



Therapie der chronischen GVHD – Kinase Hemmung und Antikörper

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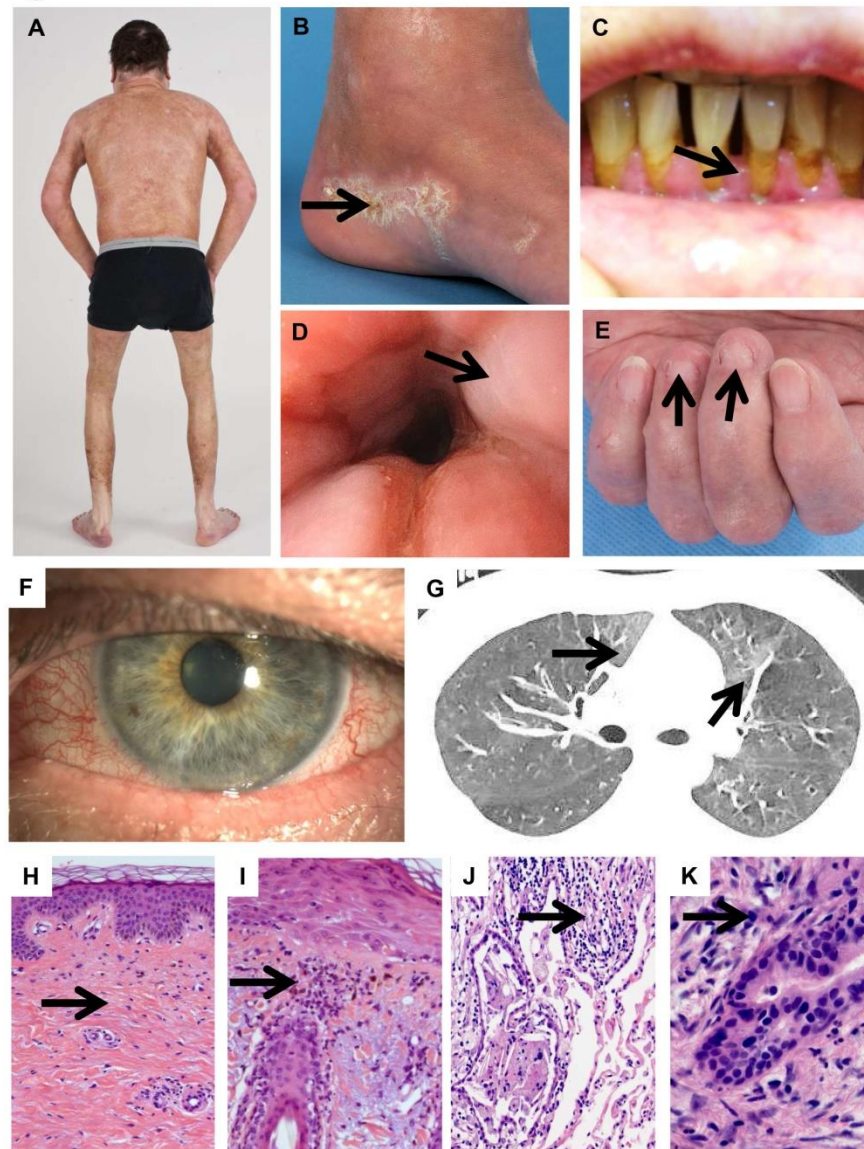
Disclosures

Honorare von Novartis, Incyte, Sanofi, MNK, VectivBio,
Medac

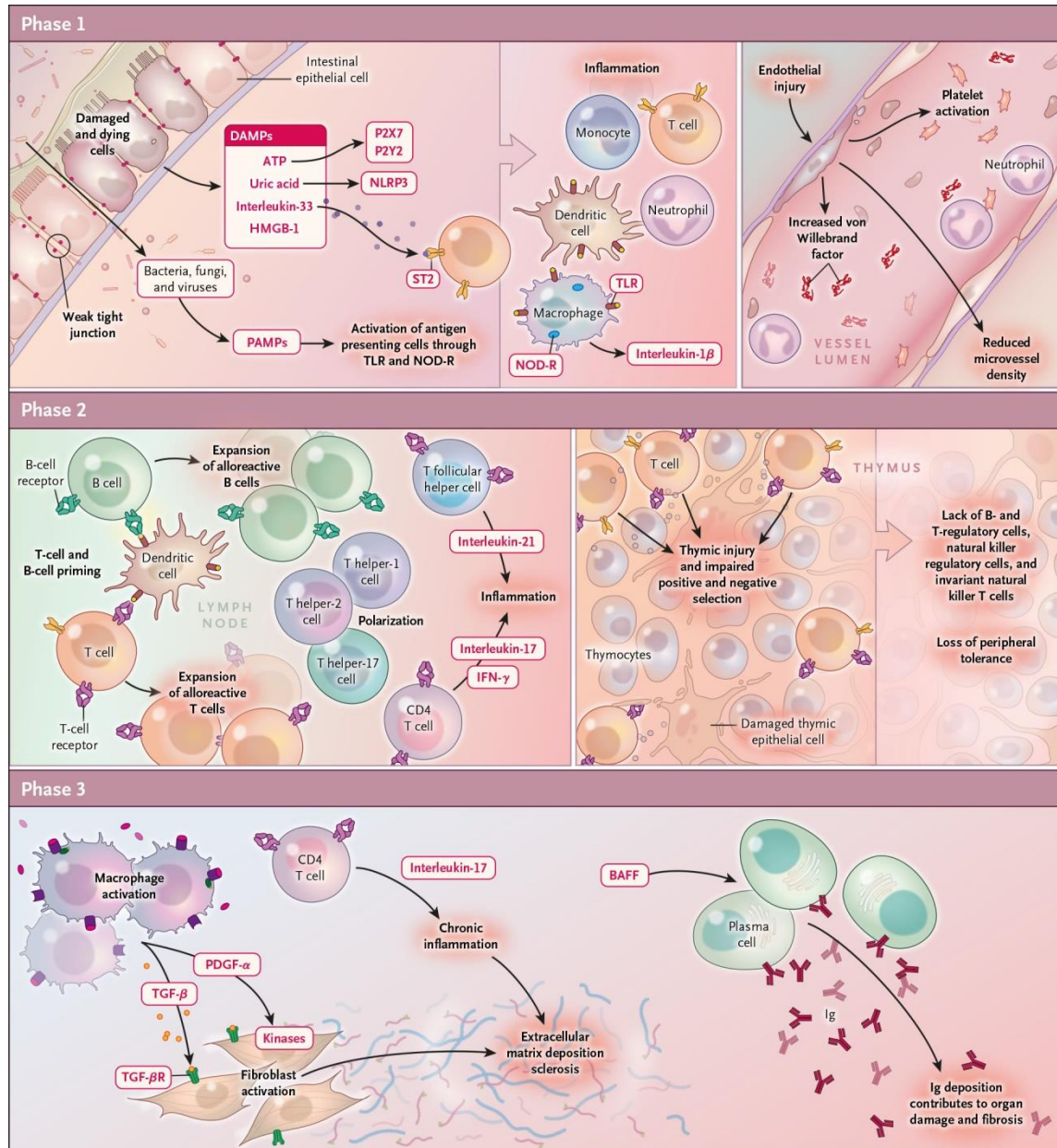
Clinical features of fibrosis and inflammation in cGvHD

chronic GVHD

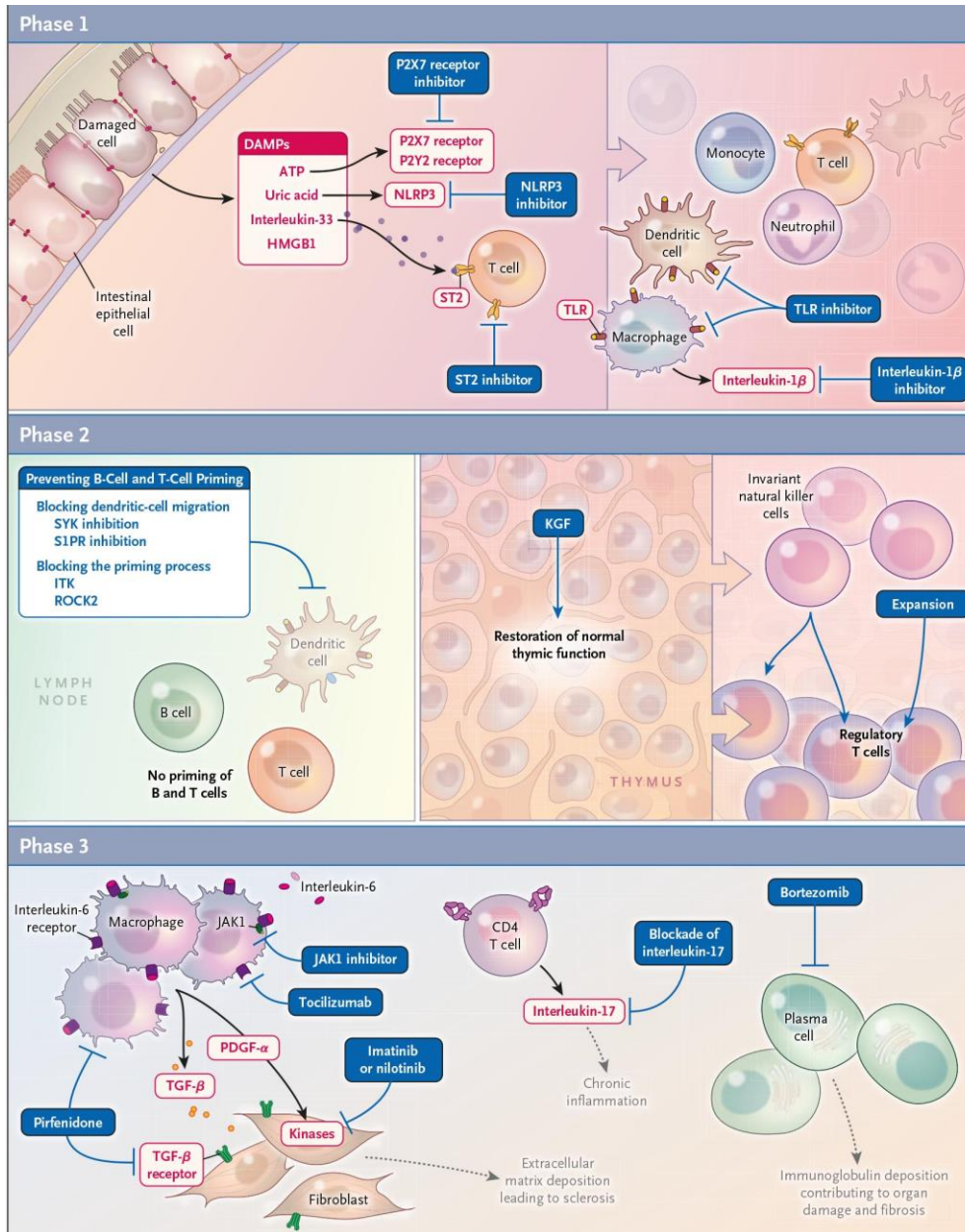
Figure 1



Pathomechanism of fibrosis in chronic GVHD

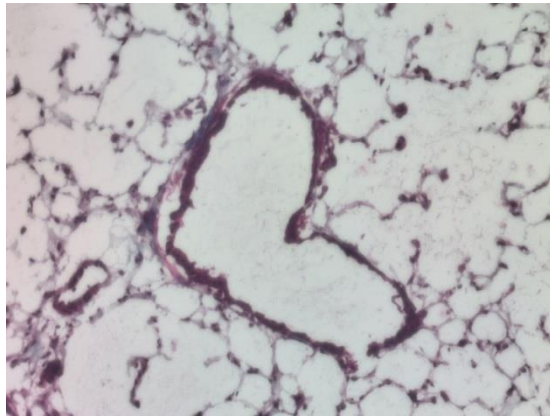


New drugs based on the pathomechanism ?

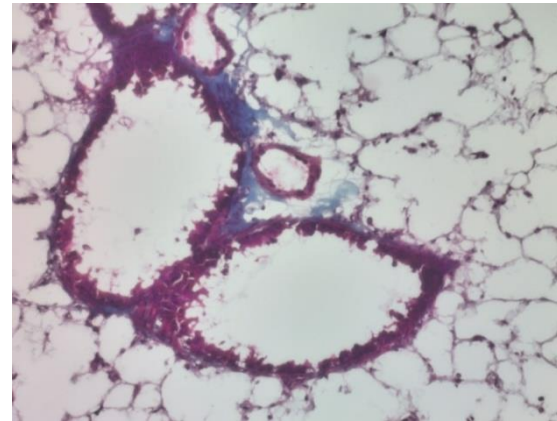


Ruxolitinib in chronic GVHD - **preclinical data**

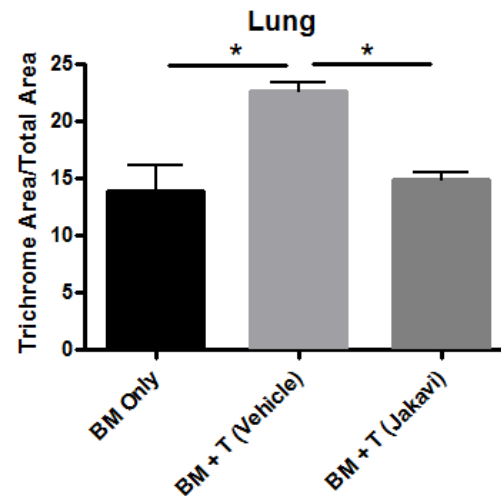
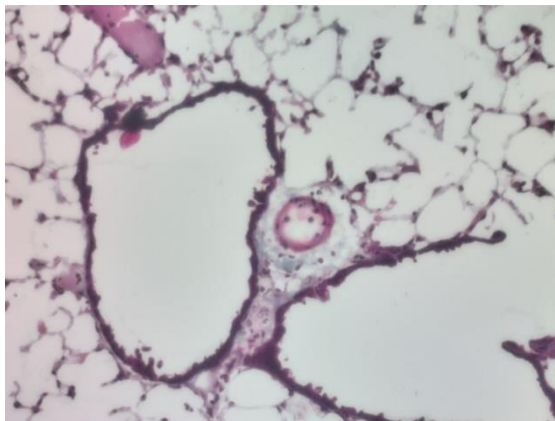
BM only



BM + T cells + vehicle



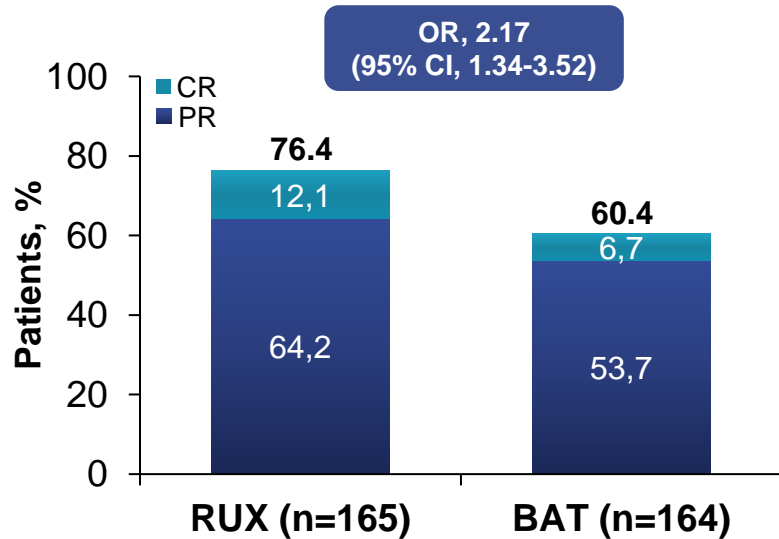
BM + T cells + ruxolitinib



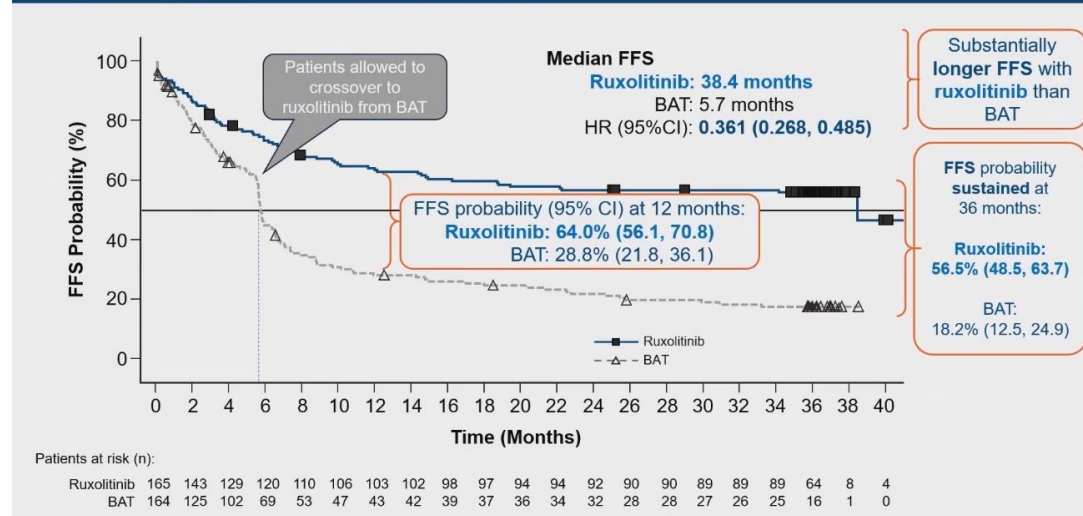
Trichrome positive area represents collagen deposition as a stigmata of chronic pulmonary GVHD (collaboration Dr. B Blazar, Minnesota)

Ruxolitinib in chronic GVHD - clinical data

Best Overall Response

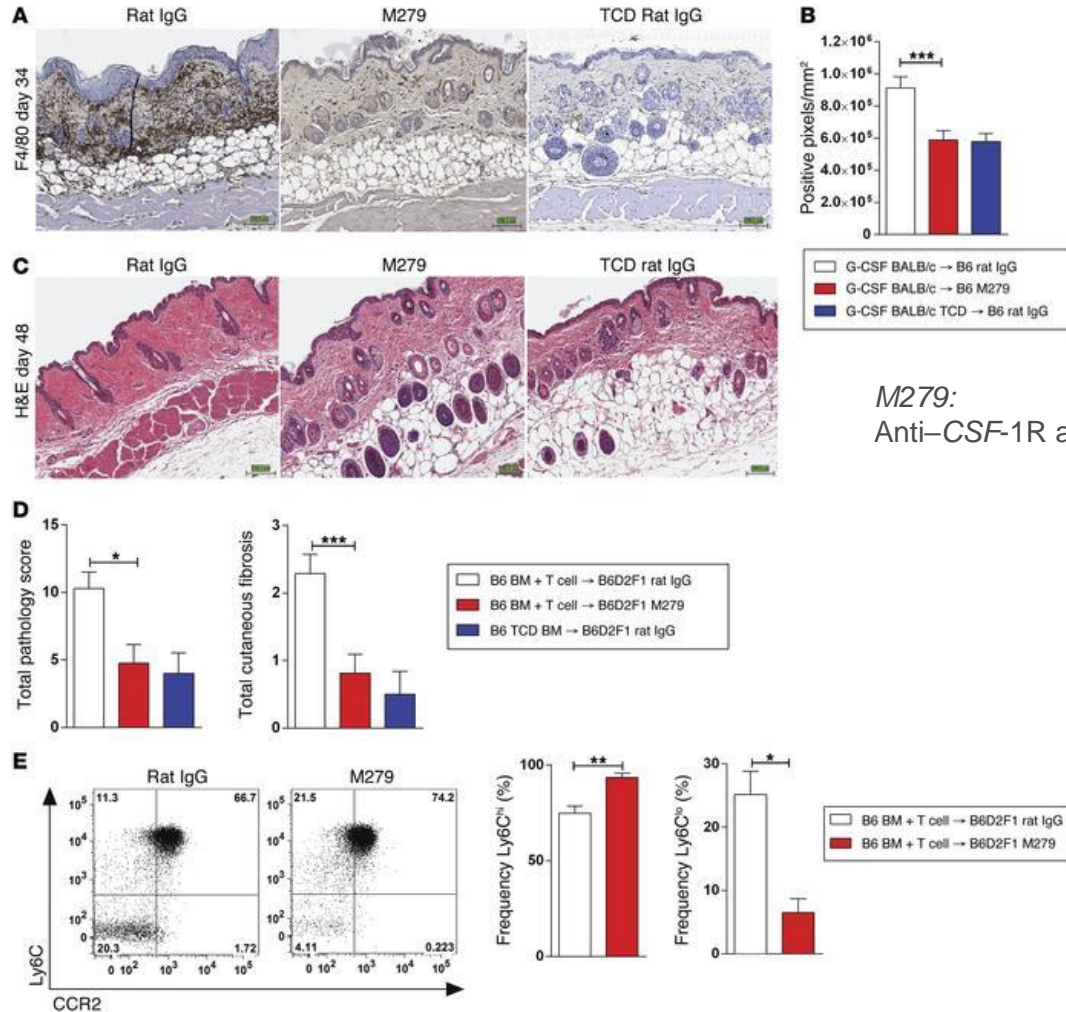


Failure free survival (full analysis set)



BAT, best available therapy; CR, complete response; OR, odds ratio; PR, partial response; RUX, ruxolitinib.
^a Among patients who achieved a CR or PR at any time up to week 24. Duration of response from first documented PR or CR.

CSF-1R inhibition in chronic GVHD - **preclinical data**



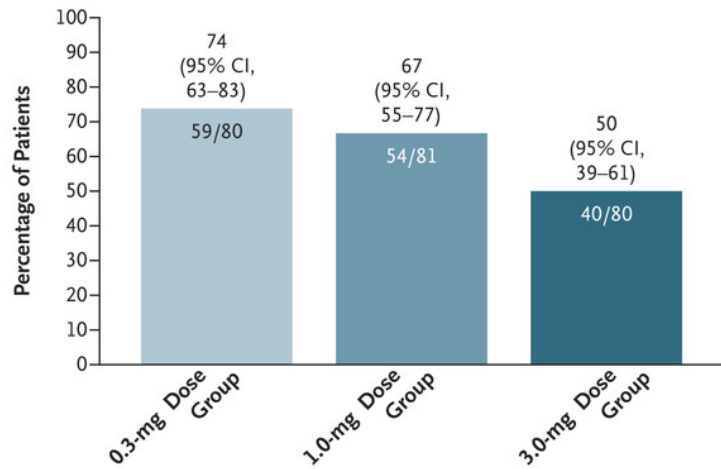
M279:
Anti-CSF-1R antibody

CSF-1-dependant donor-derived macrophages mediate chronic graft-versus-host disease

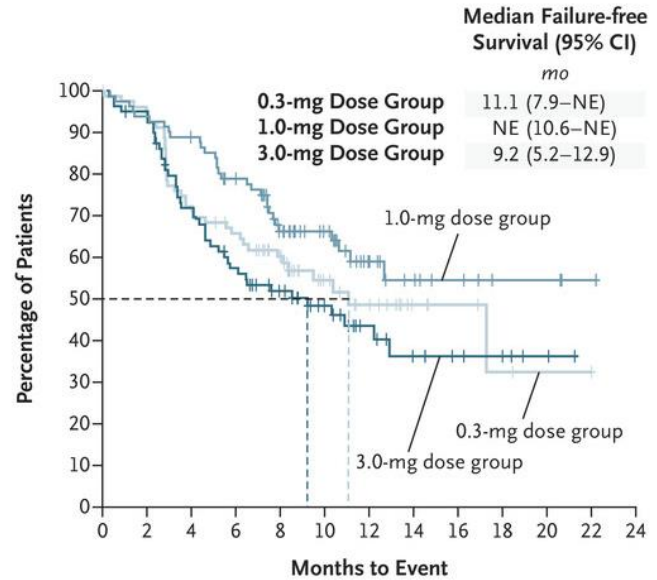
Alexander et al. J Clin Invest. 2014

CSF-1R inhibition in chronic GVHD - **clinical data**

A Overall Response in the First Six Cycles



B Failure-free Survival

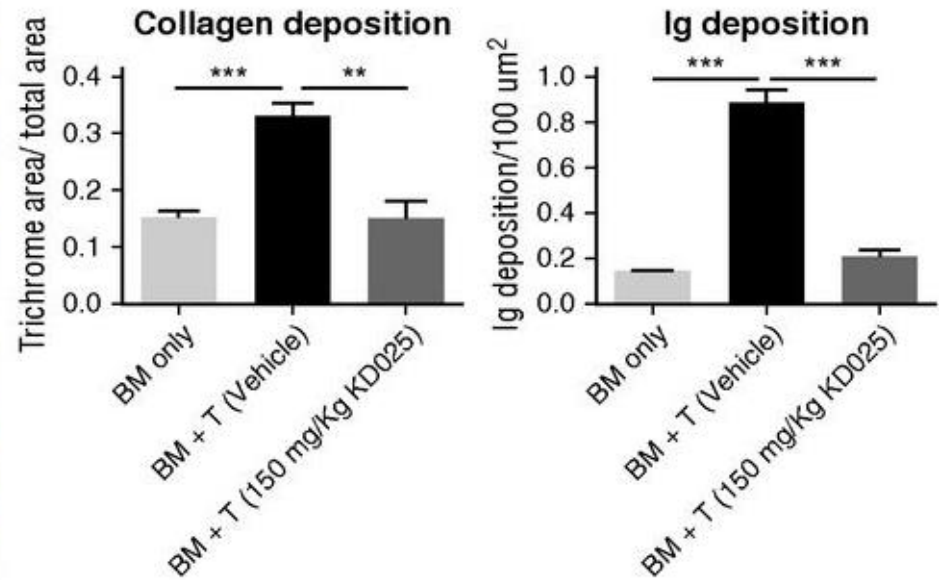
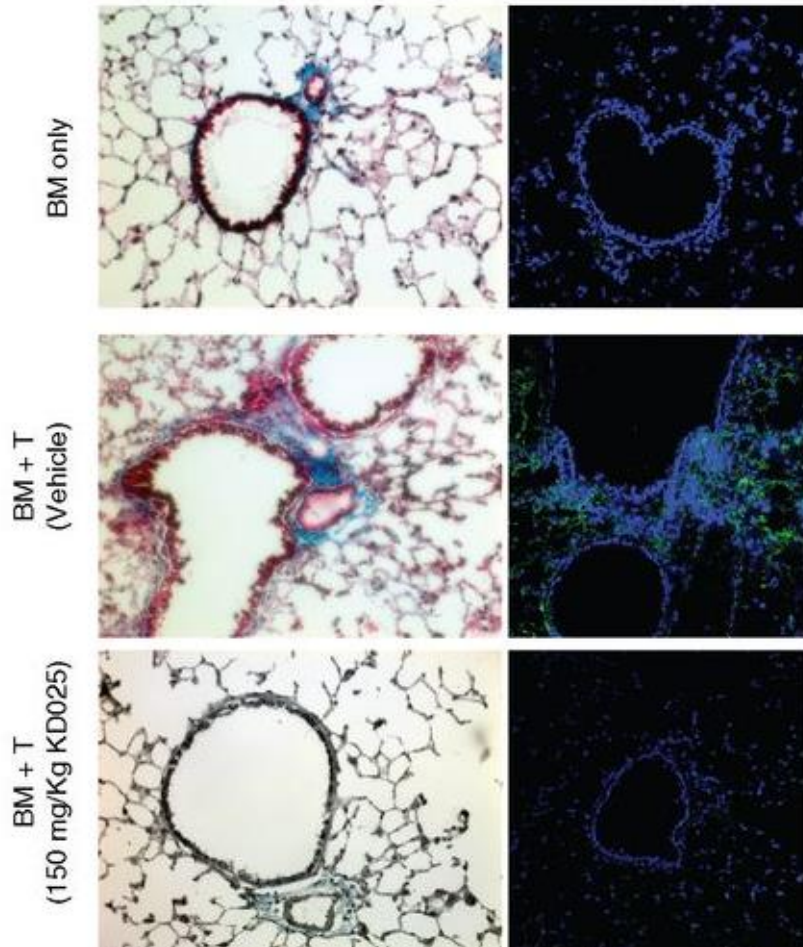


No. at Risk

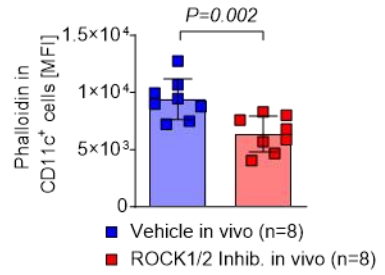
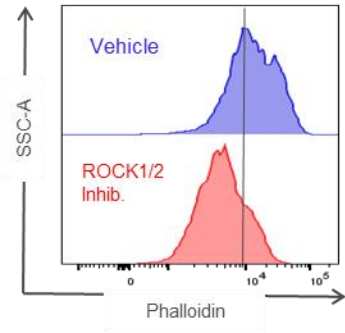
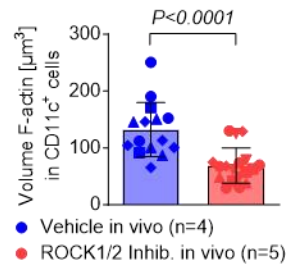
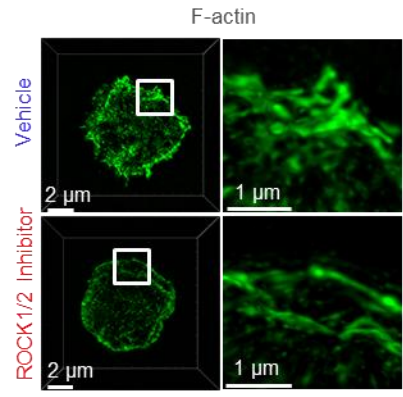
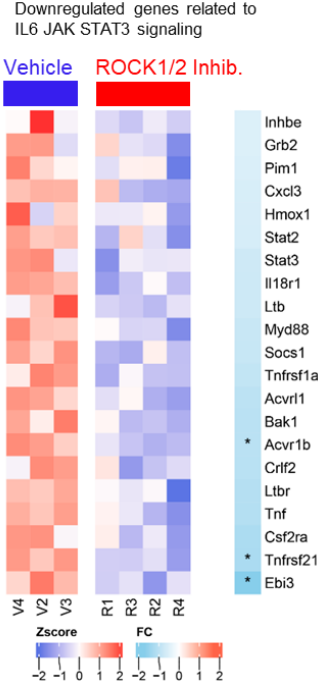
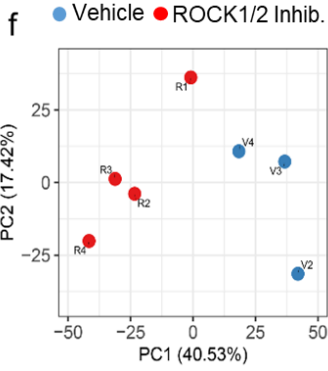
0.3-mg dose group	80	75	57	50	38	20	14	6	4	2	1	1	0
1.0-mg dose group	81	76	71	61	43	31	17	10	7	3	3	1	0
3.0-mg dose group	80	75	55	43	32	22	13	8	6	5	2	0	0

Wolff D et al. N Engl J Med. 2024 Sep 19;391(11):1002-1014

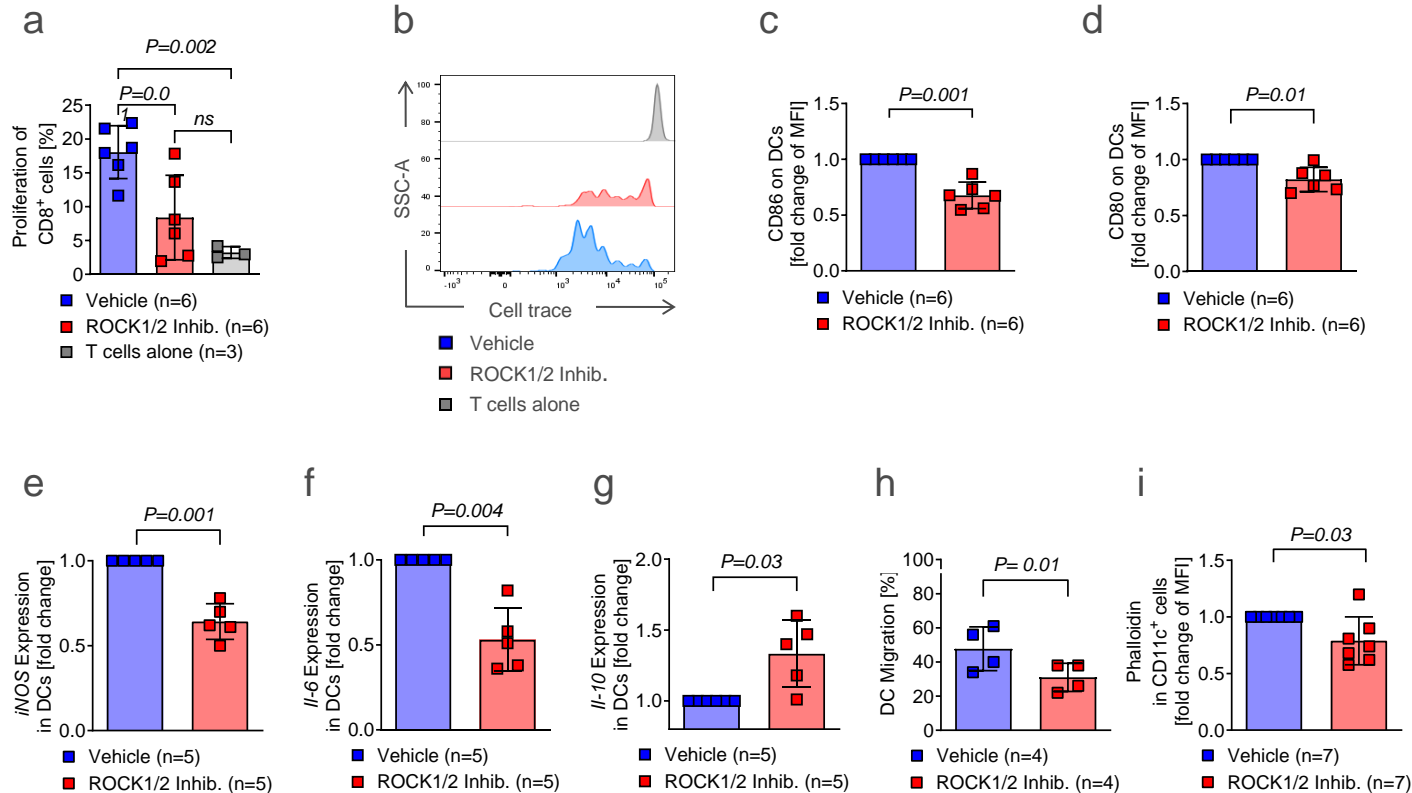
ROCK2 inhibition in chronic GVHD - **preclinical data**



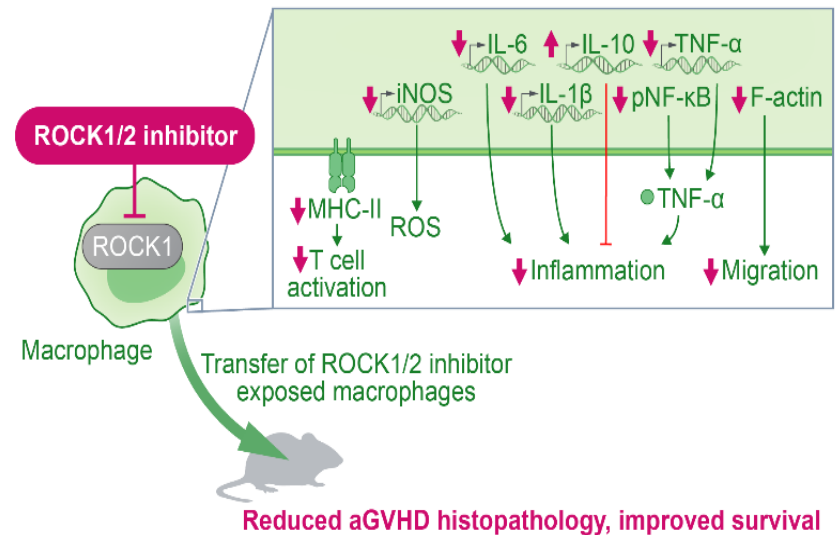
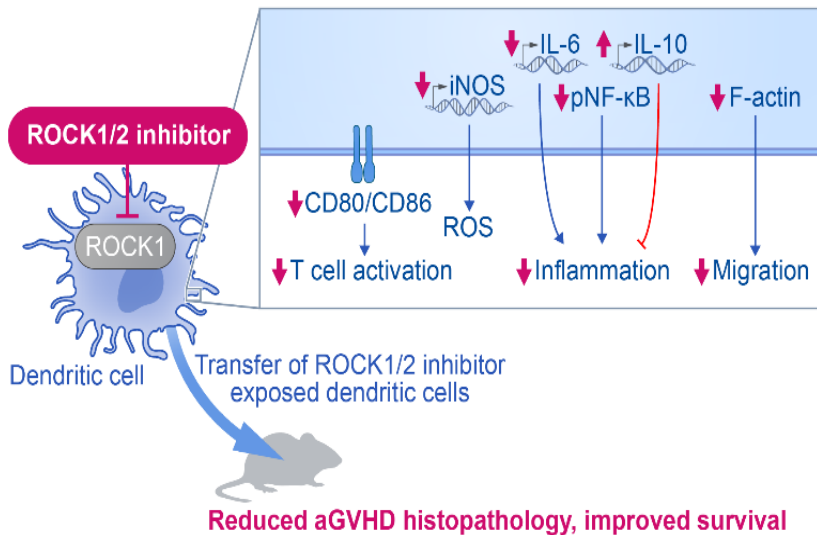
ROCK 1/2 inhibition – impact on myeloid cells - preclinical data



ROCK 1/2 inhibition – impact on T cells, costimulatory molecules and cytokine production - **preclinical data**

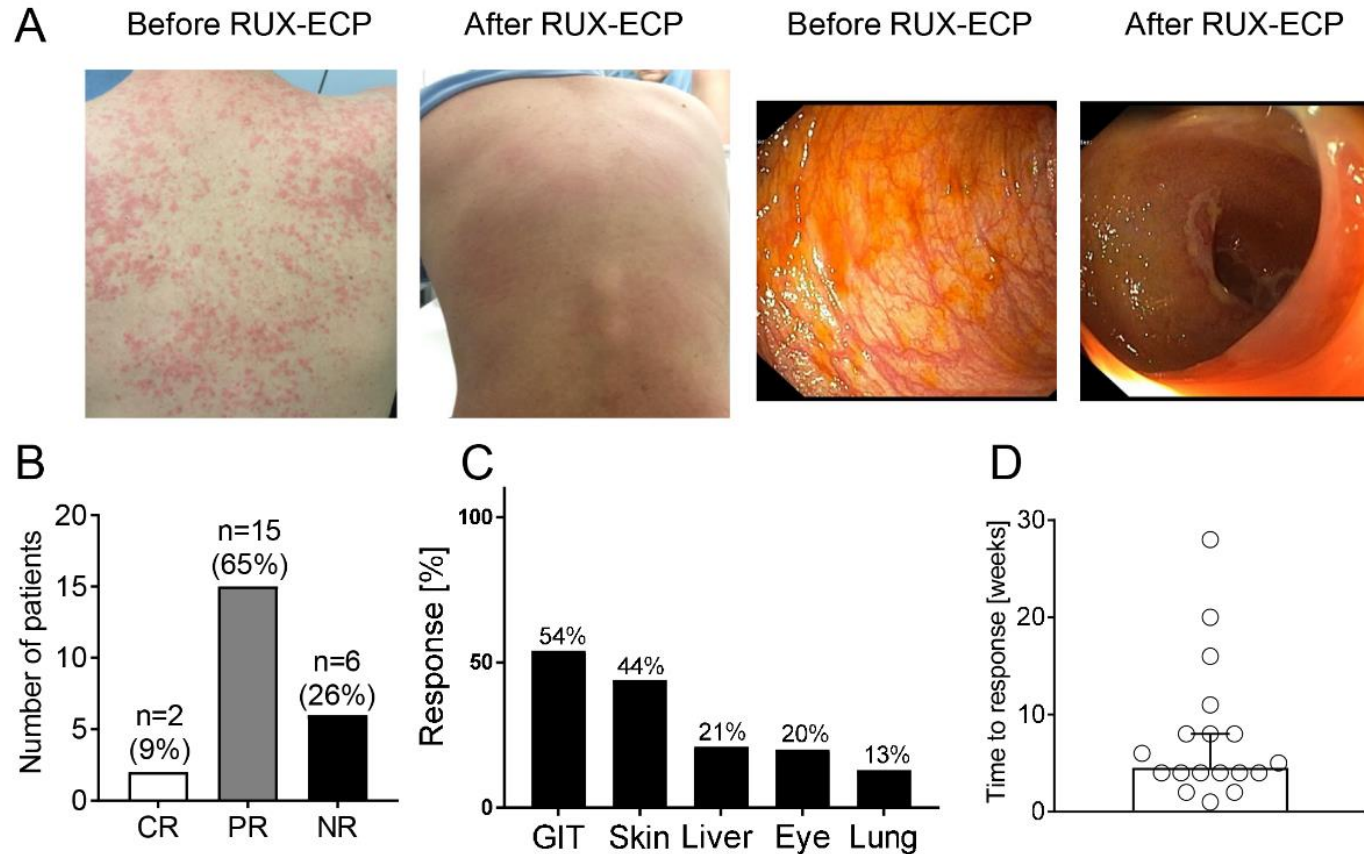


ROCK inhibition – impact on myeloid cells - **preclinical data**



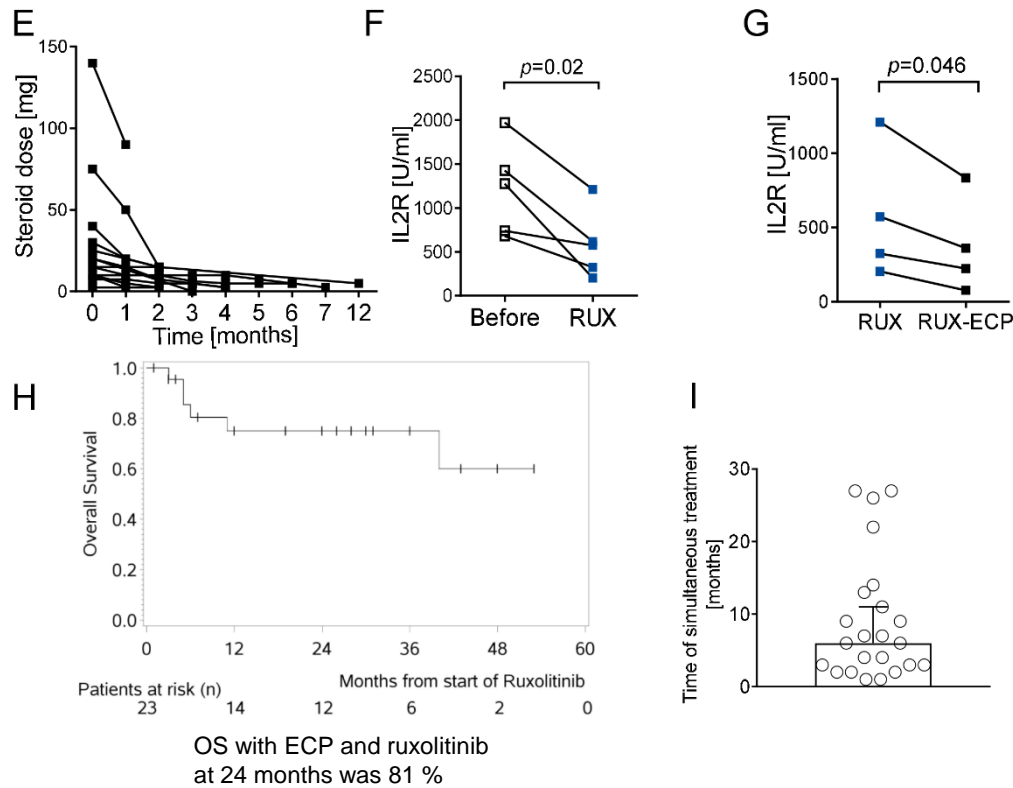
ECP plus Ruxo as combination
therapy

Rux-ECP for chronic GVHD refractory to RUX



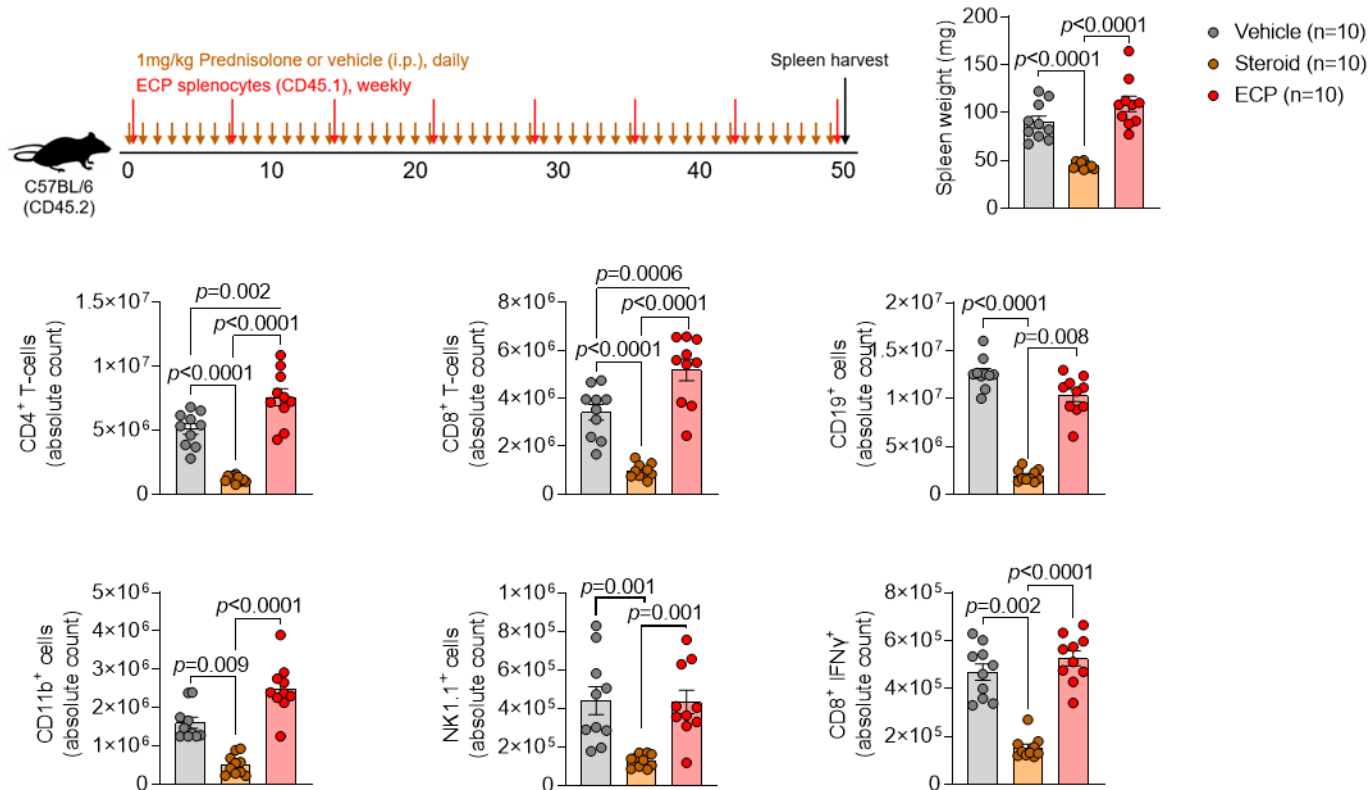
Maas-Bauer K, (...), Zeiser R. Ruxolitinib-ECP combination treatment for refractory severe chronic graft-versus-host disease. *Bone Marrow Transplant.* 2021;56(4):909-916.

Rux-ECP for chronic GVHD refractory to RUX



Maas-Bauer K, (...), Zeiser R. Ruxolitinib-ECP combination treatment for refractory severe chronic graft-versus-host disease. *Bone Marrow Transplant.* 2021;56(4):909-916.

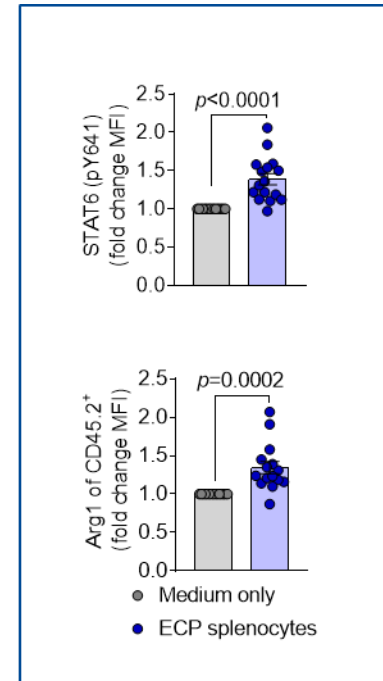
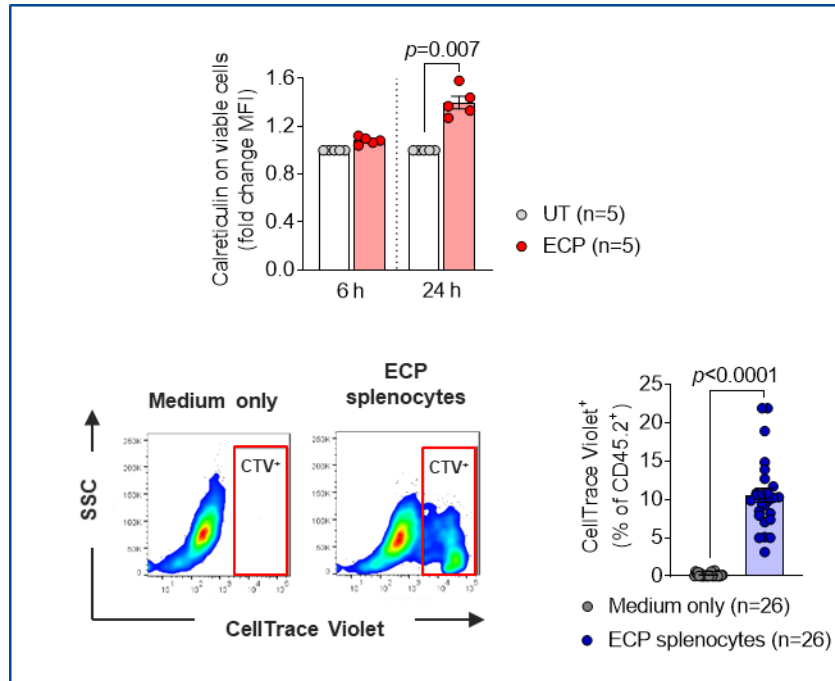
Long-term *in vivo* steroid treatment reduces lymphocytes and cytotoxic T-cells in the spleen



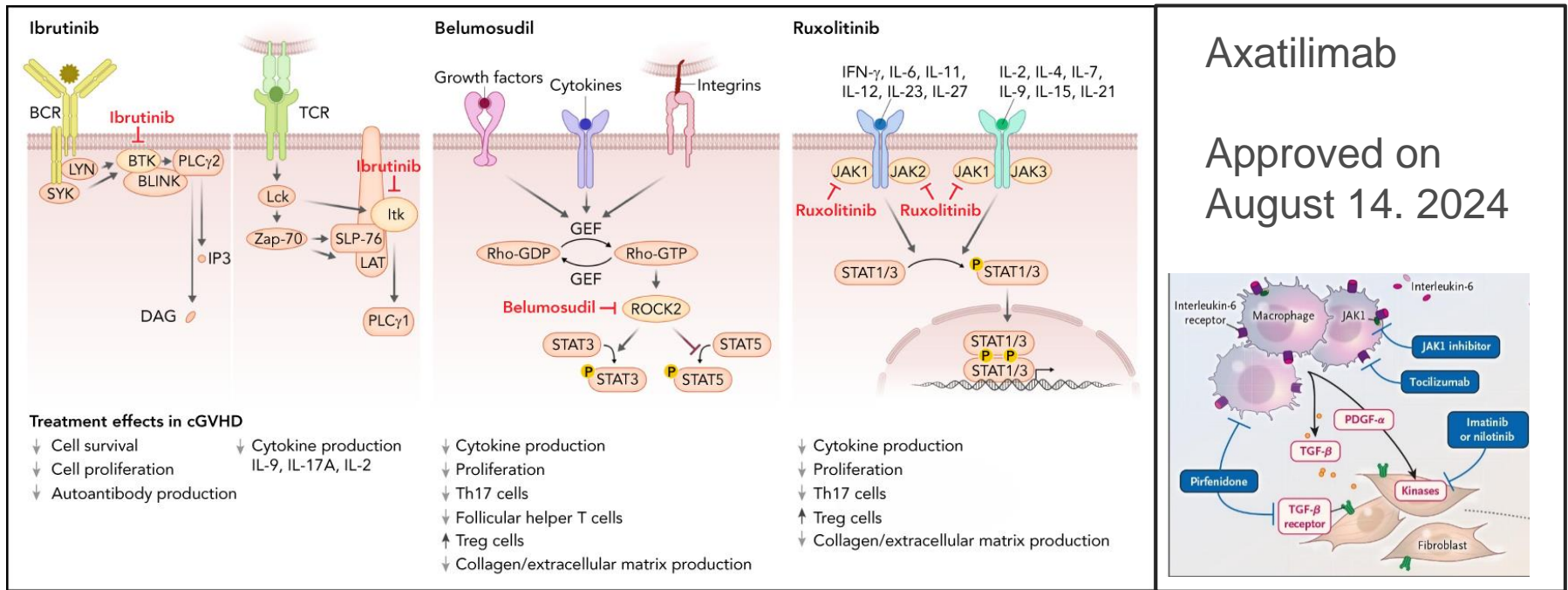
Unpublished data – please do not copy or post

How does ECP work?

Phagocytosis of ECP treated cells induces Adiponectin *in vitro*



Unpublished data – please do not copy or post



Robert Zeiser, Stephanie J. Lee,
 Three US Food and Drug Administration–approved
 therapies for chronic GVHD, Blood, 2022

Update in progress

Conclusion and Outlook

1. Ruxo, Belu, Axa and Inbrutinib are FDA approved for the treatment of SR-cGVHD in different lines.
2. The next steps are to understand what are rational combination therapies and which patients may benefit most from which treatment.

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