

Early proof of concept in cGVHD, expanding to phase 2

High affinity, IgG4 ($K_D = 4-8 \text{ pM}$)

- ✓ Chronic graft versus host disease (cGVHD):
 - 1 mg/kg Q2W cohort expanding into Phase 2
 - Expect phase 1 dose escalation results in 2H20
 - FDA approved broadening enrollment criteria for prior ibrutinib therapy and lowering age restriction

✓ Ascending dose trials in solid tumors:

- ✓ Identified RP2D in combo with IMFINZI[®] (durvalumab, AZ)
 - Monotherapy (solid tumors) ongoing

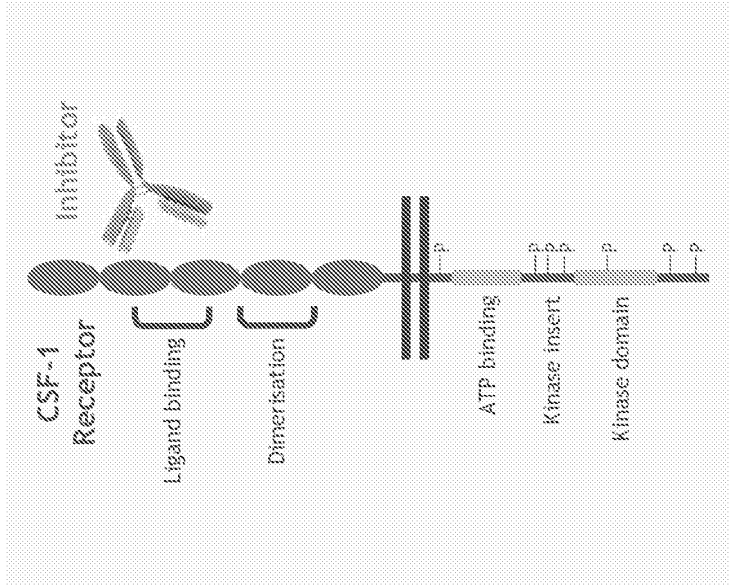


FIG. 1

Signaling through CSF-1R may play a meaningful role in cGVHD

- * cGVHD develops in 40% of HSCT^{1,2}
 - ... US prevalence ~14,000²
- * Pre-clinical evidence suggest CSF-1-dependant macrophages mediate cGVHD³
- * Phase 1 trial ongoing; data 2H20
- * Phase 2 expansion to start 1Q20

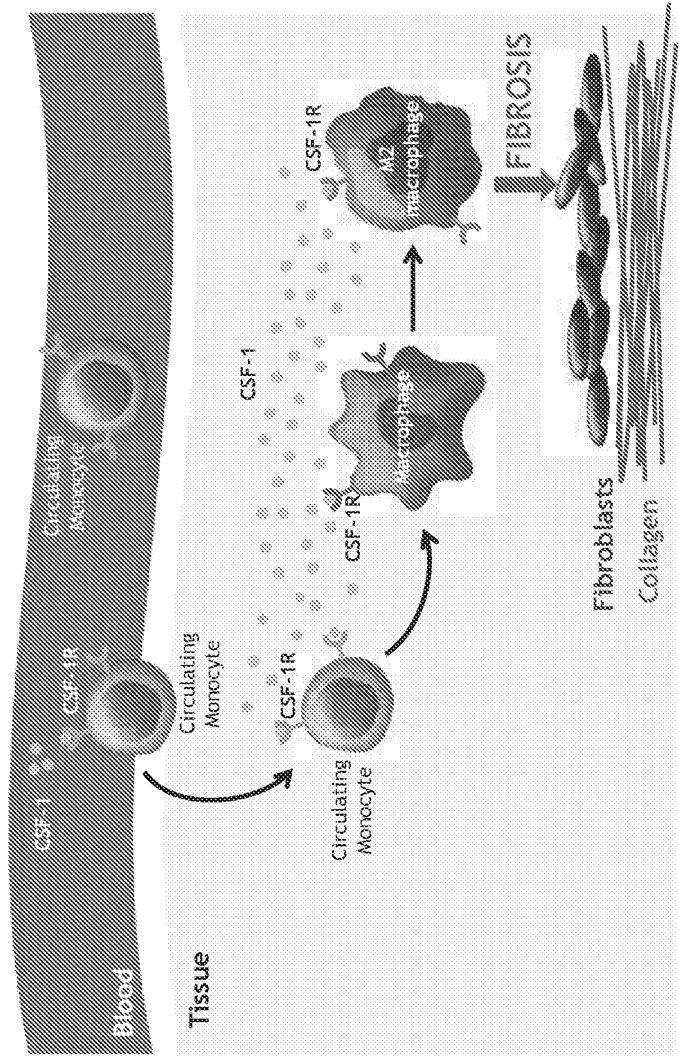
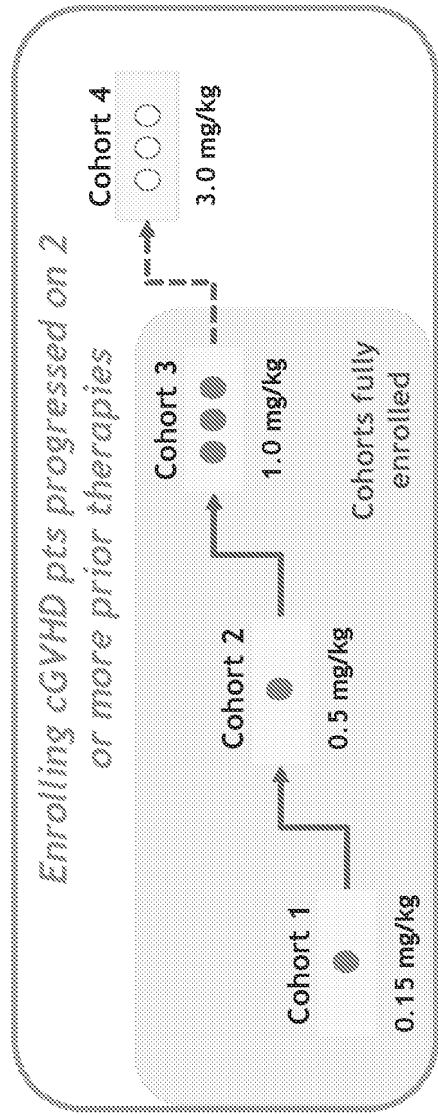


FIG. 2

Designed to identify optimal Phase 2 dose



- Study may enroll up to 30 Patients
 - Standard “3+3” dose escalation design following 0.15 and 0.5 mg/kg dose
- Patients continue to receive treatment for up to 12 months or until progressive disease or unacceptable toxicity
- Primary endpoint optimal biologic dose and recommended Phase 2 dose

FIG. 3

Responses observed in all evaluable patients as of data cutoff

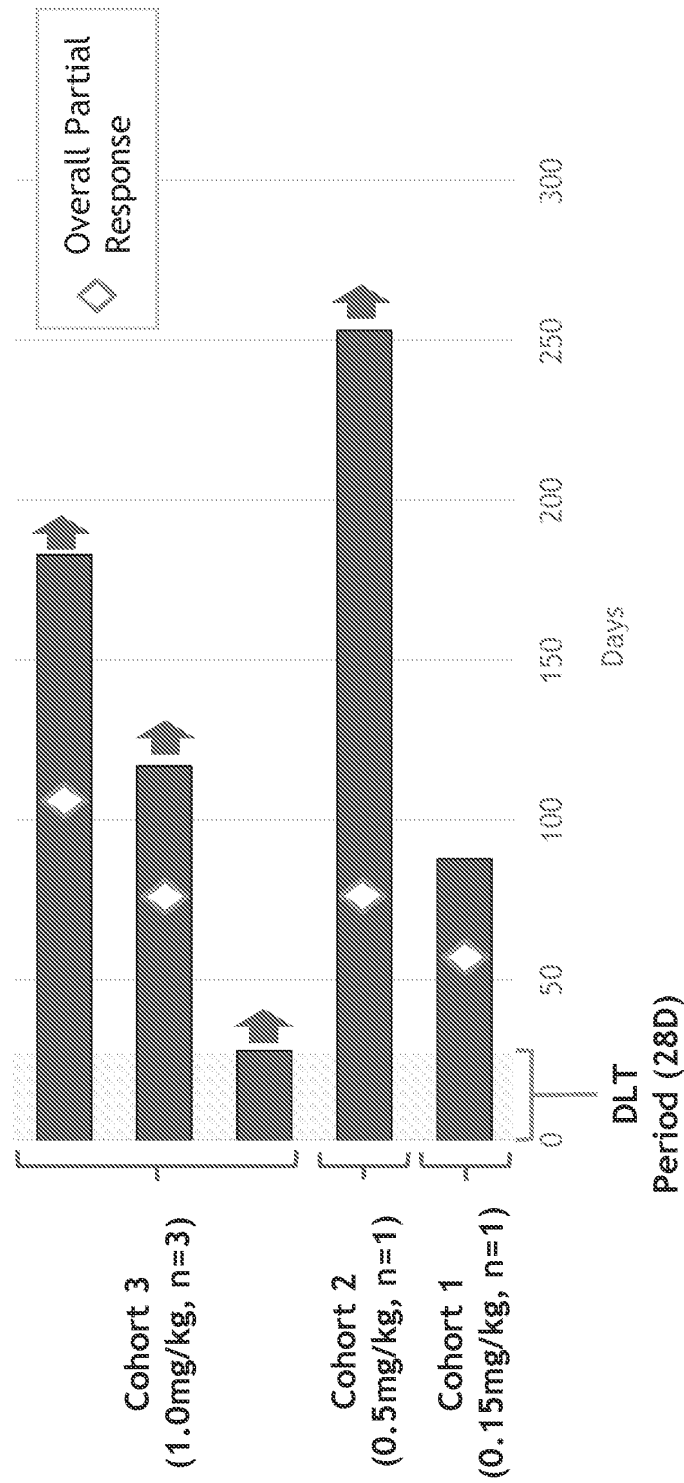


FIG. 4

First evidence of CSF-1R inhibition inducing responses in cGVHD

- Patient experienced chronic condition unresponsive to prior therapies
- Treatment with 1mg/kg Q2W Inhibitor led to significant improvement in ulceration

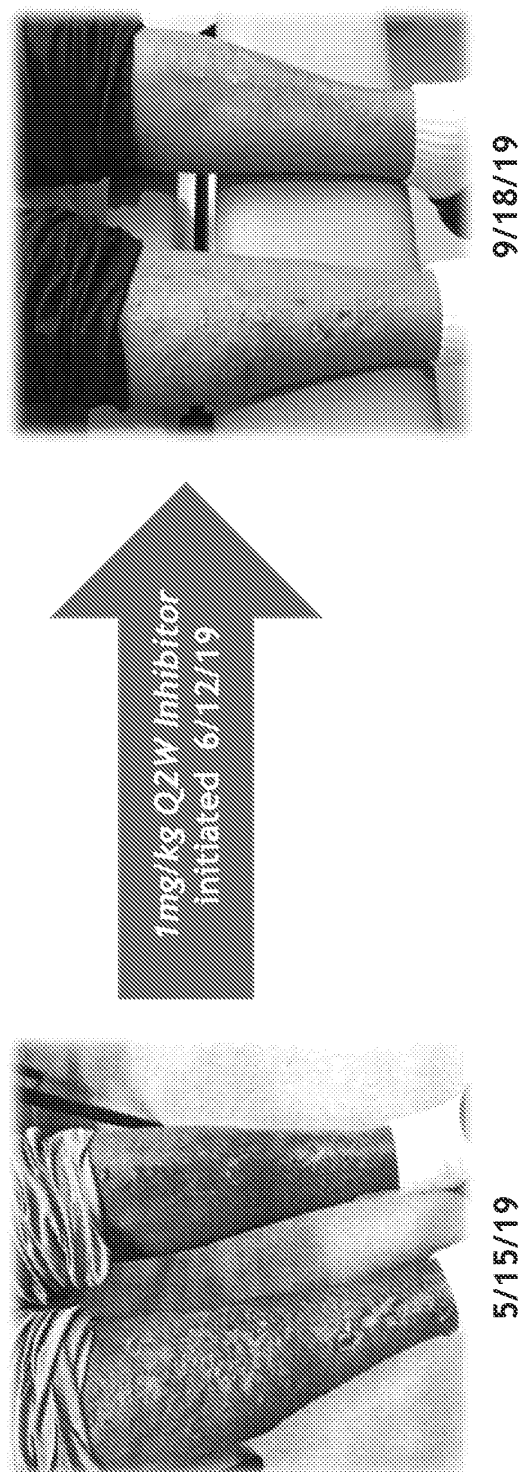


FIG. 5

Additional example of observed improvement in lower leg ulcers

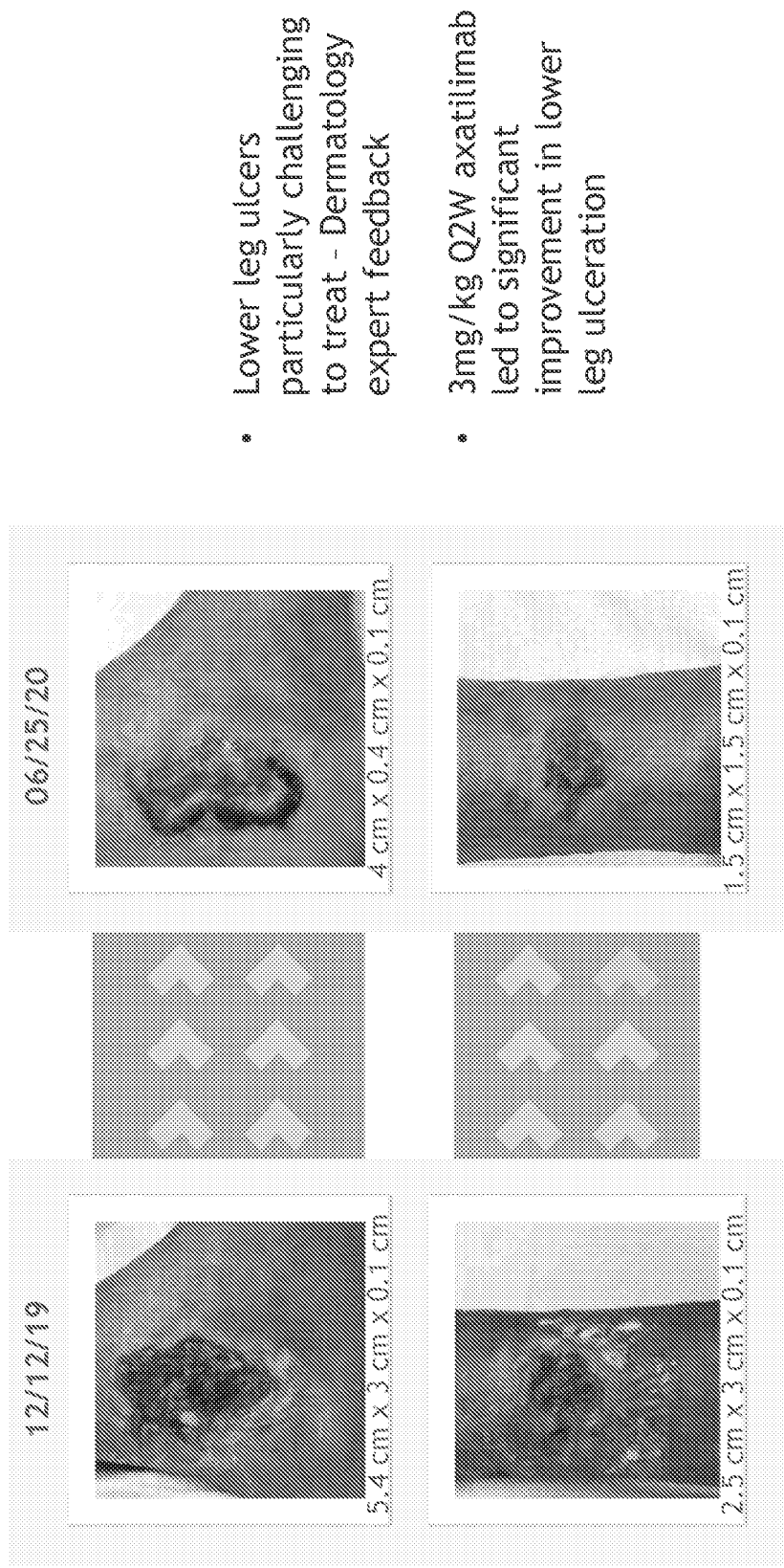


FIG. 6

Axatilimab PK and circulating monocyte pharmacodynamic changes

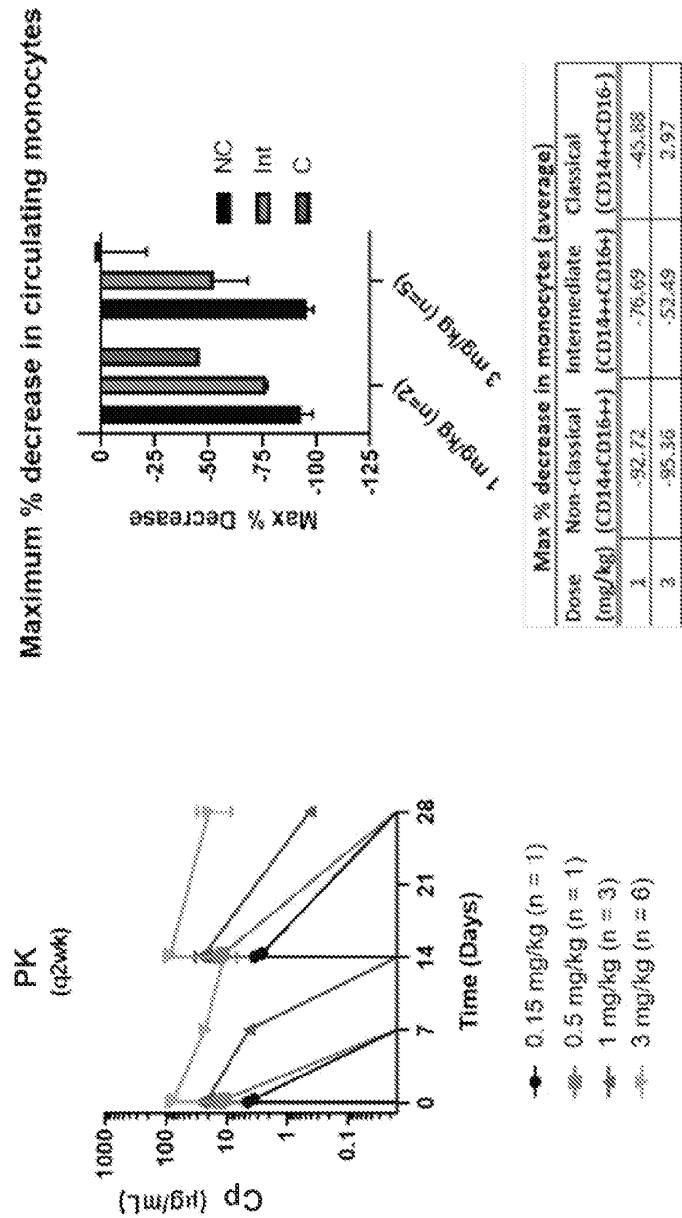


FIG. 7

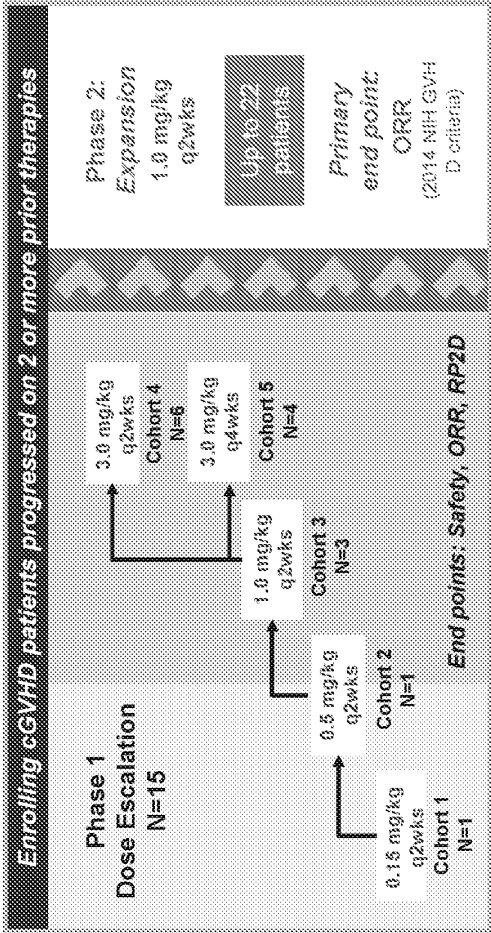
Overall Responses and by organ system (patient experience)

- Responses observed at all dose levels
- Deep and Sustained responses observed across several organ systems
- Responses seen after prior Ibrutinib = 6; Ruxolitinib = 5; KD-025 = 3
- Patients with 7-point improvement in normalized Lee Symptom Scale (LSS) = 6
- Additional responses in lungs, skin, and GI

Total (N = 12)	
Patients with at least 1 response (CR and/or PR)	7
Median time to response	12 weeks
Esophagus (n = 1)	1
Eyes (n = 10)	3
Joints/fascia (n = 9)	5
Mouth (n = 7)	1
Skin (n = 8)	3

FIG. 8

Axatilimab



No DLT's have been noted in this cohort.

FIG. 9

Study Population

- * Active cGVHD after ≥ 2 prior treatments
- * Karnofsky Performance scale ≥ 60
- * ≥ 6 years of age

Chronic GVHD incidence and limited treatment options

- * Chronic GVHD commonly affects 30-50% of allogeneic HCT recipients
- * Corticosteroids are the standard frontline treatment
- * Approximately 50% of the patients need second line treatment for disease progression or inadequate response
- * Ibrutinib is the only approved second line treatment of chronic GVHD
- * Morbidity and mortality in patients needing second or further lines of therapy remains high
- * Amongst patients with chronic GVHD, those with sclerosis and lung involvement are often difficult to treat and associated with poor outcomes
- * Development of novel agents to treat chronic GVHD remains an unmet medical need

FIG. 10

Baseline demographics & characteristics

Characteristic	<1 mg/kg q2wk n=2 ^{1,2}	1 mg/kg q2wk n=3	3 mg/kg q2wk n=6	3 mg/kg q4wk n=4	Total N=15
Age, median (range), years	56 (48, 64)	36 (29, 66)	60 (53, 73)	63 (31, 73)	60 (29, 73)
Myeloablative transplant n, (%)	1 (50) ²	1 (33)	2 (33)	3 (75)	7 (47)
Related Donor	2 (100)	2 (67)	4 (67)	1 (25)	9 (60)
Matched unrelated Donor	0	1 (33)	2 (33)	3 (75)	6 (40)
Peripheral blood SCT	2 (100)	3 (100)	5 (83)	4 (100)	14 (93)
Transplant→cGVHD, median (range), months	6.1 (3.4, 8.8)	3.7 (0.2, 5.7)	12.1 (5.2, 24.2)	9.2 (2.3, 20)	6.8 (0.2, 24.2)
cGVHD→CID1	27 (18, 36)	48.8 (34.8, 85.2)	49.2 (20.4, 187.2)	25.2 (9.6, 42)	42 (9.6, 187.2)
KPS at enrollment, median (range)	85 (60, 90)	70 (70, 90)	75 (60, 80)	80 (70, 100)	80 (60, 100)
# organs involved, median (range)	3.5 (3, 4)	3 (2, 5)	4 (1, 5)	3.5 (2, 9)	4 (1, 9)
≥4 organs involved	1 (50) ²	1 (33)	4 (67)	2 (50)	8 (53)
Prior tx, median (range)	5.5 (4, 7)	7 (4, 9)	4.5 (3, 7)	3 (2, 6)	4 (2, 9)
Ibrutinib, n (%)	2 (100)	3 (100)	6 (100)	0	11 (73)
Ruxofitinib	2 (100)	1 (33)	4 (67)	2 (50)	9 (60)
KDQ25	1 (50) ²	1 (33)	3 (50)	0	5 (33)

¹ Includes one patient from 0.15mg/kg q2wk dosing cohort. ² Includes one patient from 0.5mg/kg q2wk dosing cohort. Abbreviations: SCT=stem-cell transplant, KPS=Karnofsky Performance Score, tx=treatment, q=every

FIG. 11

Axatilimab: Response seen across cGVHD organ system involvement

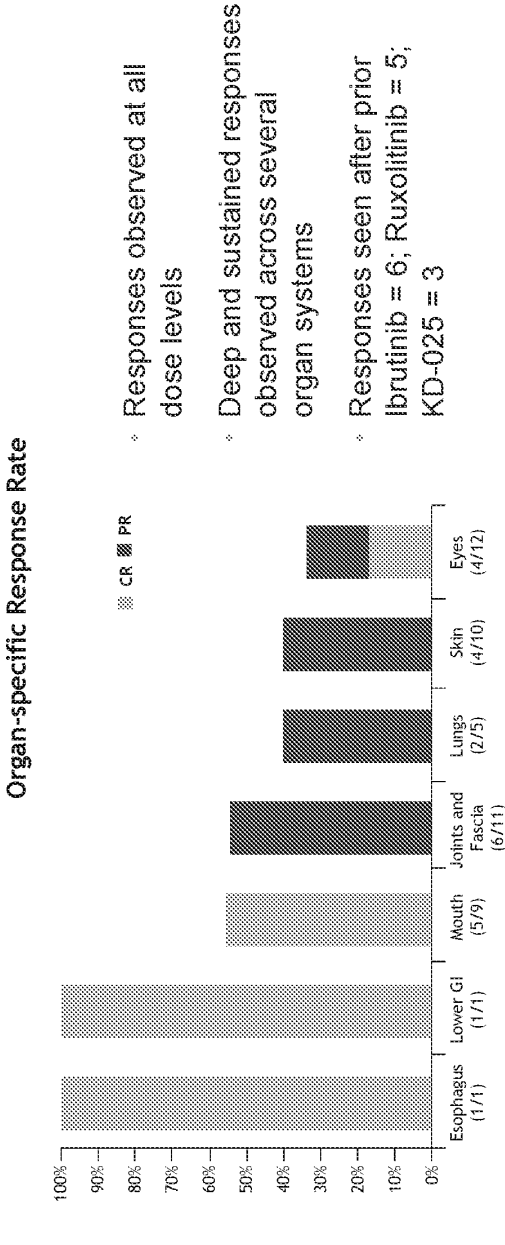
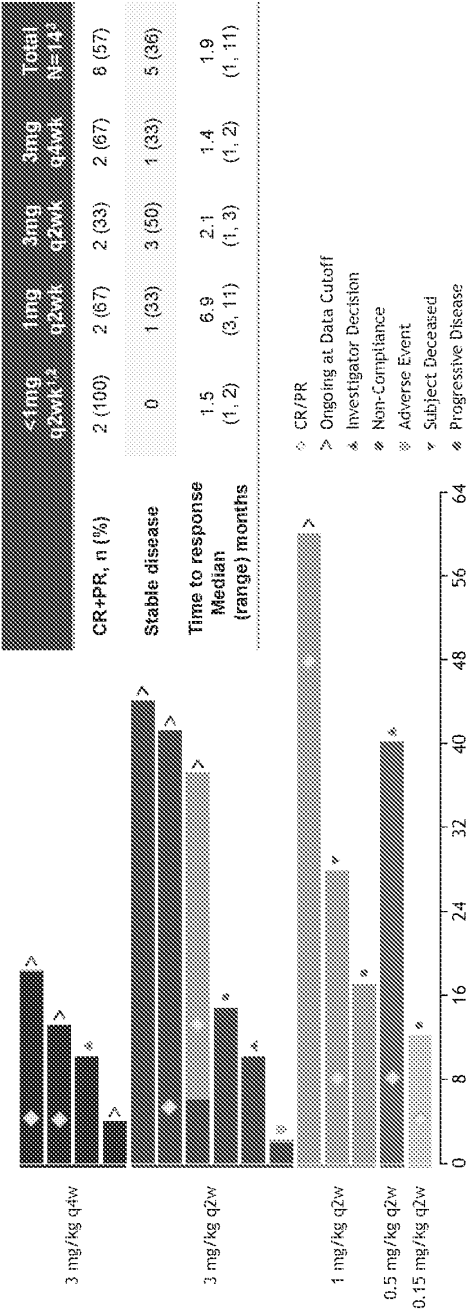


FIG. 12

Axatilimab: Early evidence of symptom control



¹ Includes one patient from 0.15mg/kg q2w dosing cohort. ² Includes one patient from 0.5mg/kg q2w dosing cohort. One patient did not have a post-baseline response assessment at time of data cut-off. Abbreviation: CR=complete response, PR=partial response, q=every

FIG. 13

Axatilimab: Improved Lee symptom scores in a majority of patients

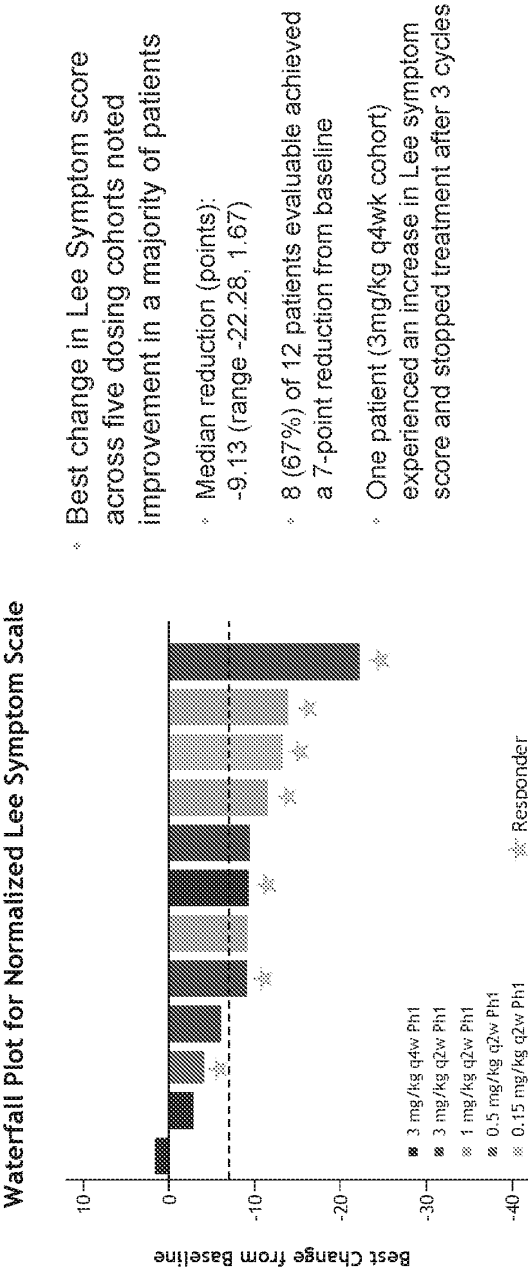


FIG. 14

Conclusions

- * Axatilimab demonstrates good tolerability with clinical activity demonstrated by a 57% (n=8) response rate in a heavily pre-treated patient population
- * Low rate of infections reported with no viral reactivations
- * Ongoing development of axatilimab will include a Phase 2 study (AGAVE-201) planned for enrollment. This will be a randomized, multicenter study to evaluate the efficacy, safety and tolerability of Axatilimab at 3 different doses in patients with recurrent or refractory active cGVHD who have received at least 2 lines of systemic therapy

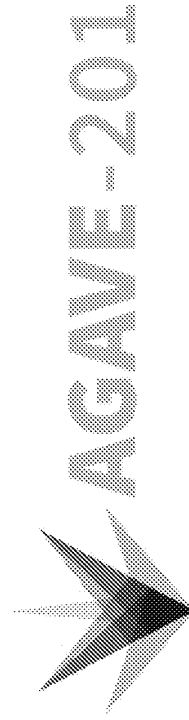


FIG. 15