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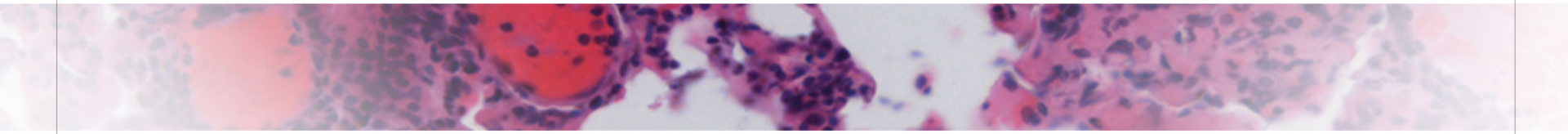

Phase 1 Study of Axatilimab (SNDX-6352), a CSF-1R Humanized Antibody, For Chronic Graft-Versus-Host Disease after 2 or More Lines of Systemic Treatment

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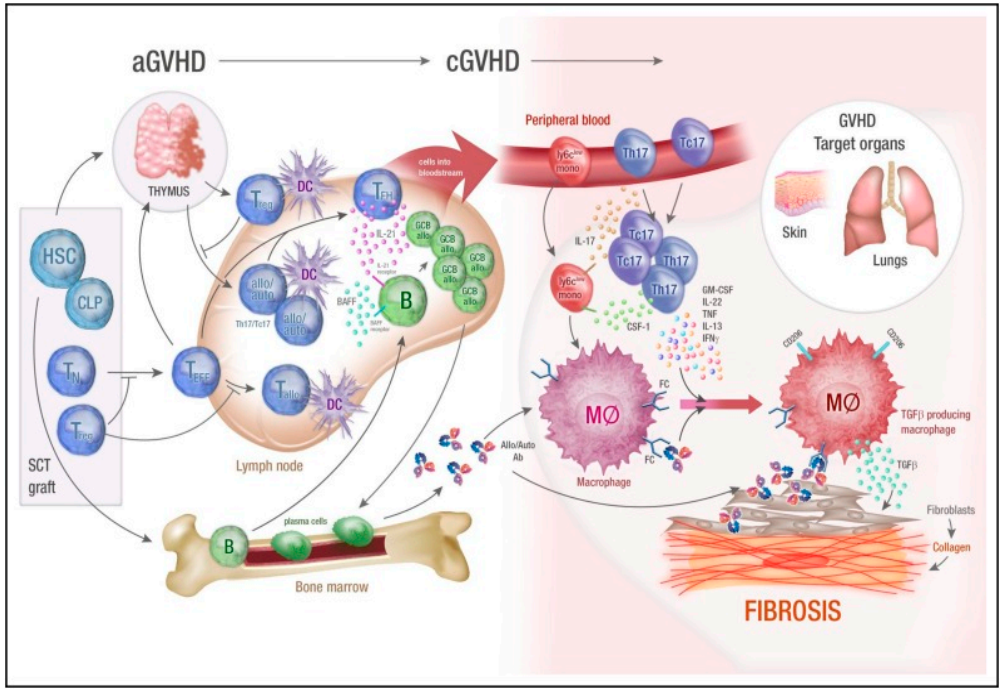
Chronic GVHD incidence and limited treatment options

- 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

CSF-1–dependent donor derived macrophages in models of cGVHD

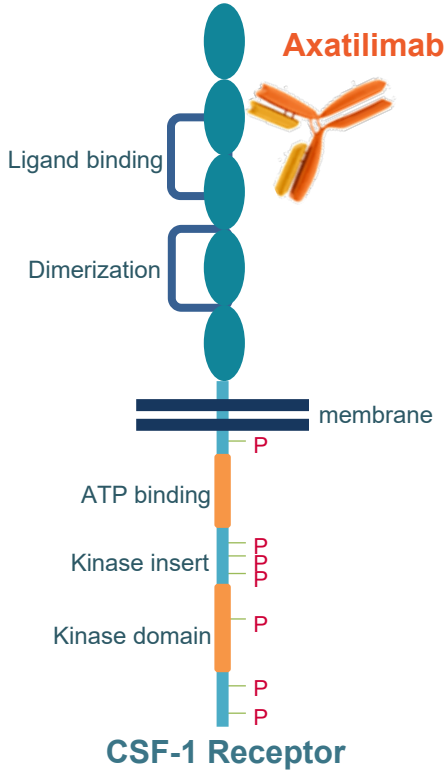


- cGVHD particularly sclerodermatous and pulmonary disease is associated with CSF-1R dependent donor macrophages
- CSF-1/CSF-1R regulates macrophage infiltration and cutaneous pathology
- Anti–CSF-1R depletes circulating non-classical monocytes, tissue macrophage infiltration and reduces GVHD associated tissue pathology

Source: Alexander KA et al 2014 JCI.
Figure Adapted from MacDonald KP et al. *Blood*. 2017;129(1):13-21. HSCT, hematopoietic stem cell transplantation.

Axatilimab, anti-CSF1R mAb targeting macrophage driven diseases

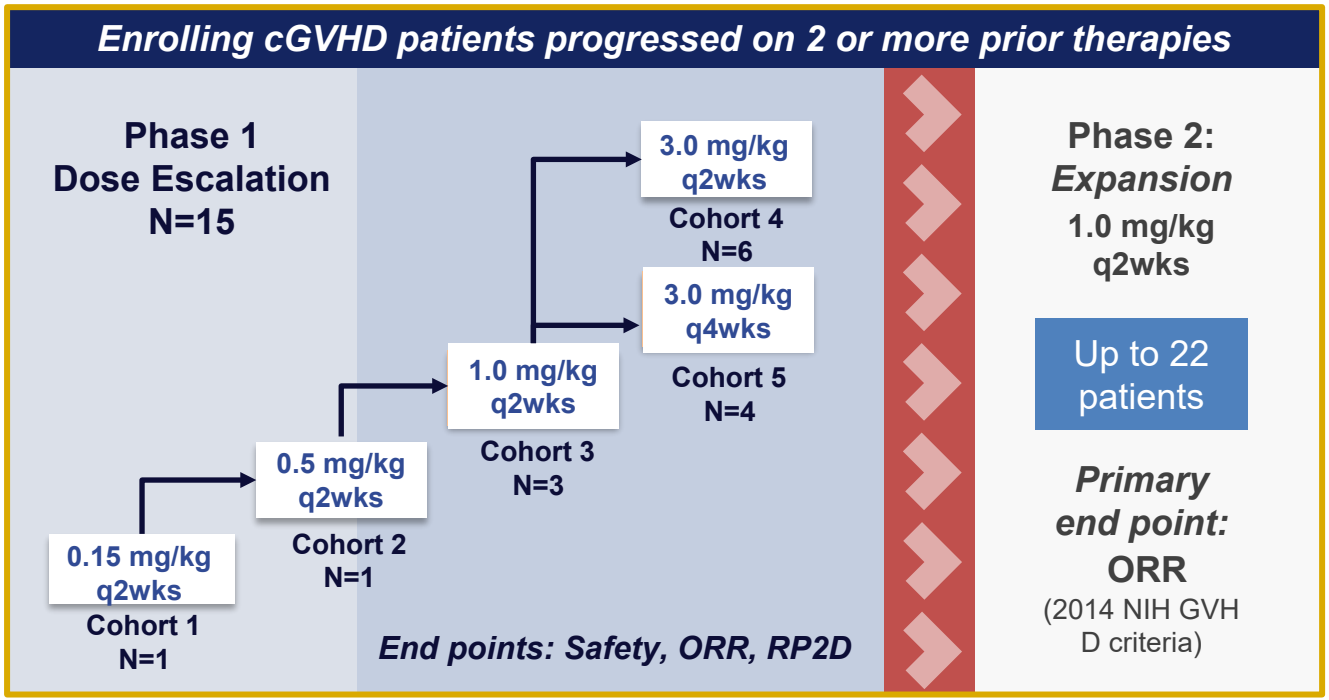
Subtype	IgG4
Binding properties	• Human CSF-1R ligand binding domain (Kd 4-8pM); • Blocks both CSF-1 and IL-34; • No evidence of antibody mediated receptor internalization or activation
Specificity	All human CSF-1R variants (V32G, A245S, P247H, V279M)
In vitro	Inhibits ligand induced monocyte activation (IC_{50} 100-400 pM)



Axatilimab: Phase 1 / 2 trial establishes proof of concept in cGVHD

Study Population

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



Baseline demographics & characteristics

Characteristic	<1mg/kg q2wk n=2[1,2]	1mg/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→C1D1	27 (18, 36)	46.8 (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 (80, 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) Ibrutinib, n (%) Ruxolitinib KD025	5.5 (4, 7) 2 (100) 2 (100) 1 (50)[2]	7 (4, 9) 3 (100) 1 (33) 1 (33)	4.5 (3, 7) 6 (100) 4 (67) 3 (50)	3 (2, 6) 0 2 (50) 0	**4 (2, 9)** **11 (73)** **9 (60)** **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

Data cut-off 30Oct2020.

Axatilimab: Summary of treatment-emergent adverse events (TEAES)

Characteristic	<1mg/kg q2wk n=2[1,2]	1mg/kg q2wk n=3	3 mg/kg q2wk n=6	3 mg/kg q4wk n=4
TEAE Related	2 (100)	3 (100)	6 (100)	4 (100)
TEAE Gr 3/4	2 (100)	2 (67)	4 (67)	2 (50)
Gr 3/4 Related	1 (50)[1]	1 (33)	3 (50)	2 (50)
Discontinued Tx	**2 (100)**	**2 (67)**	**3 (50)**	**1 (25)**
Progression	1 (100)[1]	1 (33)	0	0
Adverse Event	0	0	1 (17)	0
MD decision	1 (100)[2]	0	1 (17)	1 (25)
Deceased	0	1 (33)	0	0
Other	0	0	1 (17)	0

- **Grade 3/4 events occurring ≥ 2 patients include**: CK increased (n=3), AST increased (n=2), Pneumonia (n=2)
- **One Grade 5 event occurred unrelated to axatilimab:** Fall (n=1)

[1] Includes one patient from 0.15mg/kg q2wk dosing cohort. [2] Includes one patient from 0.5mg/kg q2wk dosing cohort Abbreviations: Gr=grade, tx=treatment, q=every
Data cut-off 30Oct2020.

Axatilimab: TEAEs occurring in at least 5 patients, all grades regardless of causality

Characteristic	<1mg/kg q2wk n=2[1,2]	1mg/kg q2wk n=3	3 mg/kg q2wk n=6	3 mg/kg q4wk n=4	Total N=15
TEAE term, n (%)					
AST increased	1 (50)[1]	1 (33)	4 (67)	3 (75)	**9 (60)**
CPK increased	0	1 (33)	5 (83)	3 (75)	**9 (60)**
LDH increased	1 (50)[2]	2 (67)	4 (67)	2 (50)	**9 (60)**
Amylase increased	1 (50)[1]	1 (33)	4 (67)	0	**6 (40)**
Fatigue	1 (50)[2]	0	3 (50)	2 (50)	**6 (40)**
Lipase increased	0	1 (33)	3 (50)	2 (50)	**6 (40)**
ALT increased	1 (50)[1]	0	3 (50)	1 (25)	**5 (33)**
Creatinine increased	0	1 (33)	2 (33)	2 (50)	**5 (33)**
Nausea	2 (100)	0	3 (50)	0	**5 (33)**
Pyrexia	0	1 (33)	4 (67)	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: q=every
Data cut-off 30Oct2020.

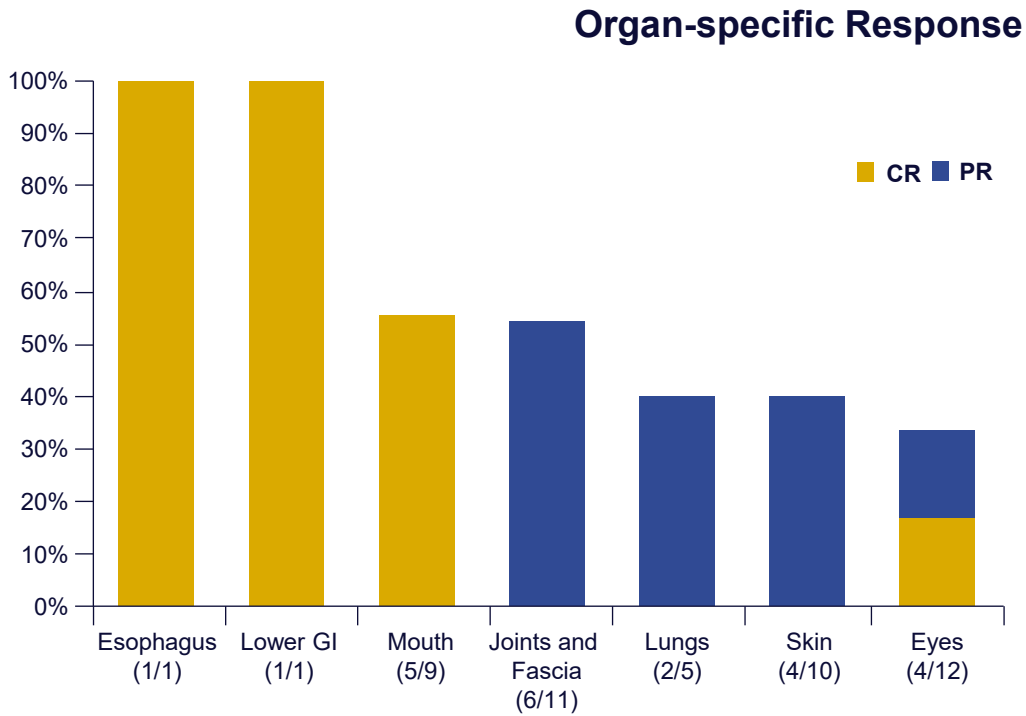
Axatilimab: All infection events, all grades regardless of causality

Characteristic	<1mg/kg q2wk n=2[1,2]	1mg/kg q2wk n=3	3 mg/kg q2wk n=6	3 mg/kg q4wk n=4	Total N=15
TEAE term, n (%)					
Pneumonia	1 (50)[2]	1 (33)	0	1 (25)	**3 (20)**
Conjunctivitis	1 (50)[1]	0	0	0	**1 (7)**
Gastroenteritis norovirus	0	0	1 (17)	0	**1 (7)**
Influenza	0	1 (33)	0	0	**1 (7)**
Lung infection	0	1 (33)	0	0	**1 (7)**
Pseudomonas infection[3]	0	0	0	1 (25)	**1 (7)**
URI	0	1 (33)	0	0	**1 (7)**

- 9 events of infection were reported in six patients with two patients experiencing multiple events (pneumonia, influenza and URI, n=1; pseudomonas and pneumonia, n=1)
- No CMV viral reactivations were reported

[1] Includes one patient from 0.15mg/kg q2wk dosing cohort. [2] Includes one patient from 0.5mg/kg q2wk dosing cohort[3] Pseudomonas infection to foot (dermal ulcers)
Abbreviations: URI=Upper-respiratory infection, q=every
Data cut-off 30Oct2020.

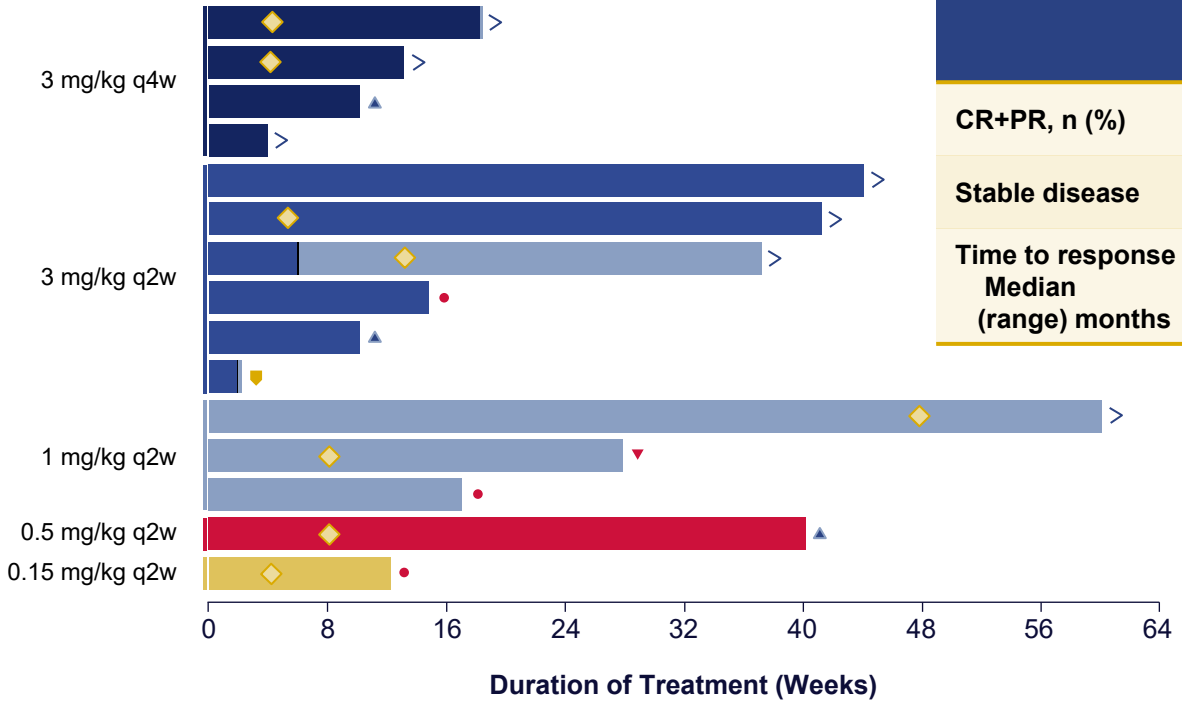
Axatilimab: Response seen across cGVHD organ system involvement



- 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

Abbreviation: CR=complete response, PR=partial response
Data cut-off 30Oct2020.

Axatilimab: Early evidence of symptom control in the heavily pretreated patients

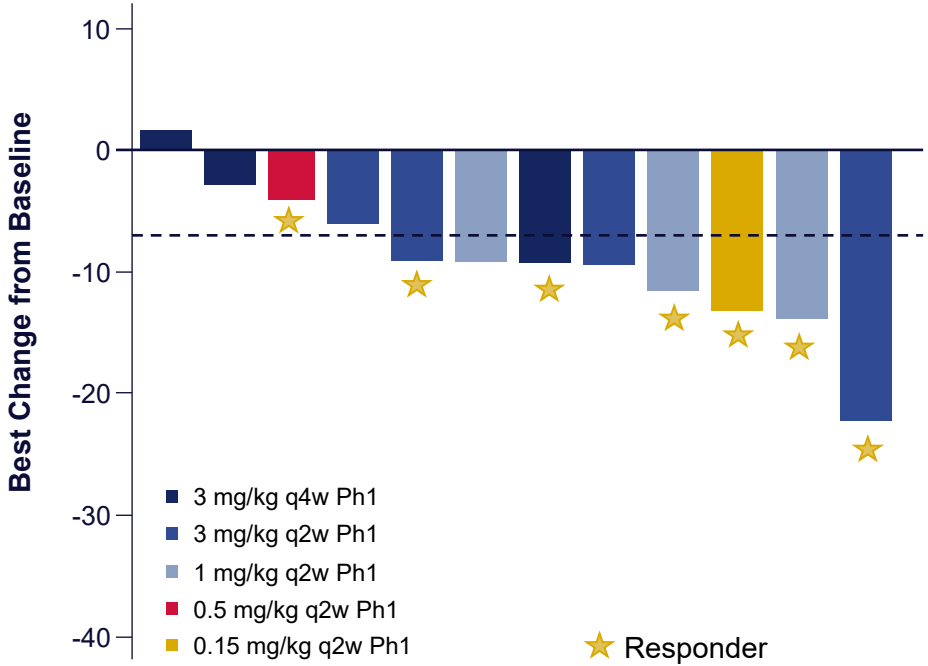


	<1mg q2wk[1,2]	1mg q2wk	3mg q2wk	3mg q4wk	Total N=14[3]
CR+PR, n (%)	2 (100)	2 (67)	2 (33)	2 (67)	8 (57)
Stable disease	0	1 (33)	3 (50)	1 (33)	5 (36)
Time to response Median (range) months	1.5 (1, 2)	6.9 (3, 11)	2.1 (1, 3)	1.4 (1, 2)	1.9 (1, 11)

[1] Includes one patient from 0.15mg/kg q2wk dosing cohort. [2] Includes one patient from 0.5mg/kg q2wk dosing cohort[3] 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
Data cut-off 30Oct2020.

Axatilimab: Improved Lee symptom scores in a majority of patients

Waterfall Plot for Normalized Lee Symptom Scale



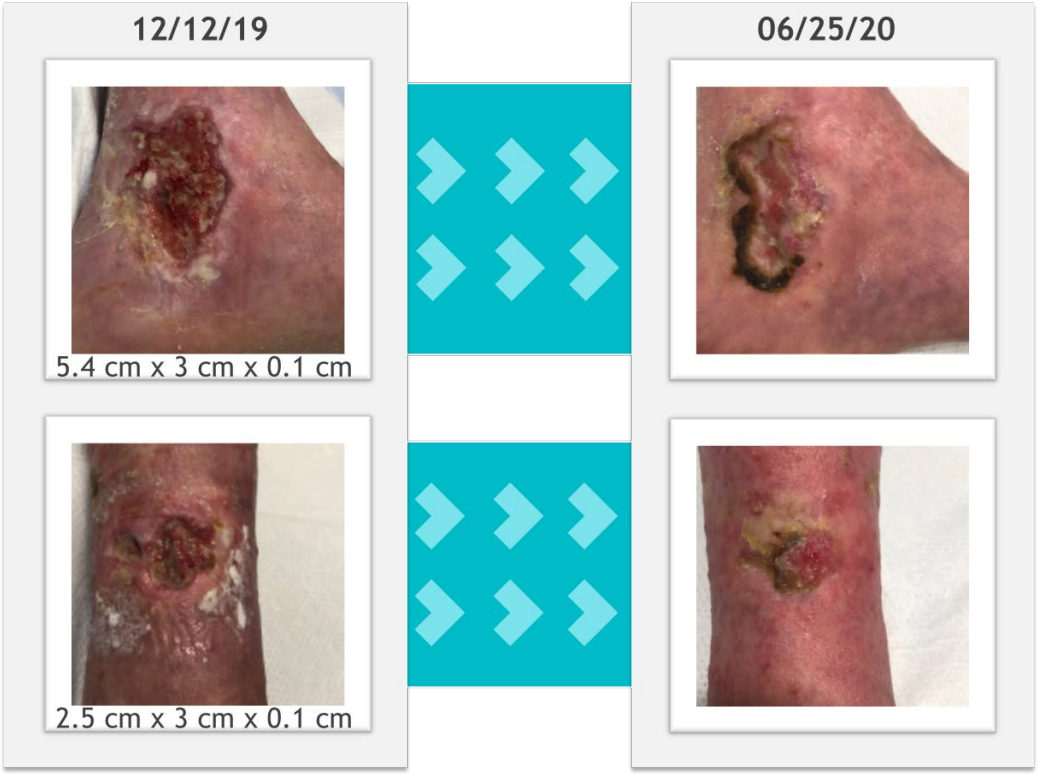
Data cut-off 30Oct2020.

- Best change in Lee Symptom score across five dosing cohorts noted improvement in a majority of patients
  - Median reduction (points): -9.13 (range -22.28, 1.67)
  - 8 (67%) of 12 patients evaluable achieved a 7-point reduction from baseline
  - One patient (3mg/kg q4wk cohort) experienced an increase in Lee symptom score and stopped treatment after 3 cycles

Axatilimab effective in sclerodermatous cGVHD

- Patient experienced chronic ulcers unresponsive to prior therapies
- Treatment with 1mg/kg q2wk axatilimab led to significant improvement in ulceration

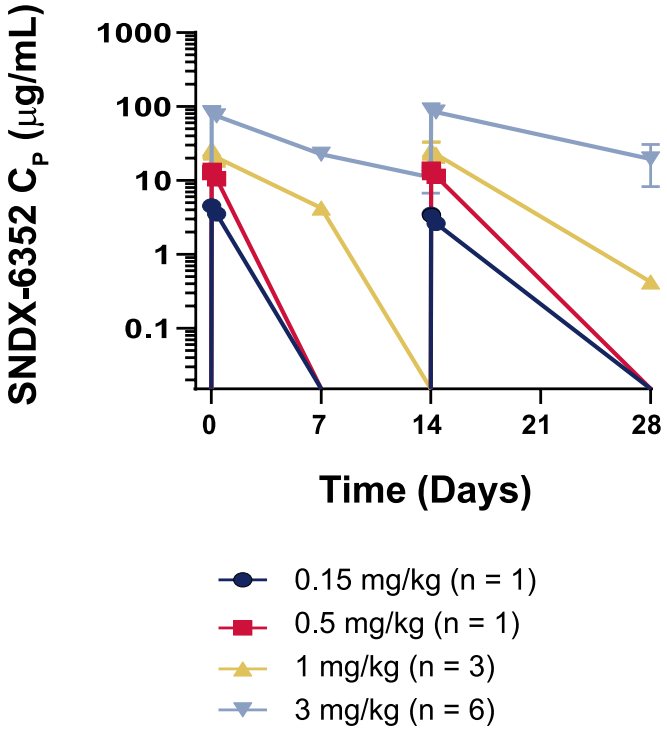
Additional example of observed improvement in sclerodermatous disease with ulcers



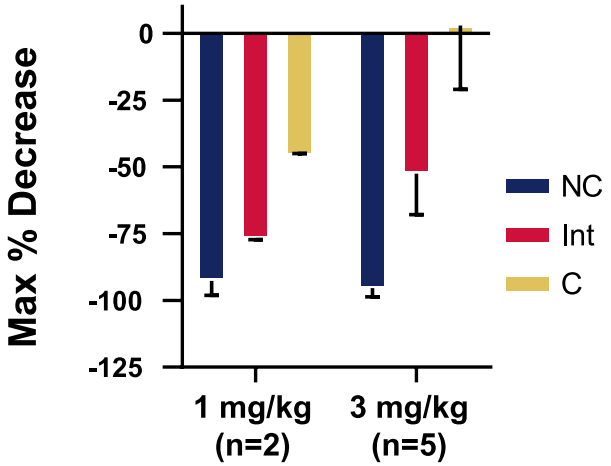
- Lower leg ulcers are particularly challenging to treat
- 3mg/kg q2wk axatilimab led to significant improvement in lower leg ulceration

Axatilimab PK and circulating monocyte pharmacodynamic changes

SNDX-6352 PK
(q2wk)



Maximum % decrease in circulating monocytes



Max % decrease in monocytes (average)

Dose (mg/kg)	Non-classical (CD14+CD16++)	Intermediate (CD14++CD16+)	Classical (CD14++CD16-)
1	-92.72	-76.69	-45.88
3	-95.36	-52.49	2.97

Max Decrease = greatest reduction at any time in the first cycle

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 in 2021. 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

Acknowledgements

- Bruce Blazar and Geoffrey Hill
- All the investigators that participated and worked on this study

Patients and their Families