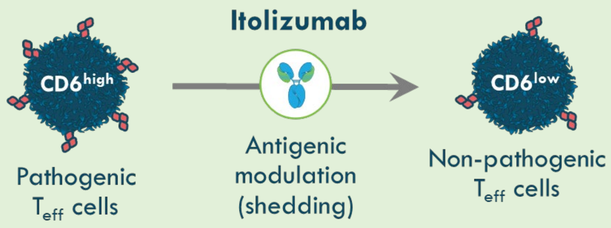
Final Safety and Efficacy Results from EQUATE, an Open-Label Study Evaluating Itolizumab, a Novel Targeted anti-CD6 Therapy, in Newly Diagnosed Acute Graft-Versus-Host Disease

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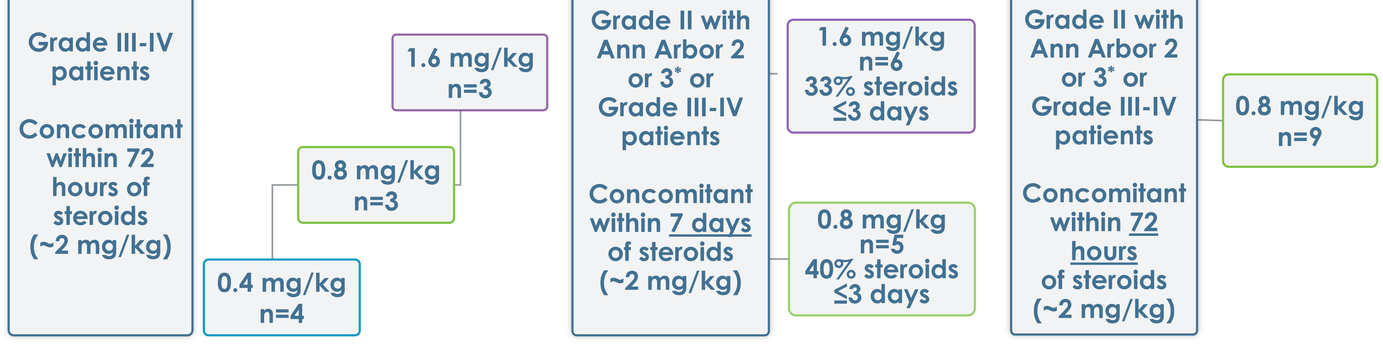
INTRODUCTION



- CD6 is a co-stimulatory receptor expressed on CD4 and CD8 T effector (T_{eff}) cells that modulates T cell activity and trafficking[1]
- The CD6 ligand, activated leukocyte cell adhesion molecule (ALCAM), is expressed on antigen presenting cells and tissues, including the skin and gastrointestinal (GI) tract
- CD6 and ALCAM are overexpressed during GI inflammation[2]
- Itolizumab is a first-in-class monoclonal antibody that targets the CD6-ALCAM pathway and causes CD6 shedding; this results in $CD6^{low}$ T cells
- $CD6^{low}$ T cells are hyporesponsive to stimulation, exhibiting decreased activation, proliferation, and cytokine production

EQUATE — **Phase 1b open-label, 3+3, dose escalation study evaluating itolizumab as first-line treatment for adult subjects with aGVHD (NCT03763318)**

Five itolizumab doses IV bi-weekly (Days 1, 15, 29, 43 & 57)
Subjects followed through Day 337



*Ann Arbor Score: 1, MAGIC Algorithm Probability (MAP) <0.141; 2, MAP 0.141-0.290; 3, MAP >0.290

RESULTS

SUBJECT DISPOSITION

- All subjects received at least 1 itolizumab dose; 33% received all 5 doses
- Study drug discontinuations after 1 dose of itolizumab were due to progressive aGVHD requiring alternative therapy (n=8), adverse event (AE; n=5), physician decision (n=3), withdrawal by subject (n=1), and death (n=1)

DEMOGRAPHICS AND BASELINE CHARACTERISTICS

	Itolizumab 0.4 mg/kg N=4	Itolizumab 0.8 mg/kg N=17	Itolizumab 1.6 mg/kg N=9	TOTAL N=30
Age (years), Mean (SD)	44 (18.0)	60 (10.9)	55 (13.0)	**56 (13.2)**
Sex (Male), n (%)	4 (100)	11 (65)	5 (56)	**20 (67)**
Race (White), n (%)	4 (100)	14 (82)	8 (89)	**26 (87)**
Primary Disease, n (%)				
Acute Myeloid Leukemia	2 (50)	8 (47)	2 (22)	**12 (40)**
Myelodysplastic Syndrome	0	4 (24)	2 (22)	**6 (20)**
Other	2 (50)	5 (29)	5 (56)	**12 (40)**
Graft Source, n (%)				
Peripheral Blood	4 (100)	15 (88)	9 (100)	**28 (93)**
Bone Marrow	0	2 (12)	0	**2 (7)**
aGVHD Clinical Grade*, n (%)				
II	0	1(6)	0	**1 (3)**
III	3 (75)	12 (71)	6 (67)	**21 (70)**
IV	1 (25)	4 (24)	3 (33)	**8 (27)**
Organ Involvement, n (%)				
Skin	1 (25)	7 (41)	4 (44)	**12 (40)**
Liver	1 (25)	2 (12)	1 (11)	**4 (13)**
Upper GI	1 (25)	10 (59)	2 (22)	**13 (43)**
Lower GI	4 (100)	14 (82)	7 (78)	**25 (83)**
Minnesota High Risk#, n (%)	4 (100)	10 (59)	7 (78)	**21 (70)**
Ann Arbor Score 3*, n (%)	4 (100)	7 (44)†	5 (56)	**16 (55)†**

*Highest clinical grade at screening or baseline. #Score calculated at Screening. †Day 1 Ann Arbor score was not available for one subject.
Abbreviations: aGVHD, acute graft-versus-host disease; GI, gastrointestinal; SD, standard deviation

KEY SAFETY RESULTS

The adverse event profile was consistent with a severe aGVHD patient population

- Three subjects had treatment-related serious AEs; one was a protocol-defined dose-limiting toxicity AE (sepsis)
- All infusion reaction AEs occurred with the first dose of 0.4 or 0.8 mg/kg itolizumab; subjects were able to complete dosing on Day 1
- No deaths were considered treatment-related

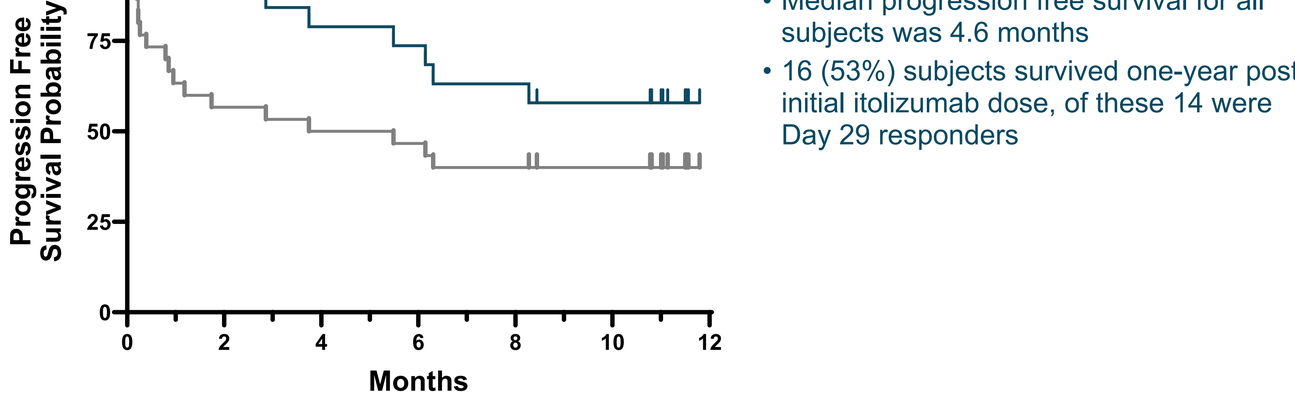
Subjects, n (%) with:	Itolizumab 0.4 mg/kg N=4	Itolizumab 0.8 mg/kg N=17	Itolizumab 1.6 mg/kg N=9	TOTAL N=30
Any AE	4 (100)	17 (100)	9 (100)	**30 (100)**
Infusion reaction AE	1 (25)	3 (18)	0 (0)	**4 (13)**
Infection AE	3 (75)	10 (59)	7 (78)	**20 (67)**
CTCAE Grade ≥3 AE	2 (50)	14 (82)	9 (100)	**25 (83)**
AE Leading to Study Drug Discontinuation	0	3 (18)	4 (44)	**7 (23)**
SAE	2 (50)	9 (53)	8 (89)	**19 (63)**
Infection SAE	1 (25)	4 (24)	6 (67)	**11 (37)**
Treatment-related SAE	0	2 (12)	1 (11)	**3 (10)**
Dose Limiting Toxicity AE	0	0	1 (11)	**1 (3)**
Deaths	1 (25)	7 (41)	6 (67)	**14 (47)**
AE Leading to Death	0	7 (41)	4 (44)	**11 (37)**

AEs were collected through Day 169 for subjects who completed dosing and Day 85 for subjects who discontinued study treatment early. Treatment-Related defined as possibly related, probably related, or related by the Investigator.
Dose-Limiting Toxicity defined as ≥Grade 3 infusion reaction or clinical finding associated with hypersensitivity or any ≥Grade 3 AE that is not related to underlying disease that is at least possibly related to study treatment as per the investigator.
Abbreviations: AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; SAE, serious adverse event

KEY EFFICACY RESULTS

Itolizumab was associated with high clinical response rates at Days 15 and 29

- High Day 29 response rates (CR and ORR) were seen in subjects who received itolizumab within 72 hours of systemic steroid initiation
- This included a high proportion of CRs following a single dose of itolizumab (Day 15)



Responses were sustained with meaningful progression free survival through one year



- Responses were sustained, with a mean duration of response of 206 days
- Median progression free survival for all subjects was 4.6 months
- 16 (53%) subjects survived one-year post initial itolizumab dose, of these 14 were Day 29 responders

Progression free survival is defined as the time from the date of first dose to the earliest observation of disease progression, rescue therapy, relapse of underlying malignancy or death. Duration of response is the time from first response to last assessment, disease progression or death.
Subjects with a PR, VGPR, or CR at Day 29 were considered Day 29 Responders. Topline data with database lock on 15 Dec 2022.
Abbreviations: aGVHD, acute graft versus host disease; CR, complete response; NR, no response; PD, progressive disease; PR, partial response; VGPR, very good partial response defined as achieving all the criteria for skin, liver, and gut involvement per Martin 2009 Consensus criteria without meeting the criteria for CR

CONCLUSIONS

Itolizumab in first-line treatment of acute GVHD resulted in rapid, durable responses with a favorable benefit-risk profile

- Itolizumab treatment in combination with systemic corticosteroids was associated with high rates of overall clinical response
- Response at Day 29 was associated with improved progression-free survival through 1 year
- Itolizumab was safe and well tolerated in severe aGVHD patients
- These data support ongoing development of itolizumab as first-line treatment for aGVHD and our pivotal Phase 3 study (EQUATOR)

ACKNOWLEDGMENTS

We would like to thank the patients and their families, the participating site investigators, research nurses, coordinators, supportive staff, our contract research organization and the EQUATE study team, including the Data Safety Monitoring Committee

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1. Consuegra-Fernandez M et al. *Cell Mol Immunol* 2018;17(5):493-503; **2.** Ma C et al. *J Crohns Colitis* 2019;13(4):510-524.

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Presented EBMT – April 23-26, 2023