San Giuseppe Moscati - Avellino
Azienda Ospedaliera di Rilievo Nazionale e di Alta Specializzazione

Avellino, Hotel de la Ville
March 30-31, 2023

1ST SYMPOSIUM ON INNOVATIVE THERAPIES IN HEMATOLOGY

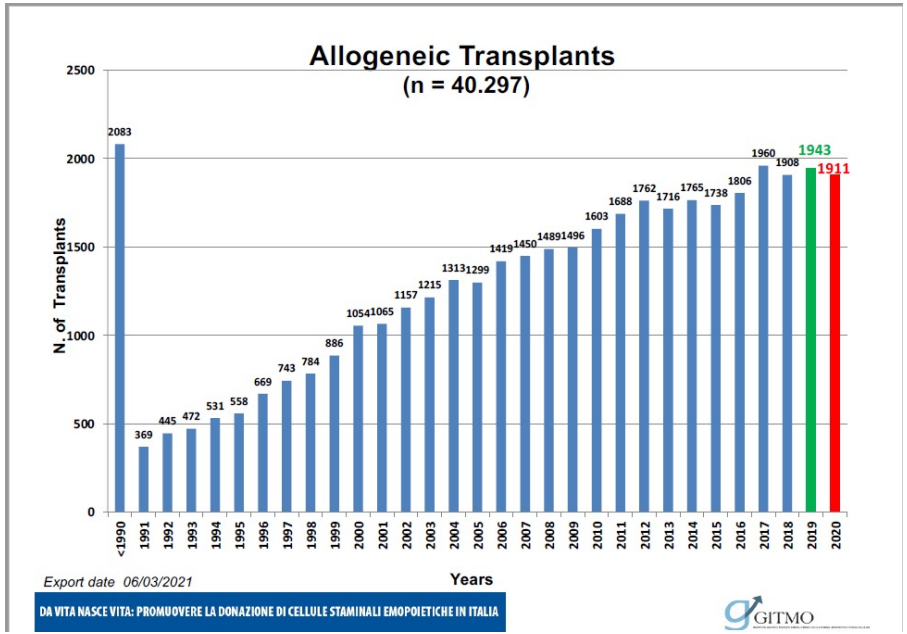
Ruxolitinib and other innovative treatments for GVHD

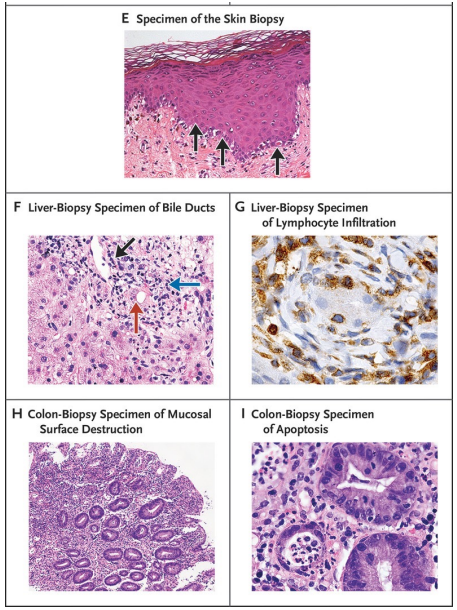
Maria Teresa Lupo-Stanghellini
Ospedale San Raffaele, IRCCS, Milano

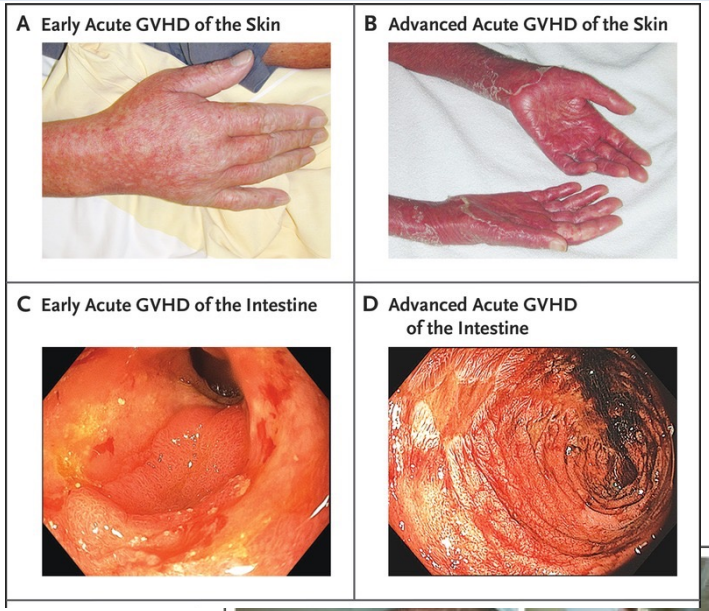
Disclosures of Maria Teresa Lupo-Stanghellini

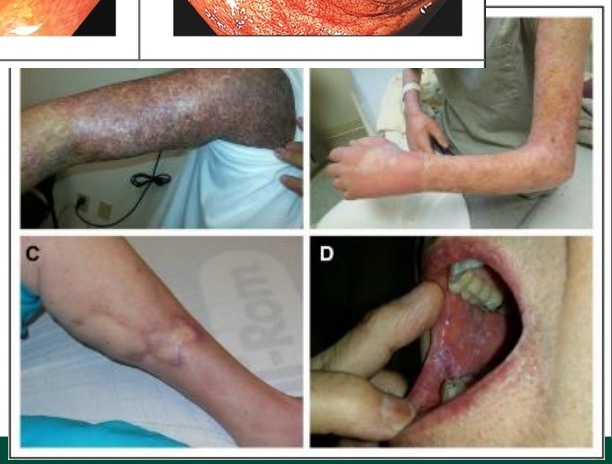
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Novartis						X	
Mallinckrodt						X	
Incyte							x
Neovii							x

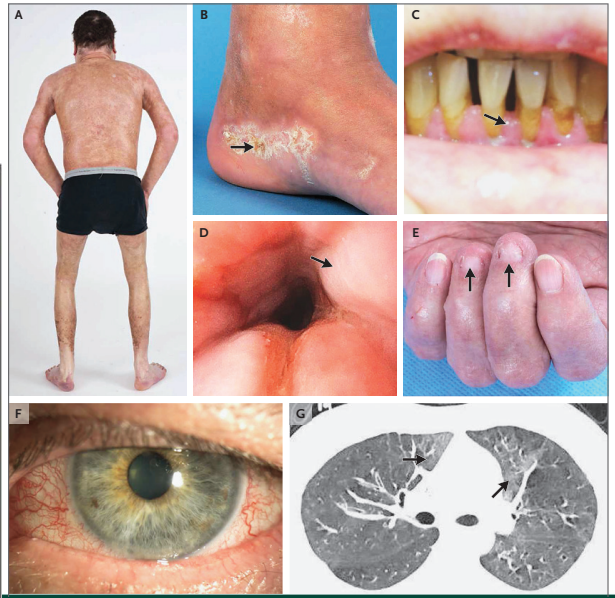
GITMO – Allo HSCT activity











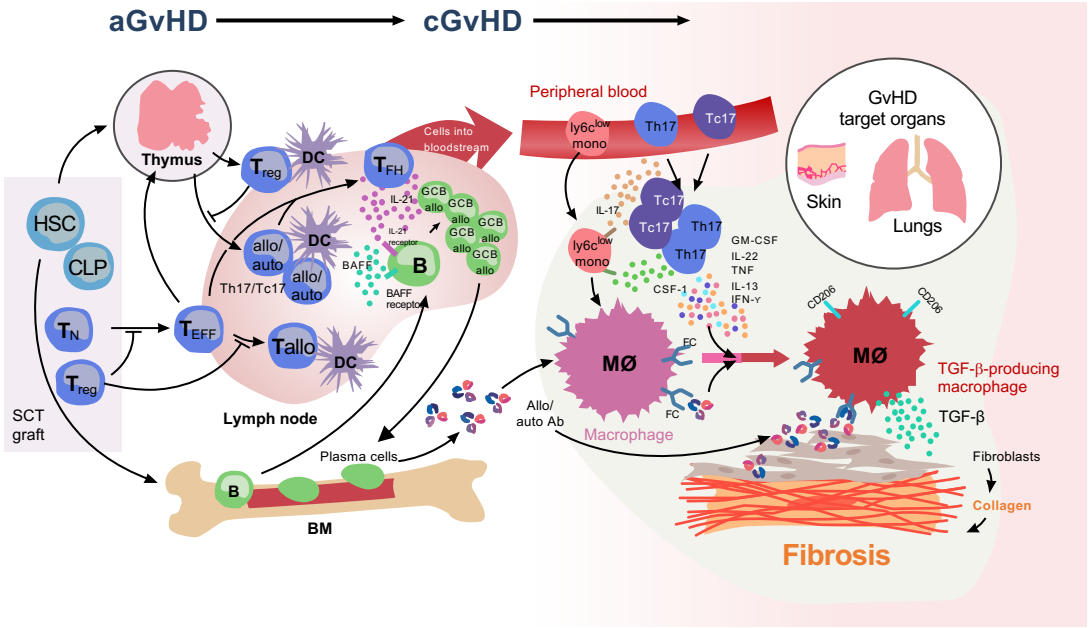
aGvHD

incidence 50%
G3-4 14%
mortality G3-4 36%
60% fail 1° line
5-30% LT-survival

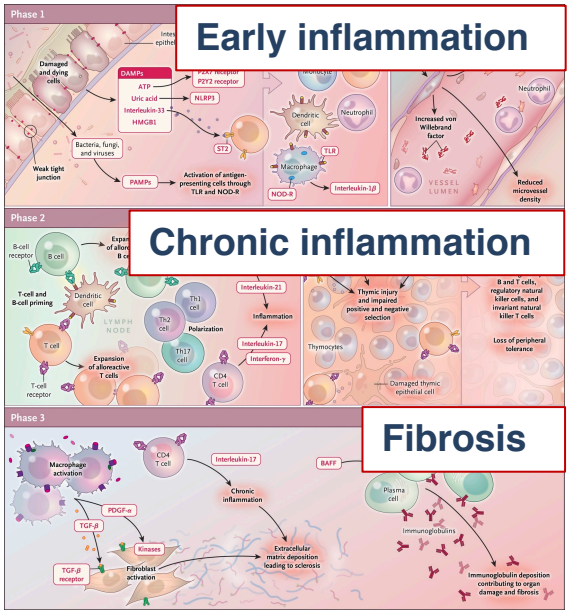
ChGvHD

1^ NRM among survivors >2y
↓ QoL e LT-outcome
↑Immune-disregulation

Cellular and molecular mediators contributing to the continuum of aGvHD and cGvHD pathology



Markey KA, et al. Blood. 2014;124:354-62.



Zeiser R, Blazar BR. N Engl J Med ;377:2565-2579

How we treat Acute GvHD

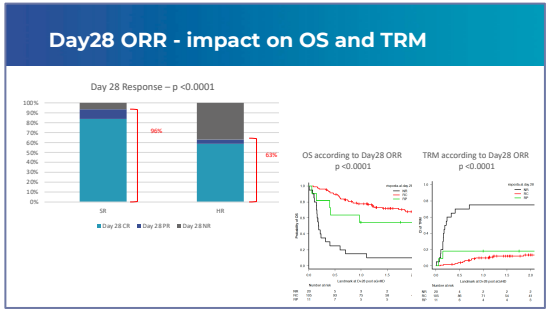
*EBMT recommendation **2020***

Clinical trials

Overall MAGIC	Topical Treatment	Systemic Treatment	When?
Grade I	**Yes**	**Not recommended**	The decision to initiate treatment for acute GVHD is based on clinical signs. Biopsies are recommended.
Grade II	**Yes**	**Yes***	
Grade III	**Yes**	**Yes***	
Grade IV	**Yes**	**Yes***	

*Systemic treatment - Methylprednisolone 2 mg/kg per day or equivalent prednisone
*Clinical trial

2^ Line and Beyond no drugs in label in Europe (FDA 2019 Ruxolitinib)
ECP – Ruxolitinib – Infliximab – MMF etc
Clinical Trial



Ardizoia F, Lorentino F, […] Lupo-Stanghellini MT, Haematologica 2022

How we treat Chronic GvHD

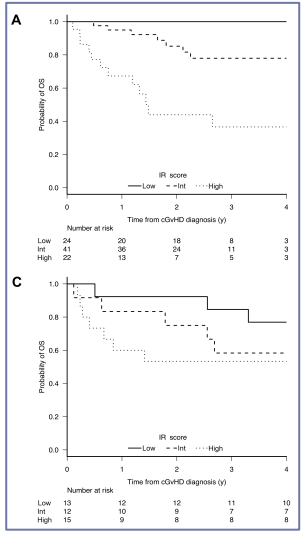
*EBMT recommendation **2020***

Clinical trials

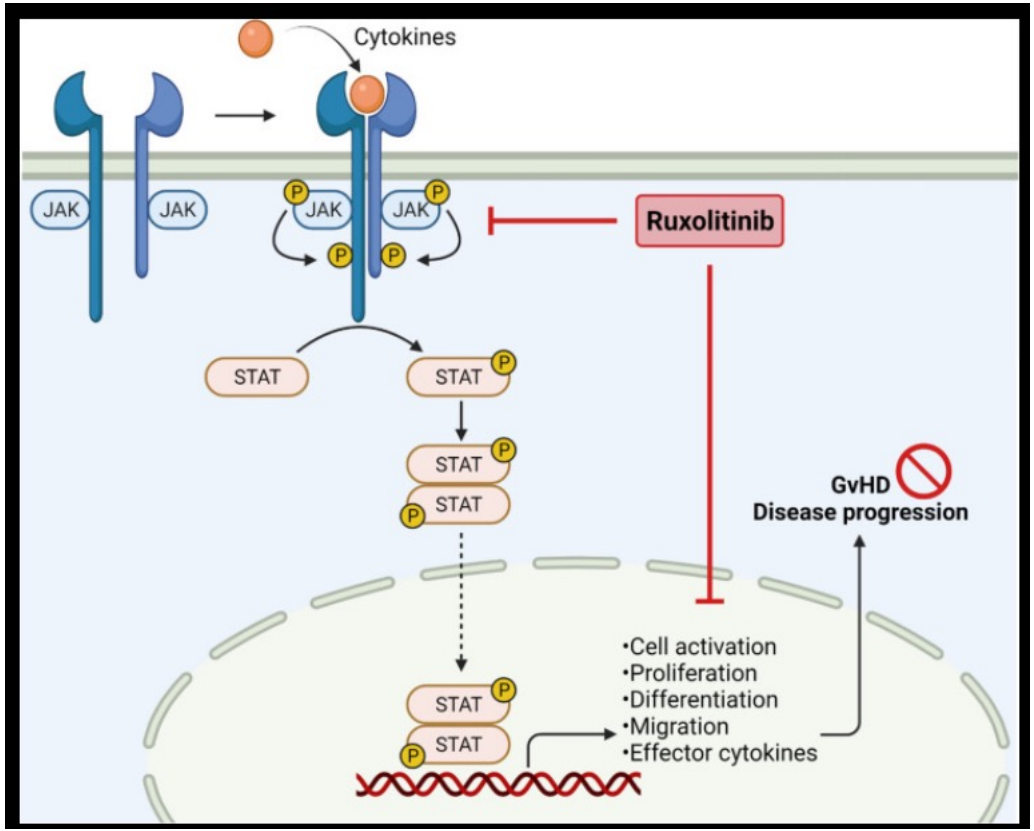
Overall NIH	Topical Treatment	Systemic Treatment	When?
Mild	**Yes**	**Not recommended**	According to symptom type, severity (moderate / severe), dynamics of progression. Other relevant variables: disease risk, chimerism, minimal residual disease.
Moderate	**Yes**	**Yes***	
Severe	**Yes**	**Yes***	

*Systemic treatment - Prednisone 1 mg/kg per day
*Clinical trial

2^ Line and Beyond no drugs in label in Europe
(FDA approved Ruxolitinib – Ibrutinib - Belumosudil)
ECP – Ruxolitinib – Infliximab – MMF – TKi – Ibrutinib - etc
Clinical Trial



Serpenti F [...] Lupo-Stanghellini MT, Frontiers in Onc, 2021



Braun & Zeiser. Front in Immun 2021

Ruxolitinib

Key players in mediating pro-inflammatory signalling

Changing Paradigm - 1

Ruxolitinib (2015&beyond)

Acute GvHD

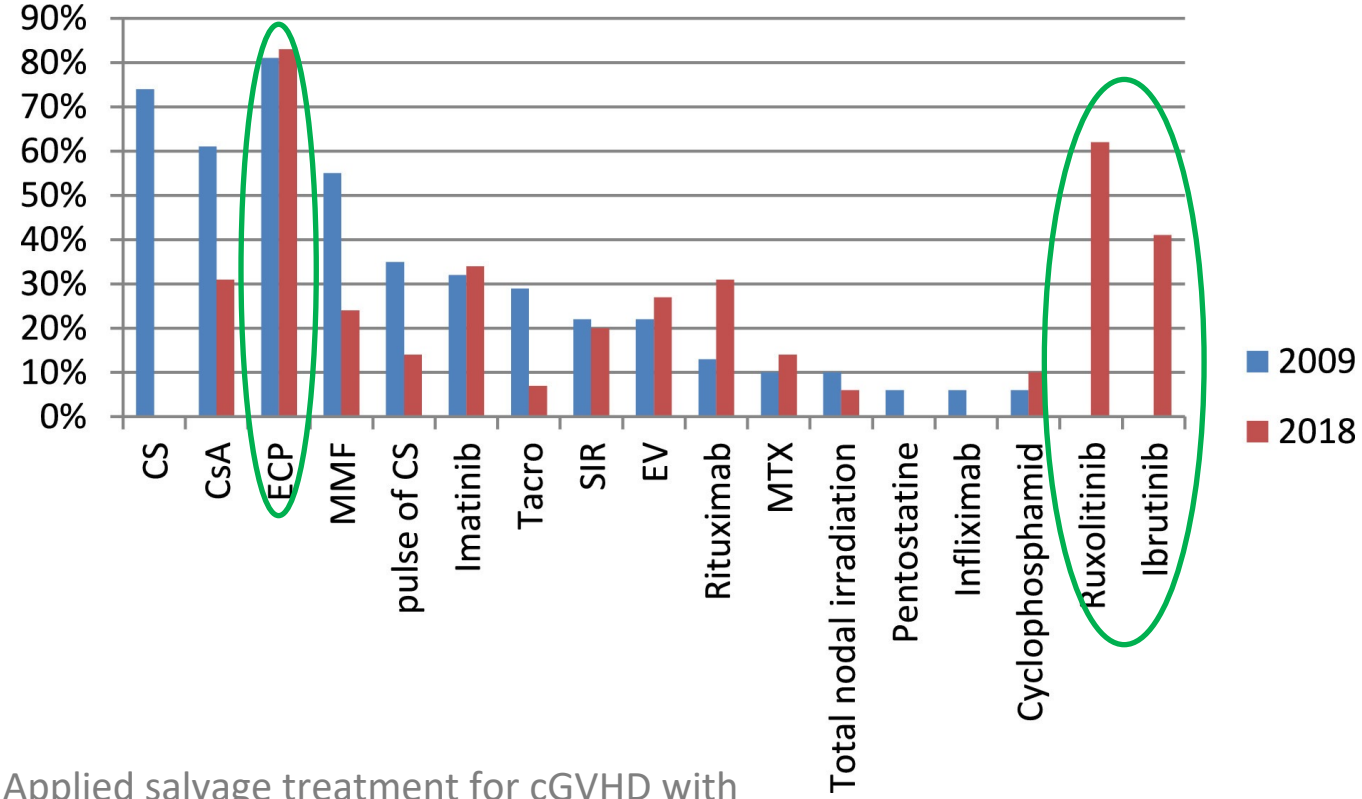
1Ph 2 & 1Ph 3	2 prospective trials	4 retrospective trials
225 pts	72 pts	126 pts
Day 28 ORR 62%	Worst outcome in liver	CMV reactivation

Chronic GvHD

1 Ph 3	1 prospective trial	9 retrospective trials
165 pts	43 pts	373 pts
Skin-Mouth-Upper/Lower GI ORR>40%	No change eyes, lung, joint, genitalia	Good mouth response, worst lung

Greinix HT, Ayuk F, Zeiser R. Leukemia. 2022.

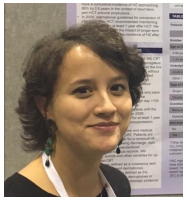
Changing Paradigm - 2



Applied salvage treatment for cGVHD with cutaneous deep sclerosis.

Wolff et al, BBMT 2019

Ruxolitinib – great expectations



Elisabetta Xue

Francesca Lorentino

Ruxolitinib for chronic steroid-refractory graft versus host disease: a single center experience

Elisabetta Xue [a], Francesca Lorentino [a,b], Francesca Pavesi [a], Andrea Assanelli [a], Jacopo Peccatori [a], Massimo Bernardi [a], Consuelo Corti [a], Fabio Ciceri [a], Maria Teresa Lupo Stanghellini [a,*]

Table 2
Overall response rate on evaluable patients from Ruxolitinib start.

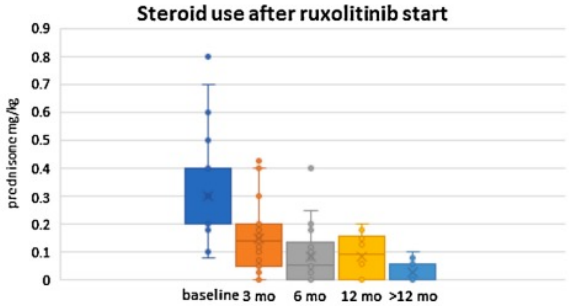
	At 3 months	At 6 months	Long term response
CR or PR	20 (59 %)	16 (62 %)	15 (75 %)
SD or PD	14 (41 %)	10 (38 %)	5 (25 %)
Not evaluable	2	10	16

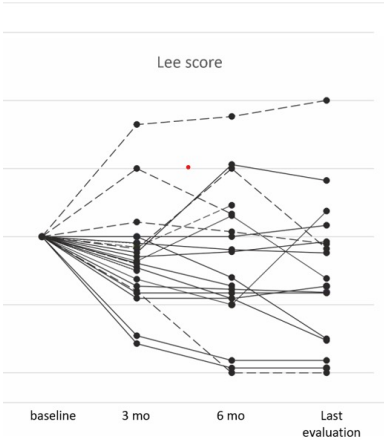
Abbreviation: CR, complete response, PR, partial response; SD, stable disease; PD, progression disease.

Table 3
Differentiated response according to Wilcoxon signed ranks test.

	Baseline ⟶ 3 months	Baseline ⟶6 months
Performance Status[¶]	0145	0058
Skin	0005	003
Eyes	0083	0046
Mouth	0002	0009
Joint-Fascia	0564	1
Lung	0317	0317
Genital Tract[*]	0046	0705
Gastro-intestinal	0317	0157
Liver	NE	NE

[¶] Performance status was calculated through Eastern Cooperative Oncology Group score.
[*] Responses were seen both among female and male patients.





Xue E., Lorentino F, et al, Leukemia Res 2021

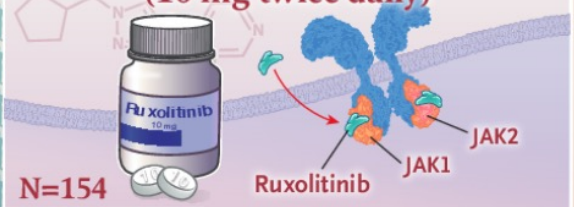
The NEW ENGLAND JOURNAL of MEDICINE

Ruxolitinib for Glucocorticoid-Refractory Acute GVHD

PHASE 3, MULTICENTER, RANDOMIZED, OPEN-LABEL TRIAL

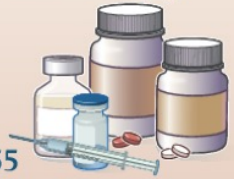
309 Patients with grade II–IV glucocorticoid-refractory acute graft-versus-host disease

Ruxolitinib (JAK inhibitor) (10 mg twice daily)



N=154

Best Available Therapy



N=155

	Ruxolitinib	Best Available Therapy
Partial or complete response at day 28	62%	39%
	Odds ratio, 2.64; P<0.001	
Treatment-associated adverse reaction	Thrombocytopenia 33%	Thrombocytopenia 18%

Ruxolitinib significantly improved efficacy outcomes as compared with best available therapy

R. Zeiser et al. 10.1056/NEJMoa1917635

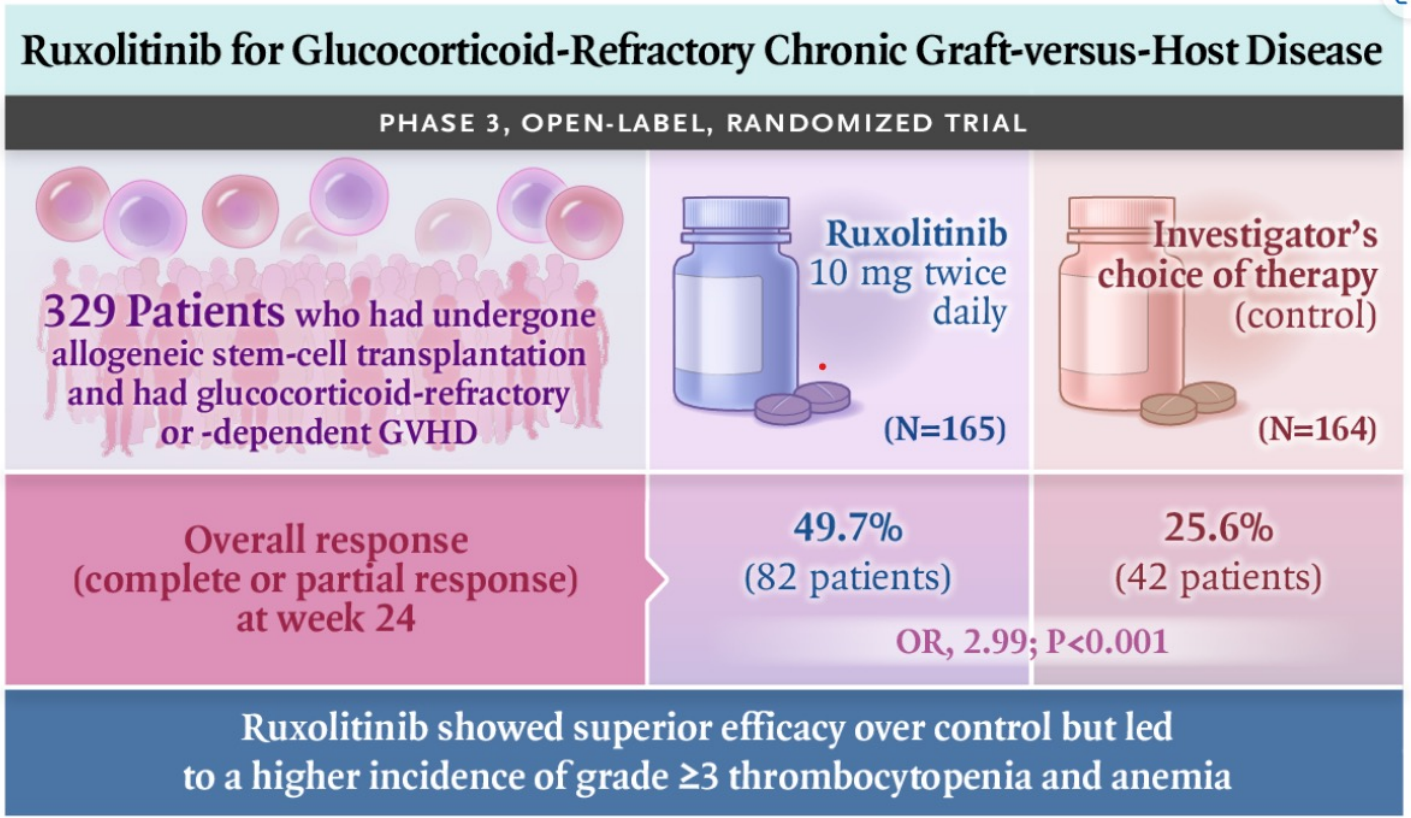
Ruxolitinib
acute GvHD phase 3

Table 1. Criteria for corticosteroid-refractory and ruxolitinib-refractory acute GVHD

Criteria
Corticosteroid-refractory acute GVHD (1) Disease progression after 3 days of treatment with MP 2 mg/kg per day equivalent, (2) Lack of improvement after 7 d of treatment with MP 2 mg/kg per day equivalent, (3) Progression to a new organ after treatment with MP 1 mg/kg per day equivalent for skin and upper gastrointestinal GVHD, or (4) Recurrence during or after a corticosteroid taper.
Ruxolitinib-refractory acute GVHD (1) Progression of GVHD compared with baseline after ≥5 to 10 days of treatment with ruxolitinib, based either on objective increase in stage/grade or new organ involvement; (2) Lack of improvement in GVHD (PR or better) compared with baseline after at least 14 days of treatment with ruxolitinib; or (3) Loss of response, defined as objective worsening of GVHD determined by increase in stage, grade or new organ involvement at any time after initial improvement.

Mohty et al, Blood 2020

The NEW ENGLAND JOURNAL of MEDICINE

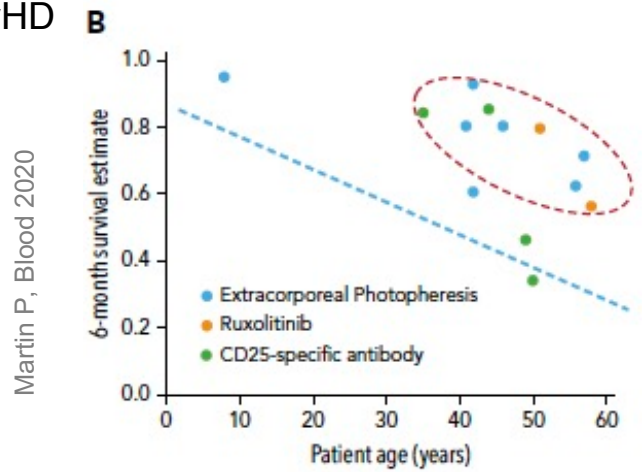


R. Zeiser et al. 10.1056/NEJMoa2033122

Ruxolitinib
chronic GvHD phase 3

Ruxolitinib is approved by FDA / EMA / AIFA for both a/c GvHD
Meta-analysis **Ruxo and ECP** are **superior to other 2^ line in SR-aGvHD**.
Preference for ECP in case of infection or severe cytopenia.

☹ Durable overall response in aGvHD 40%
☹ Unsatisfactory ORR in eyes – liver – lung ch GvHD



Martin P, Blood 2020

Changing Paradigm.3

GITMO / SIDEM BestPractice ECP 2022

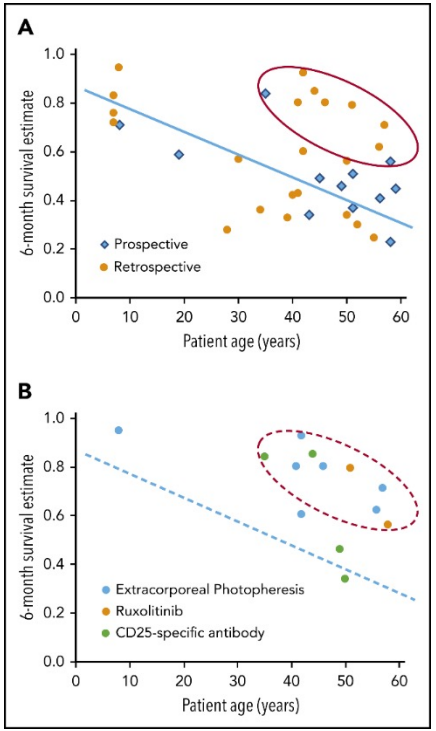
GITMO GvHD guideline → ongoing

PTCy
ECP
Ruxo
Anti-TNF
MMF

EBMT 2020 Recommendation → up-date

ECP vs Ruxolitinib

	ECP pros	ECP cons	Ruxo pros	Ruxo cons
Citopenia		X		X
Infezioni	X			X
Assenza accessi venosi periferici		X	X	
Drug Drug Interactions	X			X
Disponibilità sul territorio		X*	X*	
Acute vs Chronic	X		X	

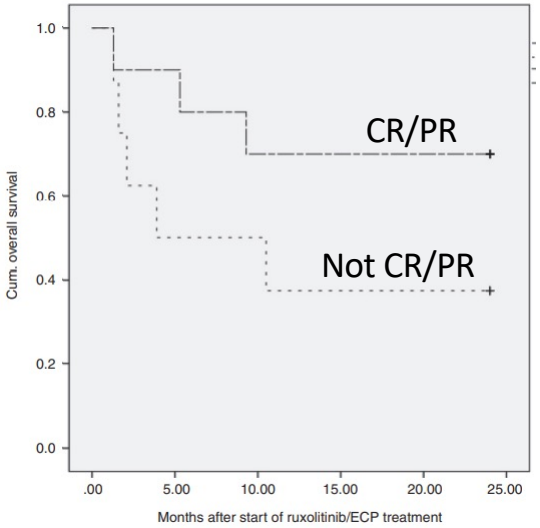


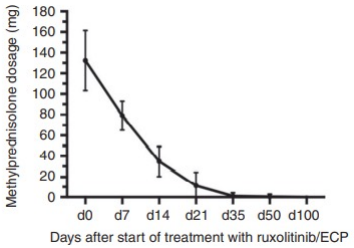
Paul J. Martin, How I treat SR aGvHD, Blood, 2020

ECP + Ruxolitinib in aGvHD

Ruxolitinib plus extracorporeal photopheresis (ECP) for steroid refractory acute graft-versus-host disease of lower GI-tract after allogeneic stem cell transplantation leads to increased regulatory T cell level

Franziska Modemann[1,2] · Francis Ayuk[1] · Christine Wolschke[1] · Maximilian Christopeit[1] · Dietlinde Janson[1] · Ute-Marie von Pein[1] · Nicolaus Kröger[1]





Single center
18 pts w steroid-refractory lower GI acute GvHD

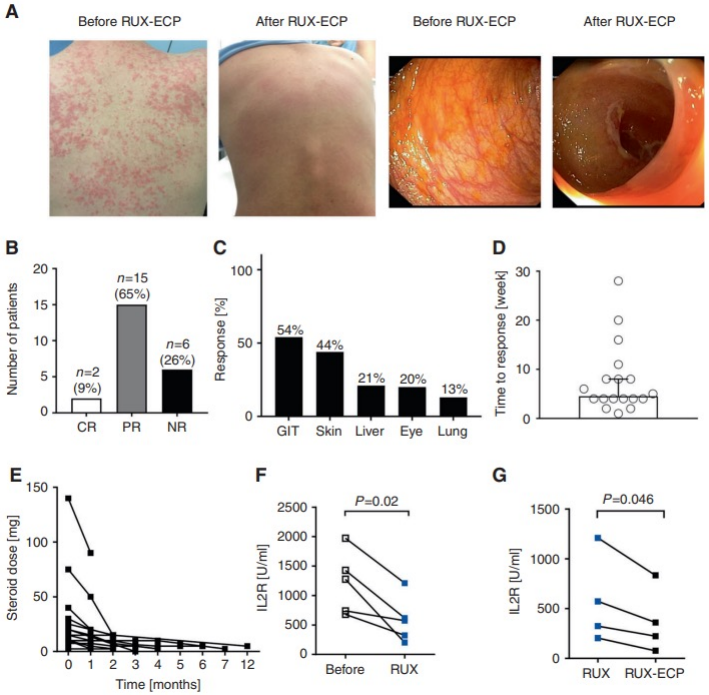
15/18 Ruxo -> Ruxo + ECP
17/18 Ruxo + ECP + 6MP+/-CsA + MMF

CR 44% - PR 11%

Table 2 Response and side effects.

Patient	Response to treatment	Leukopenia	Anemia	Thrombopenia	Other side effects	CMV reactivation
1	CR	None	None	None	None	No
2	No response	None	CTC I	None	Fever CTC I	Yes
3	PR	CTC II	None	None	Fever CTC II	Yes
4	No response	None	None	None	None	No
5	PR	CTC I	CTC I	CTC I	Elevated CRP-level CTC II	Yes
6	CR	CTC II	None	None	None	Yes
7	No response	None	None	None	Elevated CRP-level CTC II	Yes
8	No response	CTC III	None	None	Fever CTC I elevated CRP-level CTC II	No
9	CR	CTC II	None	CTC III	Elevated CRP-level CTC II	Yes
10	No response	None	None	CTC II	Elevated CRP-level CTC I	Yes
11	CR	None	None	None	Fever CTC I elevated CRP-level CTC III	Yes
12	CR	CTC I	CTC I	None	None	Yes
13	No response	None	None	None	Fever CTC II elevated CRP-level CTC III sepsis	Yes
14	CR	CTC II	None	None	Fever CTC I	Yes
15	No response	CTC I	CTC I	None	Fever CTC II elevated CRP-level CTC I	No
16	No response	None	CTC II	CTC III	None	No
17	CR	CTC I	None	CTC II	None	No
18	CR	None	None	CTC I	Fever elevated CRP-level	Yes

ECP + Ruxolitinib in chGvHD



Ruxolitinib–ECP combination treatment for refractory severe chronic graft-versus-host disease

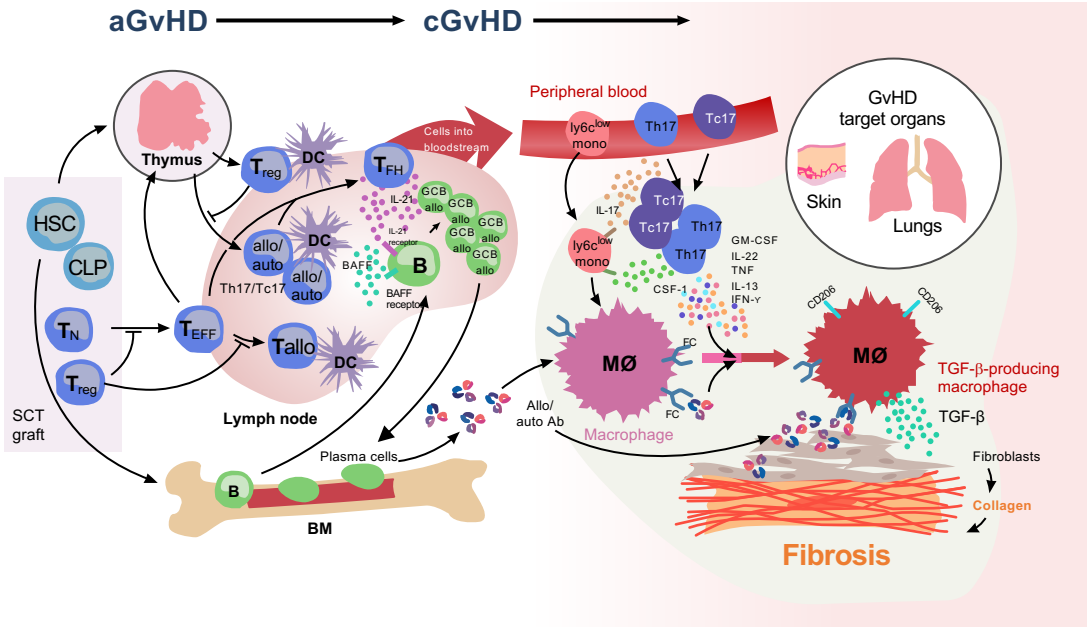
Kristina Maas-Bauer[1] · Chrissoula Kiote-Schmidt[1] · Hartmut Bertz[1] · Petya Apostolova[1] · Ralph Wäsch[1] · Gabriele Ihorst[2] · Jürgen Finke[1] · Robert Zeiser[1]

Single center
23 pts w steroid-refractory ch GvHD

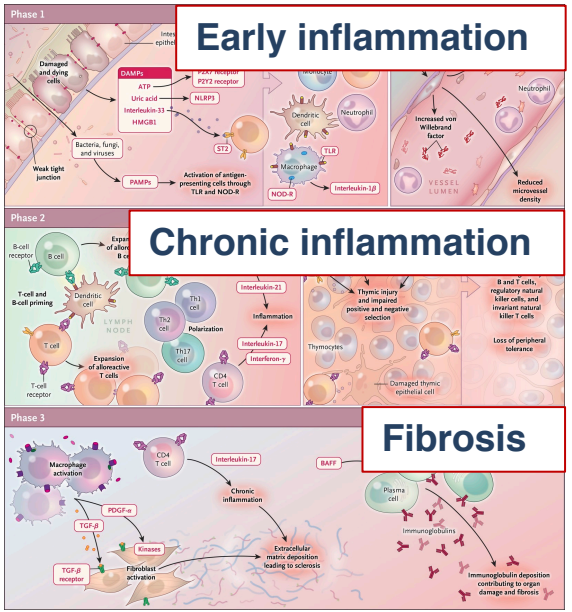
Best response rate (CR or PR) at any time point
74% (17/23) - 9% (2/23) CR and 65% (15/23) PR.
The 24-months-survival was 75% (CI 56.0–94.1).

Newly diagnosed cytopenia 22% (5/23)
CMV reactivation 26% (6/23)

Cellular and molecular mediators contributing to the continuum of aGvHD and cGvHD pathology



Markey KA, et al. Blood. 2014;124:354-62.



Zeiser R, Blazar BR. N Engl J Med ;377:2565-2579

Bone Marrow Transplantation
https://doi.org/10.1038/s41409-020-01188-4

ARTICLE

Randomized phase II trial of extracorporeal phototherapy and steroids vs. steroids alone for newly diagnosed acute GVHD

Rohtesh S. Mehta[1] · Roland Bassett[2] · Gabriela Rondon[1] · Bethany J. Overman[1] · Uday R. Popat[1] · Chitra M. Hosing[1] · Katy Rezvani[1] · Muzaffar H. Qazilbash[1] · Paolo Anderlini[1] · Roy B. Jones[1] · Partow Kebriaei[1] · David Marin[1] · Issa F. Khouri[1] · Betul Oran[1] · Stefan O. Ciurea[1] · Kayo Kondo[1] · Daniel R. Couriel[3] · Elizabeth J. Shpall[1] · Richard E. Champlin[1] · Amin M. Alousi[1]

Single center - open label – adaptively randomized
Bayesian design

- *20 pts randomized fairly*
- *Subsequent assignment to be harmonized to an arm based on probability of success in each arm*

New onset
Biopsy proven
1st line

Treatment success on day 56 (primary endpoint):

- Be alive
- Be in remission from malignancy
- Achieved aGvHD response w/o need for additional therapy
- Be on < 1mg/Kg PDN on day 28 and <0,5 mg/Kg PDN on day 56

Changing Paradigm.4

One size does not fit all – smth old

Table 2 Primary outcome: day 56 treatment success[a].

Treatment Arm	Risk group	Success	Failure	Total
Steroids alone	All patients	16 (53%)	14 (47%)	30
	Visceral	3 (43%)	4 (57%)	7
	Skin only	13 (57%)	10 (43%)	23
ECP + steroids	All patients	33 (65%)	18 (35%)	51
	Visceral	7 (47%)	8 (53%)	15
	Skin only	26 (72%)	10 (28%)	36

[a]Defined as being alive, in a remission, achieving a GVHD response (CR or PR) without additional therapy and on a prednisone (MP equivalent) dose of <1 mg/kg/day on day 28 and <0.5 mg/kg/day by day 56. The probability the ECP + steroids arm has a higher success rate compared to steroids alone for day 56 treatment success was 81.5%.

Caveat
study not powered for subgroup analyses

ECP arm higher probability of success (0.815) – response rate 65% vs 53%.

Potentially more beneficial than steroid alone in skin-only GvHD (response rate 72% vs 57%) than for visceral organ aGvHD (47% vs 43%).

Patients with treatment success (regardless of arm assignment) **had a markedly lower risk for NRM when compared to those with treatment failure** (HR 0.32 – p 0,003)

Changing Paradigm.5

One size does not fit all – smth new

*Since **Ruxolitinib** can lead to cytopenias due to co-inhibition of JAK2, specific JAK1 inhibitors – **Itacitinib** - were developed to reduce cytokine signaling w/o side effects*

Efficacy and safety of itacitinib versus placebo in combination with corticosteroids for initial treatment of acute graft-versus-host disease (GRAVITAS-301): a randomised, multicentre, double-blind, phase 3 trial

Robert Zeiser, Gérard Socié, Mark A Schroeder, Sunil Abhyankar, Carlos Pinho Vaz, Mi Kwon, Johannes Clausen, Leonid Volodin, Sebastian Giebel, Manuel Jurado Chacon, Gabrielle Meyers, Monalisa Ghosh, Dries Deeren, Jaime Sanz, Rodica Morariu-Zamfir, Michael Arbushites, Mani Lakshminarayanan, April M Barbour, Yi-Bin Chen

Highly selective JAK1 inhib (Itacitinib) + steroid
vs
steroid + placebo

Day 28 ORR 74% (CR 53%) vs 66% (CR 40%) p 0.078

Improvement did not reach the prespecified significance level

Zeiser et al, Lancet Hematol 2022

blood

American Society of Hematology
2021 L Street NW, Suite 900,
Washington, DC 20036
Phone: 202-776-0544 | Fax 202-776-0545
editorial@hematology.org

Effective treatment of low risk acute GVHD with itacitinib monotherapy

Tracking no: BLD-2022-017442R1

Itacitinib vs steroid
In Low Risk aGvHD (Minnesota RS + Ann Arbor 1)

Day 28 ORR 89% vs 86 p 0.67
Day 7 ORR 81% vs 66% p 0.02

Safe – durable
Alternative to steroid in LR aGvHD?!

Etra et al, Blood 2022

One size does not fit all
smth new & smth old

Risk stratification biomarker
(eg Ann Arbor)
clinical risk score
(eg Minnesota RS; IR score; etc)

Escalation (HR) vs Deescalation (LR)

Old drug in different **pts selection**
Comparator
Organ target
Trials' design – match pair vs randomized vs cohort comparison etc

Changing Paradigm.6

smth borrowed

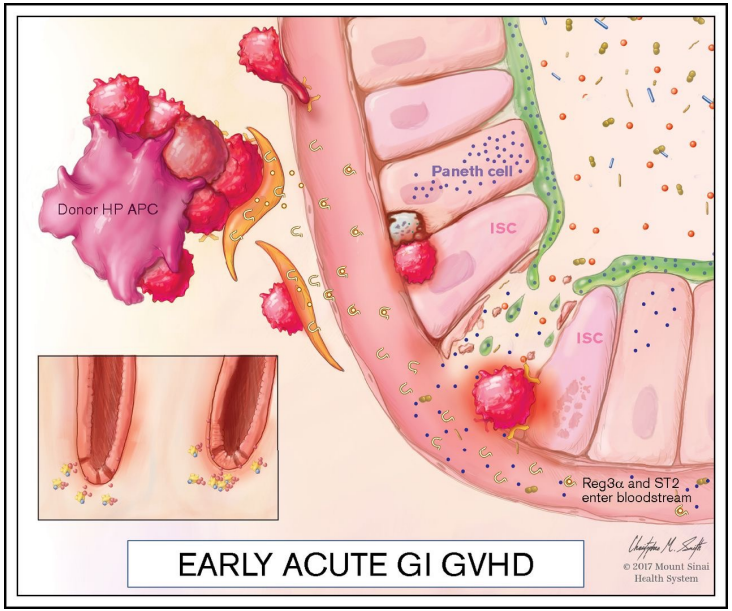
Background

- GUT aGvHD is a life-threatening complication
- Stage 4 GUT predict 6-12 month mortality
- Steroid-refractory GI-GvHD has low rate of response to therapy

Goal

Novel therapies specifically aiming at enhanced intestinal regeneration should be pursued

- **IL22**
- R-spondin
- **GLP-2 - Glucagone-like-peptide-2**



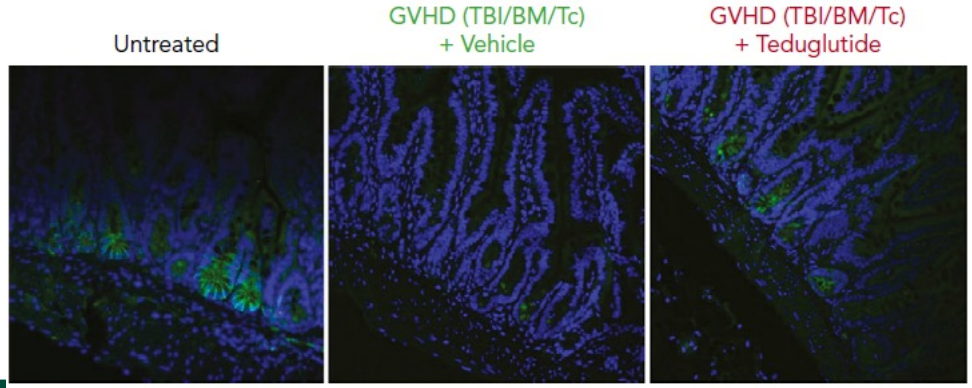
JLM Ferrara & MS Chaaudhry, Hematology 2018

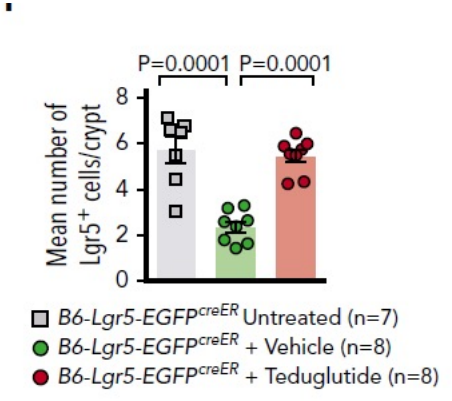
GLP-2 *Glucagone-like-peptide-2*

GLP-2 is a enteroendocrine tissue hormone produced by intestinal L cells.

- aGvHD reduce GLP-2 level (Human/Mouse)
- GLP-2 agonist reduce de novo aGvHD and SR-aGvHD, preserving GvL.
- GLP-2 agonist promote regeneration of Paneth Cells and Intestinal Stem Cells
- GLP-2 enhance production of antimicrobial peptides and caused microbiome changes

→ **intestinal homeostasis**





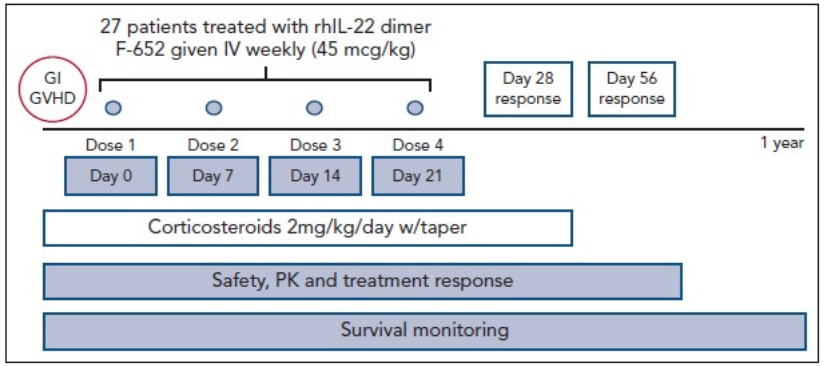
Norona J et al, Blood 2020

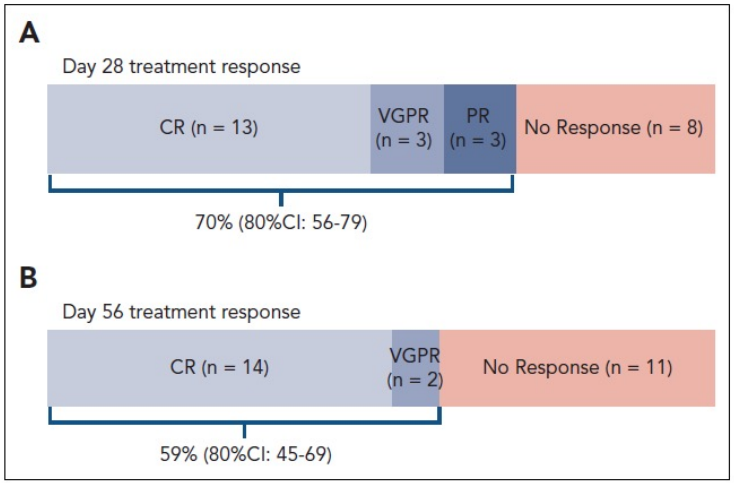
F625 *Recombinant human IL22*

Open label – single cohort – multicentre

27 pts newly diagnosed biopsy proven G1 → G4 GUT GvHD

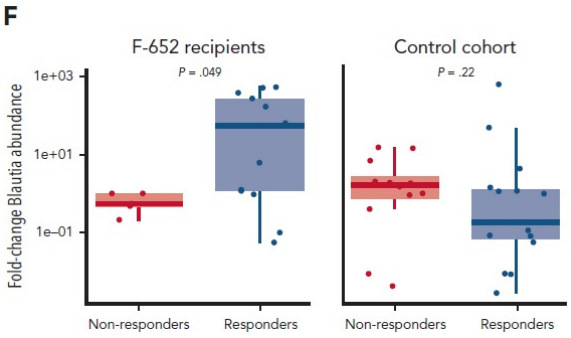
AE 20% xerostomia / 23% skin xerosis / 13% xerophtalmia





KEY POINTS

- **Use of the rhIL-22 dimer F-652 with systemic steroids appeared safe and was associated with a high response rate in newly diagnosed GI GVHD.**
- **Patients responding after tissue-targeted therapy with F-652 and corticosteroids demonstrated an expansion of healthy commensal GI flora.**



Ponce DM et al, Blood 2023

Changing Paradigm.7

smth borrowed

Background

Intestinal homeostasis <> dysbiosis is crucial for outcome in autologous / CAR-T / allogeneic HSCT

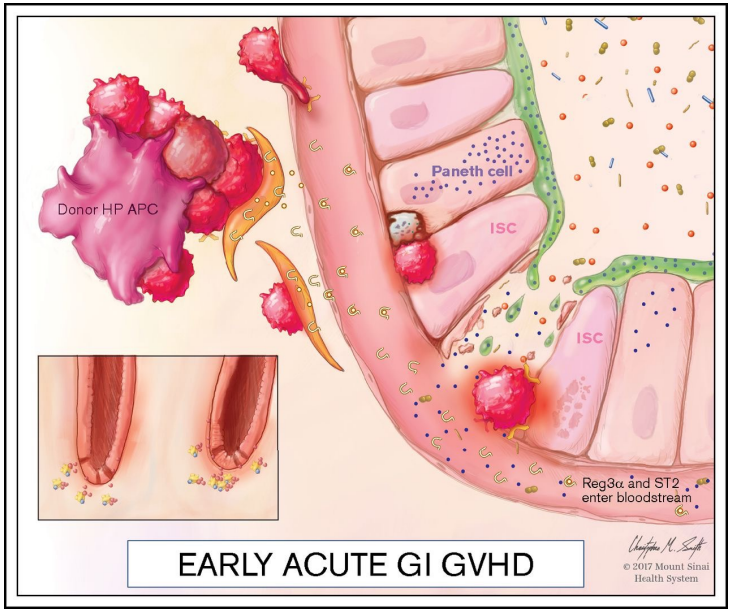
Microbiota interplays with immune system → infection, multi drug resistant germs, SR-aGvHD

Goal

Dysbiosis = disruption of balance

REVERSIBLE

FMT (faecal microbiota transplantation) restor microbiota richness and correct dysbiosis associated with chronic disease.



JLM Ferrara & MS Chaaudhry, Hematology 2018

The MaaT013 experience

76 pts w SR-GI-aGvHD
24 pts Ph2 – 52 compassionate

MaaT013 is a pooled allogeneic microbiome ecosystem therapy.
Weekly enema administration.
cGMP production.

Day 28 – ORR 38% (Ph2)
Day 28 – ORR 58% (expanded access)
Day 28 responders have an higher 12-M OS
Day 28 responders have an higher alfa-diversity indices
Day 28 responders have a better MaaT engraftment

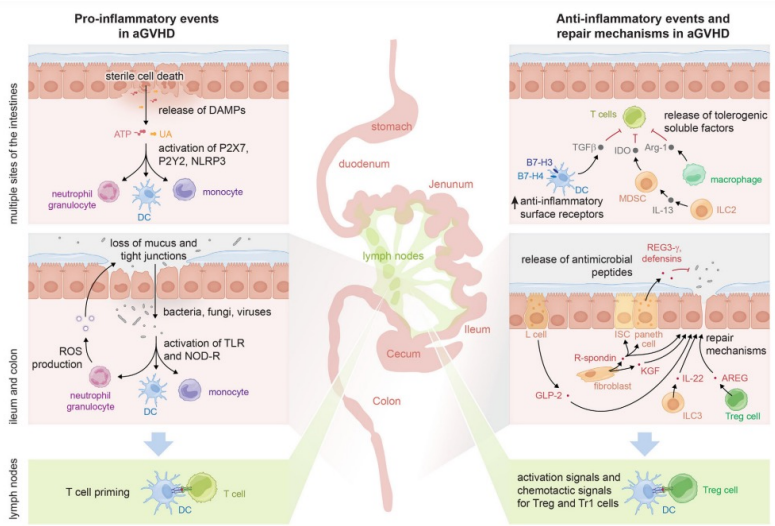
Malard F et al, ASH 2021

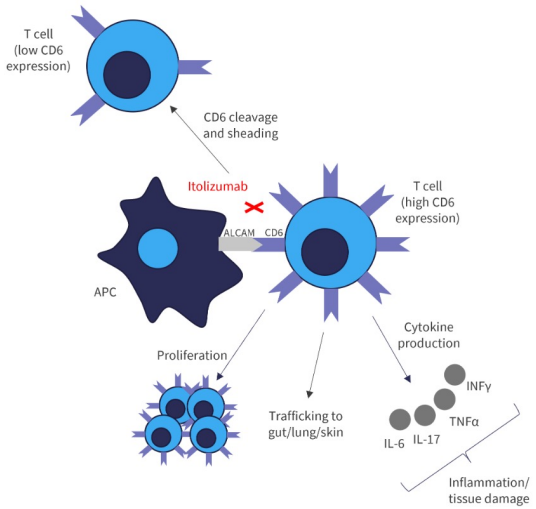
One size does not fit all
smth borrowed

GUT lesson

GVHD, IBD, and primary immunodeficiencies
The gut as a target of immunopathology resulting from impaired immunity

Zeiser et al, Eur J Immunol 2022





Changing Paradigm.8

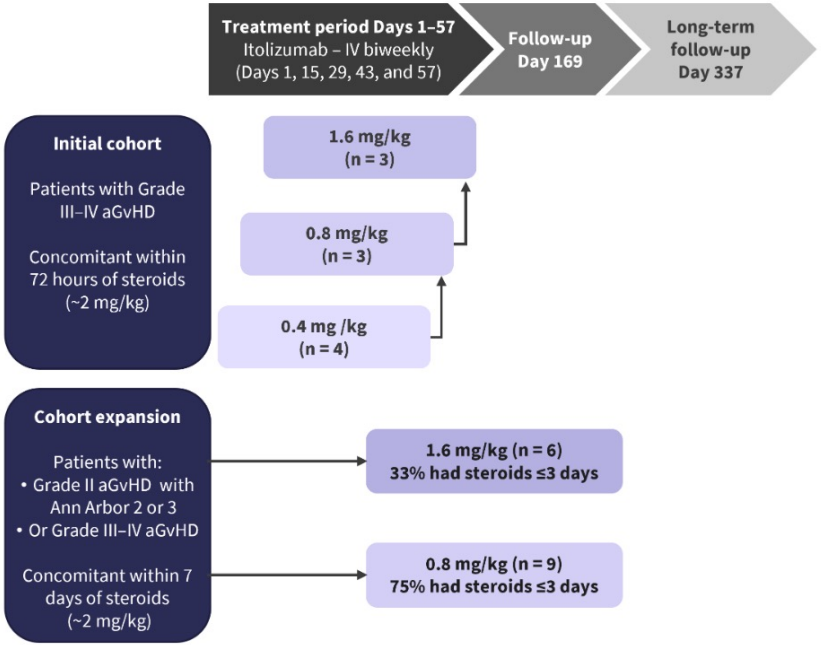
smth given as a gift

Itolizumab, a humanized immunoglobulin G1 (IgG1) anti-CD6 monoclonal antibody, inhibits CD6 signaling, consequently decreasing T-cell activation and proliferation.

The CD6-activated leukocyte cell adhesion molecule (ALCAM) pathway plays an important role in inflammation and autoimmunity.

Itolizumab binds to CD6 (at Domain-1) and causes shedding of the receptor. T cells with lower levels of CD6 exhibit reduced sensitivity to stimulation, including decreased activation, proliferation, and cytokine production

Itolizumab



Cutler C et al, EBMT 2022

Characteristic, % (unless otherwise stated)	Itolizumab 0.4 mg/kg (n = 4)	Itolizumab 0.8 mg/kg (n = 12)	Itolizumab 1.6 mg/kg (n = 9)	Total (N = 25)
aGvHD grade†				
II	0	8	0	4
III	75	58	67	64
IV	25	33	33	32
Organ involvement				
Skin	25	33	44	36
Liver	25	0	11	8
UGI	25	67	22	44
LGI	100	83	78	84
Minnesota high risk score‡	100	67	78	76
Ann Arbor Score 2 or 3	100	100	89	96

EQUATE - Phase I-II study – 1^ line in HR GvHD
25 pts

Efficacy
Day 15 CR rate 50% and ORR 71%
Day 29 CR rate 52% and ORR 64%

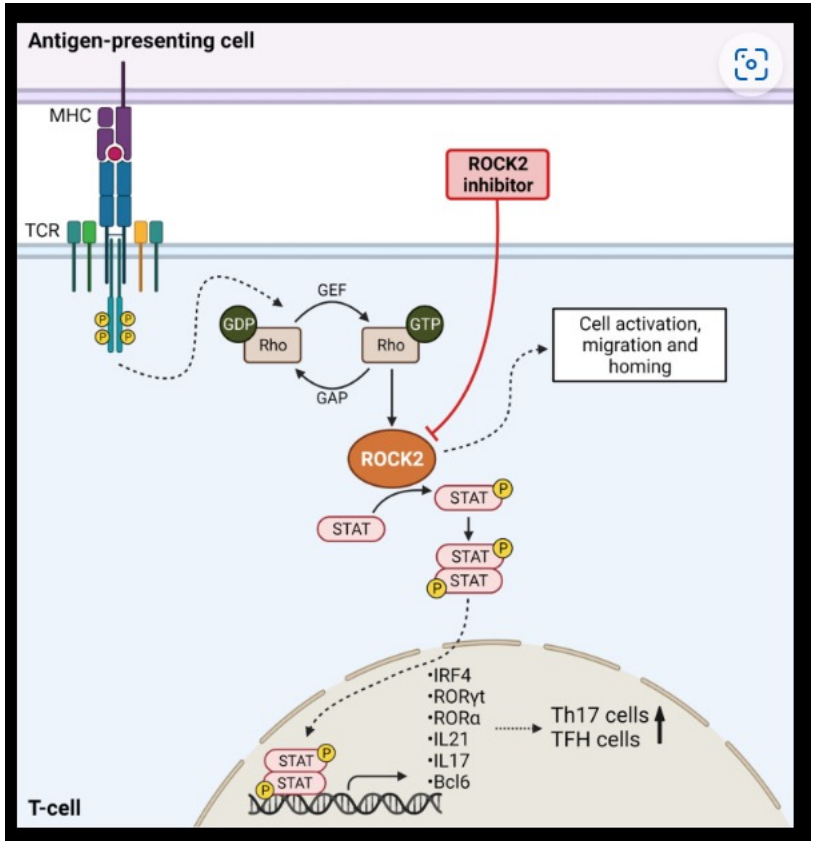
Itolizumab within 72 hours of corticosteroids
Day 29 CR rate and ORR of 61% and 67%

Day 169 durable response rate 79%
Day 337 response rate 55%

Safety
SAE 64% of patients
40% infection
8% reporting a treatment-related SAE

Cutler C et al, EBMT 2022

Phase III study has been initiated to investigate the efficacy and safety of itolizumab versus placebo as first-line-therapy in patients with Grade III–IV aGvHD (NCT05263999).



Braun & Zeiser. Front in Immun 2021

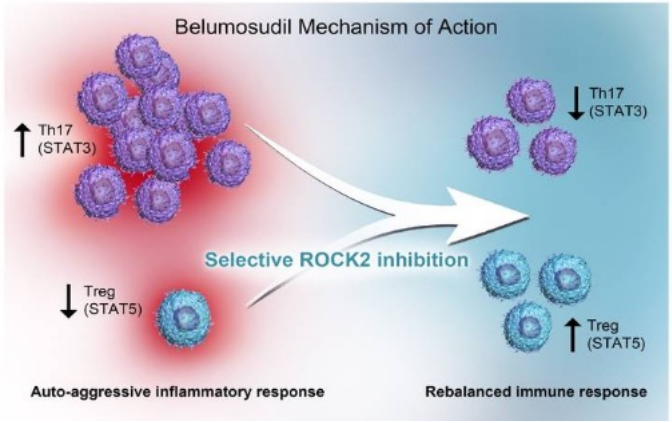
Belumosudil

Changing Paradigm.9

smth blue

Belumosudil (*Rezurock*)

Oral selective inhibitor of ROCK-2 (Rho-associated coiled-coil containing protein kinase 2).
↓ type 17 and follicular T helper cell
↓ STAT3
↑ RegT via STAT5



Jagasia M et al, JCO 2021
Cutler C et al, Blood 2022

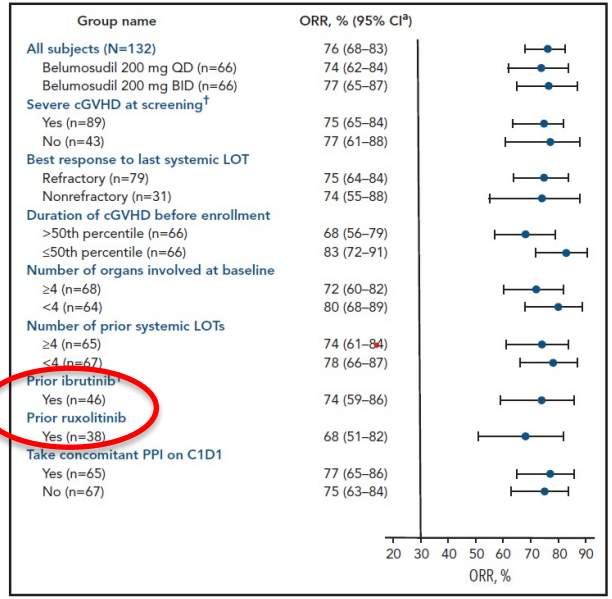
Phase IIa – open label dose-finding
54 pts 200 mg die – 200 mg bid – 400 mg mono
Phase II – randomized, multicenter study
66 pts 200 mg die vs 66 pts 200 mg bid
chGvHD 2-5 previous lines
(30% ruxo – 30% ibrutinib)

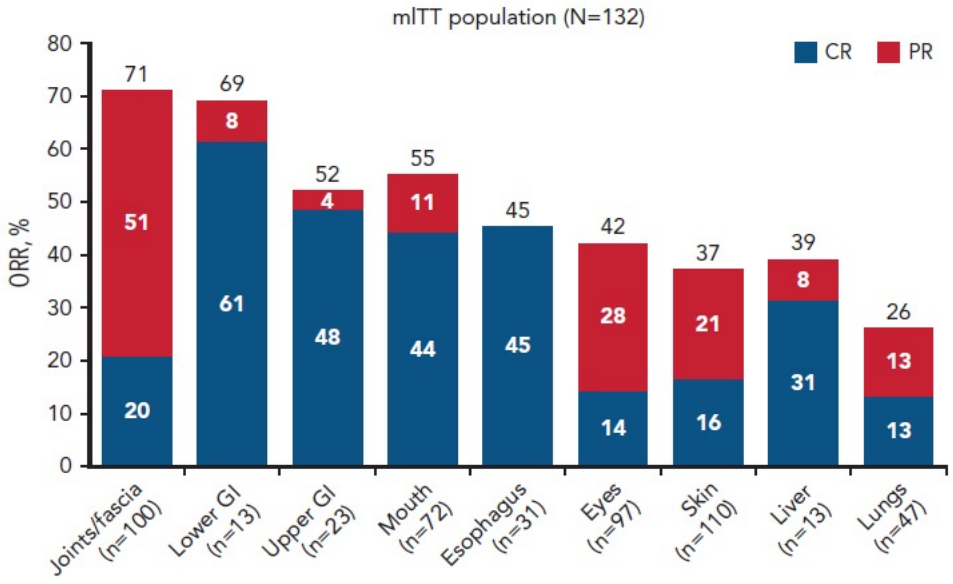
→ FDA approval

Changing Paradigm.9

smth blue

Belumosudil – ROCKstar study





Cutler C et al, Blood 2022

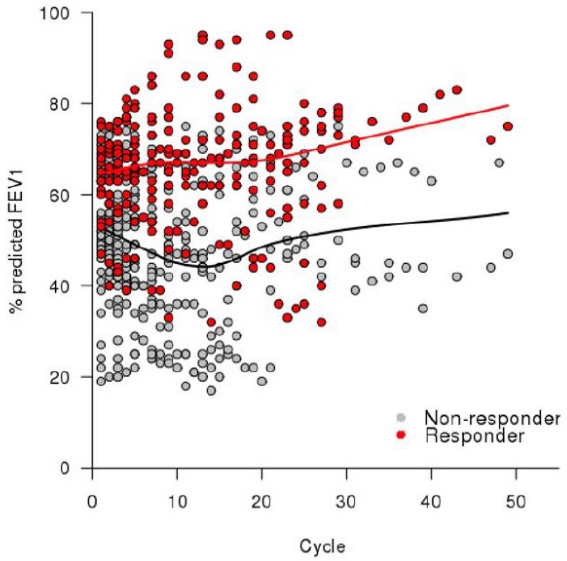
Belumosudil in Lung ChGvHD

Changing Paradigm.9
smth blue

KD025 208 (Jagasia et al JCO 2021)
KD025 213 (Cutler et al Blood 2021)

59 pts	N	ORR
NIH G1	30 (59%)	50%
NIH G2	23 (39%)	17%
NIH G3	6 (10%)	0%
Overall		32% (17 PR – 15 CR)

Multivariable analysis:
male sex, lower baseline NIH score, PR to previous lines



DeFilipp Z et al, Blood ADV 2022

Changing Paradigm.9

smth blue

Budget impact analysis of belumosudil for chronic graft-versus-host disease treatment in the United States

Carlos R. Bachier[a], Jeffrey R. Skaar[b], Sumudu Dehipawala[b], Benjamin Miao[b], Jonathan Ieyoub[c] and Haya Taitel[c]

[a]Sarah Cannon Transplant and Cellular Therapy Program, Methodist Hospital, San Antonio, TX, USA; [b]Evidence Strategy, Trinity Life Sciences, Waltham, MA, USA; [c]A Sanofi Company, Kadmon Corporation, LLC, New York, NY, USA

Figure 5. Budget percent change in 2026 with adoption of belumosudil with ibrutinib and ruxolitinib reduction.

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

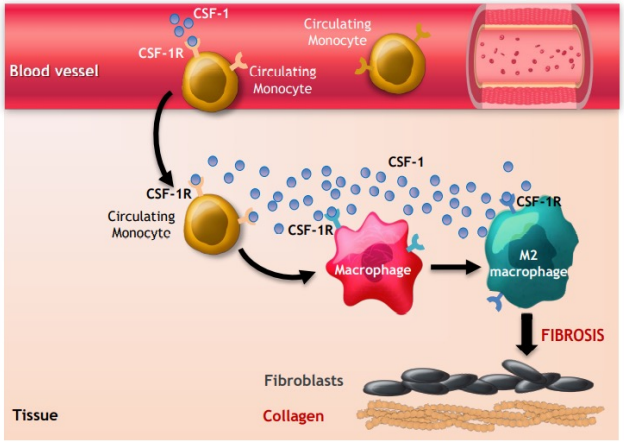


Figure Adopted from MacDonald, K.P.A. et al., *Blood*, 5 (129) 13-21;

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

Changing Paradigm.10

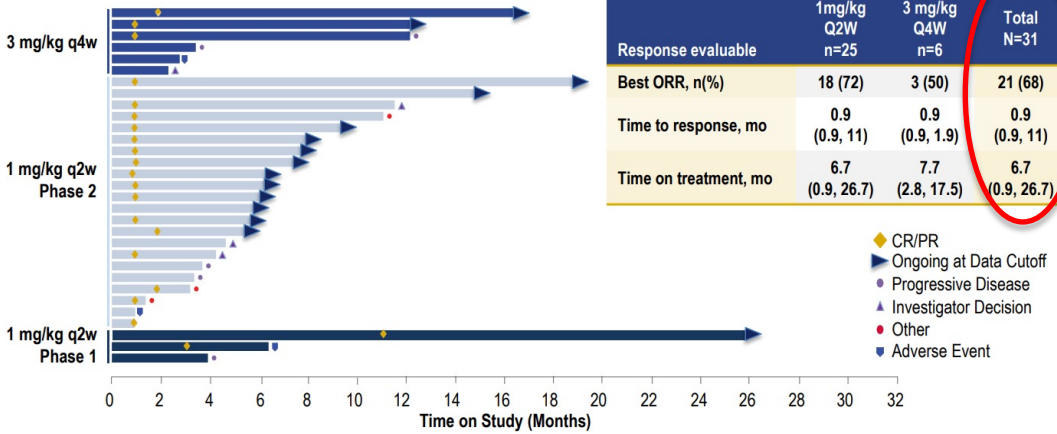
smth new

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

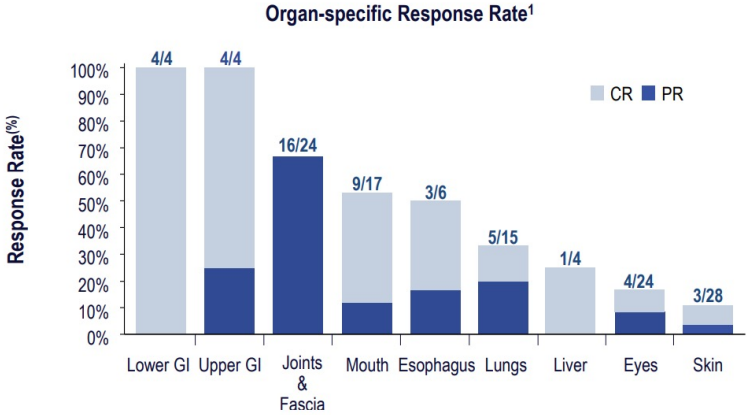
Stephanie J Lee et al, ASH 2021

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)

Axatilimab: Response seen across cGVHD organ system involvement

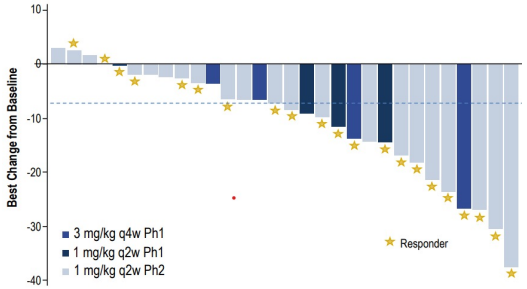


- 25 (81%) had severe skin sclerosis at baseline
- 4 (16%) improved sclerosis

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)

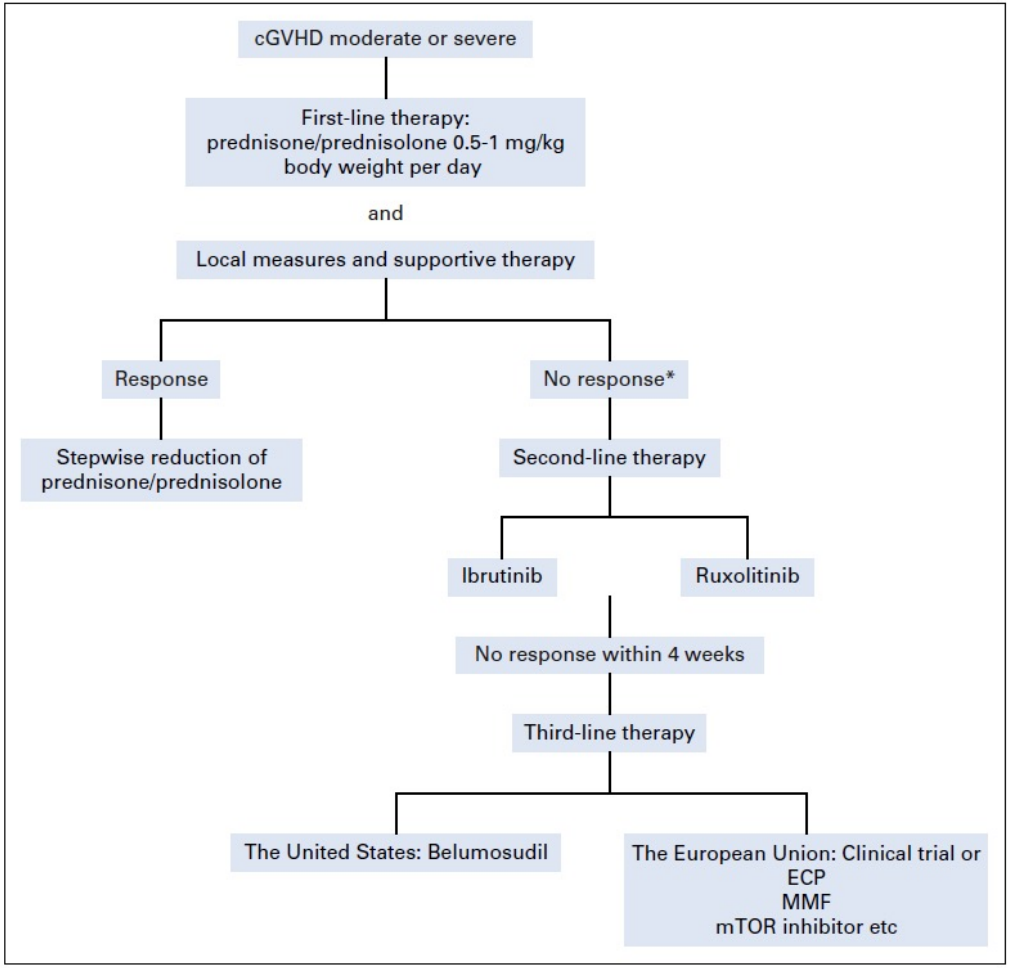
Improved Lee symptom scores in a majority



Phase II AGAVE-201 ongoing

Stephanie J Lee et al, ASH 2021

No combination therapy had shown improved response rate over GC monotherapy for therapy naive chGvHD



Zeiser R, JCO 2023

Approaches ignoring heterogeneity are likely to fail

PATIENTS REPORTED OUTCOMES (PROS) IN ROUTINE PRACTICE SUPPORT THE IMPACT OF GVHD ON LONG-TERM WORSENING OF QUALITY OF LIFE: ANALYSIS ON 105 PROSPECTIVE PATIENTS.

M.T. Lupo-Stanghellini[1], E. Dirai[1], A. Bruno[1], F. Farina[1], F. Aletti[1], S. Piemontese[1], R. Greco[1], S. Marktel[1], S. Mastaglio[1], E. Xue[1], C. Daniela[1], G. Catalano[1], M. Bernardi[1], J. Peccatori[1], M.G. Carrabba[1], C. Corti[1], F. Ciceri[1,2]

Aim: to analyze the perception of QoL in long-term survivors after HSCT according to FACT-BMT scale.

Method : Prospective single-center study

105 patients - HSCT Jan 2004 /Dec 2020

Follow-up >/=2y

FACT-BMT paper questionnaire - 5 point Likert-type scale

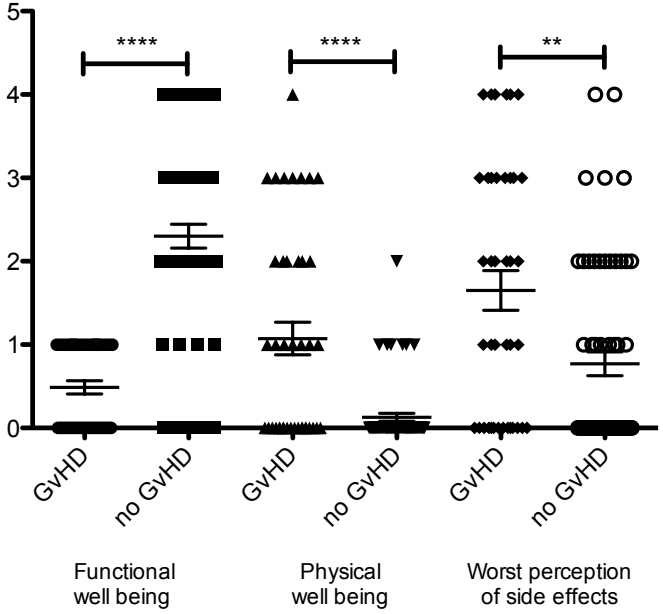
Physical Well-Being,

Social/Family Well-Being,

Emotional Well-Being,

Functional Well-Being,

BMT Subscale



- Donor Source ns
- Age <-> concern about work (p 0.0178).
- Female pts -> less satisfaction about the appearance of their body (p 0.02).

Hematology - Transplantation & Cellular Therapy Unit
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Pathology Unit

Maurilio Ponzoni
Federica Pedica
Luca Albarello

Mentore… qualcuno che ti accompagna con pensiero critico e partecipe, il cui scopo è quello di farci crescere dal punto di vista professionale e umano

Prof. Mery Flowers