EHA 2021

Interim results from the EQUATE Study: Preliminary safety and efficacy of itolizumab, a novel targeted anti-CD6 therapy, in newly diagnosed severe acute graft-versus-host disease

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Disclosures

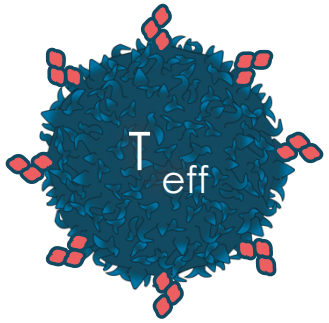
Dr. John Koreth maintains the following affiliations:

- Research Support: Bristol Myers Squibb, Miltenyi, Clinigen, Amgen, Regeneron
- Advisory Board: Therakos, Cugene, Regeneron
- Consulting: EMD Serono/Merck, Biolojic Design, Gentibio, Moderna Therapeutics, Equillium

Investigational use of Itolizumab (EQ001) for acute graft versus host disease (aGVHD)

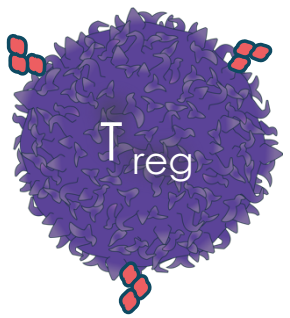
CD6-ALCAM Pathway Central to Immune Inflammation in aGVHD

- CD6 is a co-stimulatory receptor expressed on CD4 and CD8 effector T cells (T_{eff})
- Multiple CD6 ligands, including activated leukocyte cell adhesion molecule (ALCAM), expressed on both APCs and tissues, including the skin and GI tract
- CD6-ALCAM pathway modulates both T cell activity and trafficking
- CD6 and ALCAM both overexpressed during GI inflammation



$CD6^{high}$

- High proliferation
- Pathogenic phenotypes
- Pro-inflammatory cytokines



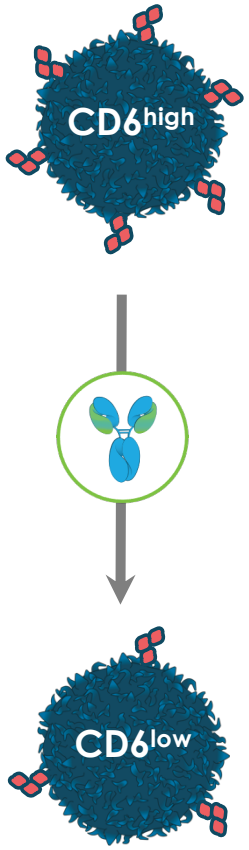
$CD6^{low/-}$

- Low proliferation
- Regulatory phenotype
- Anti-inflammatory cytokines

- Prior studies performed at DFCI validated CD6 as a target relevant to GVHD pathogenesis

Consuegra-Fernandez *et al.*, Cell Mol Immunol 2018; Ma *et al.*, J Crohns & Colitis 2019; Soiffer *et al.*, JCO 1992

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

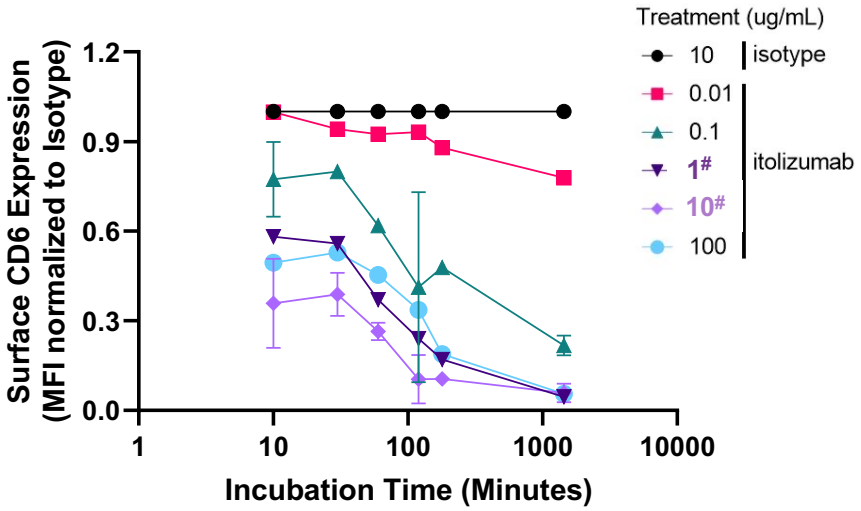


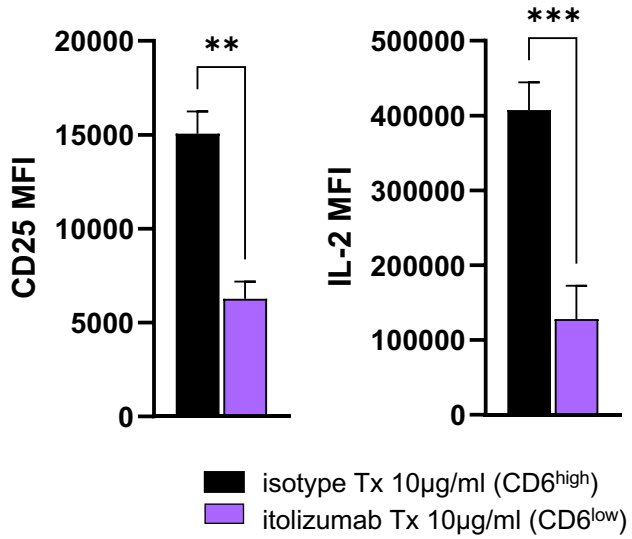
Pathogenic T_{eff} Cells

Antigenic Modulation (shedding)

Non-pathogenic T_{eff} Cells

Itolizumab leads to loss of CD6 in a dose- and time-dependent manner resulting in T cells that are hyporesponsive to TCR stimulation†





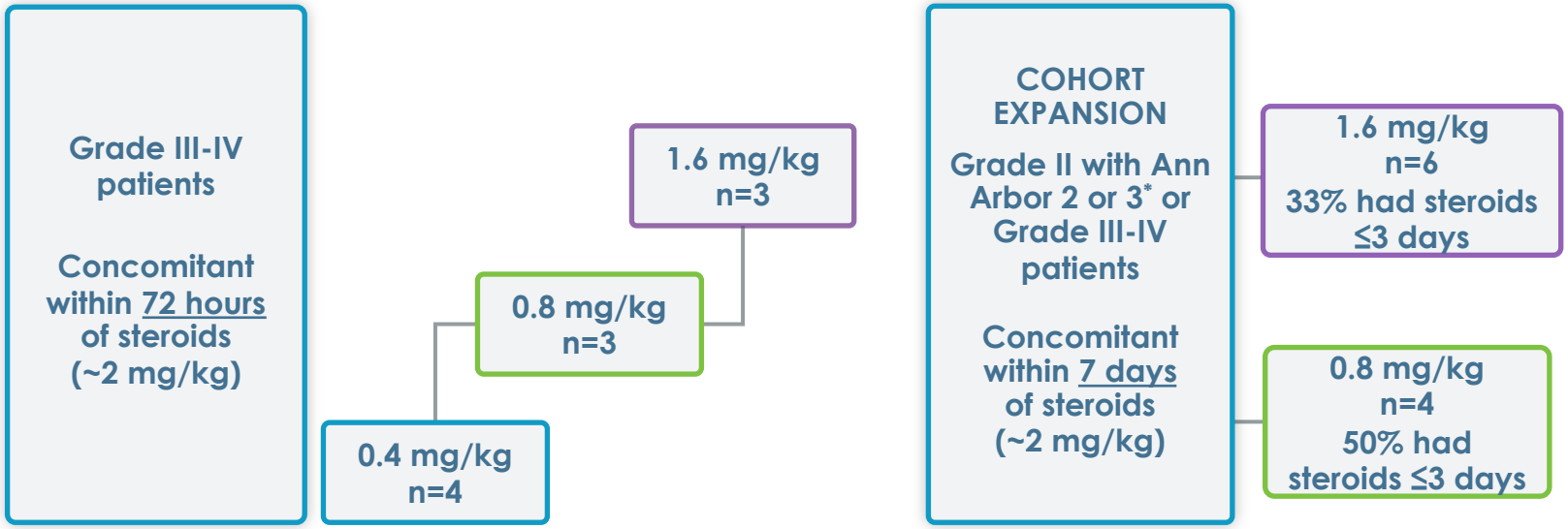
- Itolizumab binds to domain-1 of CD6 causing shedding that can be detected with a non-competing anti-CD6 antibody
- Dose-dependent CD6 loss results in hyporesponsive T cells
- CD6 pharmacodynamic marker can be monitored in patients

#clinically relevant doses
**p<0.01, ***p<0.001
†Chu, D., Ampudia, J., Connelly, S., & Ng, C. (2021). American Association of Immunologists 104th annual meeting. See Equillium website for details

EQUATE Study Enrollment: First-line Treatment of aGVHD

EQUATE

Phase 1b open-label, 3+3, dose escalation study
Five itolizumab doses IV bi-weekly (Days 1, 15, 29, 43 & 57)
Subjects followed through Day 337



- Per protocol, 3 evaluable subjects expected in each dose cohort for safety assessment
- Safety: Evaluable subjects must receive ≥ 2 doses or receive ≥ 1 dose with a DLT in the first 29 days
- Continuing to enroll patients at 0.8 mg/kg; no further dose escalation is anticipated

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
DLT 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.
Interim data with a cut-off date of 30 Apr 2021 and subject to change.

equillium

Baseline Demographics and Disease Characteristics by Dose Group

	Itolizumab 0.4 mg/kg N=4	Itolizumab 0.8 mg/kg N=7	Itolizumab 1.6 mg/kg N=9	TOTAL N=20
Age (years), Mean (SD)	44 (18.0)	56 (15.5)	55 (13.0)	**53 (14.8)**
Sex (M), n (%)	4 (100%)	4 (57%)	5 (56%)	**13 (65%)**
Race (White), n (%)	4 (100%)	4 (57%)	8 (89%)	**16 (80%)**
Primary Disease, n (%)				
AML	2 (50%)	4 (57%)	2 (22%)	**8 (40%)**
ALL	1 (25%)	1 (14%)	1 (11%)	**3 (15%)**
MDS	0 (25%)	1 (14%)	2 (22%)	**3 (15%)**
Other	1 (25%)	1 (14%)	4 (44%)	**6 (30%)**
Graft Source, n (%)				
Peripheral Blood	4 (100%)	5 (71%)	9 (100%)	**18 (90%)**
Bone Marrow	0	2 (29%)	0	**2 (10%)**
HLA Mismatched, n (%)	2 (50%)	0	1 (11%)	**3 (15%)**
Myeloablative Conditioning, n (%)	2 (50%)	4 (57%)	6 (67%)	**12 (60%)**

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; HLA, human leukocyte antigen; M, male; MDS, myelodysplastic syndrome; SD, standard deviation.
Interim data with a cut-off date of 30 Apr 2021 and subject to change.

Baseline GVHD Characteristics by Dose Group

	Itolizumab 0.4 mg/kg N=4	Itolizumab 0.8 mg/kg N=7	Itolizumab 1.6 mg/kg N=9	TOTAL N=20
Organ Involvement, n (%)				
Skin	1 (25%)	1 (14%)	4 (44%)	**6 (30%)**
Liver	1 (25%)	0	1 (11%)	**2 (10%)**
UGI	1 (25%)	4 (57%)	1 (11%)	**6 (30%)**
LGI	4 (100%)	7 (100%)	7 (78%)	**18 (90%)**
aGVHD Clinical Grade*, n (%)				
III	3 (75%)	3 (43%)	6 (67%)	**12 (60%)**
IV	1 (25%)	4 (57%)	3 (33%)	**8 (40%)**
Minnesota High Risk Score#, n (%)	4 (100%)	4 (57%)	7 (78%)	**15 (75%)**
Ann Arbor Score 2 or 3*, n (%)	4 (100%)	5 (100%)†	8 (89%)	**17 (94%)**†
Prophylaxis, n (%)				
Methotrexate	3 (75%)	4 (57%)	5 (56%)	**12 (60%)**
Tacrolimus	3 (75%)	5 (71%)	6 (67%)	**14 (70%)**
Sirolimus	2 (50%)	4 (57%)	3 (33%)	**9 (45%)**

Ann Arbor Score: 1, MAP <0.141; 2, MAP 0.141-0.290; 3, MAP >0.290 taken at Day 1 of dosing.
Abbreviations: GVHD, graft versus host disease; LGI; lower gastrointestinal; MAP; MAGIC algorithm probability; UGI, upper gastrointestinal.
*Highest clinical grade at screening or baseline. #Score calculated at Screening. †Ann Arbor Scores for 0009-0001 and 0014-0004 were not available at cut-off date.
Interim data with a cut-off date of 30 Apr 2021 and subject to change.

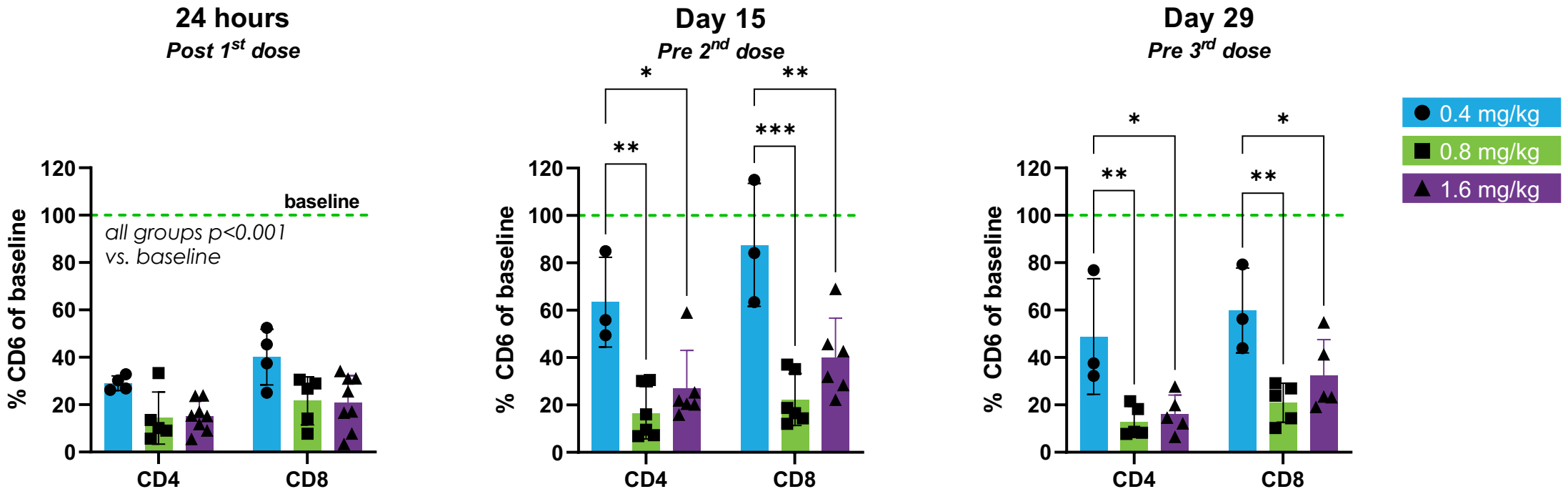
Safety: Treatment Emergent Adverse Events by Dose Group

Subjects with:	Itolizumab 0.4 mg/kg N=4 n (%)	Itolizumab 0.8 mg/kg N=7 n (%)	Itolizumab 1.6 mg/kg N=9 n (%)	TOTAL N=20 n (%)
Any AE	4 (100)	7 (100)	9 (100)	**20 (100)**
Infusion Reaction AE	1 (25.0)	2 (28.6)	0 (0.0)	**3 (15.0)**
Infection AEs	3 (75.0)	4 (57.1)	7 (77.8)	**14 (70.0)**
CTCAE Grade ≥3 AE	2 (50.0)	6 (85.7)	9 (100)	**17 (85.0)**
AE Leading to Study Treatment Discontinuation	0	2 (28.6)	4 (44.4)	**6 (30.0)**
Infection AEs With Treatment Discontinuation	0	1 (14.3)	2 (22.2)	**3 (15.0)**
SAE	2 (50.0)	2 (28.6)	8 (88.9)	**12 (60.0)**
Infection SAE	1 (25.0)	2 (28.6)	5 (55.6)	**8 (40.0)**
Treatment Related SAE	0	1(14.3)	1 (11.1)	**2 (10.0)**
Dose Limiting Toxicity AE	0	0	1 (11.1)	**1 (5.0)**
AE Leading to Death	0	1 (14.3)	3 (33.3)	**4 (20.0)**
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; 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
Interim data with a cut-off date of 30 Apr 2021and subject to change.

PD: Dose Responsive Reduction of CD6 with Itolizumab

Interim data suggests effective dose range is 0.8 to 1.6 mg/kg



- Itolizumab significantly reduces the surface levels of CD6 on T cells by 24 hours following the first dose.
- At 0.4 mg/kg, CD6 trends toward baseline by Day 15; at higher doses CD6 remains significantly reduced (p<0.001).

*p < 0.05, **p<0.01, and ***p<0.001
Interim data with a cut-off date of 30 Apr 2021 and subject to change.

Efficacy: Responses by Day 15 & Maintained at Day 29

	Early response: Day 15		Response endpoint: Day 29		Treatment naïve response Day 29 *Treatment ≤3 days of steroids*		
	CR	ORR	CR	ORR	N	CR	ORR
All Subjects, n (%)							
0.4 mg/kg (N=4)	2 (50.0)	3 (75.0)	2 (50.0)	2 (50.0)	4	2 (50.0)	2 (50.0)
0.8 mg/kg (N=7)	5 (71.4)	5 (71.4)	5 (71.4)	5 (71.4)	5	4 (80.0)	4 (80.0)
1.6 mg/kg (N=9)	4 (44.4)	7 (77.8)	4 (44.4)	7 (77.8)	5	3 (60.0)	4 (80.0)
TOTAL (N=20)	**11 (55.0)**	**15 (75.0)**	**11 (55.0)**	**14 (70.0)**	**14**	**9 (64.3)**	**10 (71.4)**
Evaluable Subjects (received ≥ 2 doses), n (%)							
0.4 mg/kg (N=3)	2 (66.7)	3 (100)	2 (66.7)	3 (100)	3	2 (66.7)	3 (100)
0.8 mg/kg (N=5)	5 (100)	5 (100)	5 (100)	5 (100)	4	4 (100)	4 (100)
1.6 mg/kg (N=6)	3 (50.0)	5 (83.3)	3 (50.0)	5 (83.3)	5	3 (60.0)	4 (80.0)
TOTAL (N=14)	**10 (71.4)**	**13 (92.9)**	**10 (71.4)**	**13 (92.9)**	**12**	**9 (75.0)**	**10 (83.3)**

- Six subjects received only one itolizumab dose and were not evaluable per protocol, of which 67% received systemic steroids for ≥4 days prior to itolizumab dosing
- Discontinuation of study drug after one itolizumab dose due to:
  - Requiring subsequent administration of alternate anti-GVHD therapy for progressive disease (n=4)
  - Adverse event unrelated to study drug (n=2)

Evaluable subjects must receive ≥ 2 doses or receive ≥ 1 dose with a dose limiting toxicity in the first 29 days.
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.
Interim data with a cut-off date of 30 Apr 2021 and subject to change.

Evaluable Subjects Had Early Responses, Maintained Off-treatment

	Subject aGVHD Grade	Initial Steroid Dose† ≤ 3 days	Treatment Period				Off-Treatment Follow-up Period			
			Day 15	Day 29	Day 43	Day 57	Day 85	Day 169	Day 253	Day 337
Itolizumab 0.4 mg/kg	Gr III	Yes	**CR**	**CR**	**CR**▼	**CR**	CR	CR	PD#	--
	Gr IV	Yes	**PR**	**PD#**	--	--	--	--	--	--
	Gr III	Yes	**CR**	**CR**	**CR**	**PR**	CR	CR	CR	CR
Itolizumab 0.8 mg/kg	Gr IV	Yes	**CR**	**CR**	CR	CR▼	CR	CR	CR	CR
	Gr IV	Yes	**CR**	CR	**CR**	**CR**	CR	CR	CR ○	
	Gr III	Yes	**CR**	CR	CR	CR▼	CR	--	CR	
	Gr III	No (6 days)	**CR**	**CR**	**CR**	**CR**	CR			
	Gr III	Yes	**CR**	**CR**	**CR**▼	**CR**				
Itolizumab 1.6 mg/kg	Gr III	Yes	**CR**	**CR**	**CR**▼	**CR**	PD ●			
	Gr III	Yes	**CR**	CR	CR▼	CR	CR	CR ○		
	Gr III	Yes	**PR**	**VGPR**	**CR**	**CR**▼	CR	CR		
	Gr IV	No (4 days)	**NR**	**PR**	**CR**	**CR**▼	CR	CR		
	Gr III	Yes	**PR** ●							
	Gr III	Yes	CR	**CR**	**CR**▼	**CR**	CR			

Enrolled in primary cohort

Enrolled in expansion cohort

BOLD = Itolizumab dosing

▼Achieved prednisone or equivalent dose of ≤0.25 mg/kg/day

Discontinued study due to:
- ○ Primary disease relapse
- ● Unrelated AE leading to death
- ○ Death due to primary disease relapse

Abbreviations: CR, complete response; NR, No response; PD, progressive disease; PR, partial response; VGPR, very good partial response.
Evaluable subjects must receive ≥ 2 doses or receive ≥ 1 dose with a dose limiting toxicity in the first 29 days.
†Initial systemic dose of ~1-2 mg/kg prednisone or equivalent prior to itolizumab dosing.
#Disease response after rescue treatment is not included.
Interim data with a cut-off date of 30 Apr 2021 and subject to change.

Six-Month Outcomes Post-Itolizumab Therapy

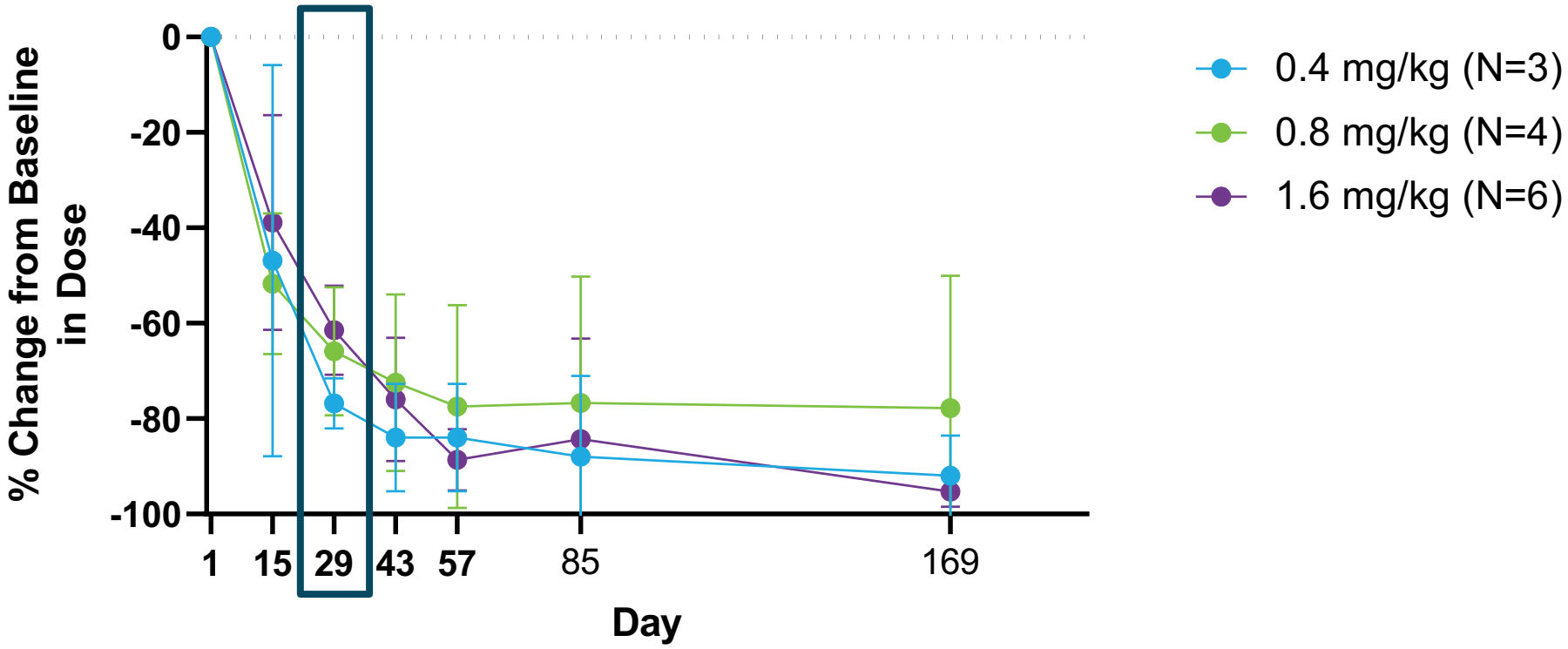
	Outcomes Through Day 169 Visit (Month 6)					
	Overall Survival	CR at Day 169	Durable response*	Non-Relapse Mortality	Recurrent aGHVD	cGVHD
All Subjects, n (%)						
0.4 mg/kg (N=4)	3 (75.0)	2 (50.0)	2 (50.0)	1 (25.0)	2 (50.0)	1 (25.0)
0.8 mg/kg (N=4)	3 (75.0)	3 (75.0)	3 (75.0)	1 (25.0)	0	1 (25.0)
1.6 mg/kg (N=7)	4 (57.1)	4 (57.1)	4 (57.1)	3 (42.9)	1 (14.3)	0
TOTAL (N=15)	**10 (66.7)**	**9 (60.0)**	**9 (60.0)**	**5 (33.3)**	**3 (20.0)**	**2 (13.3)**
Evaluable Subjects (Received ≥ 2 doses), n (%)						
0.4 mg/kg (N=3)	3 (100)	2 (66.7)	2 (66.7)	0	2 (66.7)	1 (33.3)
0.8 mg/kg (N=3)	3 (100)	3 (100)	3 (100)	0	0	1 (33.3)
1.6 mg/kg (N=5)	3 (60.0)	3 (60.0)	3 (60.0)	2 (40.0)	1 (20.0)	0
TOTAL (N=11)	**9 (81.8)**	**8 (72.7)**	**8 (72.7)**	**2 (18.2)**	**3 (27.3)**	**2 (18.2)**

- Only subjects that have met endpoint or have been studied for 6 months (up to 4 months post-treatment) are included

Abbreviations: CR, complete response; ORR, overall response rate; 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.
All subjects received 1-5 doses of itolizumab.
*Durable response is defined as PR, CR, or VGPR from Day 29 through Day 169.
Interim data with a cut-off date of 30 Apr 2021 and subject to change.

Itolizumab Associated with Dose Reduction in Systemic Steroid Use

Evaluable Patients



- Most subjects maintained the reduction from Day 29 and/or continued tapering through Day 169

Data presented as mean (SD); equivalent prednisone dose was calculated for methylprednisolone and dexamethasone to determine systemic corticosteroid use at each visit.
Evaluable subjects must receive ≥ 2 doses or receive ≥ 1 dose and have a dose limiting toxicity (DLT) in the first 29 days, who received 1-2 mg/kg prednisone or equivalent at baseline.
Interim data with a cut-off date of 30 Apr 2021and subject to change.

Conclusions: First-line Itolizumab Treatment Resulted in Rapid and Durable Response in High Risk Acute GVHD

- CD6-ALCAM pathway is a validated and attractive target for further investigation in GVHD
  - Dose-dependent reduction of CD6 expression on CD4+ and CD8+ T cells consistent with MoA
- Itolizumab was well tolerated across all doses
  - Adverse events, including SAEs, are consistent with aGVHD population
  - No direct drug toxicities reported to date
- Early CRs observed with itolizumab (Days 1-57), durable up to Day 337
  - Greater responses observed with 0.8 mg/kg and 1.6 mg/kg doses
  - Responses associated with rapid reduction in systemic corticosteroid use
  - Overall survival of 67% at 6 months in subjects across treatment groups
- 0.4 mg/kg dose appears subtherapeutic response compared to higher doses

Itolizumab offers a favorable benefit-risk profile that supports evaluation in future studies

Thank you to our patients, sites, and advisors!



- Leslie Kean, MD, PhD
- Jerome Ritz, MD
- Robert Soiffer, MD
- EQUATE DSMC Committee