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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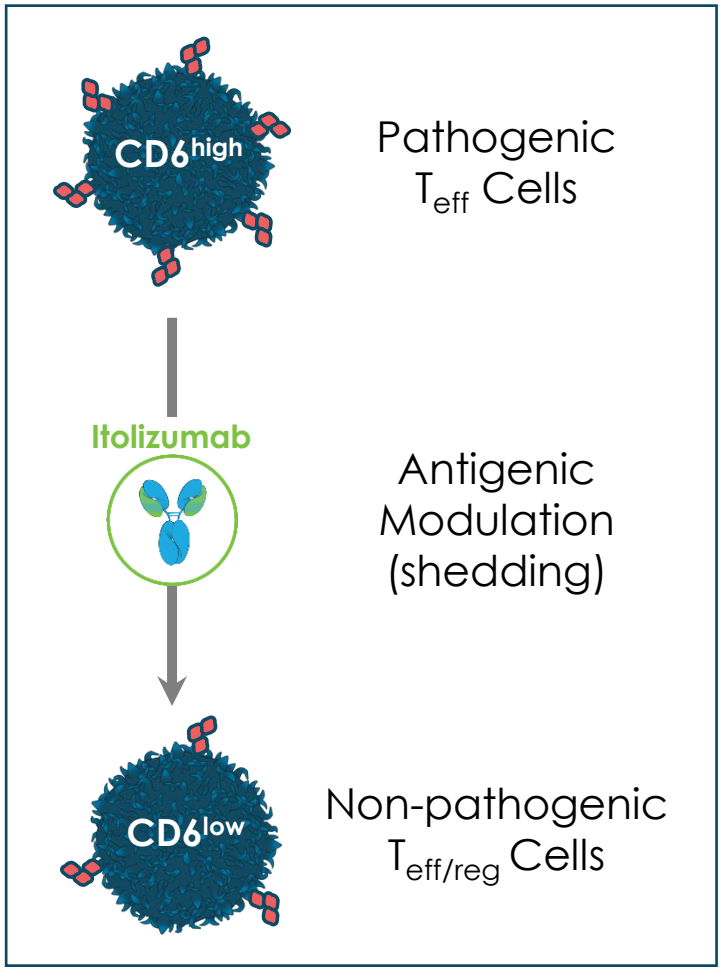
Disclosures

- The EQUATE study is funded by Equillium, Inc. (NCT03763318)
- John Koreth has received research funding from Bristol Myers Squibb, Miltenyi Biotec, Clinigen Labs, Regeneron, and Equillium; attended advisory boards with Biolojic Design, Mallinckrodt, and Cugene; received consulting fees from EMD Serono/Merck, Gentibio, Moderna Therapeutics, and Amgen
- Alison Loren, Ryotaro Nakamura, Edmund Waller, Joseph Pidala, and Marco Mielcarek have no disclosures
- Joel Rothman and Stephen Connelly are currently employees, stockholders, and officers of Equillium
- Cherie Ng, Lisette Acevedo and Maple Fung are currently employees and stockholders of Equillium
- Corey Cutler has received consulting fees from Mesoblast, Syndax, Omeros, Incyte, CareDx, Mallinckrodt, Pfizer, Kadmon (pro bono), Editas, Cimeio, Deciphera, and Jazz

Itolizumab-induced Loss of Cell Surface CD6 Inhibits T_{eff} Cells

- **CD6 is a co-stimulatory receptor** expressed on CD4 and CD8 T_{eff} cells and modulates **T cell activity and trafficking**
- The CD6 ligand ALCAM is **expressed on APCs and tissues**, including the skin and GI tract
- CD6 and ALCAM are both **overexpressed during GI inflammation**
- Prior clinical studies confirmed CD6 is a **validated target in the pathogenesis of aGVHD**



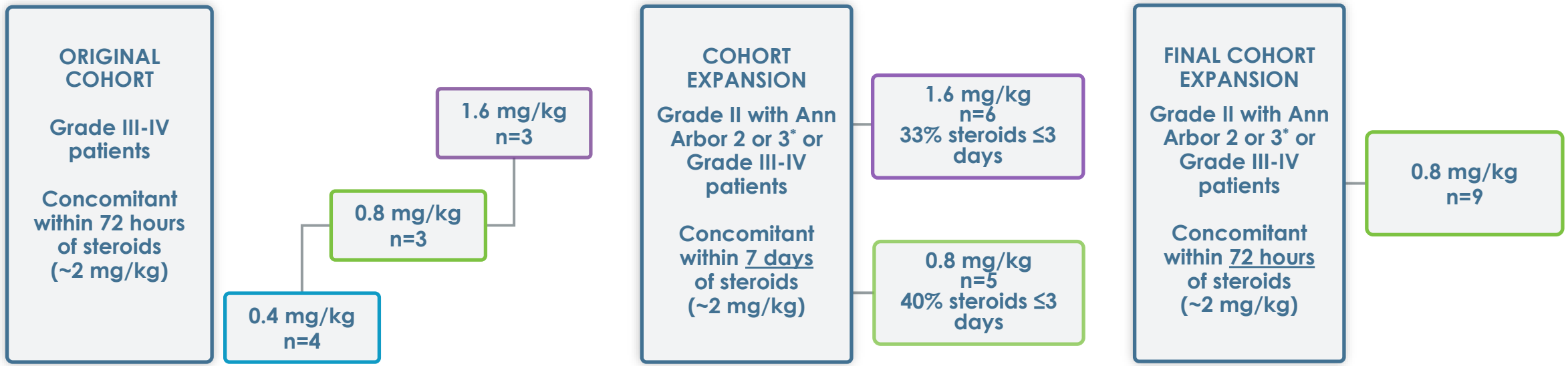
- **Itolizumab is a first-in-class mAb** targeting the CD6-ALCAM pathway
- **Itolizumab binds to $CD6^{high}$ T cells causing receptor shedding** to produce non-pathogenic $CD6^{low}$ T cells
- **$CD6^{low}$ T cells are hyporesponsive** to stimulation, exhibiting decreased activation, proliferation, and cytokine production
- **Itolizumab is being evaluated as a treatment for multiple immuno-inflammatory diseases** in which T_{eff} cells play a central role

References: Consuegra-Fernandez et al., Cell Mol Immunol 2018; Ma et al., J Crohns & Colitis 2019; Soiffer et al., JCO 1992
Abbreviations: aGVHD, acute graft versus host disease; ALCAM, activated leukocyte cell adhesion molecule; APC, antigen presenting cell; GI, gastrointestinal; Teff, T effector

Phase 1b Study of Itolizumab as First-line Treatment for aGVHD

EQUATE

Open-label, 3+3 Dose Escalation Study
Five itolizumab doses IV bi-weekly (Days 1, 15, 29, 43 & 57)
Subjects followed through Day 337



Primary Objectives

- Assess the safety and tolerability of IV dosing of itolizumab
- Determine optimal IV dose level(s) of itolizumab

Secondary Objectives

- Characterize the pharmacokinetics (PK) and pharmacodynamics (PD) of itolizumab
- Assess the clinical activity of itolizumab: GVHD ORR, NRM, chronic GVHD, durability

*Ann Arbor Score: 1, MAP <0.141; 2, MAP 0.141-0.290; 3, MAP >0.290
Topline data with database lock on 15 Dec 2022.

Baseline Demographics and GVHD 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 (M), n (%)	4 (100%)	11 (65%)	5 (56%)	**20 (67%)**
Race (White), n (%)	4 (100%)	14 (82%)	8 (89%)	**26 (87%)**
Primary Disease, n (%)				
ALL	2 (50%)	8 (47%)	2 (22%)	**12 (40%)**
AML	1 (25%)	1 (6%)	1 (11%)	**3 (10%)**
MDS	0	4 (24%)	2 (22%)	**6 (20%)**
Other	1 (25%)	4 (24%)	4 (44%)	**9 (30%)**
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%)**
UGI	1 (25%)	10 (59%)	2 (22%)	**13 (43%)**
LGI	4 (100%)	14 (82%)	7 (78%)	**25 (83%)**
Minnesota High Risk Score#, n (%)	4 (100%)	10 (59%)	7 (78%)	**21 (70%)**
Ann Arbor Score 3†, n (%)	4 (100%)	7 (44%)†	5 (56%)	**16 (55%)†**

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; GVHD, graft versus host disease; LGI; lower gastrointestinal; M, male; MDS, myelodysplastic syndrome; SD, standard deviation; UGI, upper gastrointestinal

† Ann Arbor score was assessed on Day 1 and was not available for one subject' *Highest clinical grade at screening or baseline. #Score calculated at Screening

Topline data with database lock on 15 Dec 2022

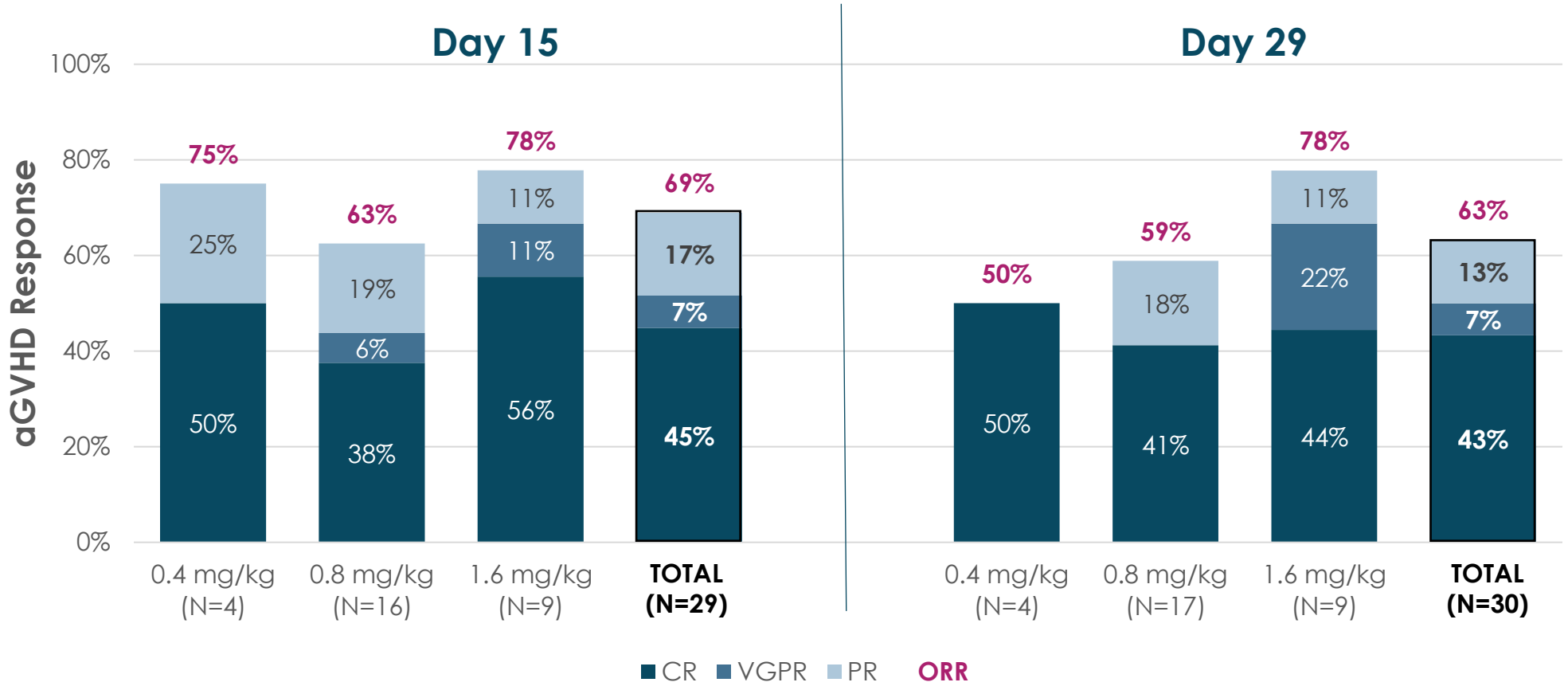
Treatment Emergent Adverse Events

Subjects 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 n (%)
Any AE, n (%)	4 (100)	17 (100)	9 (100)	**30 (100)**
Infusion reaction AE	1 (25.0)	3 (17.6)	0 (0.0)	**4 (13.3)**
Infection AEs	3 (75.0)	10 (58.8)	7 (77.8)	**20 (66.7)**
CTCAE Grade ≥3 AE	2 (50.0)	14 (82.4)	9 (100)	**25 (83.3)**
AE Leading to Study Treatment Discontinuation, n (%)	0	3 (17.6)	4 (44.4)	**7 (23.3)**
Infection AEs With treatment discontinuation	0	1 (5.9)	2 (22.2)	**3 (10.0)**
SAE, n (%)	2 (50.0)	9 (52.9)	8 (88.9)	**19 (63.3)**
Infection SAE	1 (25.0)	4 (23.5)	6 (66.7)	**11 (36.7)**
Treatment-related SAE	0	2 (11.8)	1 (11.1)	**3 (10.0)**
Dose Limiting Toxicity AE, n (%)	0	0	1 (11.1)	**1 (3.3)**
Deaths, n (%)	1 (25.0)	7 (41.2)	6 (66.7)	**14 (46.7)**
AE Leading to Death, n (%)	0	7 (41.2)	4 (44.4)	**11 (36.7)**
Deaths related to study treatment	0	0	0	**0**

AEs were collected through Day 169 for subjects who completed dosing and Day 85 for subjects who discontinued study treatment early. With Protocol Amendment 6, SAEs and AEs of special interest were collected through Day 337. Treatment related is defined as possibly related, probably related, or related by the Investigator. Dose Limiting Toxicity is 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
Topline data with database lock on 15 Dec 2022.

Early Response Rates to Itolizumab Treatment

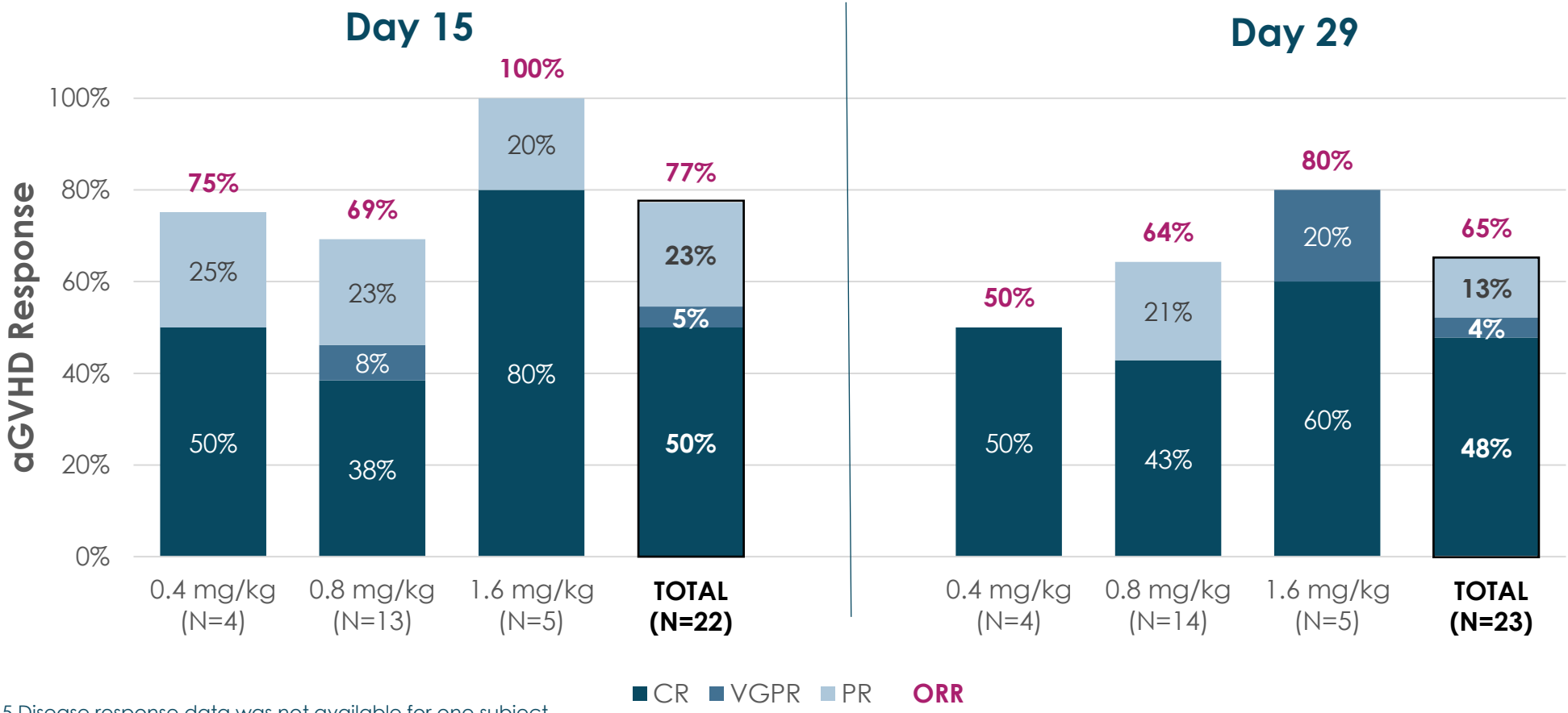
Itolizumab was associated with high clinical response rates at Day 15 and 29



* Day 15 Disease response data was not available for one subject.
Abbreviations: CR, complete response; ORR=PR+VGPR+CR, overall response rate; 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.
Topline data with database lock on 15 Dec 2022.

Early Response Rates in Treatment Naïve Subjects

High response rates to itolizumab in treatment naïve subjects (≤3 days of steroids)



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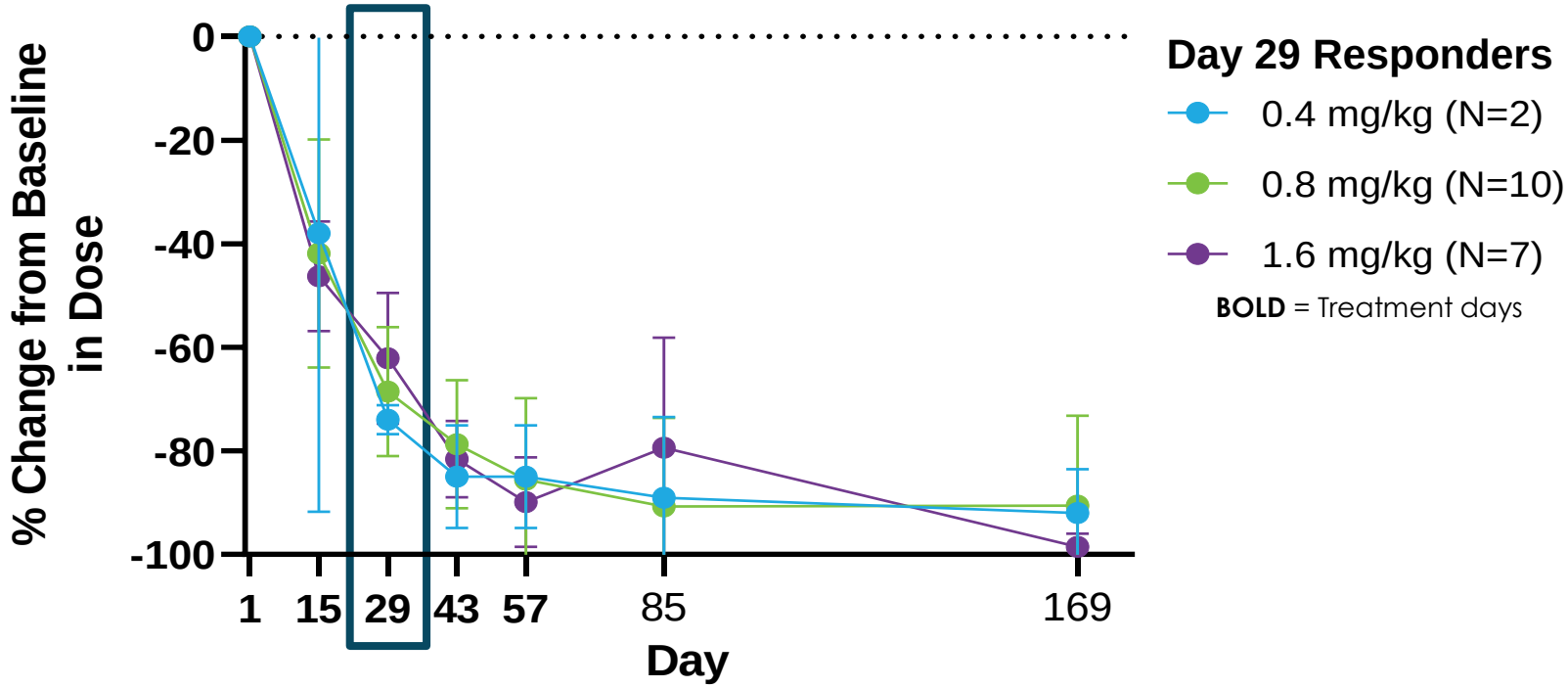
Corticosteroid Use

Itolizumab responders were able to reduce systemic steroids quickly

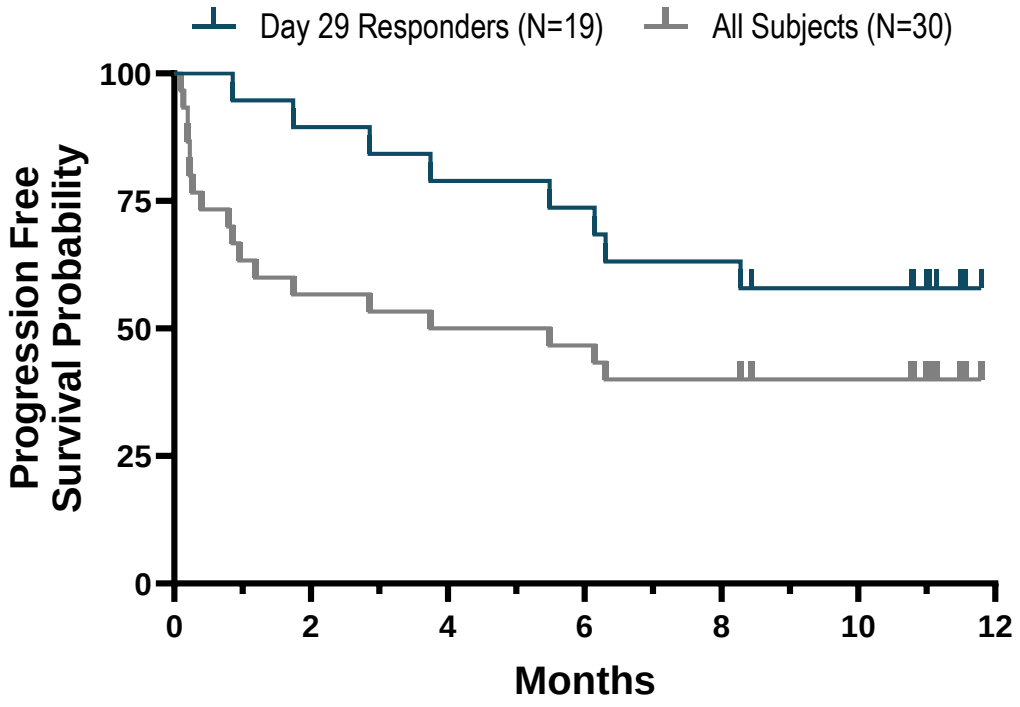


Median steroid dose reduction for Responders was 70% at Day 29 and 99% at Day 169

Data presented as mean (SD); equivalent prednisone dose calculated for methylprednisolone and dexamethasone to determine systemic steroid use at each visit
Subjects with a PR, VGPR, or CR at Day 29 were considered Day 29 Responders (n=19), whereas those with NR or PD were considered Day 29 Non-Responders (n=11)
Topline data with database lock on 15 Dec 2022.
Abbreviations: CR, complete response; NR, no response; PD, progressive disease; PR, partial response; SD, standard deviation; VGPR, very good partial response

Progression Free Survival

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
- Responders were able to taper steroids by 70% at Day 29 and 99% at Day 169
- Itolizumab was safe and well tolerated in severe aGVHD patients
- These data support our ongoing pivotal Phase 3 study (EQUATOR)

ClinicalTrials.gov NCT05263999; https://clinicaltrials.gov/ct2/show/NCT05263999?term=itolizumab&draw=2&rank=1. Accessed January 2023.

Abbreviations: aGVHD, acute graft versus host disease; CR, complete response; ORR overall response rate

Thank You to Our Patients, Sites and Advisors!



Advisors

- Leslie Kean, MD, PhD
- Jerome Ritz, MD
- Robert Soiffer, MD
- EQUATE Data Safety Monitoring Committee

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THANK YOU