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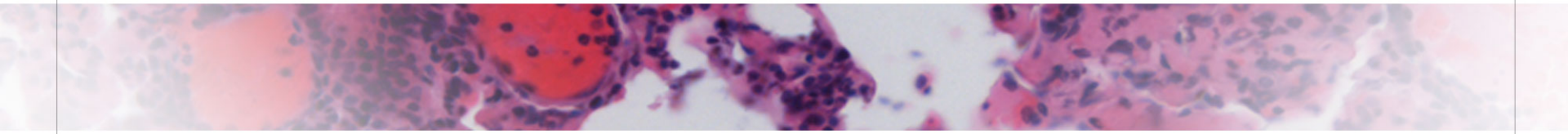

Safety, Tolerability, and Efficacy of Axatilimab, a CSF-1R humanized antibody, for Chronic Graft-versus-Host Disease after 2 or more Lines of Systemic Treatment

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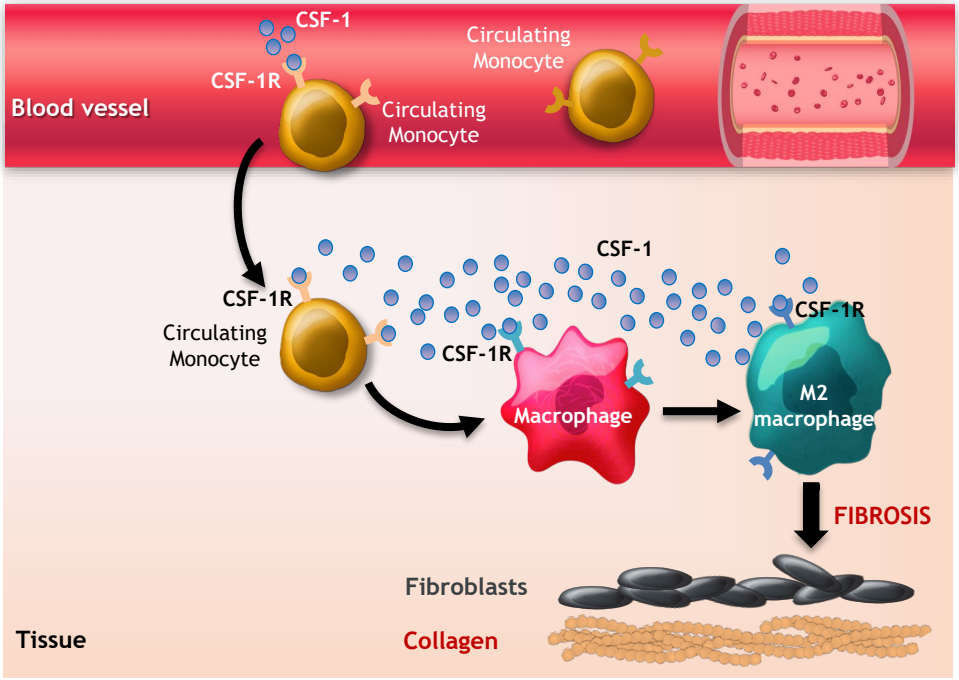
Disclosures

Year	Source	Topic	Activity
2018	Pfizer	inotuzumab AML	Consulting
2018	Kadmon	belumosudil (KD025)	Consulting
2018	Millennium Pharmaceuticals Inc.	ixazomib	Research funding
2018	Novartis Inc.	ofatumumab	Research funding
2018	Amgen Inc.	efavaleukin alfa (AMG592)	Travel and lodging
2018 -	Kadmon Corporation LLC	belumosudil (KD025)	Research funding
2018 -	Amgen Inc.	efavaleukin alfa (AMG592)	Research funding
2019 -	Pfizer Inc.	glasdegib	Research funding
2019 -	Syndax Pharmaceuticals Inc.	axatilimab (SNDX-6352)	Research funding
2019 -	Incyte	ruxolitinib	Research funding
2019 -	AstraZeneca Pharmaceuticals LP	acalabrutinib	Research funding
2021	Mallinckrodt	extracorporeal photopheresis	Consulting
2021	Amgen	efavaleukin alfa (AMG592)	Consulting
2021-	National Marrow Donor Program	member	Board of Directors

Background

- Chronic GVHD affects 30-50% of allogeneic HCT recipients
  - Systemic disease with dysregulated inflammatory and fibrotic features
  - Multiorgan involvement is common, most often skin, mouth, eye, liver
- Major cause of late morbidity and mortality after allogeneic HCT
- Corticosteroids are standard frontline treatment
- Approximately 50% of patients need second line treatment for disease progression or inadequate response
- Ibrutinib, Ruxolitinib and Belumosudil are FDA-approved for systemic treatment of chronic GVHD after 1-2 prior lines of systemic therapy, including steroids
- Amongst patients with chronic GVHD, many still fail to respond to available therapies or eventually progress, and those with sclerosis and lung involvement are often difficult to treat and have poor outcomes

CSF-1R signaling is critical for macrophage-driven cGVHD pathophysiology



- Preclinical models demonstrate the role of CSF-1R-dependent macrophages in disease development
- Blocking CSF-1 / CSF-1R signaling may prevent and treat cGVHD

Figure Adopted from MacDonald, K.P.A. et al., *Blood*, 5 (129) 13-21;

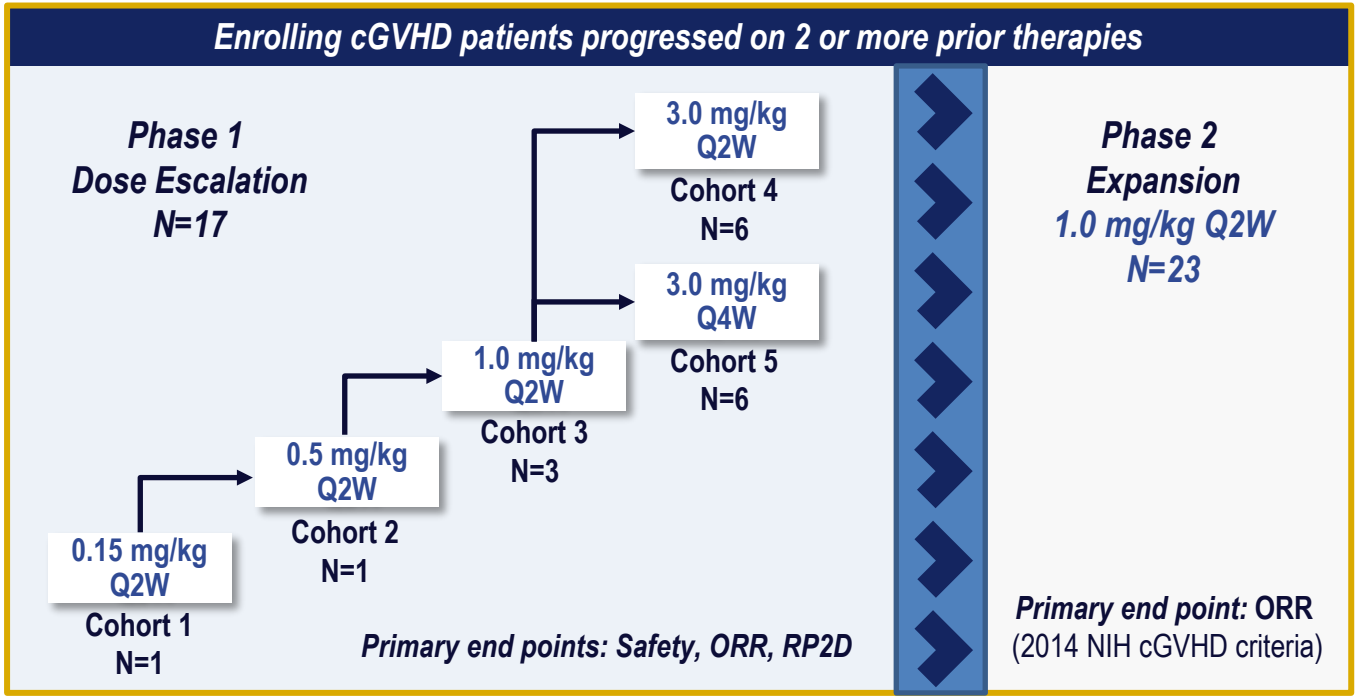
Axatilimab: Anti-CSF-1R mAb targeting macrophage-driven diseases

- High affinity humanized IgG4 monoclonal antibody
- Binds to ligand binding domain on CSF-1R
- Blocks binding of both CSF-1 & IL-34 ligands
- Administered via 30-minute infusion every 2-4 weeks
- Highly effective in selectively reducing levels of circulating pro-fibrotic/non-classical monocytes
- Intermittent dosing allows for monocyte recovery prior to subsequent dose

Axatilimab: Phase 1 / 2 trial enrolled 40 patients

Study Population

- Active cGVHD after ≥ 2 prior treatments
- KPS ≥ 60
- ≥ 6 years of age



Abbreviations: KPS=Karnofsky Performance Score; Q=every

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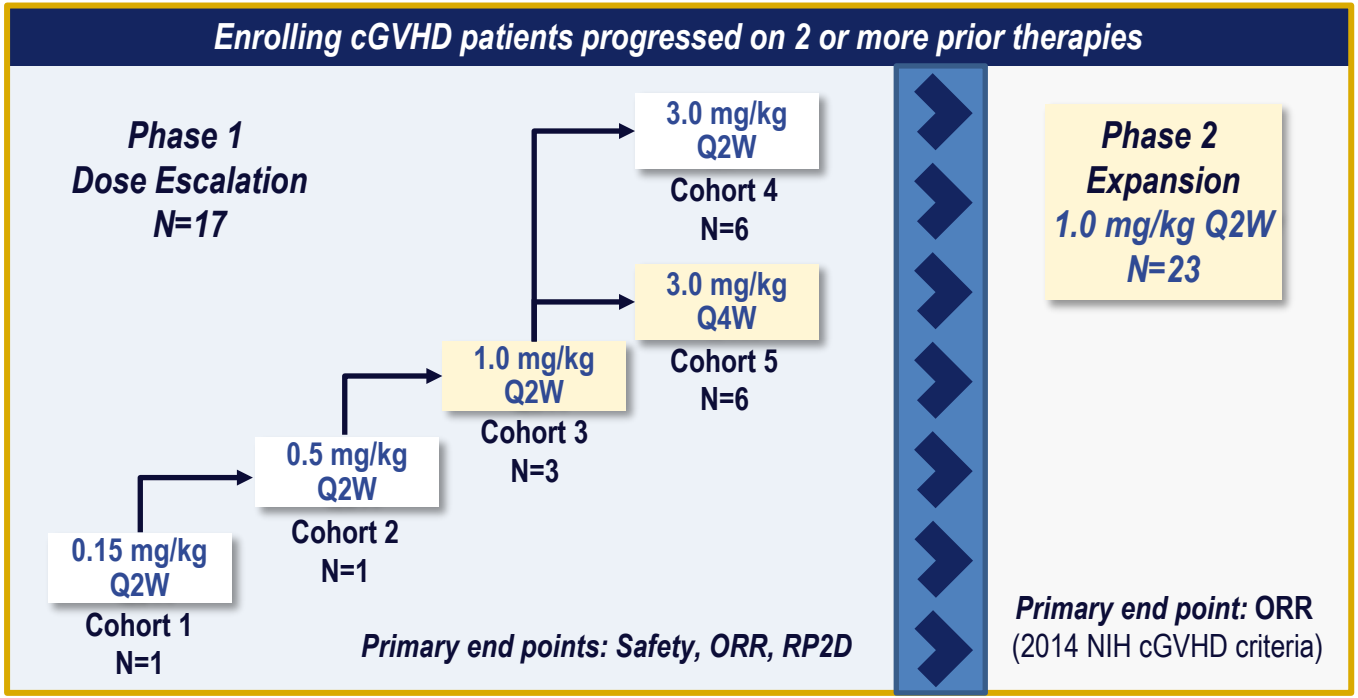


Abbreviations: KPS=Karnofsky Performance Score; Q=every

Baseline characteristics demonstrate a heavily pre-treated patient population

	PHASE 1 ALL DOSES n=17	PHASE 2 1mg/kg Q2W n=23	TOTAL N=40
Age, median (range),yrs	60 (29, 73)	57 (16, 69)	59 (16, 73)
Male, n (%)	11 (65)	14 (61)	25 (63)
Myeloablative transplant, n (%)	9 (53)	17 (74)	26 (65)
Related Donor, n (%)	9 (53)	9 (39)	18 (45)
Peripheral blood transplant, n (%)	16 (94)	21 (91)	37 (93)
KPS at enrollment, median (range)	80 (60, 100)	80 (60, 90)	80 (60, 100)
# organs involved, median (range)	4 (1, 5)	4 (1, 9)	4 (1, 9)
≥4 organs involved, n (%)	**10 (59)**	**16 (70)**	**26 (63)**
Prior treatment, median n (range)	**4 (1, 9)**	**3 (2, 11)**	**4 (1,11)**
Ibrutinib, n (%)	**13 (77)**	**13 (57)**	**26 (65)**
Ruxolitinib, n (%)	**10 (59)**	**11 (51)**	**21 (53)**
Belumosudil, n (%)	**6 (35)**	**2 (9)**	**8 (20)**
cGVHD→C1D1, median (range), yrs	**3.5 (0.11, 15.6)**	**3.0 (0.3, 6.7)**	**3.2 (0.11, 15.6)**

No significant differences in baseline characteristics across Phase 1 and Phase 2

Abbreviations: KPS=Karnofsky Performance Score, Q=every; Data cutoff 22Oct2021; extract is from an active database

Disposition demonstrates low rate of discontinuation due to toxicity

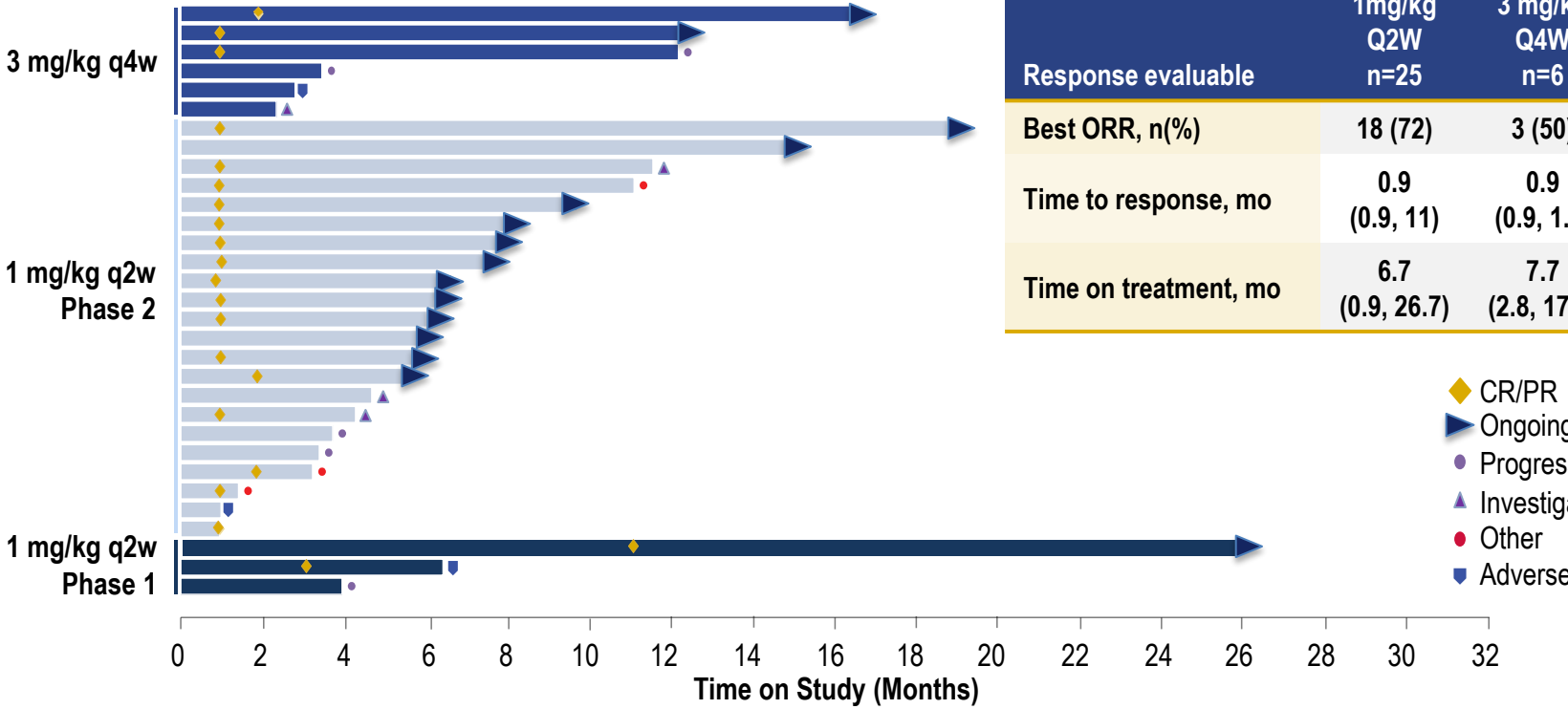
	PHASE 1 ALL DOSES n=17	PHASE 2 1mg/kg Q2W n=23	TOTAL N=40
Ongoing, n (%)	**5 (29)**	**12 (52)**	**17 (43)**
Discontinued, n (%)	**12 (71)**	**11 (48)**	**23 (58)**
Progression	4 (24)	3 (13)	7 (18)
Adverse Event	3 (18)	1 (4)	4 (10)
MD decision	3 (18)	3 (13)	6 (15)
Pt decision	1 (6)	1 (4)	2 (5)
Other[1]	1 (6)	3 (13)	4 (10)

[1]Other = non-compliance (1), hip-fracture (1), difficulty attending appts (1), Pt desired new treatment for ocular cGVHD (1)

4 patients discontinued due to adverse events
(CPK increased, periorbital edema, hypersensitivity, fall)

Q=every; Data cutoff 22Oct2021; extract is from an active database

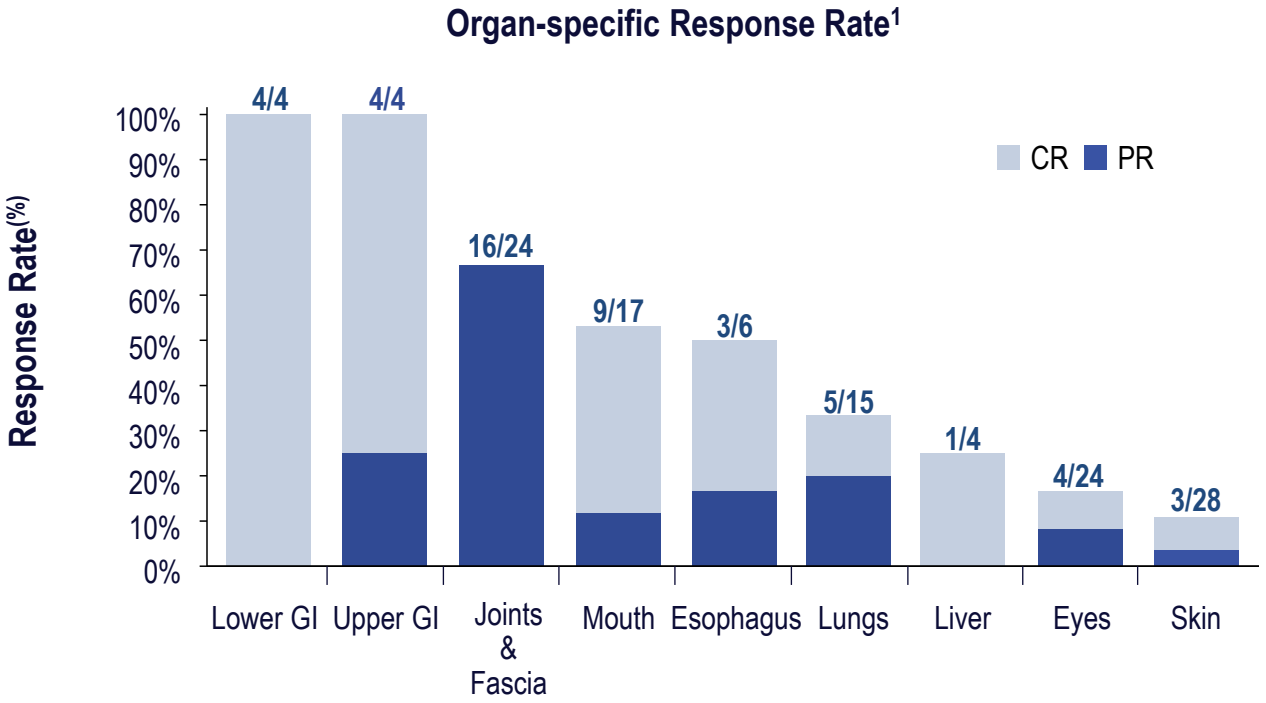
Rapid and durable responses in doses advanced to pivotal trial



Response evaluable	1mg/kg Q2W n=25	3 mg/kg Q4W n=6	Total N=31
Best ORR, n(%)	18 (72)	3 (50)	21 (68)
Time to response, mo	0.9 (0.9, 11)	0.9 (0.9, 1.9)	0.9 (0.9, 11)
Time on treatment, mo	6.7 (0.9, 26.7)	7.7 (2.8, 17.5)	6.7 (0.9, 26.7)

[1] Inclusive of patients treated in Phase 1 (1mg/kg Q2W n=3, 3mg/kg Q4W n=6) and Phase 2 (1mg/kg Q2W n=23) [2]One patient did not have a post-baseline response assessment at time of data cutoff.
Abbreviation: CR=complete response, PR=partial response, Q=every; Data cutoff 22Oct2021; extract is from an active database

Axatilimab: Response seen across cGVHD organ system involvement



- 25 (81%) had severe skin sclerosis at baseline
- 4 (16%) improved sclerosis

[1]Inclusive of patients treated in Phase 1 (1mg/kg Q2W n=3, 3mg/kg Q4W n=6) and Phase 2 (1mg/kg Q2W n=25) Abbreviation: CR=complete response, PR=partial response
Data cutoff 22Oct2021

Incidence of related AEs demonstrates an acceptable safety profile

All related Grades in ≥20%

	1mg/kg Q2W n=26	3 mg/kg Q4W n=6	All patients N=40
Related TEAE, n (%)	**17 (65)**	**5 (83)**	**29 (73)**
AST increased	6 (23)	3 (50)	14 (35)
CPK increased	3 (12)	4 (67)	13 (33)
ALT increased	3 (12)	2 (33)	10 (25)
Lipase increased	3 (12)	3 (50)	9 (23)
Amylase increased	4 (15)	--	9 (23)
Fatigue	6 (23)	2 (33)	12 (30)
Periorbital edema	3 (12)	3 (50)	8 (20)

All related Grade 3/4

	1mg/kg Q2W n=26	3 mg/kg Q4W n=6	All patients N=40
Related Gr 3/4 TEAE, n (%)	**2 (9)**	**2 (33)**	**8 (20)**
CPK increased	--	1 (17)	3 (8)
Lipase increased	--	1 (17)	2 (5)
Hypersensitivity	1 (4)	--	1 (3)
Periorbital edema	--	1 (17)	1 (3)
Septic arthritis	1 (4)	--	1 (3)

- **Serum enzyme elevations likely reflect the on-target effect of axatilimab on Kupffer cells in the liver**
- **No evidence of end-organ damage, myositis/pancreatitis with enzyme elevations**

Q=every; Data cutoff 22Oct2021; extract is from an active database

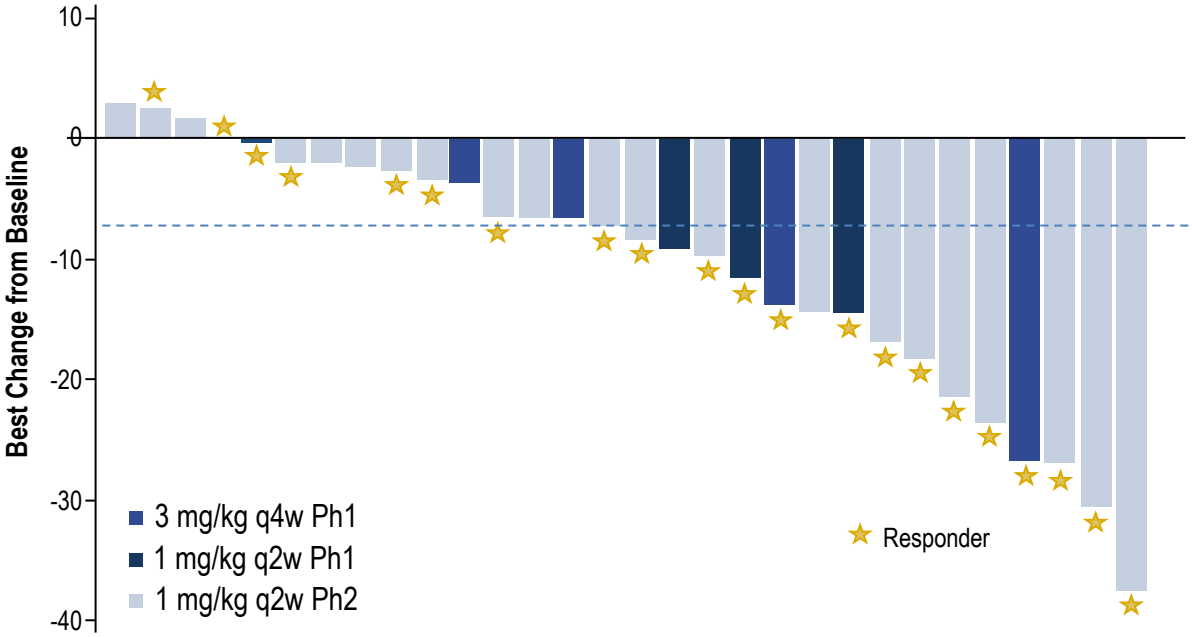
Infection rates in line with contemporary experience in cGVHD

	1mg/kg Q2W n=26	3 mg/kg Q4W n=6	All patients N=40
TEAE term, n (%)	**12 (46)**	**4 (67)**	**19 (48)**
Upper respiratory infection	7 (27)	2 (33)	**9 (18)**
Cellulitis	2 (8)	2 (33)	**4 (10)**
Pneumonia	2 (8)	--	**2 (5)**
Pseudomonas infection	1 (4)	1 (17)	**2 (5)**
Urinary tract infection	1 (4)	1 (17)	**2 (5)**
Influenza	1 (4)	--	**2 (5)**
COVID	--	1 (17)	**1 (3)**
Eye infection	--	1 (17)	**1 (3)**
Klebsiella infection	1 (4)	--	**1 (3)**
Esophageal candidiasis	1 (4)	--	**1 (3)**
Septic arthritis	1 (4)	--	**1 (3)**

No CMV or EBV reactivations were reported

Combined terms: URI+Bronchitis; Pneumonia+Lung infection; URI+Parainfluenza; Abbreviations: Q=every;
Data cutoff 22Oct2021; extract is from an active database

Improved Lee symptom scores in a majority of patients[1]



Best change in normalized Lee Symptom score

- Median change (points): -7.8 (range 3.1, -37.6)
- 16 (53%) of 30 LSS-evaluable patients achieved a 7-point reduction from baseline
- Improvement seen regardless of response by NIH consensus criteria

[1]Inclusive of patients treated in Phase 1 (1mg/kg Q2W n=3, 3mg/kg Q4W n=5) and Phase 2 (1mg/kg Q2W n=25)
Data cutoff 22Oct2021

Axatilimab advances to pivotal phase 2

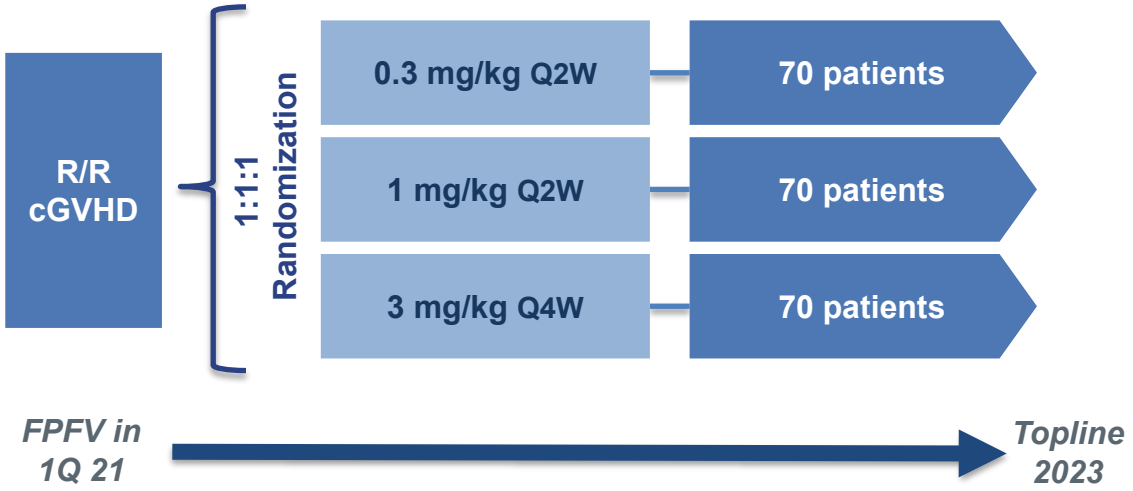
AGAVE-201

Inclusion criteria:

- 2 years and older[1]
- Recurrent or refractory active cGVHD after ≥ 2 lines of systemic therapy

Stratification factors:

- Prior therapy (ibrutinib, ruxolitinib, belumosudil)
- Severity of cGVHD



[1] Age inclusion criteria differs by country

Study Milestones

AGAVE-201

First site activated: January 2021
16 countries
~120 sites

- Australia
- Belgium
- Canada
- France
- Germany
- Greece
- Israel
- Italy
- Poland
- Portugal
- Singapore
- South Korea
- Spain
- Taiwan
- United Kingdom
- United States

Conclusions

AGAVE-201

- Phase 1/2 study observed a response rate of 68% at 2 doses selected for further investigation in AGAVE-201
- 53% of patients reported clinically meaningful improvement in their symptoms via the Lee symptom scale
- 43% were continuing treatment as of data cutoff
- Treatment appears well tolerated. No viral reactivations
- Development of axatilimab is proceeding with Phase 2 study (AGAVE-201) a global, open-label pivotal study enrolling patients with active cGVHD despite 2 prior lines of systemic therapy