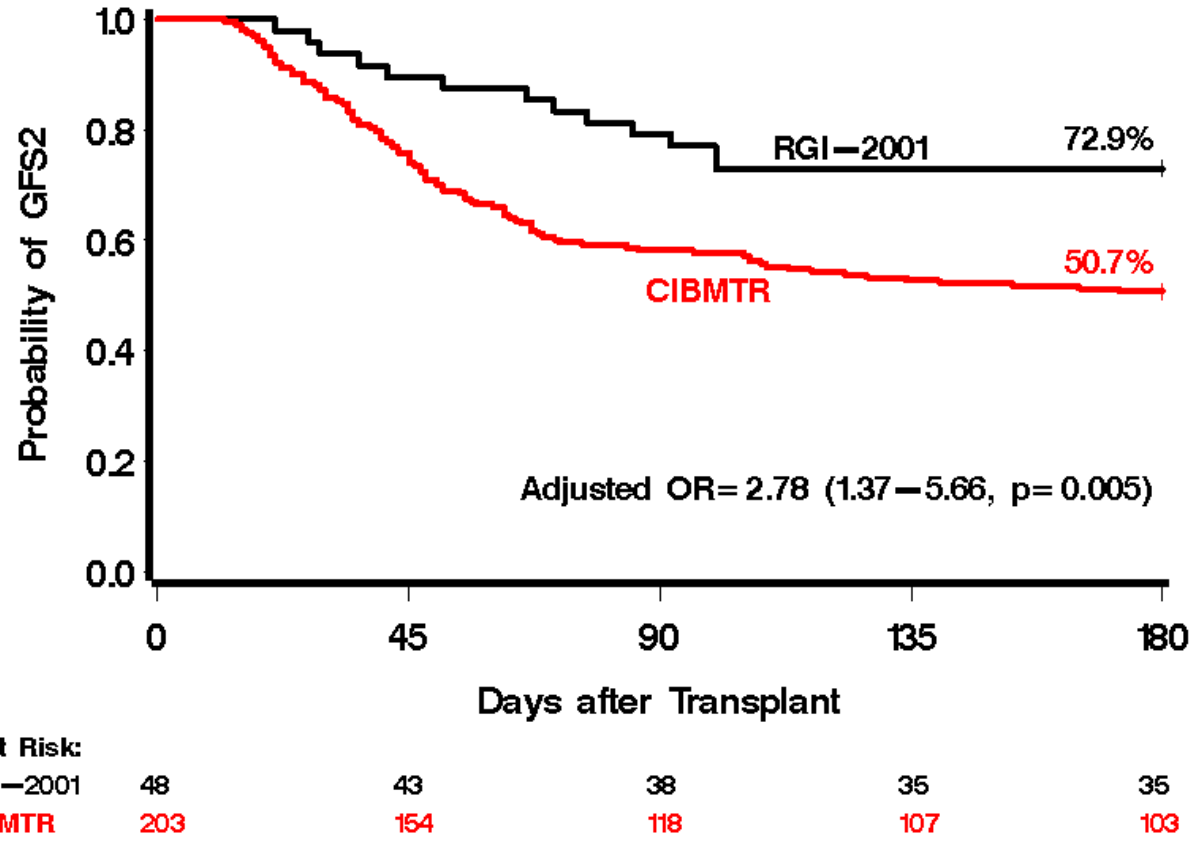
Neutrophil and Platelet Engraftment

	RGI-2001 N=48	CIBMTR cohort N=207
ANC engraftment	48/48 (100%)	207/207 (100%)
Median (days)	13	13
Min, Max	4, 34	1, 33
Platelet engraftment	48/48 (100%)	201/207 (97%)
Median (days)	18	18
Min, Max	**4, 61**	**1, 97**

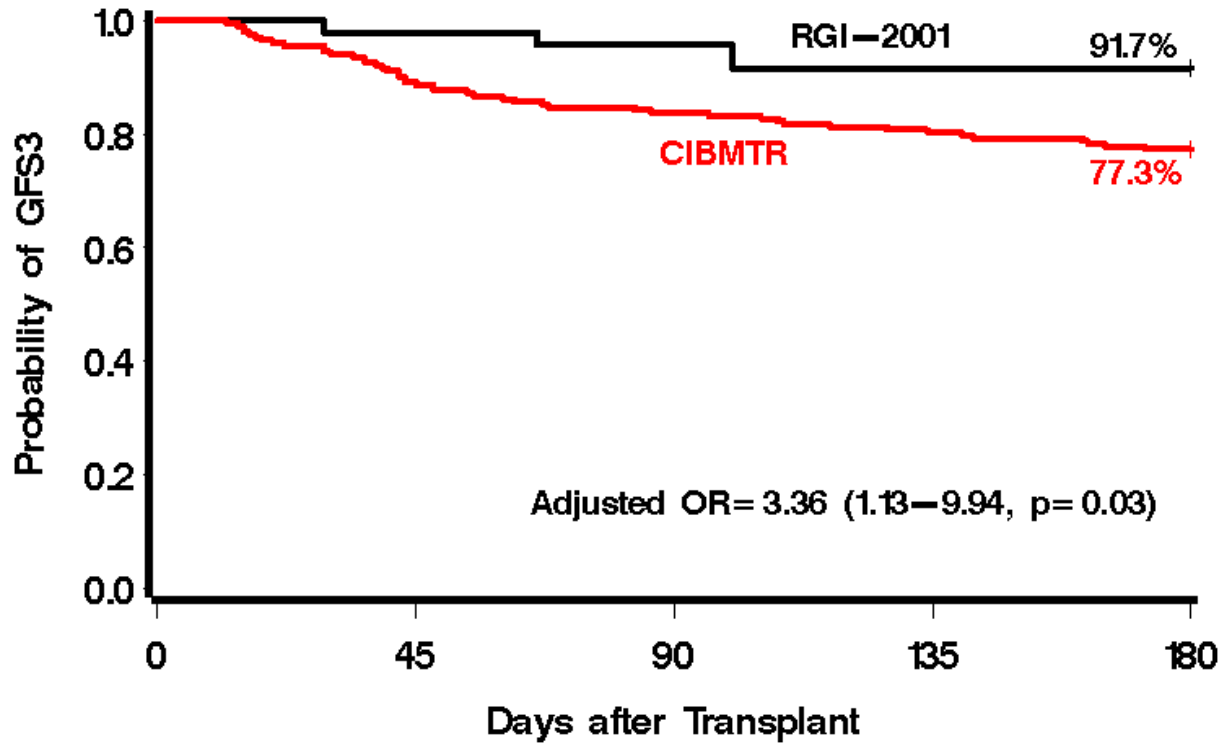
Acute and Chronic GVHD

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

Grades II-IV acute GVHD-Free Survival

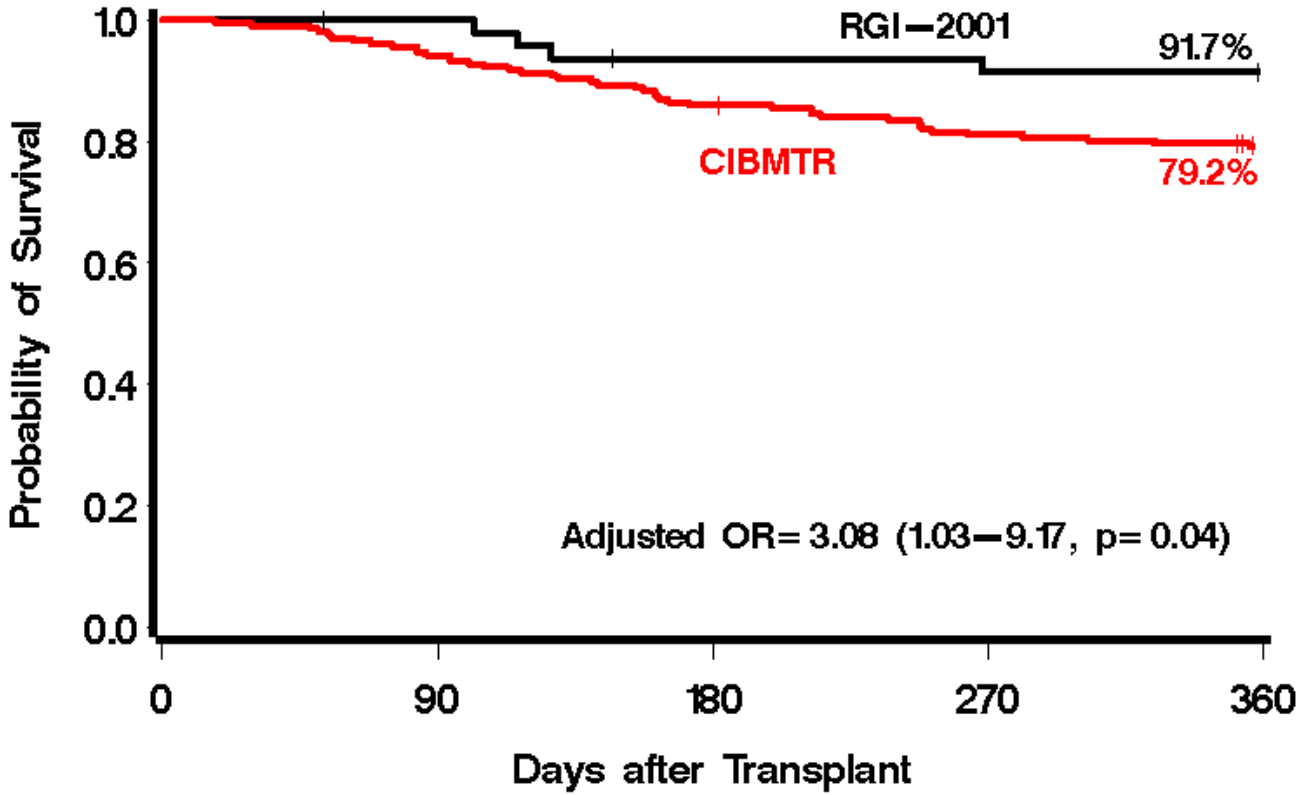


Grades III-IV acute GVHD-Free Survival



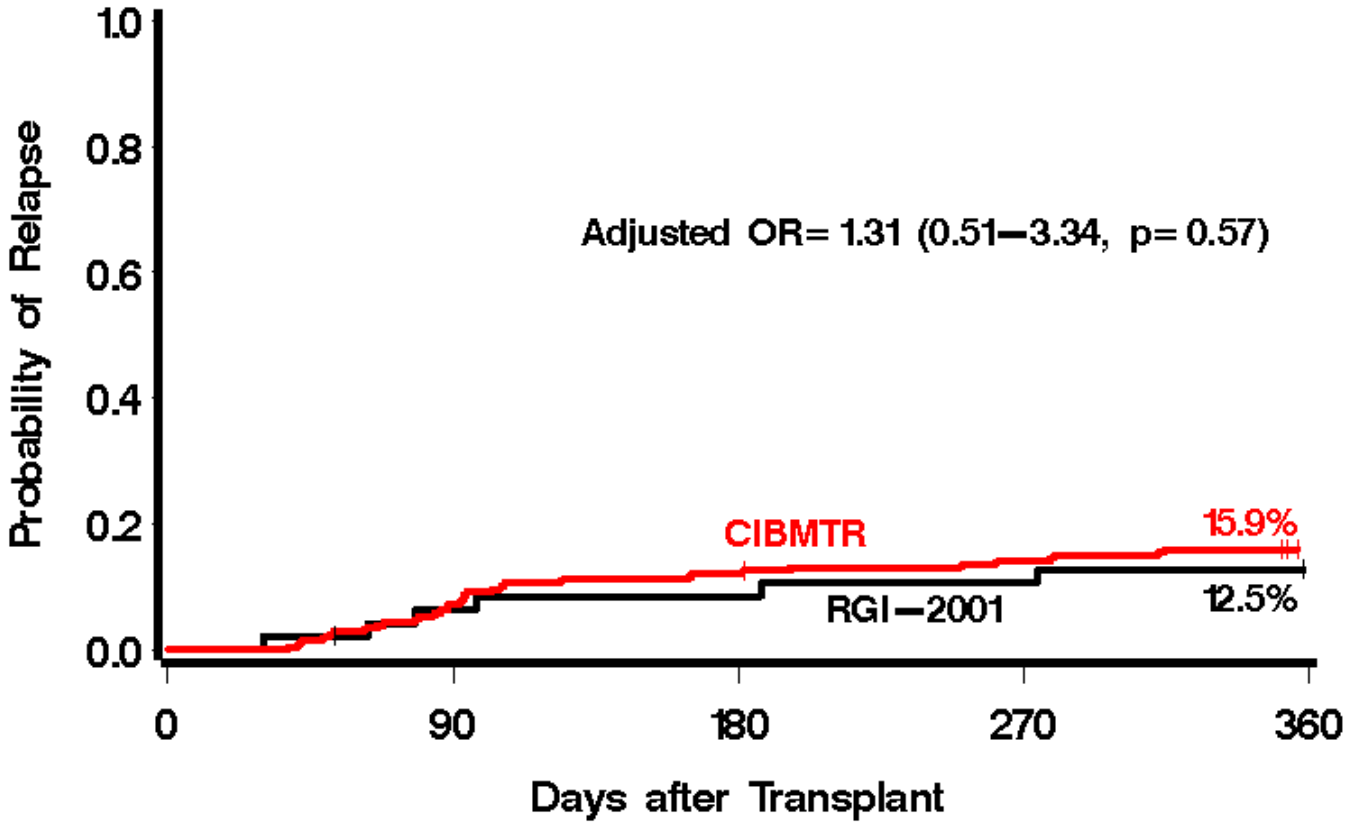
N at Risk:					
RGI—2001	48	47	46	44	44
CIBMTR	203	181	170	163	157

Overall Survival



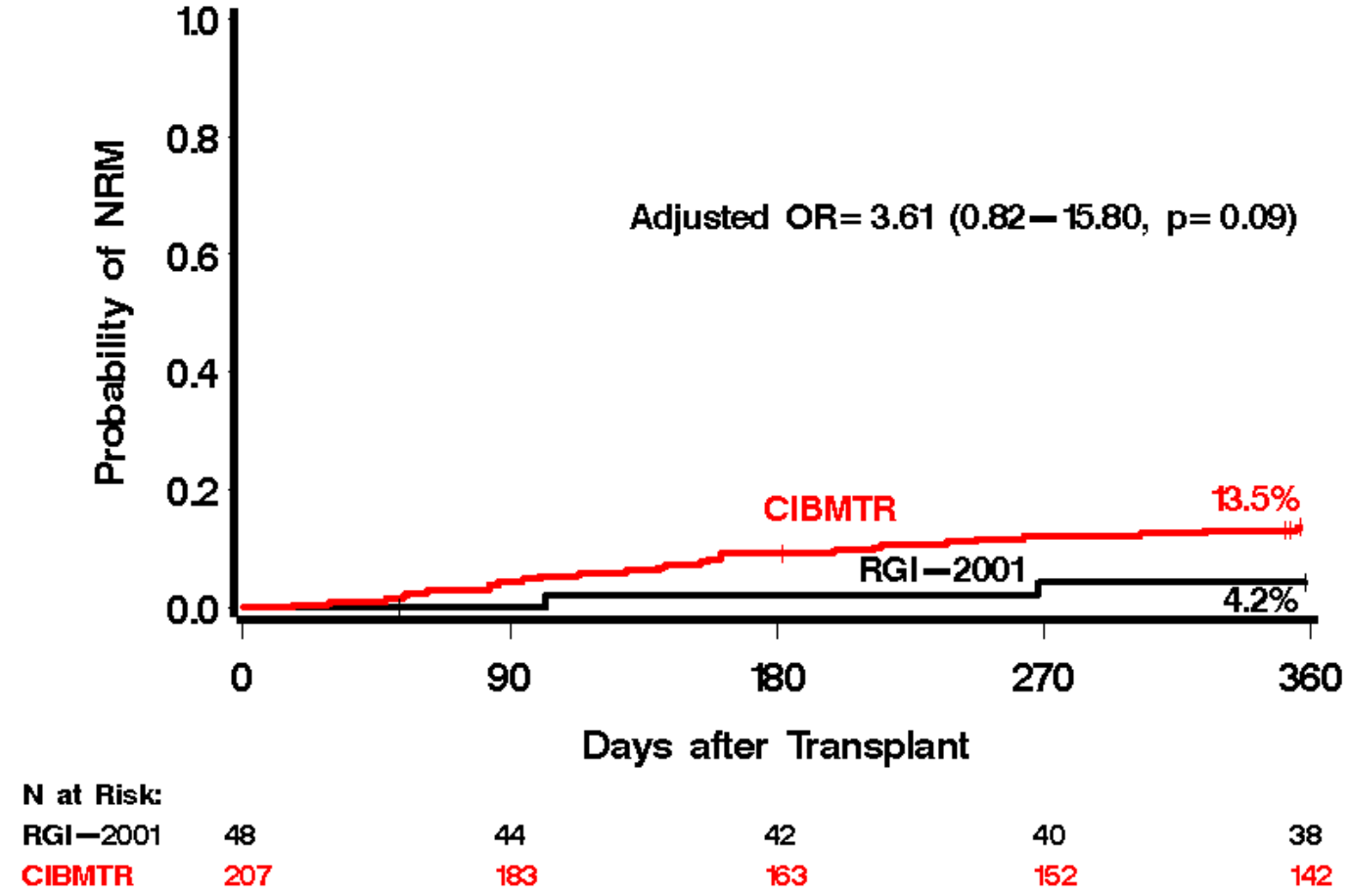
N at Risk:					
RGI—2001	48	47	43	42	40
CIBMTR	207	195	178	167	160

Relapse



N at Risk:					
RGI–2001	48	44	42	40	38
CIBMTR	207	183	163	152	142

Non-Relapse Mortality



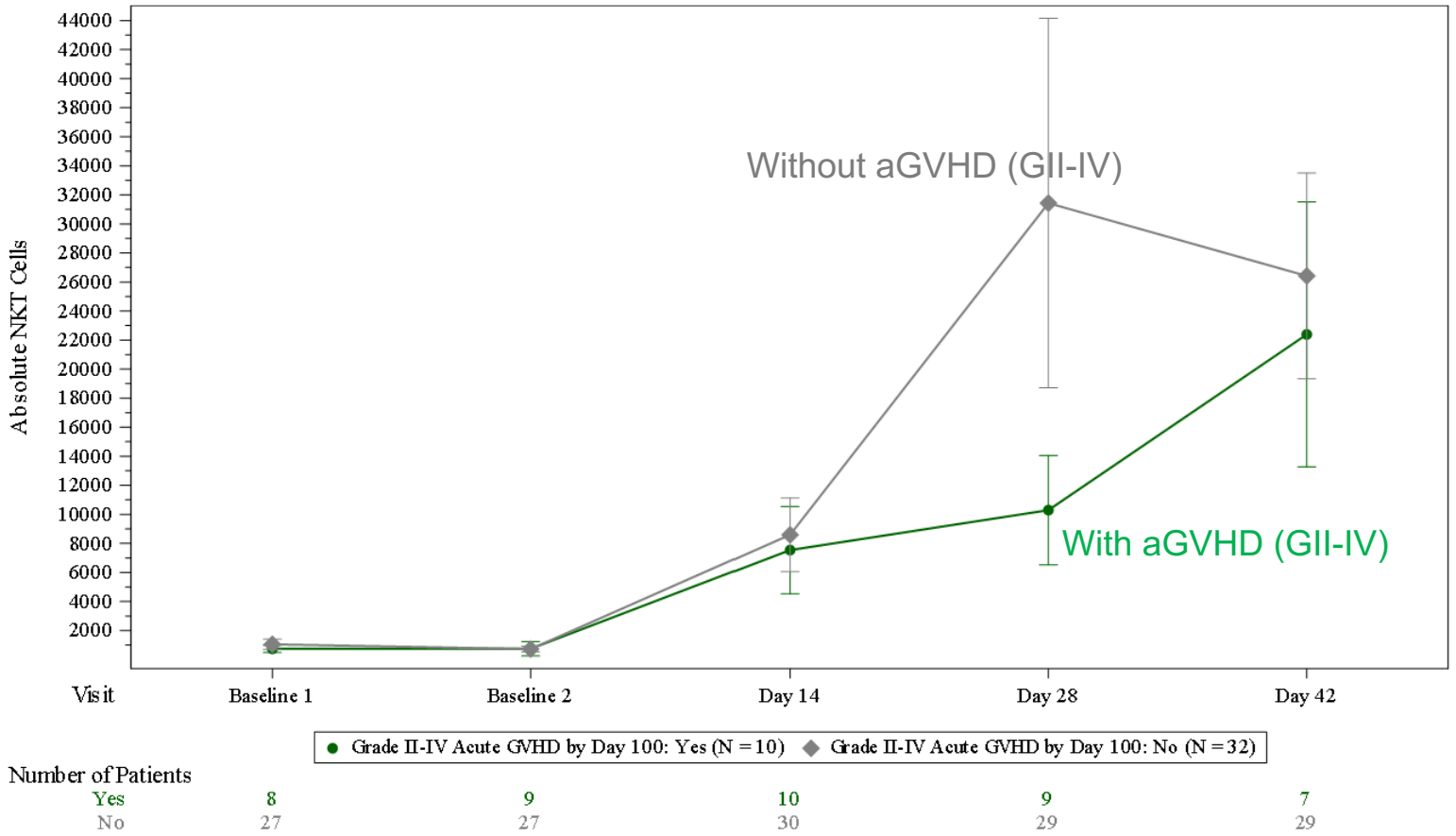
RGI-2001 Treatment-Related AEs (>10%)

All subjects enrolled (N=49)

	Adverse Events	All Grade TEAE N=49	Grade 3 or 4 TEAE N=49
Hematologic AEs	Platelet count decreased	7 (14.3%)	4 (8.2%)
	Anemia	6 (12.2%)	2 (4.1%)
	Neutrophil count decreased	6 (12.2%)	2 (4.1%)
Non-Hematologic AEs	Nausea	11 (22.4%)	1 (2.0%)
	Rash	10 (20.4%)	1 (2.0%)
	Diarrhea	9 (18.4%)	1 (2.0%)
	Stomatitis	9 (18.4%)	4 (8.2%)
	Decreased Appetite	9 (18.4%)	6 (12.2%)
	Abdominal pain	7 (14.3%)	0
	ALT increased	6 (12.2%)	0
	Fatigue	6 (12.2%)	0
	Hypomagnesemia	6 (12.2%)	0
	Mucosal inflammation	6 (12.2%)	3 (6.1%)
	Dyspnea	6 (12.2%)	0

Correlative Science

Absolute NKT cells over time for subjects treated with RGI-2001 with or without GII-IV aGVHD by Day 100



Higher numbers of iNKT cells have reduced risk of GVHD[1] and participants with rapid iNKT cells have lower risk of GVHD and improved survival[2]

NKT cells on Day 28 were on average higher in participants without GII-IV aGVHD

Baseline 1 = prior to transplant, baseline 2 = post transplant, prior to RGI-2001 treatment

[1]Rubio et al. Leukemia 31:903, 2017, Rubio et al. Blood 120: 2144, 2012; [2]Chaidos et al, Blood 119:5030, 2012, Malard et al, Blood 127:1828, 2016

Conclusions

- RGI-2001 with CNI-based prophylaxis results in low rates of acute GVHD and high acute GVHD-free survival.
- Compared to a contemporaneous CIBMTR Cohort:
  - RGI-2001 with CNI-based prophylaxis was associated with lower rates of Grade II-IV acute GVHD and higher acute GVHD-free survival (Grades II-IV and III-IV).
- Relapse rates between the 2 cohorts are similar, suggesting no compromise of the GVL effect.
- The similar rates of chronic GVHD in the 2 cohorts suggests that the activity of RGI-2001 is limited to acute GVHD with the current dosing regimen

Limitations and Future Directions

- RGI-2001+ CNI based regimen shows positive results for acute GVHD prevention with survival benefit and no increase in relapse vs CIBMTR control.

- Based on these results, a Phase 3 randomized controlled study is being planned to confirm the efficacy and safety of RGI-2001 in Allo-HCT.

- Correlative analyses are ongoing to evaluate changes in Treg and NK cell populations to evaluate the proposed mechanism of action on RGI-2001.