Determined to realize a future in which people with cancer live longer and better than ever before

Syndax

AXATILIMAB CONFERENCE CALL| DECEMBER 2020

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Syndax pipeline targets indications with significant unmet need

SNDX-5613 Menin Inhibitor

- Acute leukemias
- Ph 1 data validates new target
- Ph 2 init expected early 2021
- Complete Ph 1 expected end of 1Q21 or April 2021
- Potential fast-to-market reg path

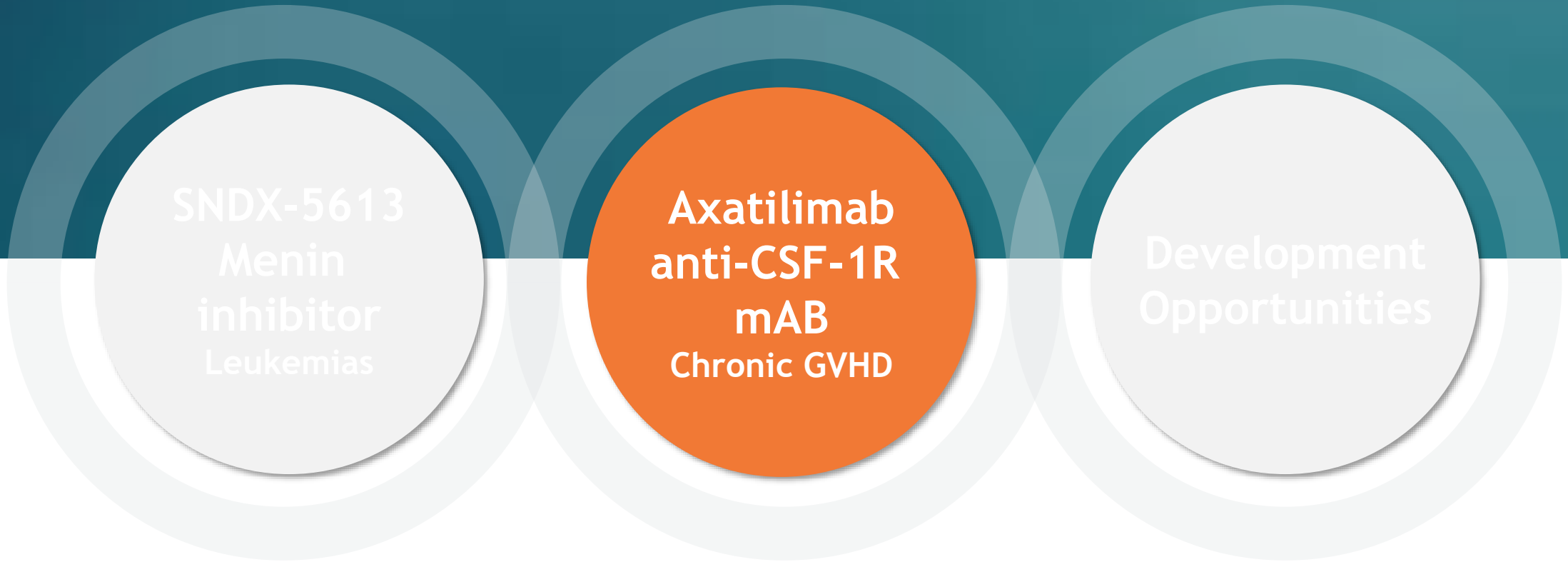
Axatilimab Anti-CSF-1R mAB

- Macrophage driven diseases
- POC for cGVHD
- Initiation of pivotal trial expected by YE20
- Inflammatory/fibrotic franchise opportunity

Development opportunities

- Focused on expanding pipeline through new asset acquisition

Syndax pipeline addresses key areas of unmet need in cancer



Expert participants

Mukta Arora, M.D., M.S.

Professor of Medicine, Division of Hematology, Oncology and Transplantation,
University of Minnesota Medical School

Geoffrey Hill, M.D.

José Carreras/E. Donnall Thomas Endowed Chair for Cancer Research and Director of The Immunotherapy Integrated Research Center,
Fred Hutchinson Cancer Research Center

Agenda

Introduction
Briggs W. Morrison, M.D., *Chief Executive Officer of Syndax*

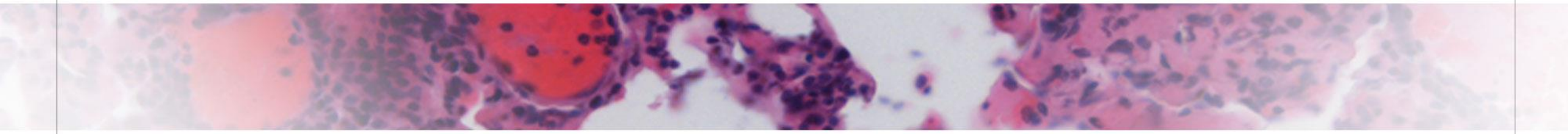
Summary of ASH data and select case studies
Mukta Arora, M.D., M.S.

cGVHD biology and treatment landscape
Geoffrey Hill, M.D.

Axatilimab cGVHD development path and closing remarks
Briggs W. Morrison, M.D.

Q&A session
- Guest speakers:
  - Mukta Arora, M.D. M.S. and Geoffrey Hill, M.D.
- Syndax:
  - Briggs W. Morrison, M.D.
  - Peter Ordentlich, Ph.D., *Chief Scientific Officer and Founder*
  - Michael Meyers M.D., Ph.D., *Chief Medial Officer*
  - Michael Metzger, *President and Chief Operating Officer*
  - Daphne Karydas, *Chief Financial Officer and Treasurer*
  - Anjali Ganguli, Ph.D., *Vice President, Corporate Development*

American Society of Hematology
Helping hematologists conquer blood diseases worldwide



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

Mukta Arora, MD MS[1], Madan Jagasia, MD[2], Antonio Di Stasi, MD[3], Michael L. Meyers, MD PhD[4], Christine Quaranto[4], Serap Sankoh, PhD[4], Mohamed Abu Zaid, MD[5], Geoffrey Hill, MD[6], Daniel J.Weisdorf[1], Bruce R. Blazar, MD[1], Peter Ordentlich, PhD[4], Stephanie J Lee, MD MPH[6]

[1]University of Minnesota, [2]Vanderbilt University, [3]University of Alabama at Birmingham, [4]Syndax Pharmaceuticals, Inc, [5]Simon Cancer Center, Indiana University [6]Fred Hutchinson Cancer Research Center

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

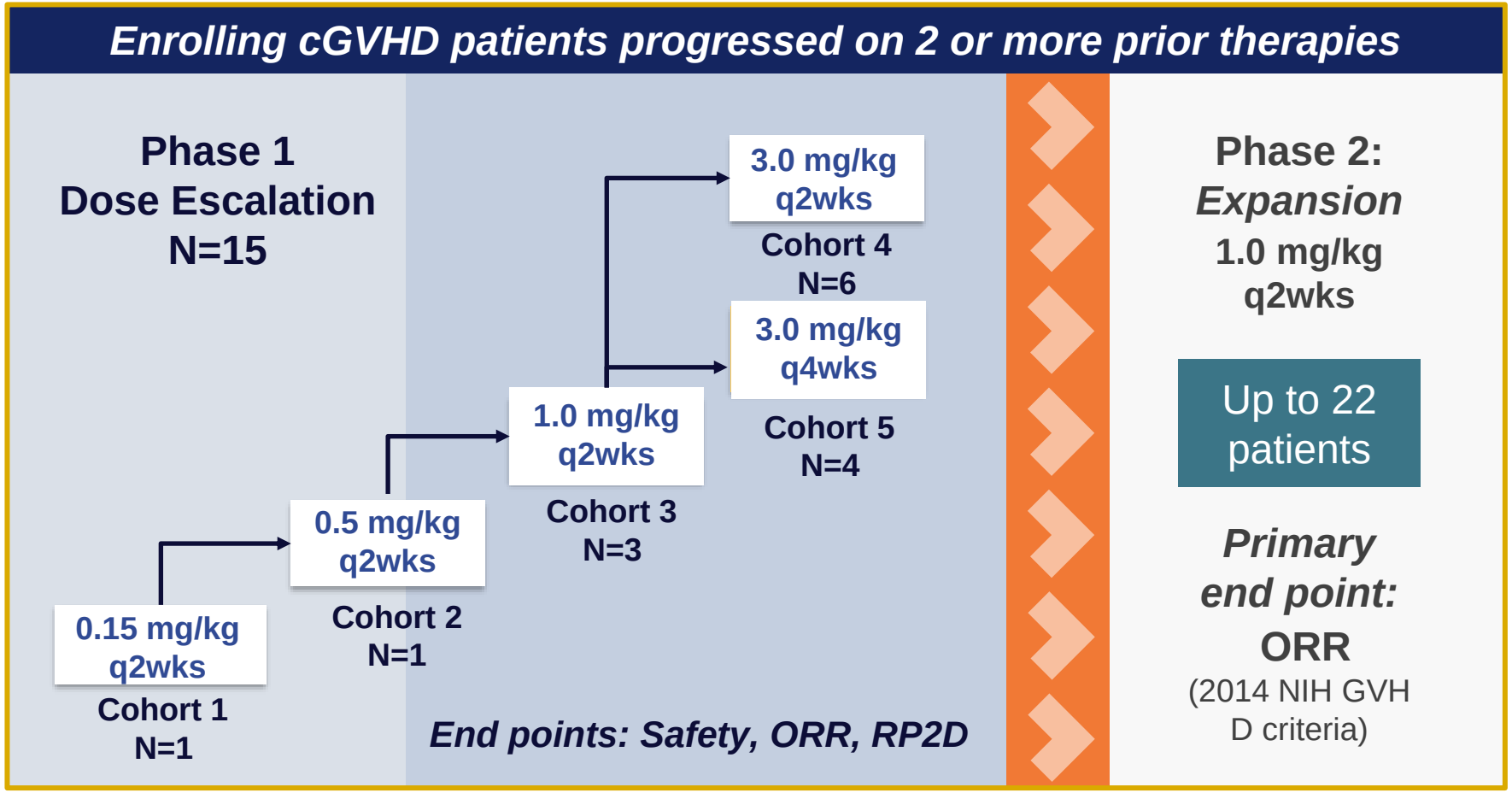
Axatilimab: Phase 1 / 2 trial establishes proof of concept in cGVHD

Study Population

Active cGVHD after ≥ 2 prior treatments

Karnofsky Performance scale ≥ 60

≥ 6 years of age



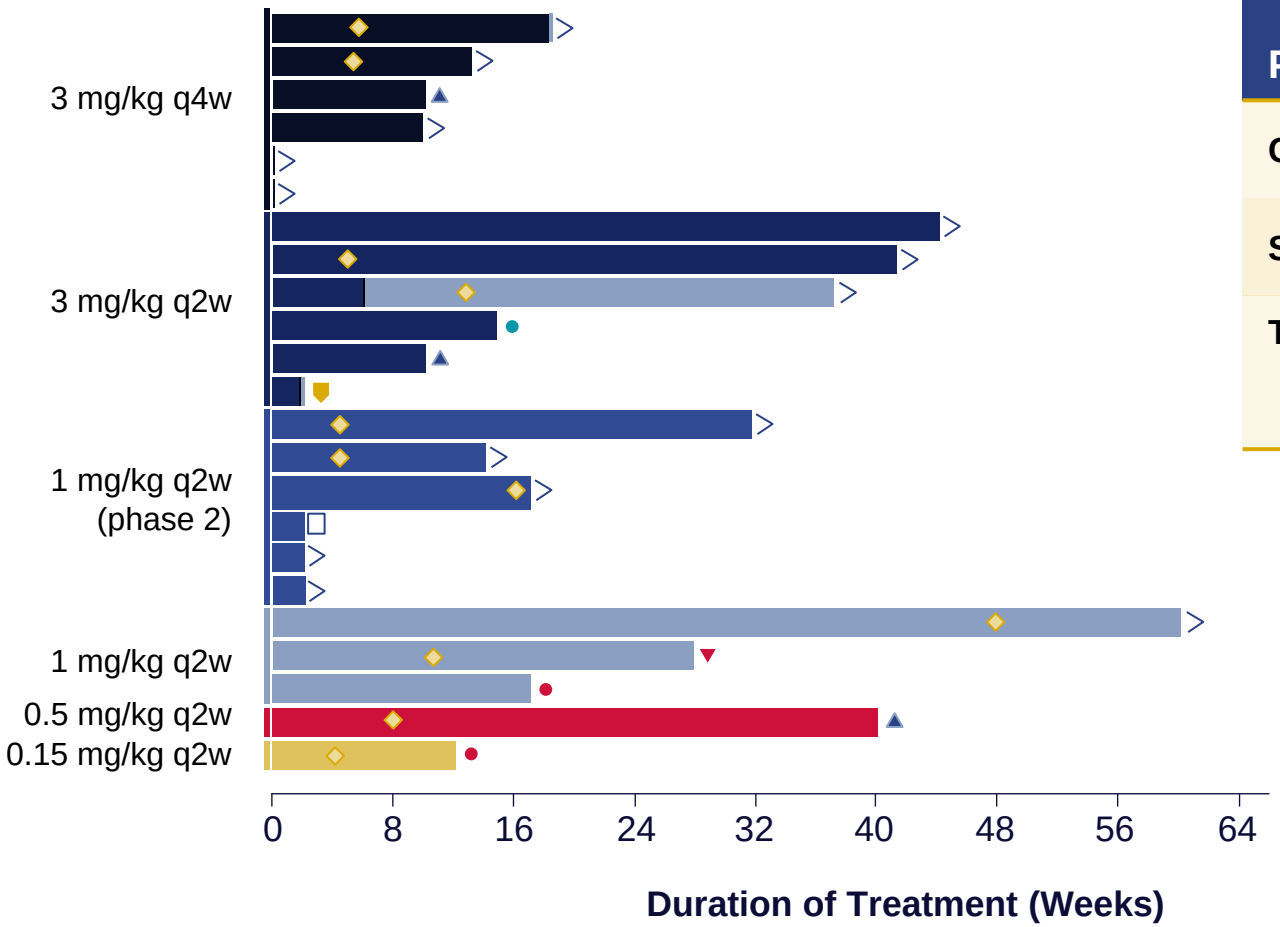
Baseline demographics & characteristics

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: Early evidence of symptom control in the heavily pretreated patients

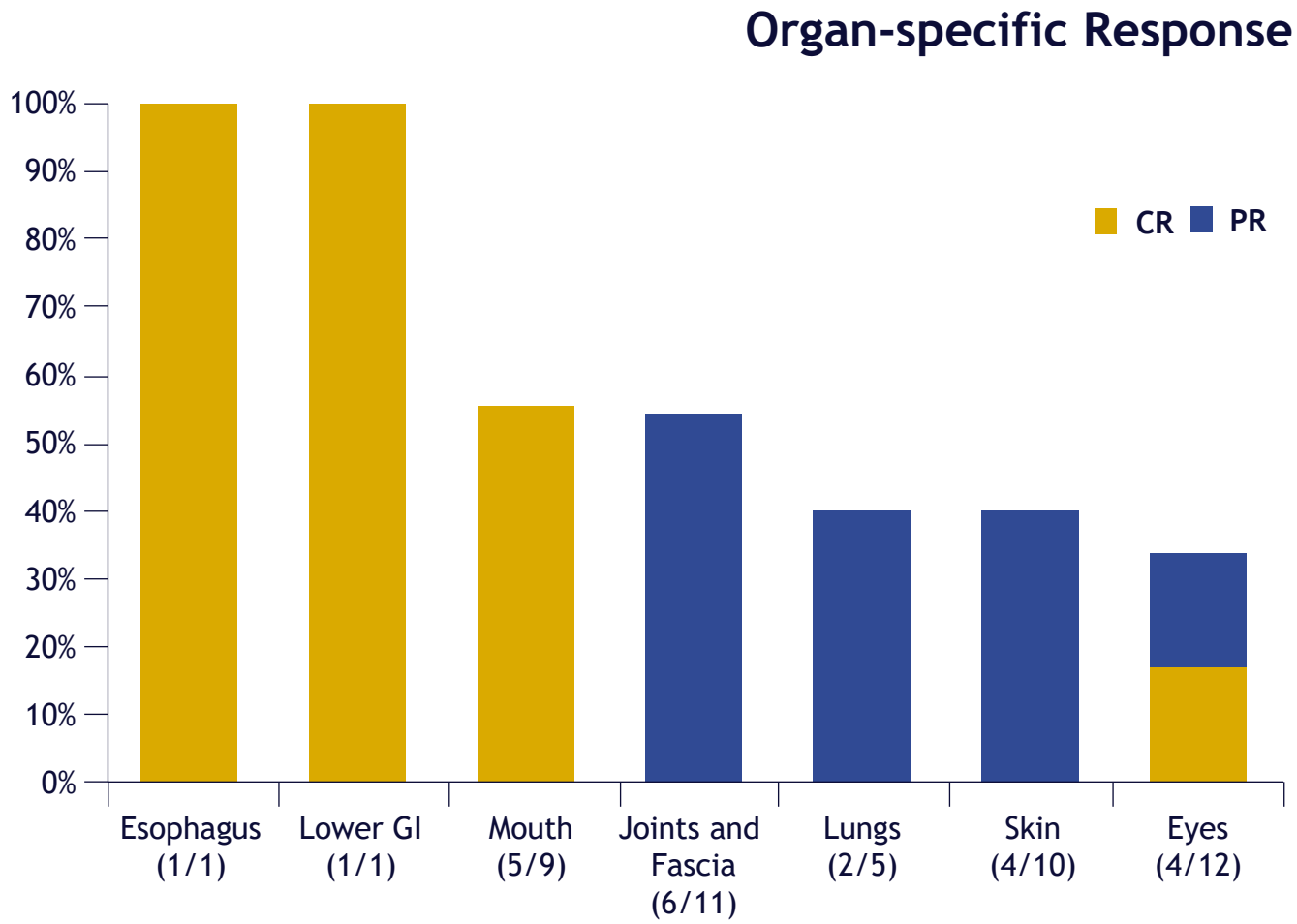
Phase 2 experience mirrors Phase 1



PHASE 1 ONLY	<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: Response seen across cGVHD organ system involvement

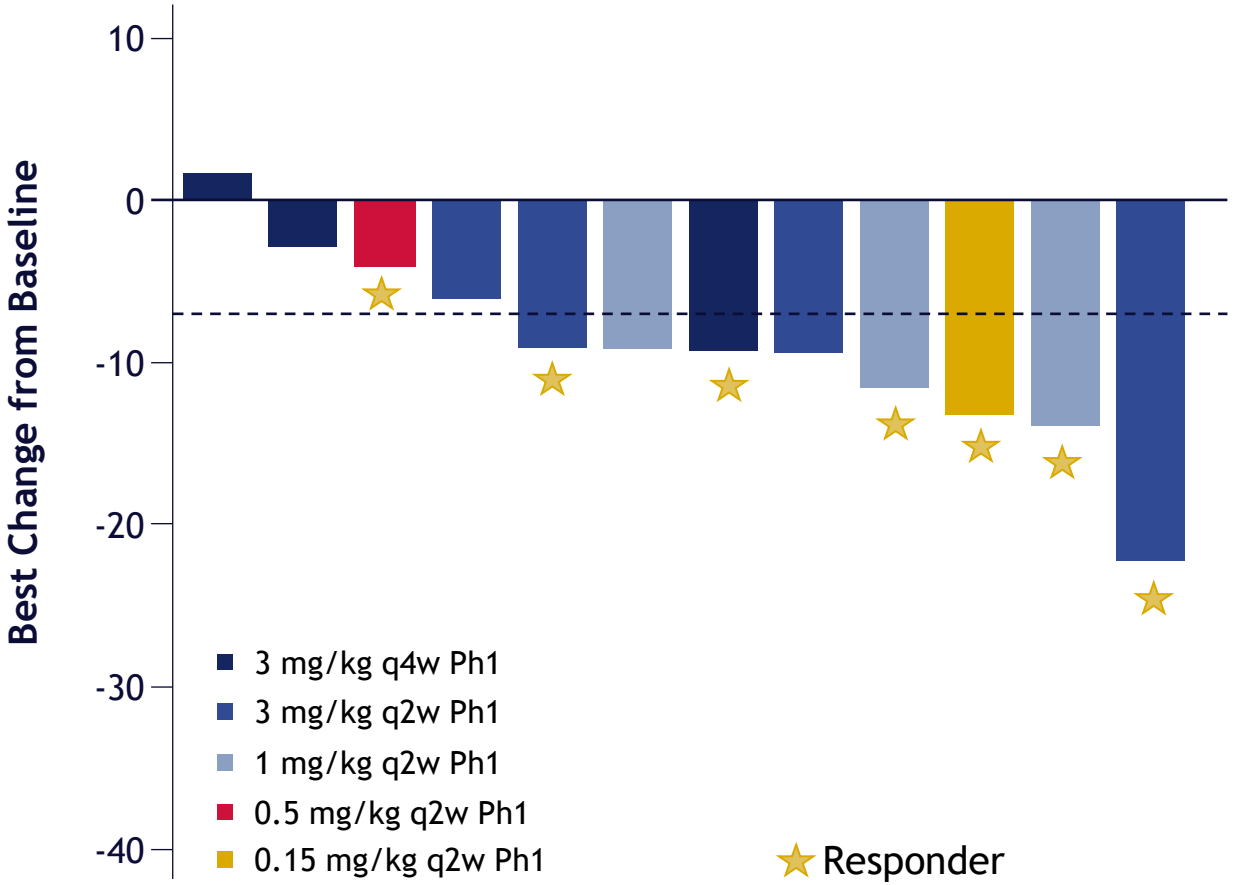


- Responses observed at all dose levels
- Deep and sustained responses observed across several organ systems
- Responses seen after prior Ibrutinib = 6; Ruxolitinib = 5; KD-025 = 3

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

Axatilimab: 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: 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

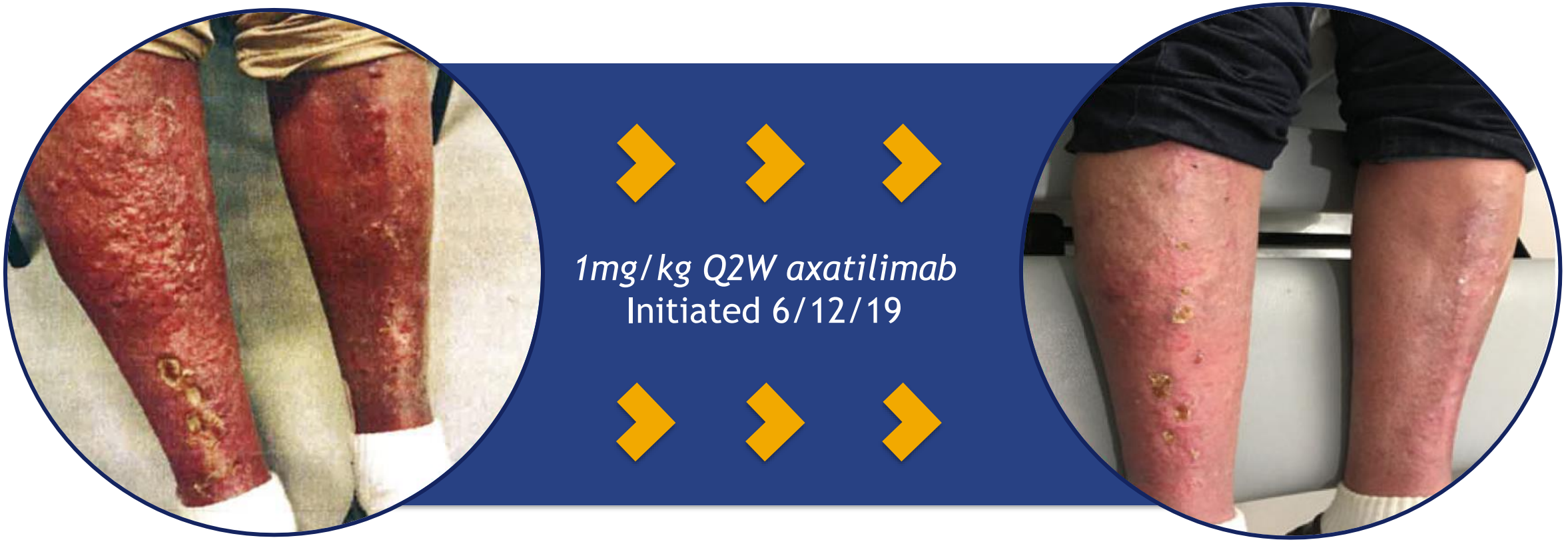
Characteristic	<1mg/kg q2wk n=2[1,2]	1mg/kg q2wk n=3	3 mg/kg q2wk n=6	3 mg/kg q4wk n=4	Total N=15
TEAE term, n (%)					
Pneumonia	1 (50)[2]	1 (33)	0	1 (25)	**3 (20)**
Conjunctivitis	1 (50)[1]	0	0	0	**1 (7)**
Gastroenteritis norovirus	0	0	1 (17)	0	**1 (7)**
Influenza	0	1 (33)	0	0	**1 (7)**
Lung infection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

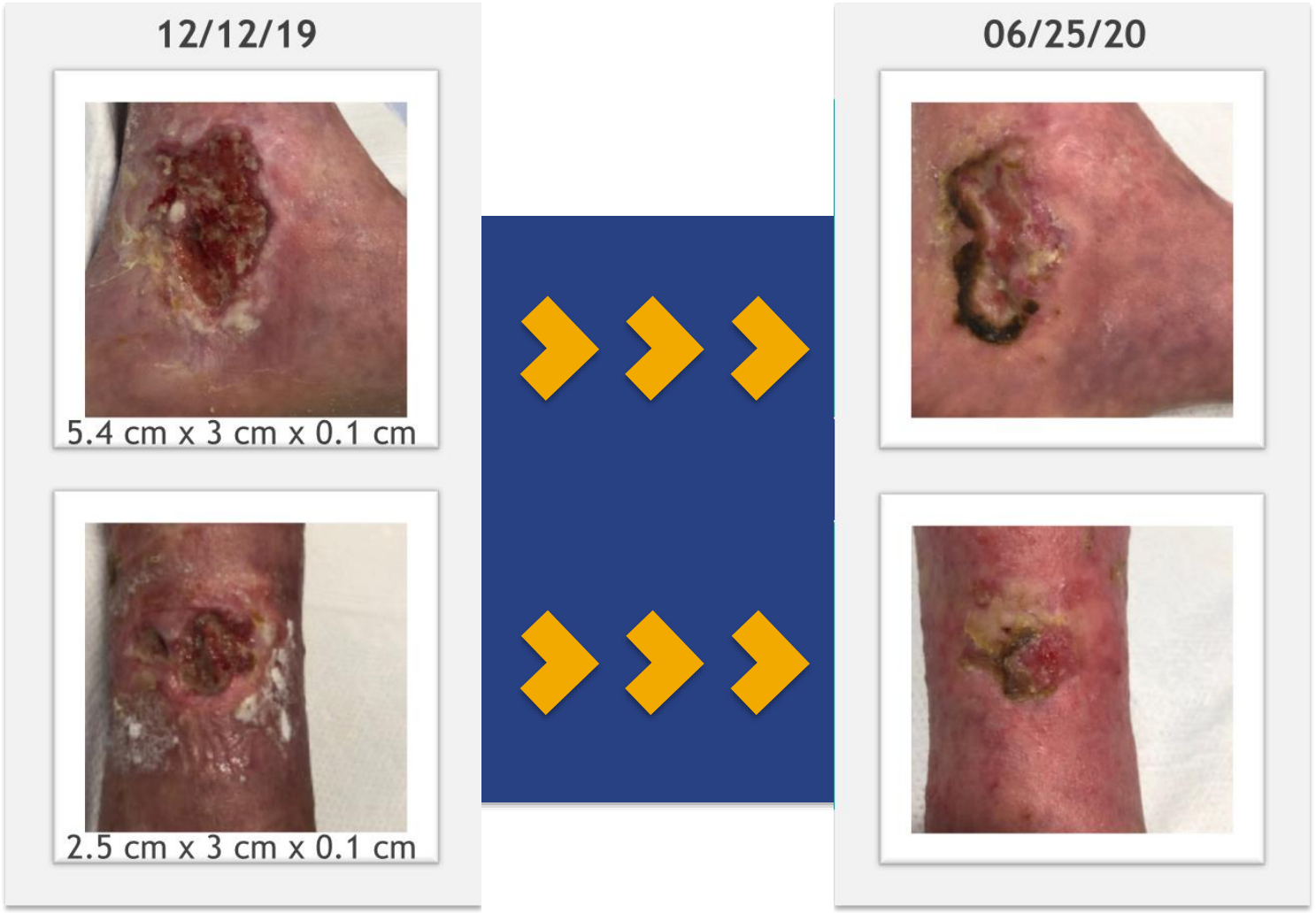
[1] Includes one patient from 0.15mg/kg q2wk dosing cohort. [2] Includes one patient from 0.5mg/kg q2wk dosing cohort [3] Pseudomonas infection to foot (dermal ulcers)
Abbreviations: URI=Upper-respiratory infection, q=every
Data cut-off 30Oct2020.

Axatilimab shows significant improvement in sclerodermatous cGVHD

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

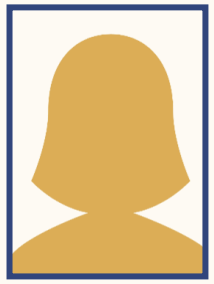


Additional example of observed improvement in sclerodermatous disease with ulcers



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

Case studies illustrate early results from this Phase 1 trial



30 Years Old,
Severe cGVHD

> *"I have not experienced any side effects since beginning the therapy; significantly fewer episodes of shortness of breath; first time I've noticed improvement from a treatment in years"*
>
> – Patient

Aug 2009
Hodgkin's Lymphoma

March 2012
Second Stem cell transplant

Apr 2012
aGVHD diagnosis

Jul 2012
cGVHD diagnosis involving skin, eyes mouth, lungs, joints & fascia

Prior to Aug 2019
Prior treatments included ibrutinib, ECP, rituximab, imatinib, ursodiol

Aug 2019
Enrolled in study AXA 1mg/kg q2w

Patient struggled with weight loss, loss of appetite & difficulty swallowing

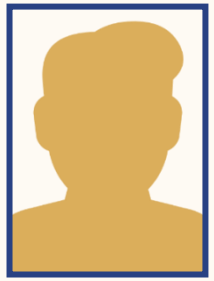
Baseline weight: 91.3lbs INCREASED to 101.9lbs

Global lung improvement with **PARTIAL RESPONSE**

FEV1:	FVC:	DLCO:
44% improved to 57%	48% improved to 55%	13% improved to 53%

AXA, axatilimab; DLCO, diffusing capacity of carbon monoxide; ECP, extracorporeal photopheresis; FEV1, forced expiratory volume in one second; FVC, forced vital capacity.

Case studies illustrate axatilimab benefit in heavily pre-treated GVHD



16 Years Old,
Severe cGVHD

Significant burden of disease despite 10 prior therapies

Jun 2014
AML diagnosed

Nov 2014
Stem cell transplant

Dec 2014
Diagnosed aGVHD

Jul 2015
Diagnosed cGVHD involving skin, mouth, joints & fascia

Prior to Mar 2020
10 prior regimens
including ibrutinib, ruxolitinib, ECP, rituximab, sirolimus, imatinib, steroids

Mar 2020
Enrolled in study
AXA 1mg/kg q2w

Cycle 2: Response in joints and fascia

Healing of leg ulcers and areas of sclerodermatous improvement

Back to physical activity including cross-country running, working part-time

Continues on treatment receiving AXA 1 mg/kg q4w

AML, acute myeloid leukemia; AXA, axatilimab; ECP, extracorporeal photopheresis.

Conclusions

- **Axatilimab demonstrates good tolerability with clinical activity demonstrated by a 57% (n=8) response rate in a heavily pre-treated patient population**
- **Clinical benefit observed across multiple organ manifestations of cGVHD**
- **A majority of patients experienced a significant benefit in their Lee Symptom Score with median change of -9.13 points.**
- **Low rate of infections reported with no viral reactivations**

- **Ongoing development of axatilimab will include a registration enabling randomized Phase 2 study (AGAVE-201) in patients with R/R cGVHD**

AGAVE-201

New Insights into the Pathophysiology and Treatment of Chronic GVHD

Prof Geoffrey Hill

José Carreras/E. Donnall Thomas Endowed Chair for Cancer Research

Fred Hutchinson Cancer Research Center

Seattle WA, USA

Conflicts of interest

Consulting
Regeneron

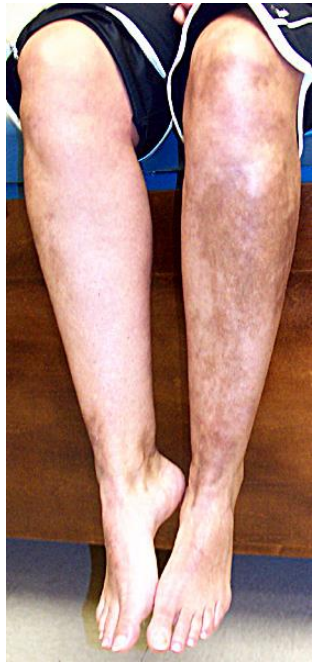
Research funding
Roche
Syndax
Compass Therapeutics
Applied Molecular Transport

Chronic GVHD

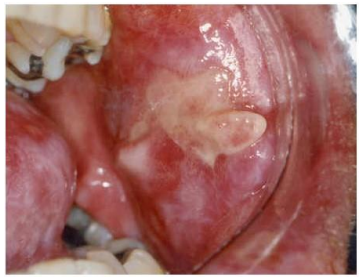
Occurs late post-transplant, follows acute GVHD

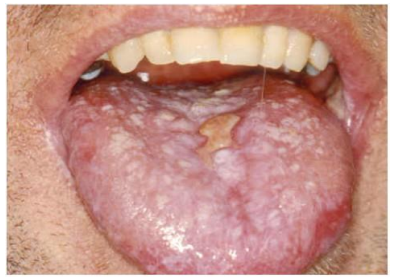
Primary target organs are skin, lung, mouth, salivary/lacrimal glands

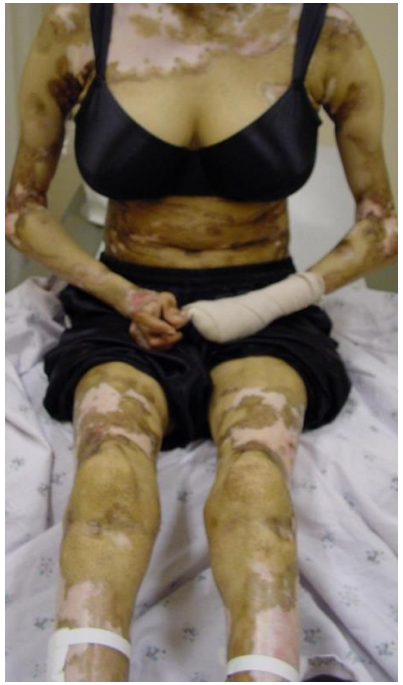
Cardinal feature is <u>fibrosis</u>



Up to 50% patients following allogeneic SCT





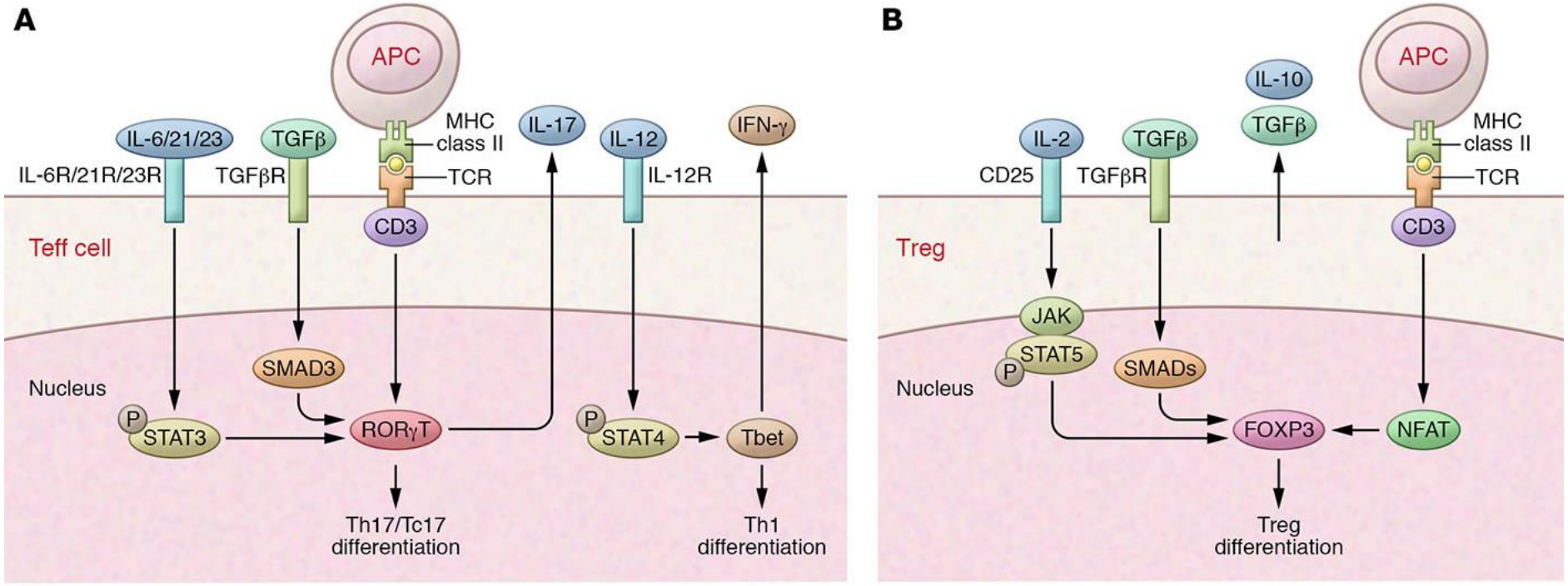


Effective therapy historically limited

Pathways of cGVHD

- Aberrant T cell differentiation (Th17, Tfh)
- Aberrant germinal centre B cell expansion and antibody secretion
- Regulatory T cell defects
- Excess IL-17A
- Alternatively activated macrophage differentiation

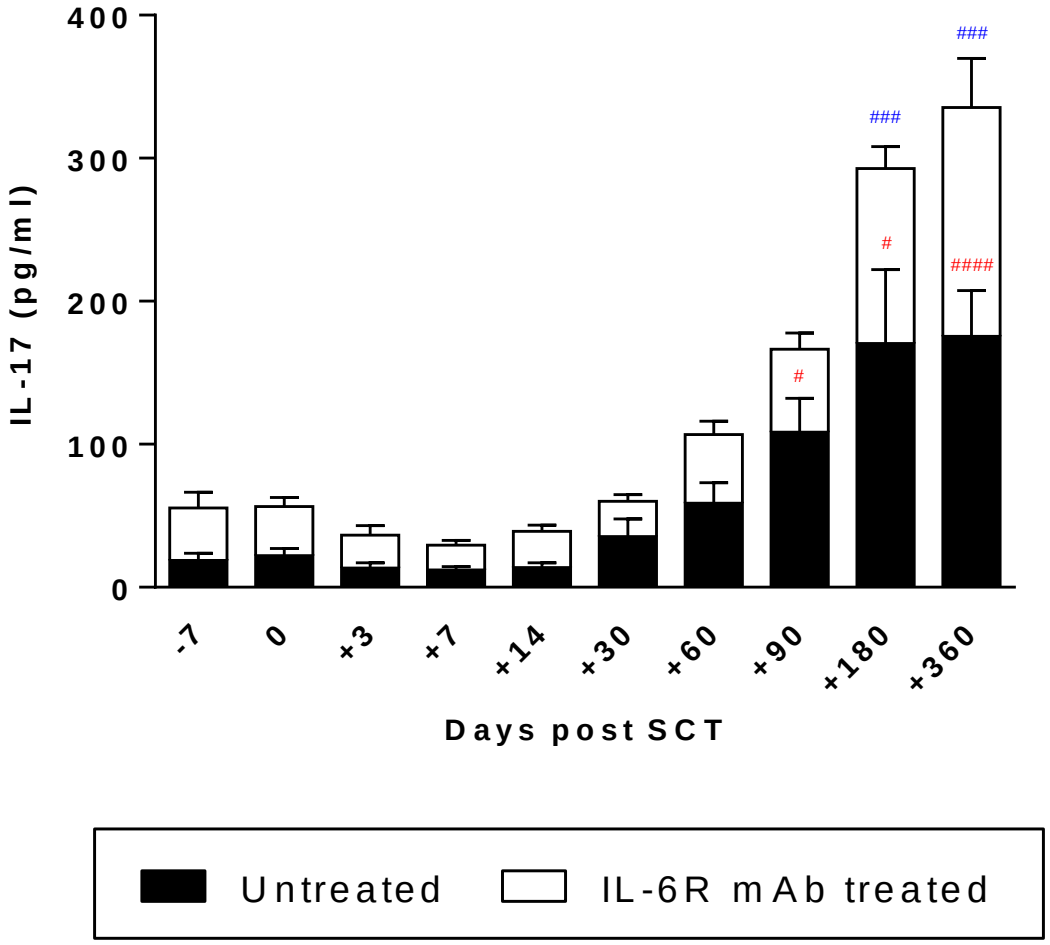
T cell differentiation



MacDonald, Blazar, Hill. *J Clin Invest* 2017

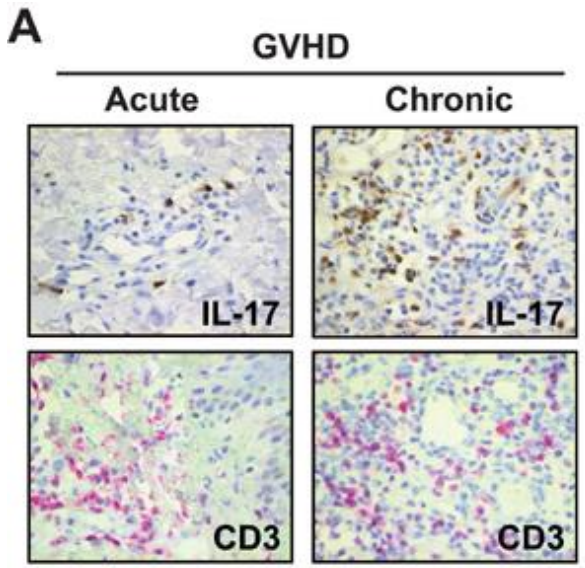
4. Th17/Th22 differentiation

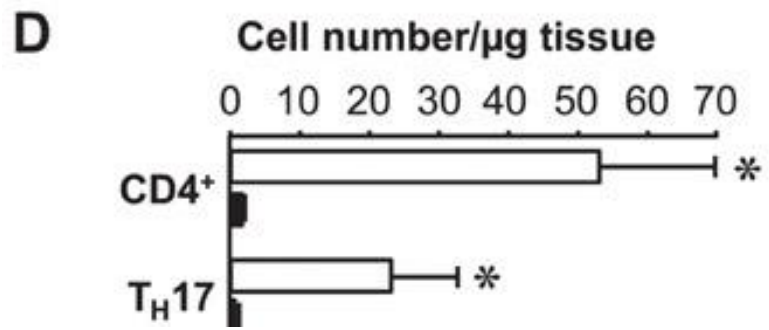
Chronic GVHD is associated with systemic IL-17 dysregulation



Kennedy G et al, *Lancet Onc* 2014

High amounts of Th17 cells are found in sites of chronic diseases

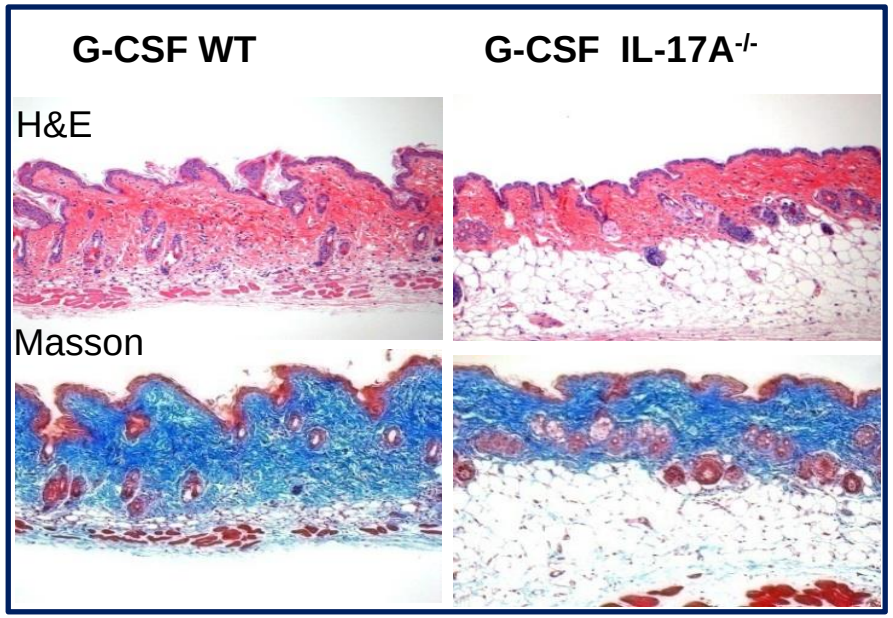




Ilona Kryczek et al., *Sci Transl Med* 2011

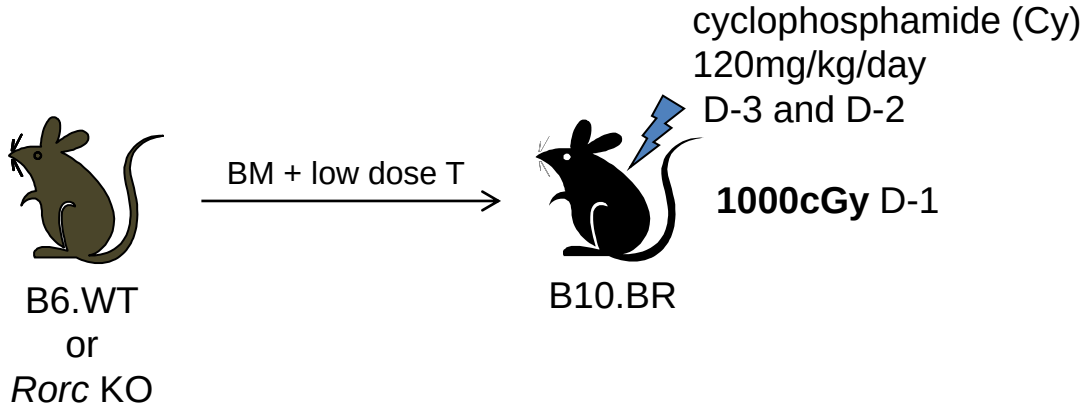
Scleroderma is IL-17 dependant

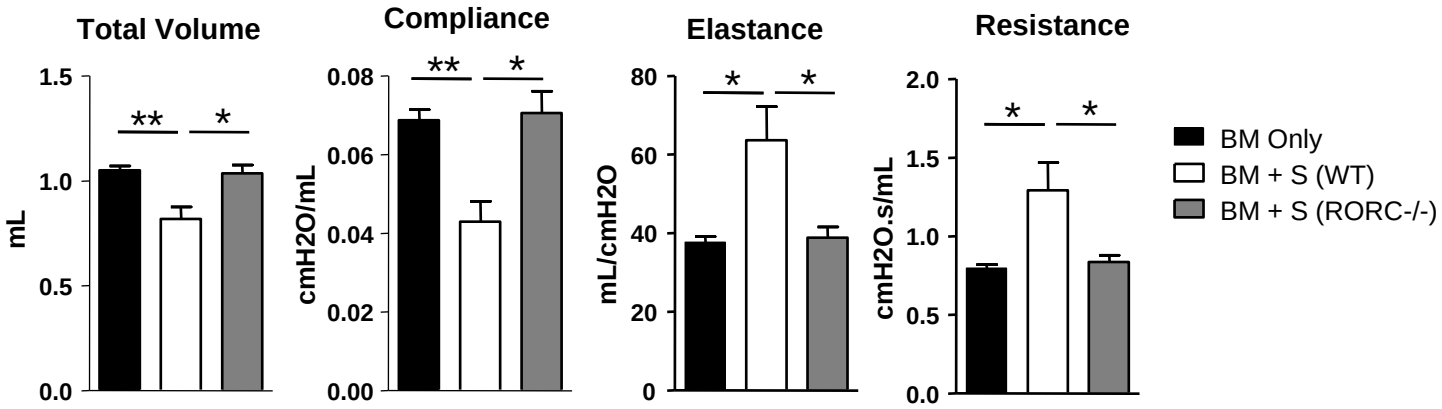
Day 70



Hill GR et al, ***Blood*** 2012;116:819-28.

IL-17 is a mediator Bronchiolitis Obliterans





IL-17 and chronic GVHD

What's the cellular mechanism of fibrosis?

Kelli MacDonald

Kylie Alexander

Pathways of cGVHD

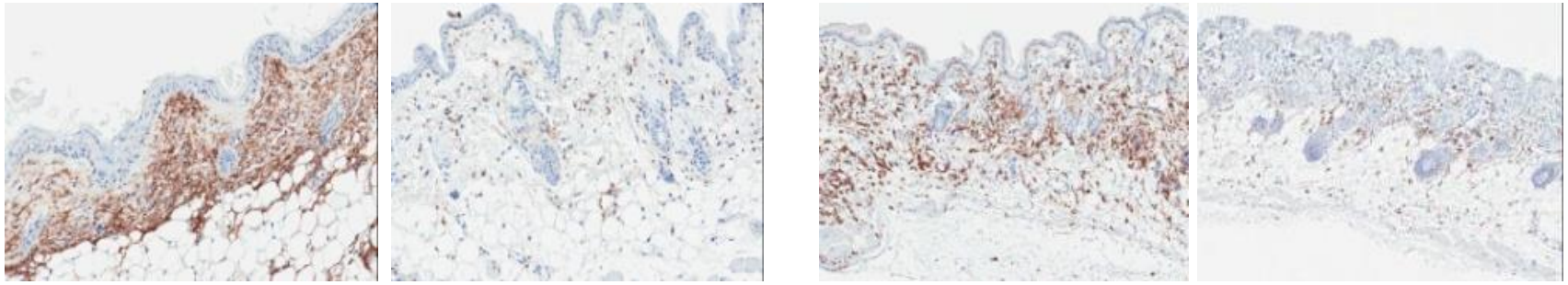
- Aberrant T cell differentiation (Th17, Tfh)
- Aberrant germinal centre B cell expansion and antibody secretion
- Regulatory T cell defects
- Excess IL-17A
- Alternatively activated macrophage differentiation

Scleroderma is associated with IL-17-dependent macrophage infiltration

F4/80^{+}

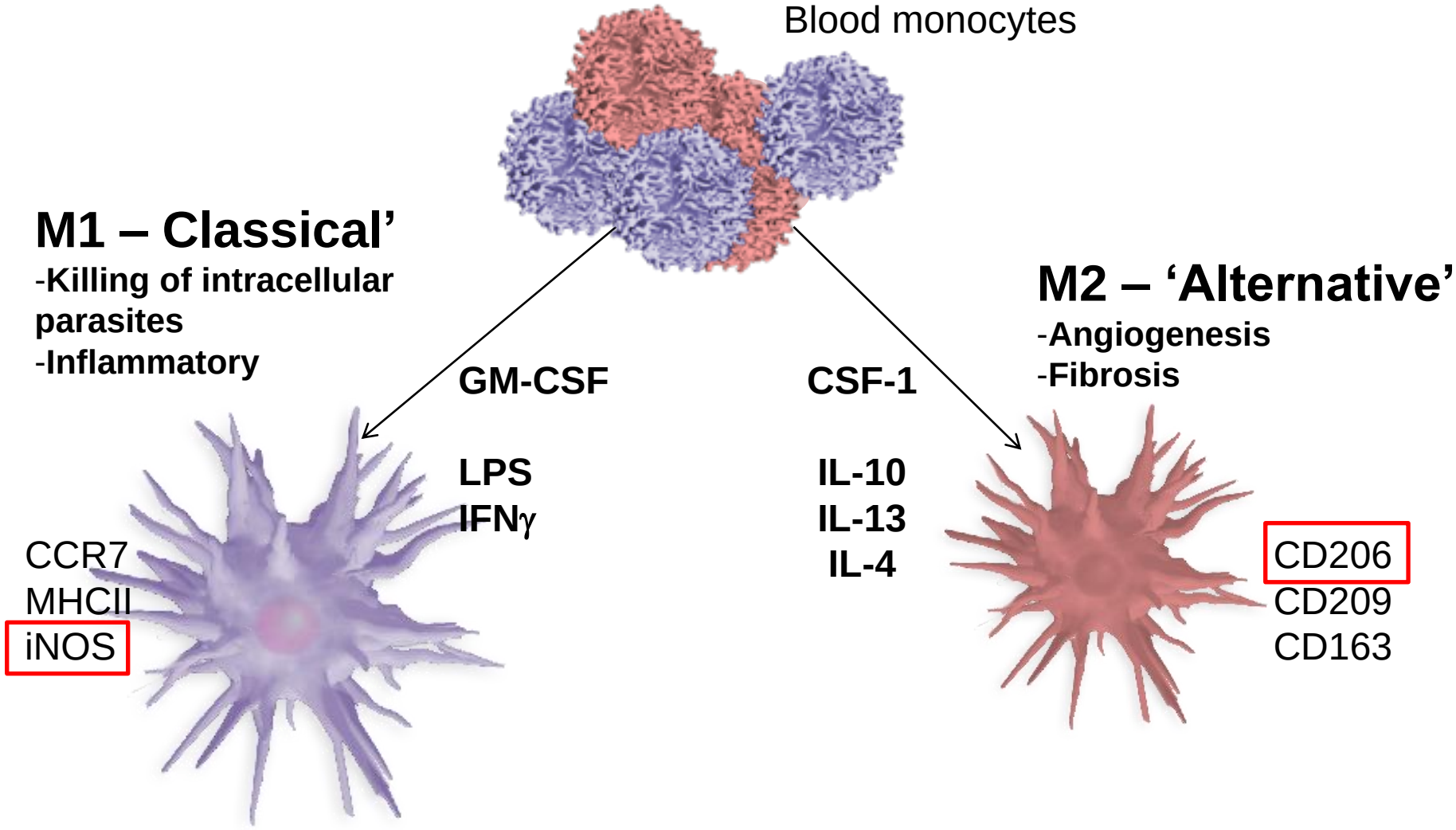
Day 28 | **Day 70**

WT | **IL-17A$^{-/-}$** | **WT** | **IL-17A$^{-/-}$**



Hill GR et al, ***Blood*** 2010

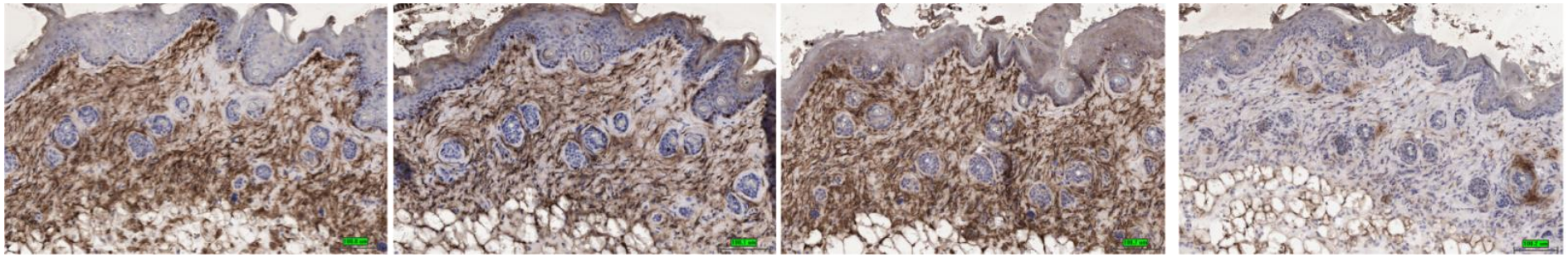
Phenotype of F4/80^{+} macrophages



F4/80^{+} macrophages are donor ‘M2’

D21

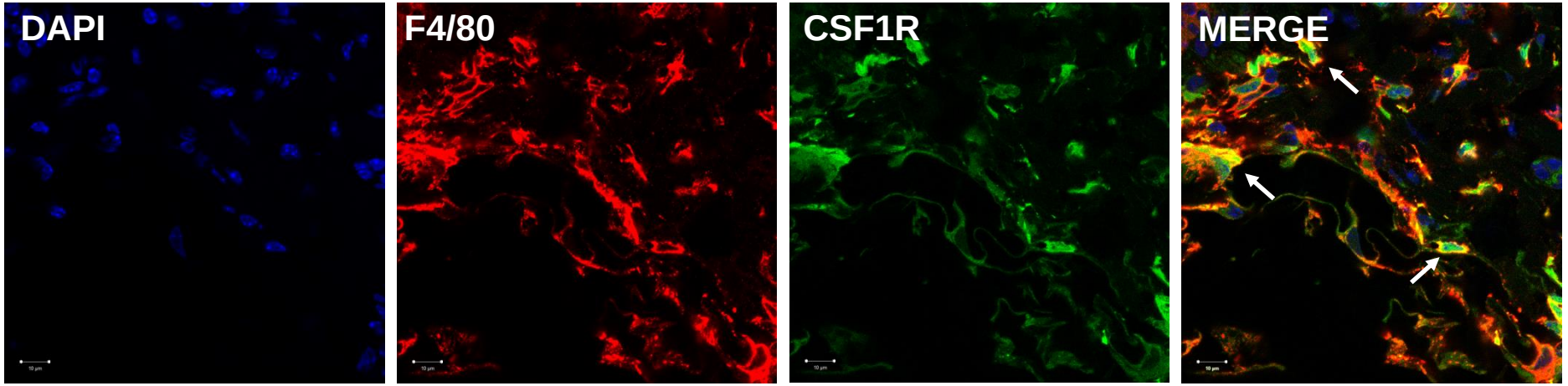
F4/80 | CD45.1 (donor) | CD206 (M2) | iNOS (M1)



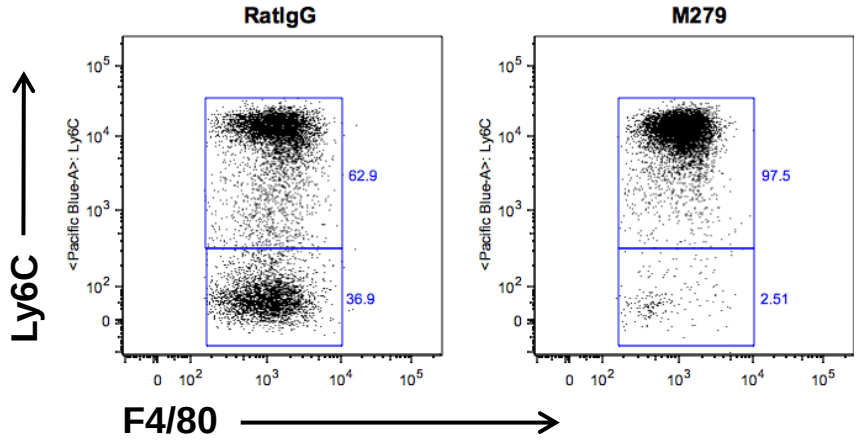
Alexander K et al, *J Clin Invest* 2014

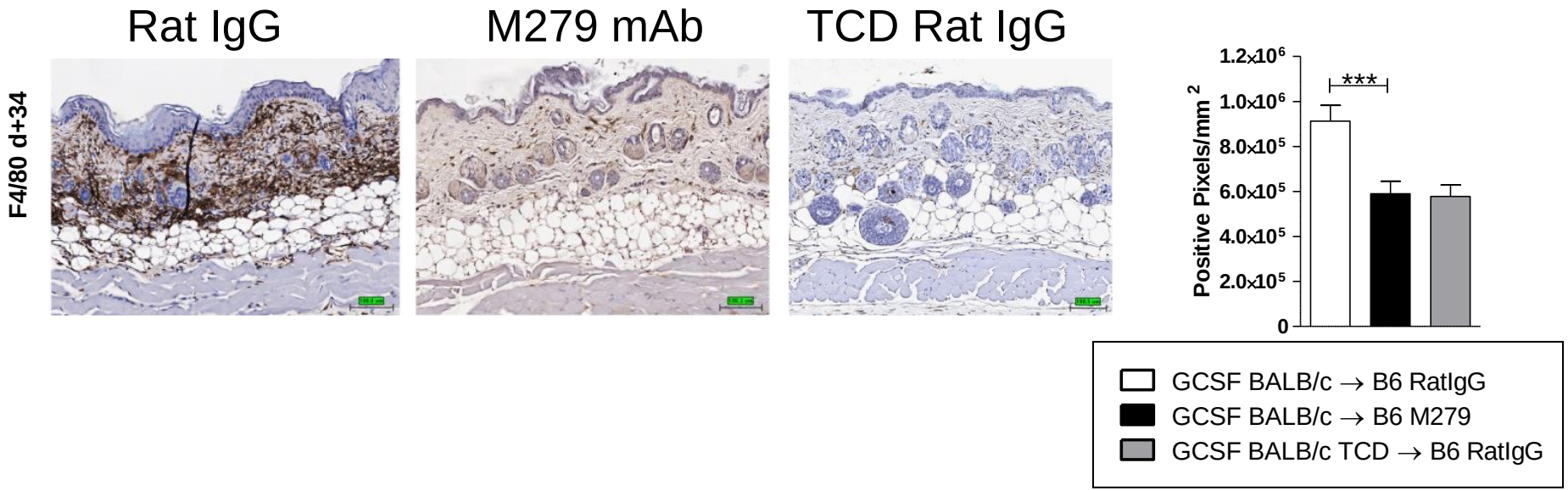
F4/80^{+} macrophages express C-CSF-1R

B6.MacGreen BM + T → B6D2F1

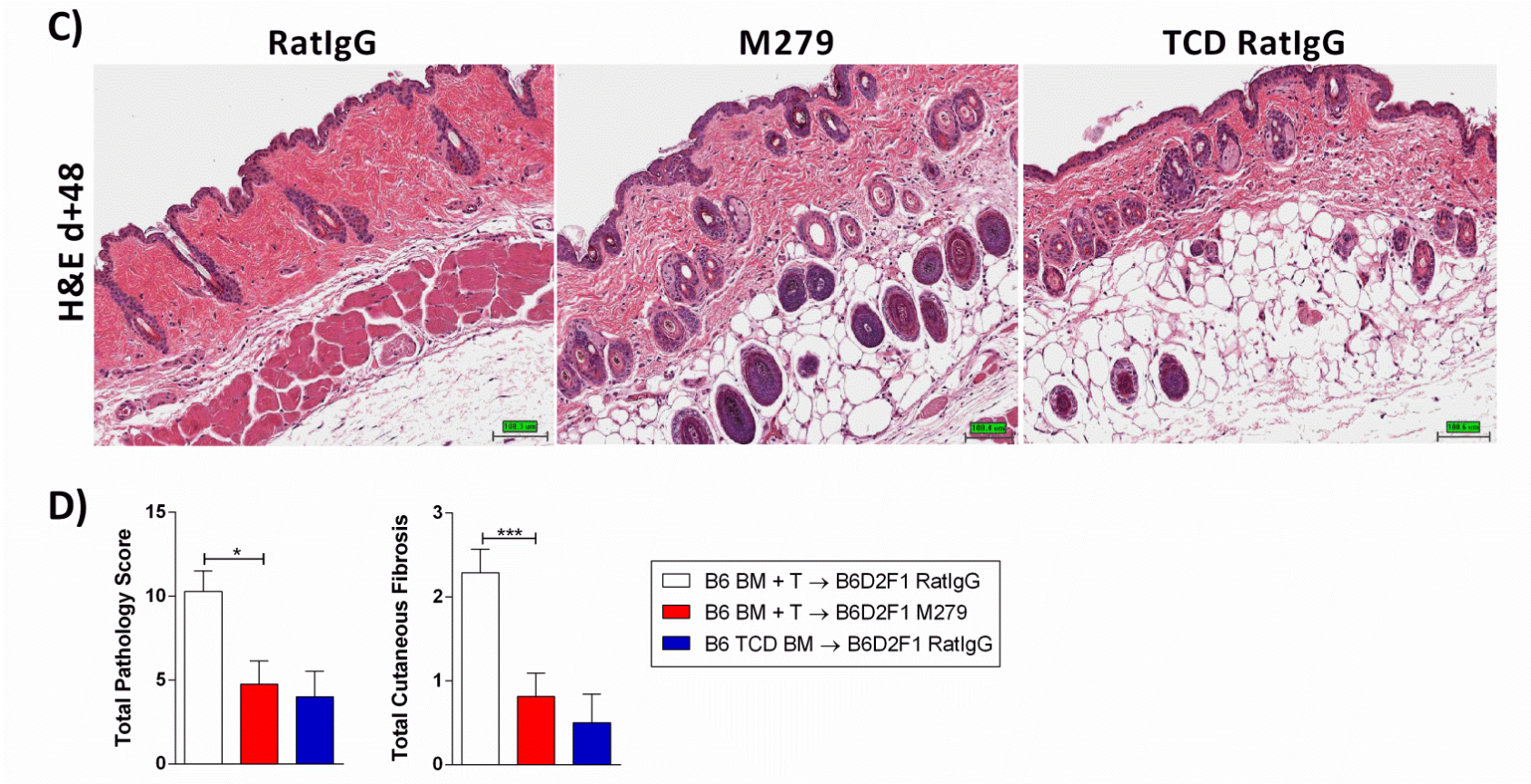


Anti-CSF-1R (M279) blockade post transplant depletes resident tissue precursor macrophages

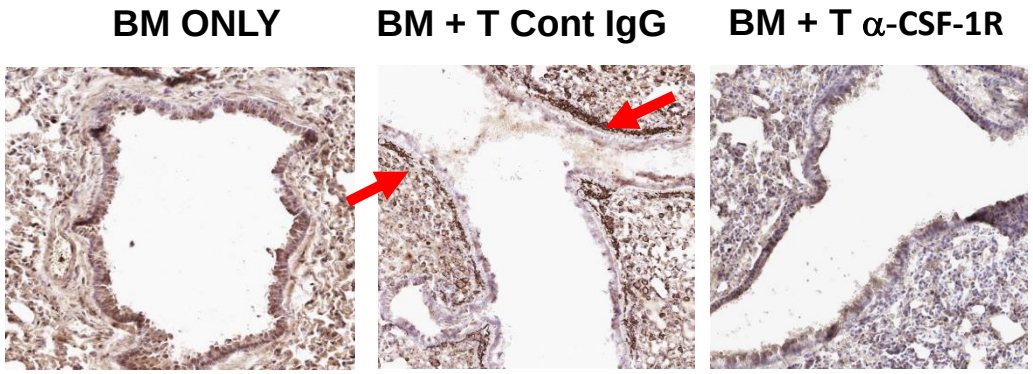


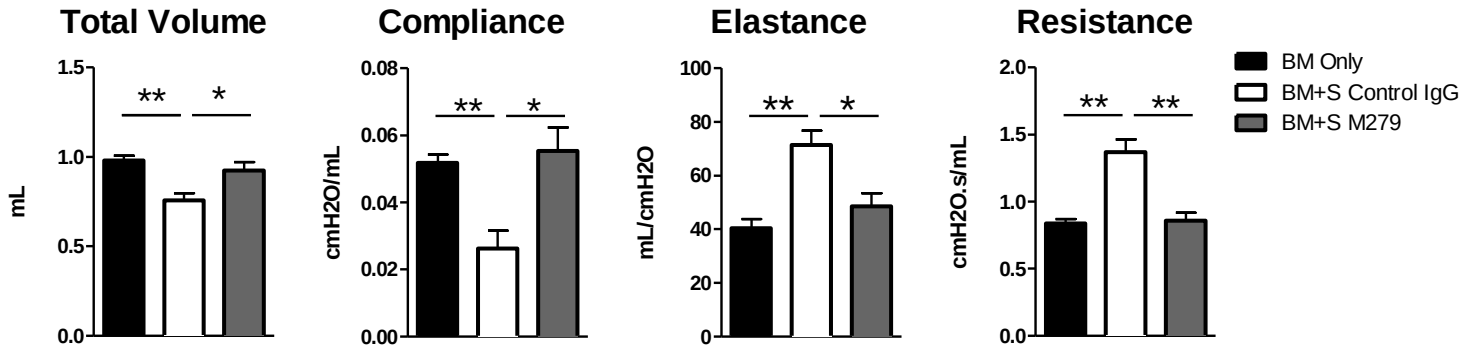


CSF-1R blockade prevents scleroderma



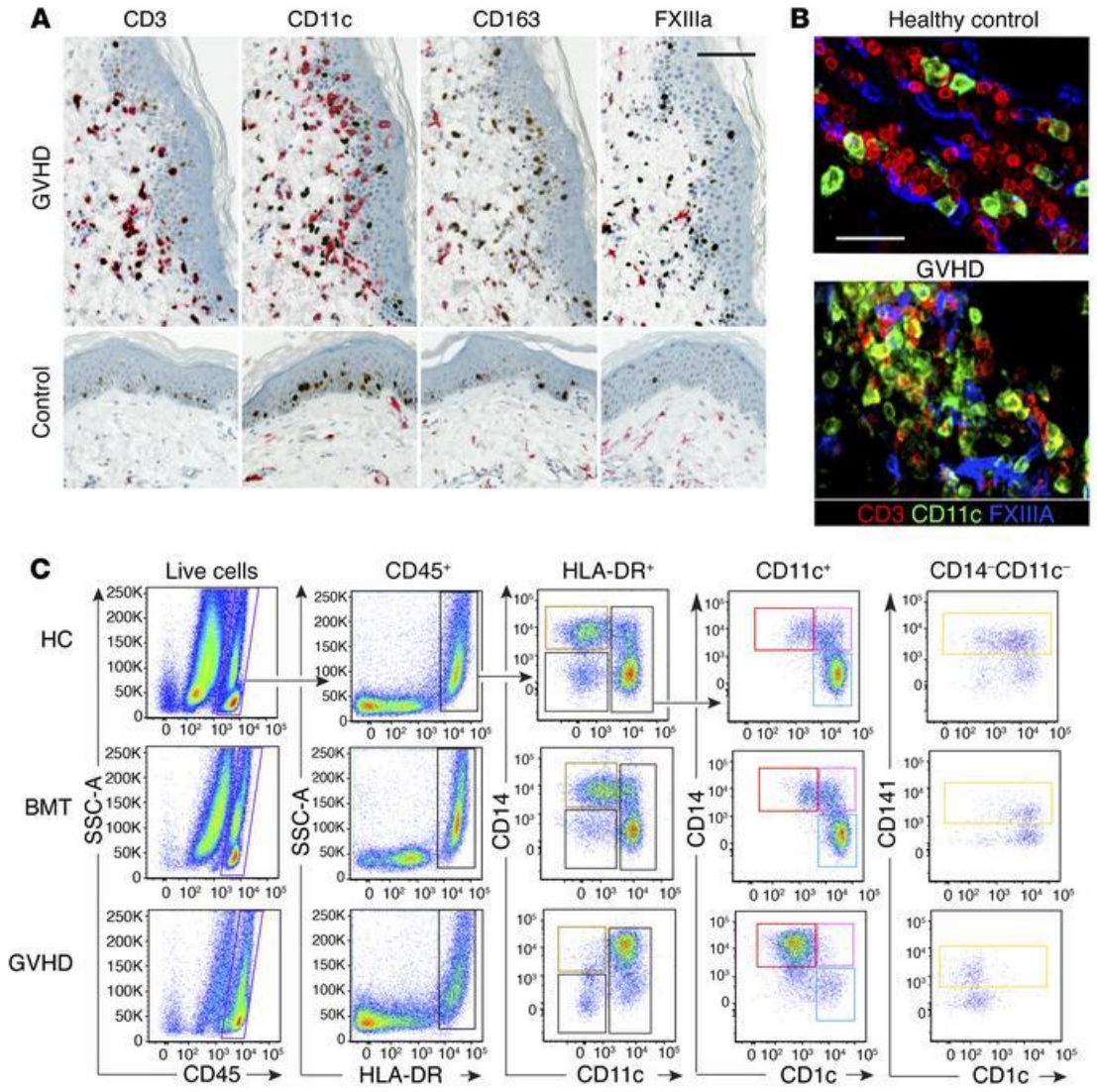
Macrophage depletion with anti-CSF1R mAb abrogates Bronchiolitis Obliterans



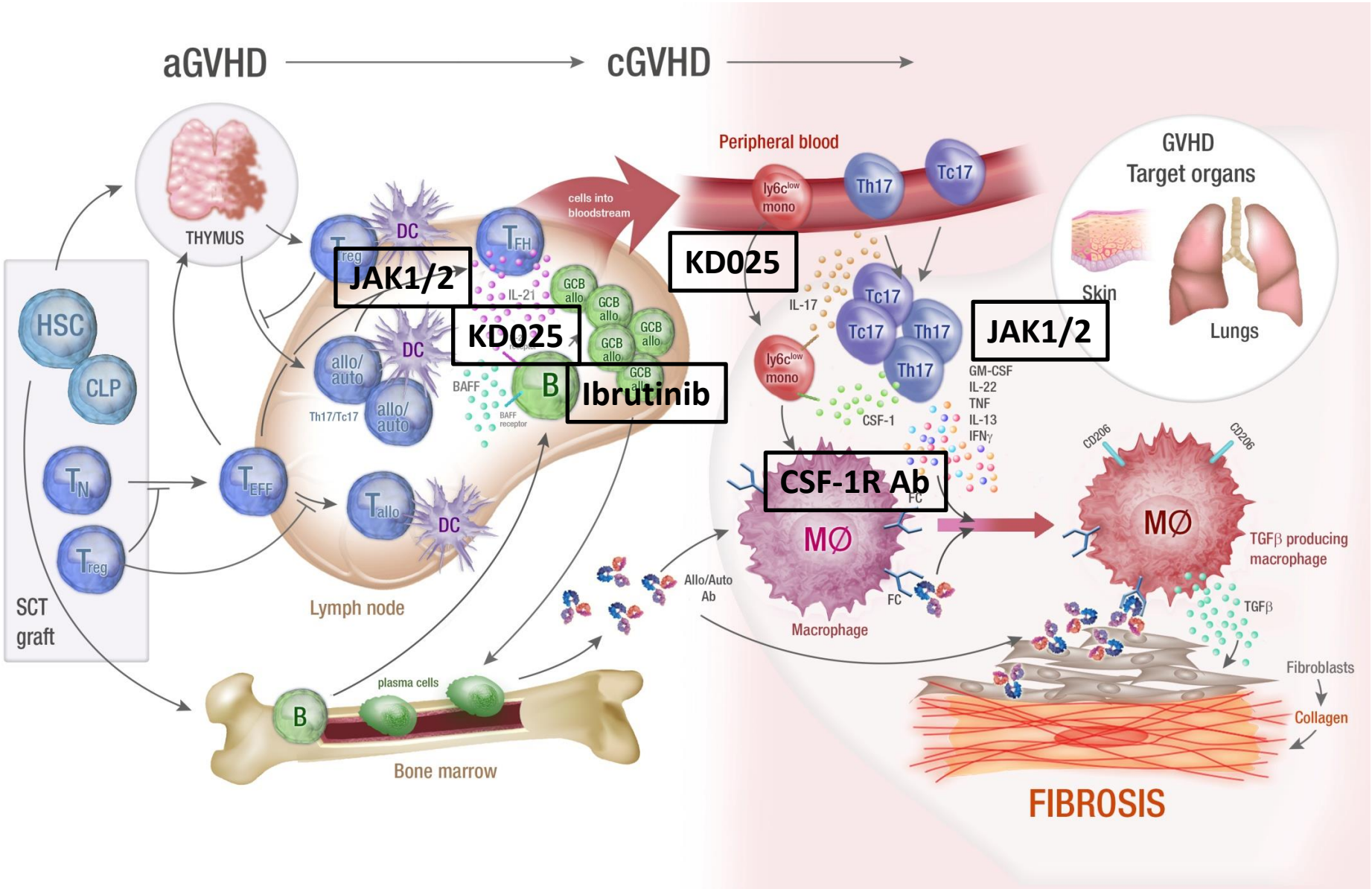


Alexander K et al, *J Clin Invest* 2014

Monocyte-derived macrophages dominate human GVHD skin



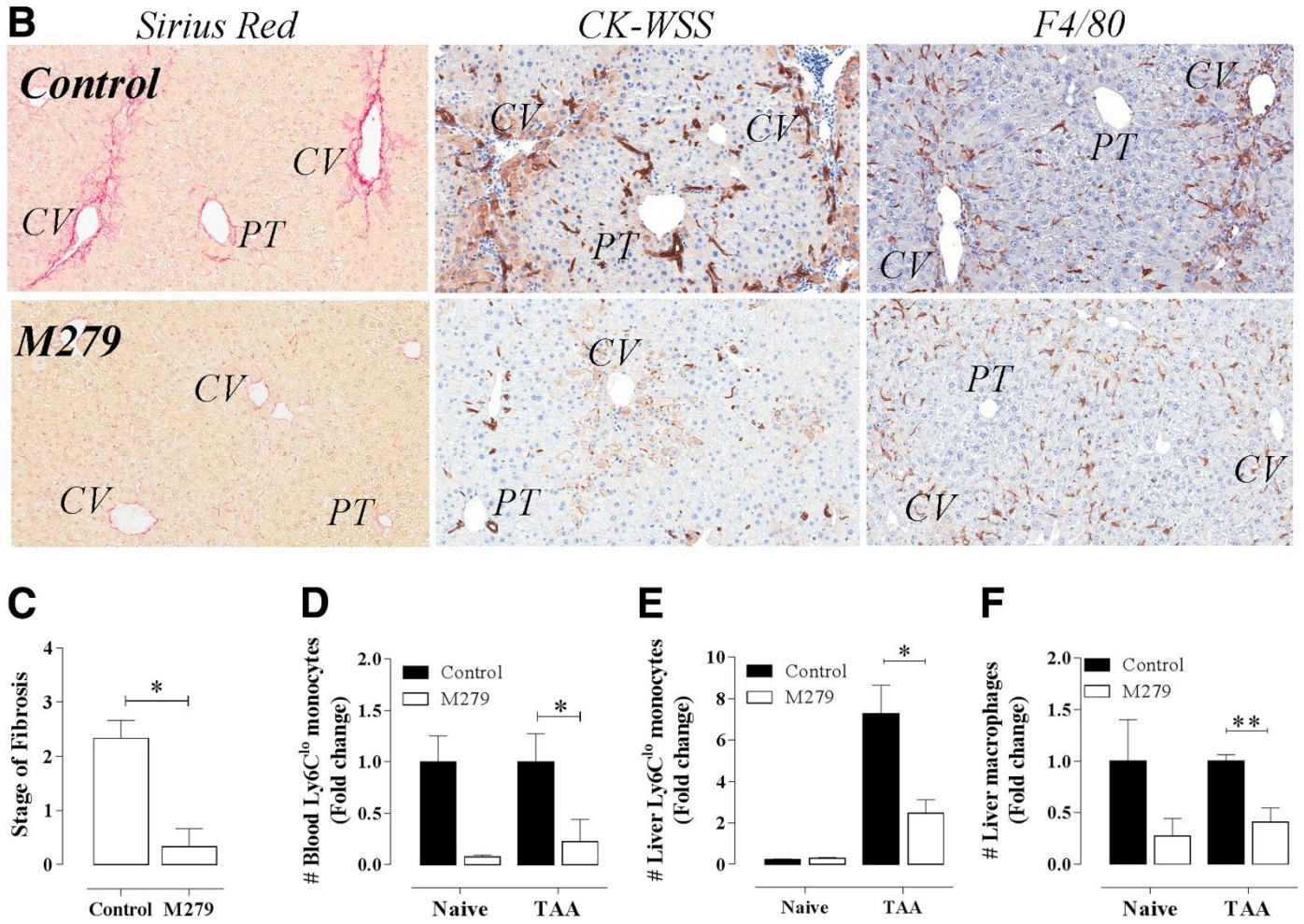
Jardine L et al. *J Clin Invest* 2020



MacDonald, Hill, Blazar. ***Blood*** 2017

What about other disease characterized by fibrosis?

Potential for activity in systemic sclerosis, pulmonary fibrosis, hepatic fibrosis



Melino M et al. ***Am J Pathol.*** **2016**

Conclusions

- **CSF-1R-dependent macrophages appear to represent a common terminal pathway of tissue fibrosis in cGVHD**

- **CSF-1R inhibition offers theoretical advantages over agents acting more proximally (e.g. on T cells or B cells)**

- **CSF-1R inhibition is active in both scleroderma and BO in preclinical cGVHD models**

- **Moving CSF-1R inhibition earlier into the treatment phase of cGVHD, before dense fibrosis has established is an attractive next step**

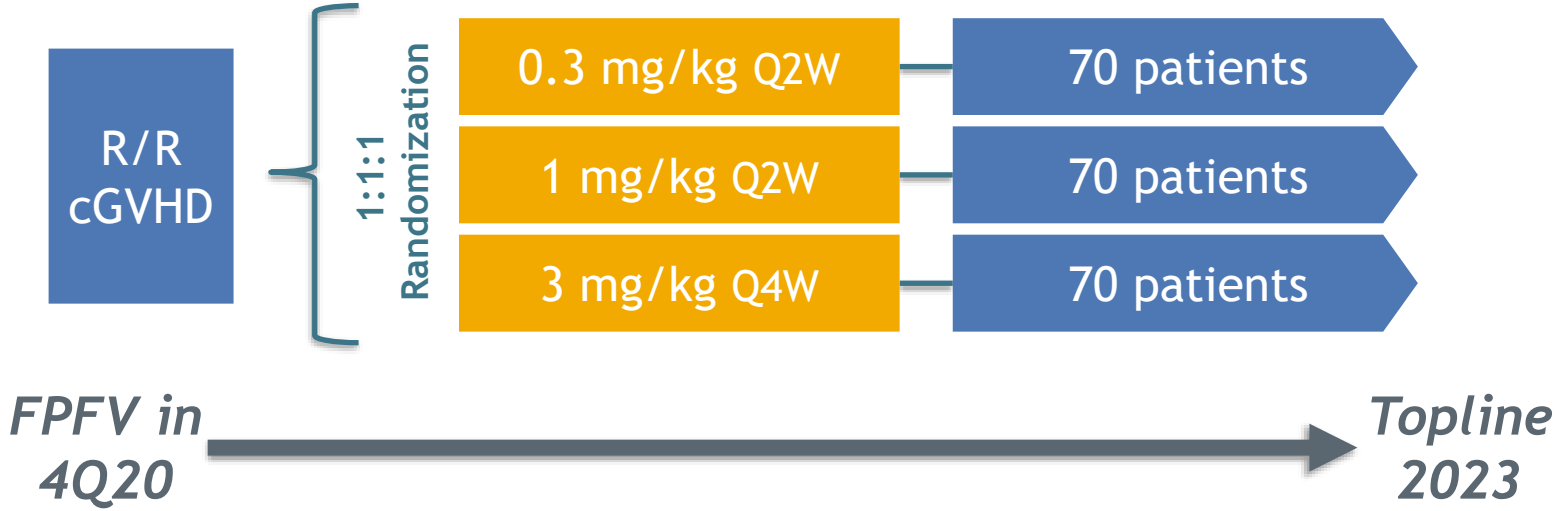
- **Fibrosis in other diseases and target organs also appear to involve the CSF-1R axis**

Axatilimab cGVHD development plans and closing remarks

AGAVE-201 global chronic GVHD pivotal trial expected to initiate by year end

Inclusion criteria:

- 6 years and older
- Recurrent or refractory active cGVHD after at least 2 lines of systemic therapy



Primary Endpoint: Objective Response Rate (ORR) by 2014 NIH GVHD Criteria

Key Secondaries: Duration of response, improvement in modified Lee Symptom Scale

Questions?

Syndax