POST STEROIDS ERA: WHAT'S NEXT FOR TREATMENT OF CHRONIC GVHD AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT

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Disclosures

Disclosure Statement: These individual(s) have the following to disclose concerning possible financial or personal relationships with commercial entities (or their competitors) that may be referenced throughout this presentation.

- Merrie Barnett-Brock, PharmD (nothing to disclose)
- Breanne Peyton-Thomas, PharmD, BCOP-Consultant for Precision AQ

Objectives

- Describe chronic graft vs host disease characteristics, pathophysiology, and risk factors following allogeneic hematopoietic stem cell transplantation
- Examine the use of novel agents for steroid refractory chronic graft vs host disease

Definitions

- **HSCT:** hematopoietic stem cell transplant
- **cGVHD:** chronic graft vs host disease
- **JAK:** Janus Associated Kinases
- **CSF-1R:** colony stimulating factor-1 receptor
- **ROCK:** rho-associated, coiled-coil containing protein kinase
- **BTK:** Bruton’s tyrosine kinase
- **STATs:** signal transducers and activators of transcription
- **OR:** overall response
- **CR:** complete response
- **BCR:** B-cell antigen receptor
- **Tbili:** total bilirubin
- **FFS:** failure free survival
- **CS:** corticosteroid
- **DOR:** duration of response
- **OS:** overall survival
- **SR-cGVHD:** steroid refractory cGVHD

Chronic Graft vs Host Disease Background

Chronic Graft vs Host Disease

An immunological disorder affecting multiple organ systems resulting from donor T cells responding to foreign recipient antigens→ injury of host organs

Host cells are attacked by the donor T cells

Symptoms: Scarring (fibrosis), Drying (sicca)

Results in tissue destruction and fibrosis over time

Hematology. 2021;2021(1):648-654
New England Journal of Medicine. 2017;377(26):2565-2579

cGVHD Background

Occurs in 30-70% of patients who have undergone allogeneic hematopoietic stem cell transplantation

- Even in those who received standard prophylaxis with a calcineurin inhibitor and an antimetabolite

Can affect GI tract, liver, skin, lungs, and any other organ system

- Hair, nails, genital tissue, esophageal, musculoskeletal, joint, fascial, ocular

Response rates to corticosteroids is 40-60%

Most patients have 3 or more organs involved

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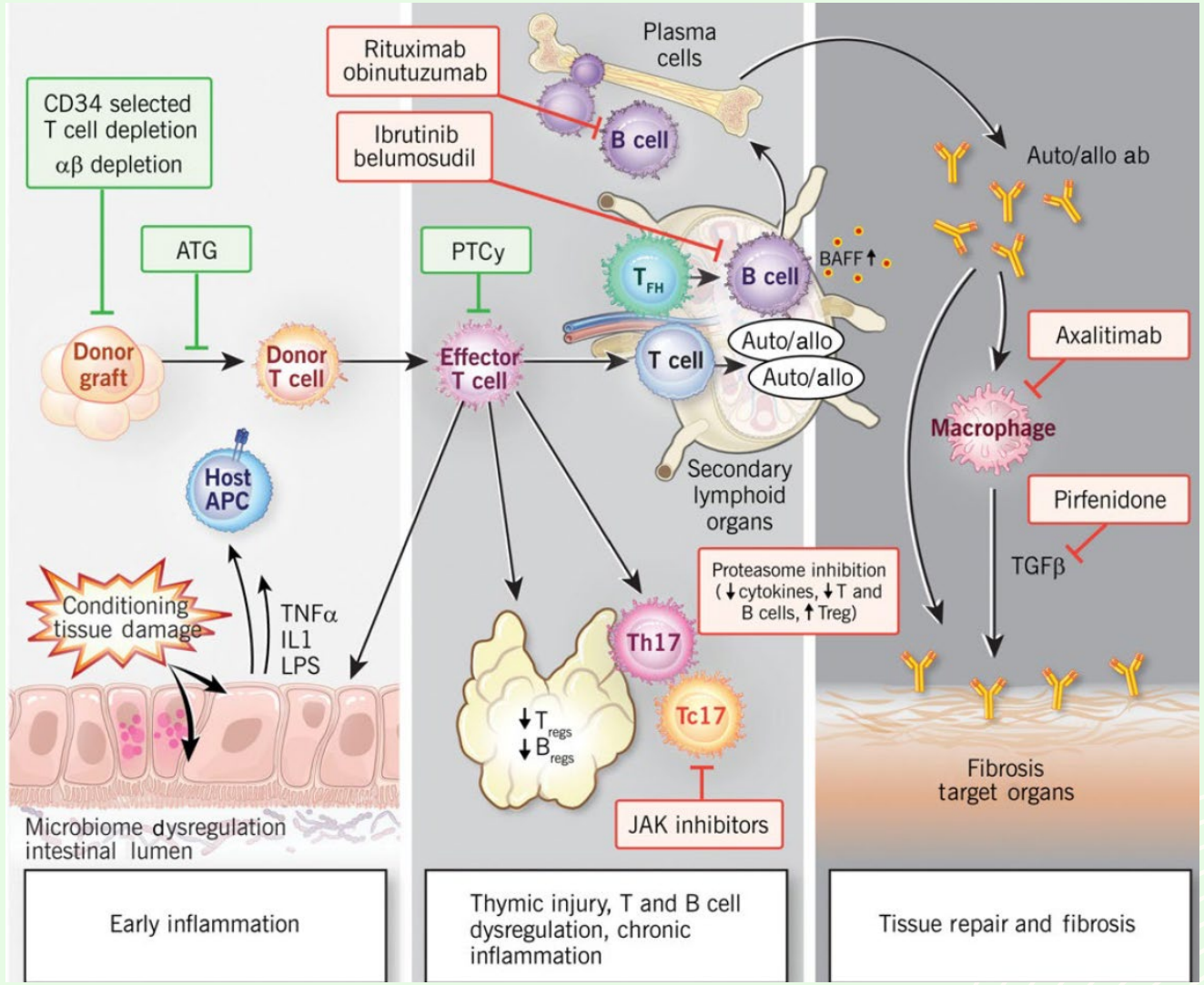
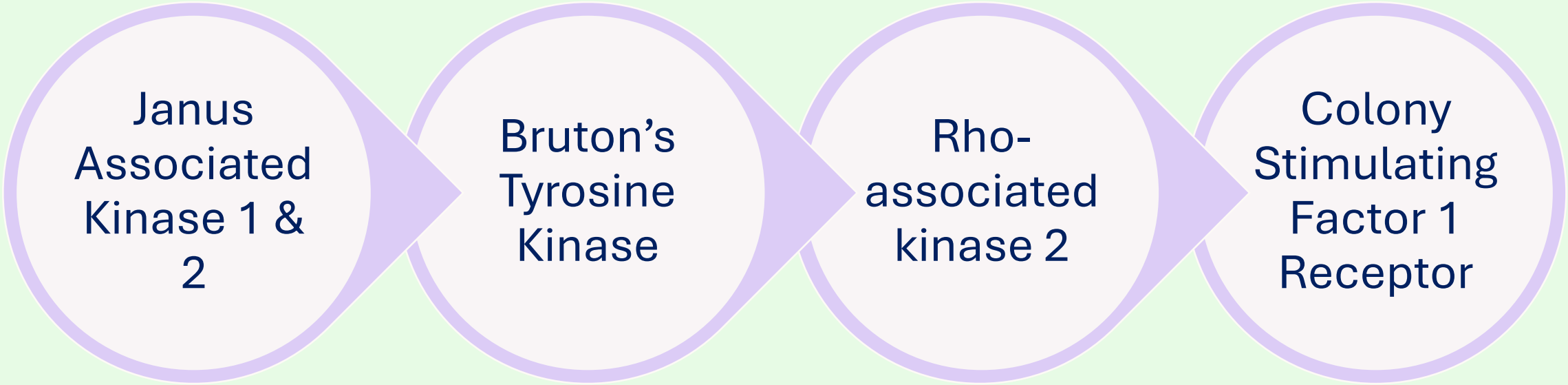
CGVHD PATHOPHYSIOLOGY

Hematology. 2021;2021(1):648-654



cGVHD Pathophysiology Key Pathways



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cGVHD Risk Factors

- Growth factor mobilized peripheral stem cells
- Mismatched or unrelated donor grafts
- Female-male transplantation
- Older age
- Acute GVHD history

Hematology. 2021;2021(1):648-654
New England Journal of Medicine. 2017;377(26):2565-2579

Emerging therapies for steroid refractory cGVHD

cGVHD TREATMENT TIMELINE

Ibrutinib FDA Approved August 2017 for Adults

Ruxolitinib FDA approved July 2021

Belumosudil FDA approved September 2021

Ibrutinib FDA approved August 2022 for Pediatrics

Axatilimab-csfr FDA approved August 2024

FDA APPROVED AGENTS FOR STEROID REFRACTORY cGVHD

Ruxolitinib (Category 1)
JAK1/2 Inhibitor

Ibrutinib
BTK inhibitor

Belumosudil
ROCK1/2 inhibitor

Axatilimab
CSF1-R Inhibitor

NCCN Clinical Practice Guidelines in Oncology: Hematopoietic Cell Transplantation (Version 2.2025).
Ruxolitinib.[package insert]. Delaware: DSM Pharmaceuticals Inc; 2011.
Ibrutinib. [package insert]. Pennsylvania: Jansenn Biotech, 2022.
Belumosudil.[package insert]. Pennsylvania: Kadmon Pharmaceuticals; 2021.
Axatilimab. [package insert]. Delaware: Incyte corporation; 2024.

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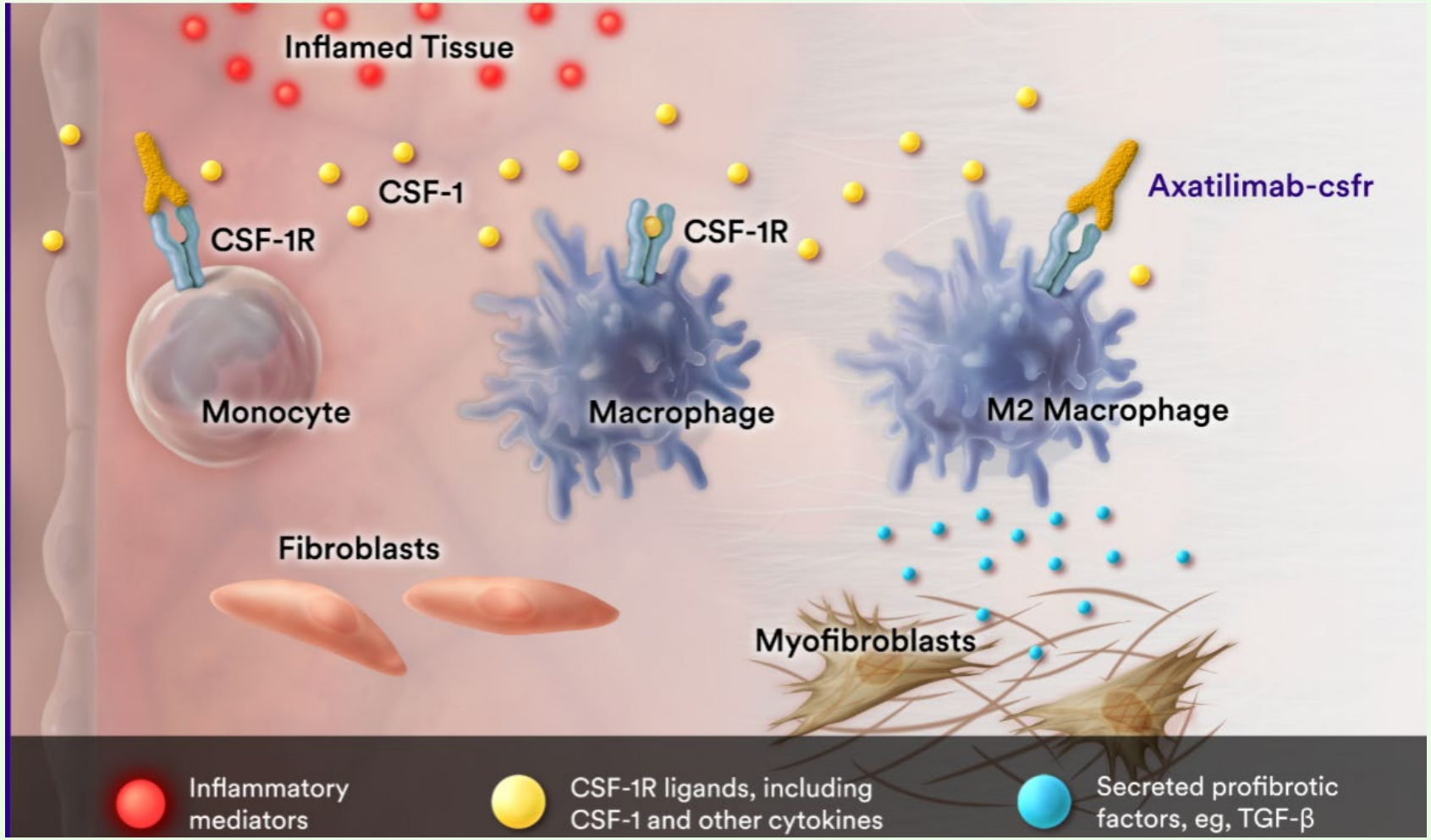
Axatilimab MOA



Niktimvo. Accessed 10/1/2025.

Axatilimab (Niktimvo)

FDA Approval: 2024
FDA Approved Use: treatment of cGVHD after failure of at least two prior lines of systemic therapy in adult and pediatric patients weighing at least 40 kg
Dose: IV 0.3 mg/kg Q2W-maximum dose 35 mg infused over 30 min
ADR: infections, musculoskeletal pain, fatigue, nausea, headache, cough, pyrexia, dyspnea

- ❑ **Warnings:** infusion reactions-interrupt or slow the infusion rate
- ❑ **Laboratory abnormalities:**
  - Increased: ALT, AST, GGT, lipase, amylase, ALP, CPK, calcium
  - Decreased: hemoglobin, phosphate,

Drug Interactions:

- ❑ No known

Monitoring: AST, ALT, ALP, CPK, amylase, lipase, prior to start of therapy and every 2 weeks for the first month→ every 1-2 months after

Axatilimab. [package insert]. Delaware,: Incyte corporation; 2024.

Axatilimab (Niktimvo)

ADR	Severity	Dosage Modification
Infusion reactions	Grade 1 or 2	❑ Interrupt infusion and decrease rate by 50% ❑ Initiate symptomatic management: antihistamines and antipyretics ❑ For subsequent infusions: pre-medicate and resume infusion at 50% of the prior rate
	Grade 3 or 4	❑ Permanently discontinue
AST/ALT elevation	Grade 3 with Tbili ≤ grade 1	❑ Hold until recovery to grade 2 and resume at 0.2 mg/kg (max 23 mg)
	ALT or AST ≥ 3xULN with Tbili ≥ 2xULN and ALP <2xULN	❑ Hold-if evidence of drug-induced liver injury permanently discontinue
	Grade 4	❑ Permanently discontinue
Elevation of CPK, amylase, or lipase	Grade ≥ 3	❑ IF end organ damage: discontinue ❑ IF no end organ damage-continue without dose reduction
	Symptomatic grade ≥ 3	❑ Permanently discontinue

Axatilimab. [package insert]. Delaware,: Incyte corporation; 2024.

Axatilimab in Recurrent or Refractory Chronic Graft-versus-Host Disease-the AGAVE 201 study

New England Journal of Medicine. 2024;391(11):1002-1014

Study Design

Randomized → Phase 2 → Multi Center → Open-label

Objective: Evaluate the efficacy and safety of axatilimab at three different doses

New England Journal of Medicine. 2024;391(11):1002-1014

Study Design

Patients

- Refractory or recurrent cGVHD
- Active signs/symptoms of cGVHD
- Received ≥ 2 lines of systemic therapy

Random Assignment

- 1:1:1 ratio
- 0.3 mg/kg Q2W
- 1 mg/kg Q2W
- 3 mg/kg Q4W

Primary Endpoint	Secondary Endpoint
Overall response: ❑ Complete or partial response defined by NIH Consensus criteria	❑ Clinically significant reduction in symptoms

New England Journal of Medicine. 2024;391(11):1002-1014

Patient Characteristics

Baseline Characteristics:			
Characteristic	0.3 mg/kg dose	1 mg/kg dose	3 mg/kg dose
Median age (years)	50	56	53
Median number of organs involved	4	4	3
Median # of previous lines of therapy	4	4	4
Previously used therapies			
Ibrutinib	34%	23%	36%
Ruxolitinib	71%	79%	72%
Belumosudil	20%	23%	26%
Best response to most recent previous cGVHD treatment			
Complete	5%	2%	2%
Partial	32%	33%	26%
No change	40%	48%	56%
Progression	8%	9%	11%

New England Journal of Medicine. 2024;391(11):1002-1014

AGAVE 201-Results

241 patients enrolled

41% still receiving axatilimab at the data cutoff

Primary Outcome:

0.3 mg/kg group: 74% ORR

Median time to response:

< 2 mo

Durable response at 12 months:

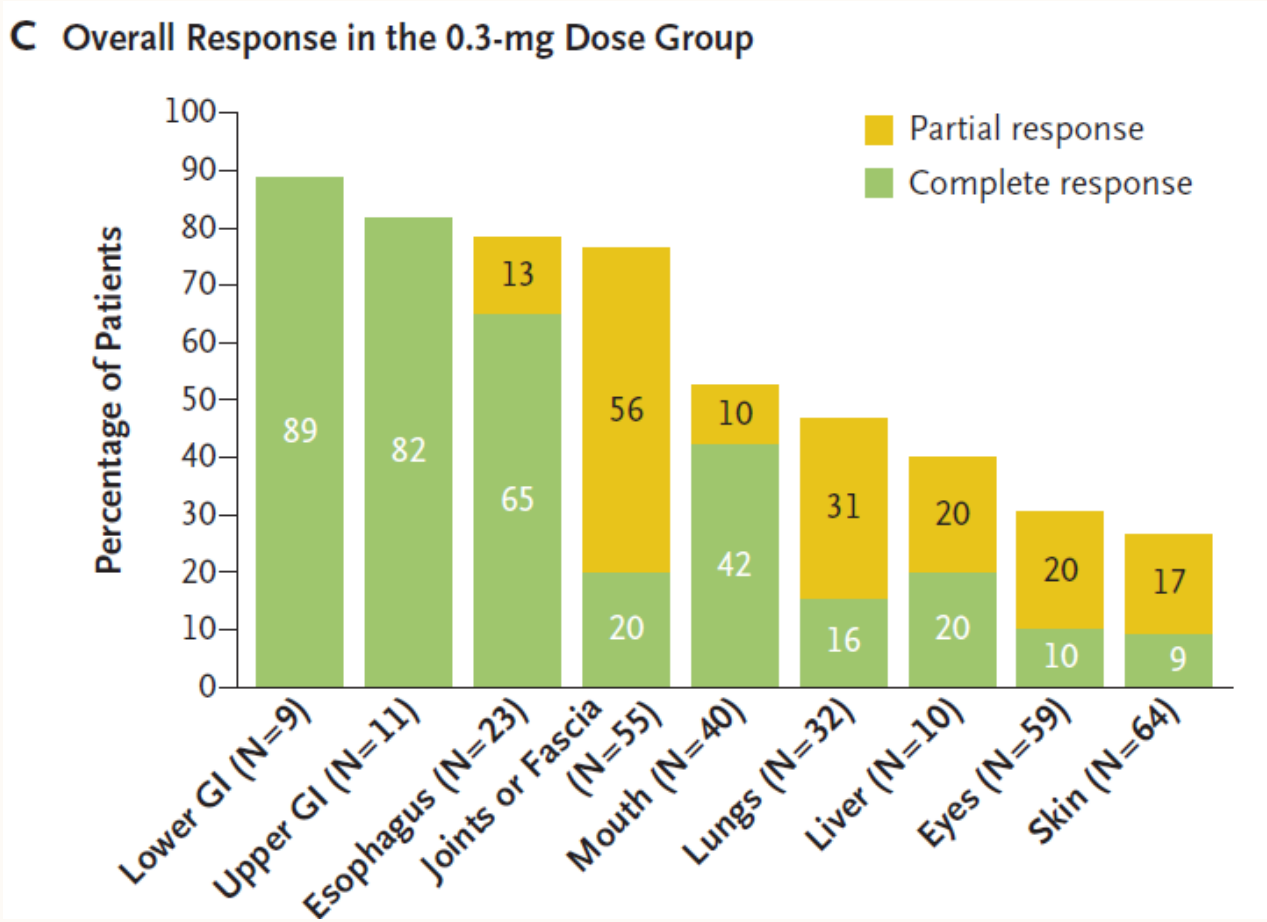
0.3 mg/kg group: 60 %

Clinically meaningful reduction in symptoms:

0.3 mg/kg group: 60 %

New England Journal of Medicine. 2024;391(11):1002-1014

AGAVE 201



New England Journal of Medicine. 2024;391(11):1002-1014

AGAVE 201-Safety

Most Common Adverse Events:

- Transient lab abnormalities
- Periorbital edema was dose dependent
- Infusion related reactions occurred most in the 0.3 mg/kg group
- Infections

ADRs leading to discontinuation:

- 0.3 mg/kg group: 6%
- 1 mg/kg group: 22%
- 3 mg/kg group: 18 %

New England Journal of Medicine. 2024;391(11):1002-1014

Key Takeaways:

Improved ORR

Response not influenced by disease severity

Response even with prior treatment failure

Quick clinically meaningful reduction in symptoms

New England Journal of Medicine. 2024;391(11):1002-1014

Key Takeaways

- cGVHD is highly prevalent with occurrence of steroid refractory disease in 40-60% of patients
- Emerging agents provide good ORR in studies and durable response
- Axatilimab shows promising side effect profile with no drug interactions, and shows promising results in GI cGVHD

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