PD-1 Agonist (Rosnilimab) R&D Event

Wednesday, Oct. 25, 2023

1:15pm PT/4:15pm ET

AnaptysBio

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This presentation and any accompanying oral presentation contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to: the timing of initiation of the Company's clinical trials, including rosnilimab's clinical trial and in ulcerative colitis; the timing of the release of data from the Company's clinical trials, including rosnilimab's Phase 2b clinical trial in rheumatoid arthritis and rosnilimab's Phase 2 clinical trial in ulcerative colitis; the timing of ANB033's IND filing; whether any of the Company's product candidates will be best in class or are optimized; the potential to receive any additional royalties from the GSK collaboration; the Company's ability to find a licensing partner for imsidolimab or etokimab and the timing of any such transaction; and the Company's projected cash runway. Statements including words such as "plan," "continue," "expect," or "ongoing" and statements in the future tense are forward-looking statements. These forward-looking statements involve risks and uncertainties, as well as assumptions, which, if they do not fully materialize or prove incorrect, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Forward-looking statements are subject to risks and uncertainties that may cause the company's actual activities or results to differ significantly from those expressed in any forward-looking statement, including risks and uncertainties related to the company's ability to advance its product candidates, obtain regulatory approval of and ultimately commercialize its product candidates, the timing and results of preclinical and clinical trials, the company's ability to fund development activities and achieve development goals, the company's ability to protect intellectual property and other risks and uncertainties described under the heading "Risk Factors" in documents the company files from time to time with the Securities and Exchange Commission. These forward-looking statements speak only as of the date of this presentation, and the company undertakes no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date hereof.

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Agenda

TOPIC	SPEAKER
Rosnilimab: a best-in-class PD-1 agonist	**Dan Faga** **Chief Executive Officer**
MOA and differentiation	Martin Dahl, Ph.D. Senior Vice President, Research
Rosnilimab in RA	
Unmet patient needs and opportunity for PD-1 agonists	Jonathan Graf, M.D. Professor, Medicine University of California, San Francisco
Targeting RA with rosnilimab and translational data	Cailin Sibley, M.D., MHS, FACR Vice President, Translational Medicine
Rosnilimab in UC	
Unmet patient needs, disease biology, and rationale for PD-1 agonist in UC	Bruce Sands, M.D., M.S. Professor and Chief, Gastroenterology Icahn School of Medicine, Mount Sinai
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PD-1 safety data and Phase 2 development plans in RA and UC	Paul Lizzul, M.D., Ph.D. Chief Medical Officer
Market opportunity and closing remarks	Dan Faga
Q&A	AnaptysBio

Developing best-in-class immune cell modulators to restore immune balance across autoimmune & inflammatory diseases

Immune Cell Modulators

Rosnilimab
(PD-1 agonist)

P2b in
Rheumatoid Arthritis

P2 in
Ulcerative Colitis

ANB032
(BTLA agonist)

P2b in
Atopic Dermatitis

ANB033
(CD122 antagonist)

IND-enabling

Potential development in additional diseases areas across dermatology, gastroenterology and rheumatology

Cytokine Antagonists (legacy programs for out-licensing)

Imsidolimab
(IL-36R)
P3 in GPP

Etokimab
(IL-33)
P2b/3-ready in
Epithelial-driven diseases

Research-driven

Preclinical pipeline of immunology targets

Strong capital position

Cash runway to YE 2026

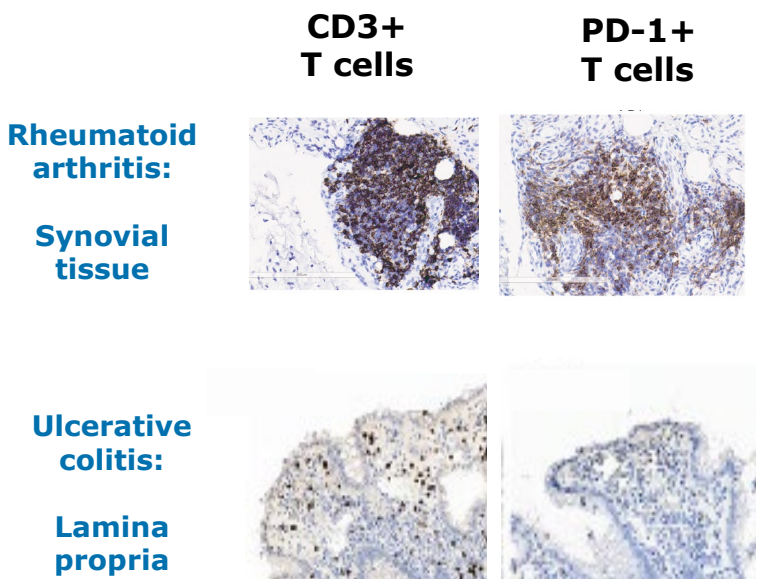
GSK immuno-oncology financial collaboration

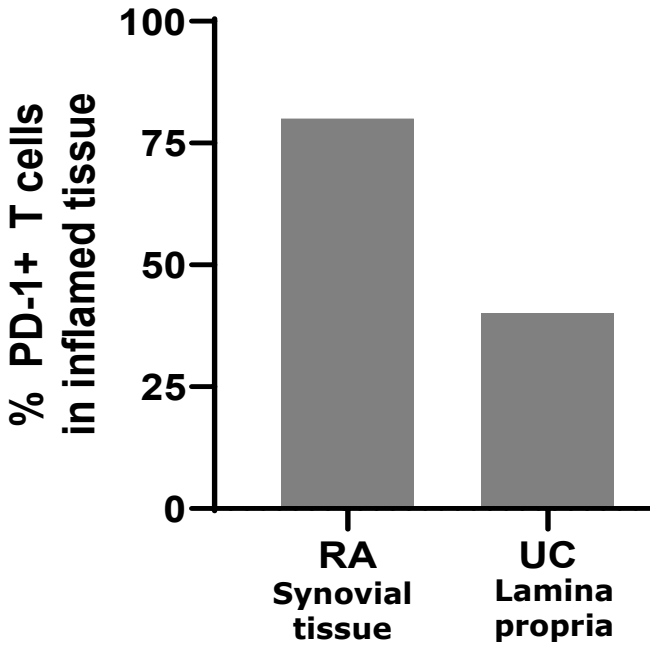
Significant royalty potential

Immune cell modulator development plan: initiation of three P2 trials across three therapeutic areas

Antibody Program	Therapeutic Indication	Development Stage and Anticipated Milestones				
		Lead Optimization	IND Enabling	Phase 1	Phase 2	Phase 3
Rosnilimab (PD-1 agonist)	**Rheumatoid Arthritis**				**P2b initiated Q3 2023** **Top-line data mid 2025**	
	Ulcerative Colitis				**Ph2 initiation Q4 2023** **Top-line data H1 2026**	
ANB032 (BTLA agonist)	**Atopic Dermatitis**				**P2b initiated Q2 2023** **Top-line data YE 2024**	
ANB033 (CD122 antagonist)	**Inflammatory Diseases**		**IND submission H1 2024**			

PD-1+ T cells are prevalent in inflamed tissue and periphery in RA and UC



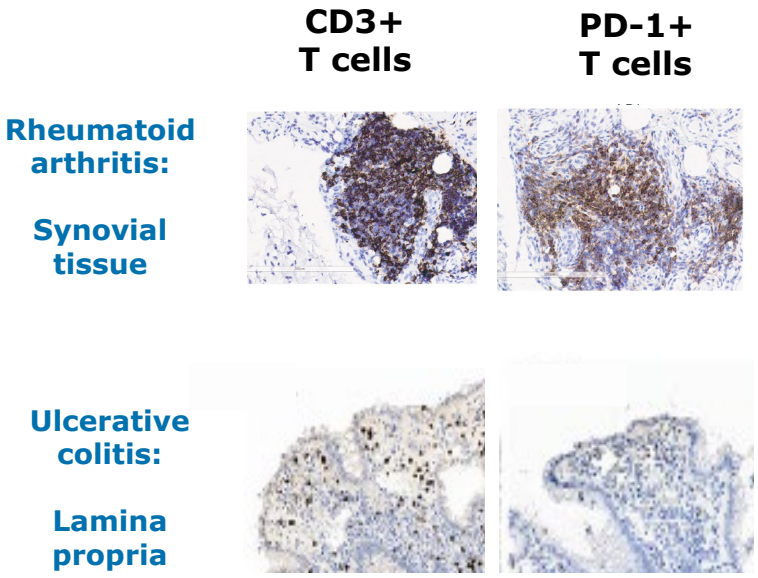


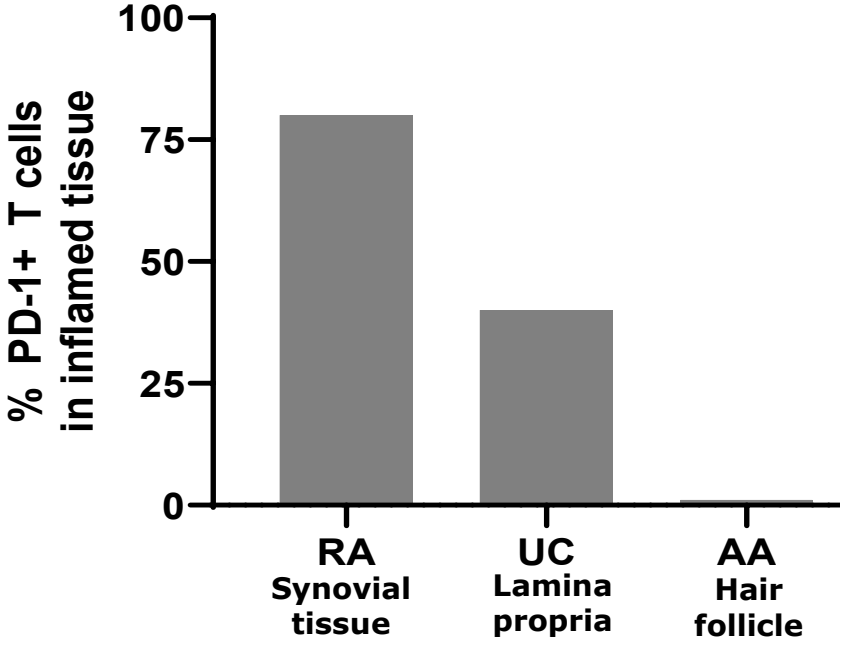
In systemic inflammatory diseases, a **multiple fold increase of PD-1+ T cells** is observed in periphery compared to healthy controls[1]

- **~1.5x in RA**
- **~2x in UC**

Adapted from Nguyen et al, Human Pathology (2022) 126, 19e27; Guo et al, PLoS One 2018; 13(2): e0192704. Shi et al. (2023), PeerJ, DOI 10.7717/peerj.15481. 1. Murray-Brown et al, RMC Open, 2022, Shi et al. (2023), PeerJ, DOI 10.7717/peerj.15481.

PD-1+ T cells are prevalent in inflamed tissue and periphery in RA and UC, but lacking in AA



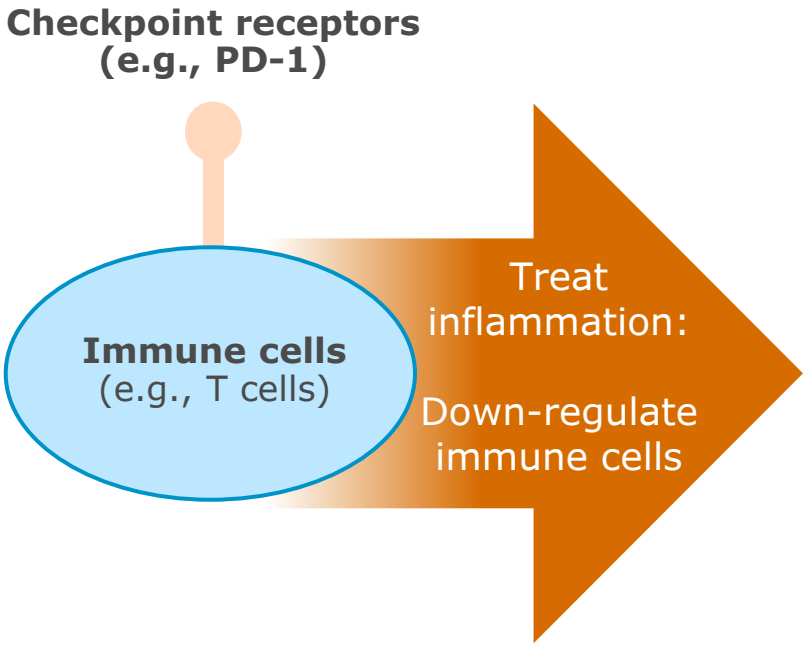


In systemic inflammatory diseases, a **multiple fold increase of PD-1+ T cells** is observed in periphery compared to healthy controls[1]

- **~1.5x in RA**
- **~2x in UC**
- **Not increased in AA**

Adapted from Nguyen et al, Human Pathology (2022) 126, 19e27; Guo et al, PLoS One 2018; 13(2): e0192704. Shi et al. (2023), PeerJ, DOI 10.7717/peerj.15481. 1. Murray-Brown et al, RMC Open, 2022, Shi et al. (2023), PeerJ, DOI 10.7717/peerj.15481.

Checkpoint agonists “hit the brakes” to restore immune balance



Rosnilimab targets PD-1+ T cells through 3 MOAs:

1. Deplete PD-1^{high} Teff cells
2. Deplete PD-1^{high} Tfh/Tph cells
3. Agonize PD-1^{int} Teff cells

Rosnilimab’s membrane-proximal binding epitope results in best-in-class potency vs. Lilly’s PD-1 agonist

Teff=T effector cells; Tph cells=Peripheral helper cells; Tfh cells=Follicular helper cells.

Rosnilimab's impact in inflamed tissue and periphery has potential to deliver differentiated efficacy and safety

Rosnilimab's impact on T cells	**Reduce PD-1^{high} Teff cells**	**Reduce PD-1+ T cell activation**	**Reduce PD-1^{high} Tfh/Tph cells**
Immunologic outcomes	Reduce T cell migration, proliferation & cytokine secretion		Reduce plasma cell generation & autoantibody levels

Relevant Approved Treatments[1]

[1]Other efficacious treatments have less specific MOAs causing safety liabilities, including Rinvoq (JAKs), Rituxan (broad B cell depleter), Lemtrada (broad lymphocyte depleter)

Rosnilimab has potential to treat wide range of systemic inflammatory diseases, including RA and UC

Rheumatoid arthritis:

~500,000 patients
>$10bn U.S. sales in "post TNF" market[1]

20-25% cycle
all treatment classes
not achieving low disease activity[2]

Ulcerative colitis:

~100,000 patients
>$6.5bn U.S. sales, excluding TNF, market[3]

1/3 to 1/2 relapse
within 1 year following
remission on induction therapy[4]

Large commercial markets

- Biologic experienced patients

Standard of care is insufficient

- RA (Post TNF): ~20–35% ACR50
- UC: ~25-30% clinical remission induction

Significant room to differentiate

- Drive deeper responses across broader patient population
- Restore immune balance

1. Expected by 2028 (Evaluate 29 Nov 2022); 2. Market research conducted by Ambit in 2022; 3. Expected by 2028 (Evaluate 21 Aug 2023);
4. Phase 3 registrational data from product labels

Rosnilimab targets PD-1+ T cells broadly impacting pathogenic drivers of autoimmune & inflammatory diseases

PD-1 agonists deplete and agonize PD-1+ T cells, in both inflamed tissue and the periphery

Rosnilimab, a best-in-class PD-1 agonist, reduces T cell migration, proliferation & cytokine secretion and reduces plasma cell generation & autoantibody levels

Translational and clinical data support Rosnilimab's potential for deep responses across heterogenous patient populations while restoring immune balance in RA and UC

RA: global Phase 2b trial initiated Q3:23 with top-line data mid:25
UC: global Phase 2 trial initiating Q4:23 with top-line data H1:26

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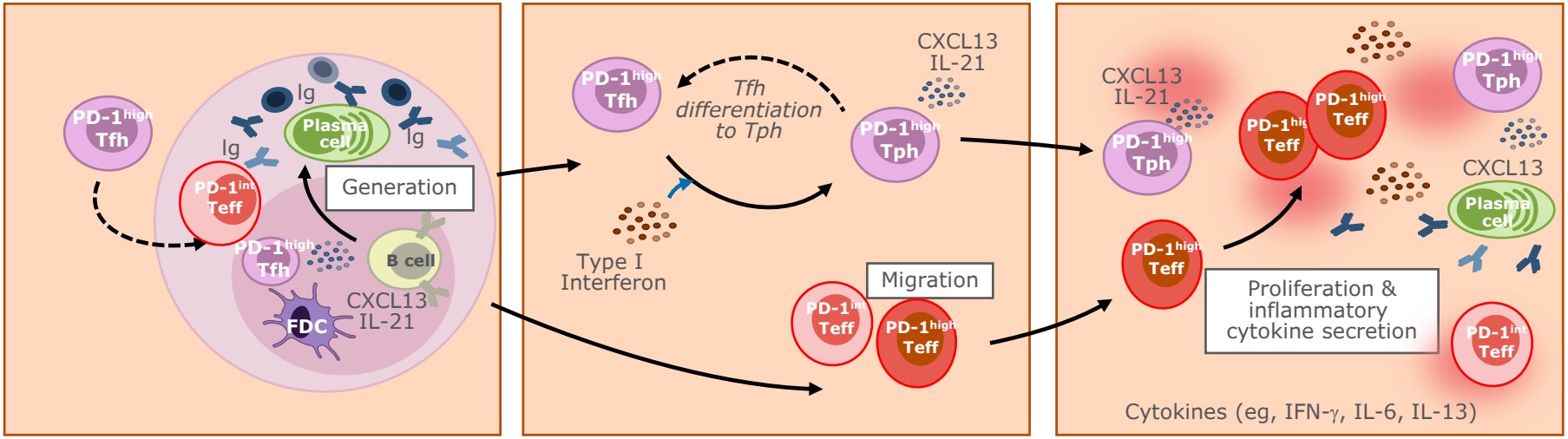
PD-1 expressed preferentially on activated Teff and Tfh/Tph cells mediating autoimmune pathology

Teff (effector)

- In response to stimulation, become highly activated (PD-1^{high}) or moderately activated (PD-1^{int})
- Secrete inflammatory cytokines, cause tissue damage and perpetuate inflammatory cycle

Tfh (follicular helper)
Tph (peripheral helper)

- Secrete CXCL13 and IL-21 which recruit and mature B cells into "autoantibody secreting" plasma cells
- Are PD-1^{high}

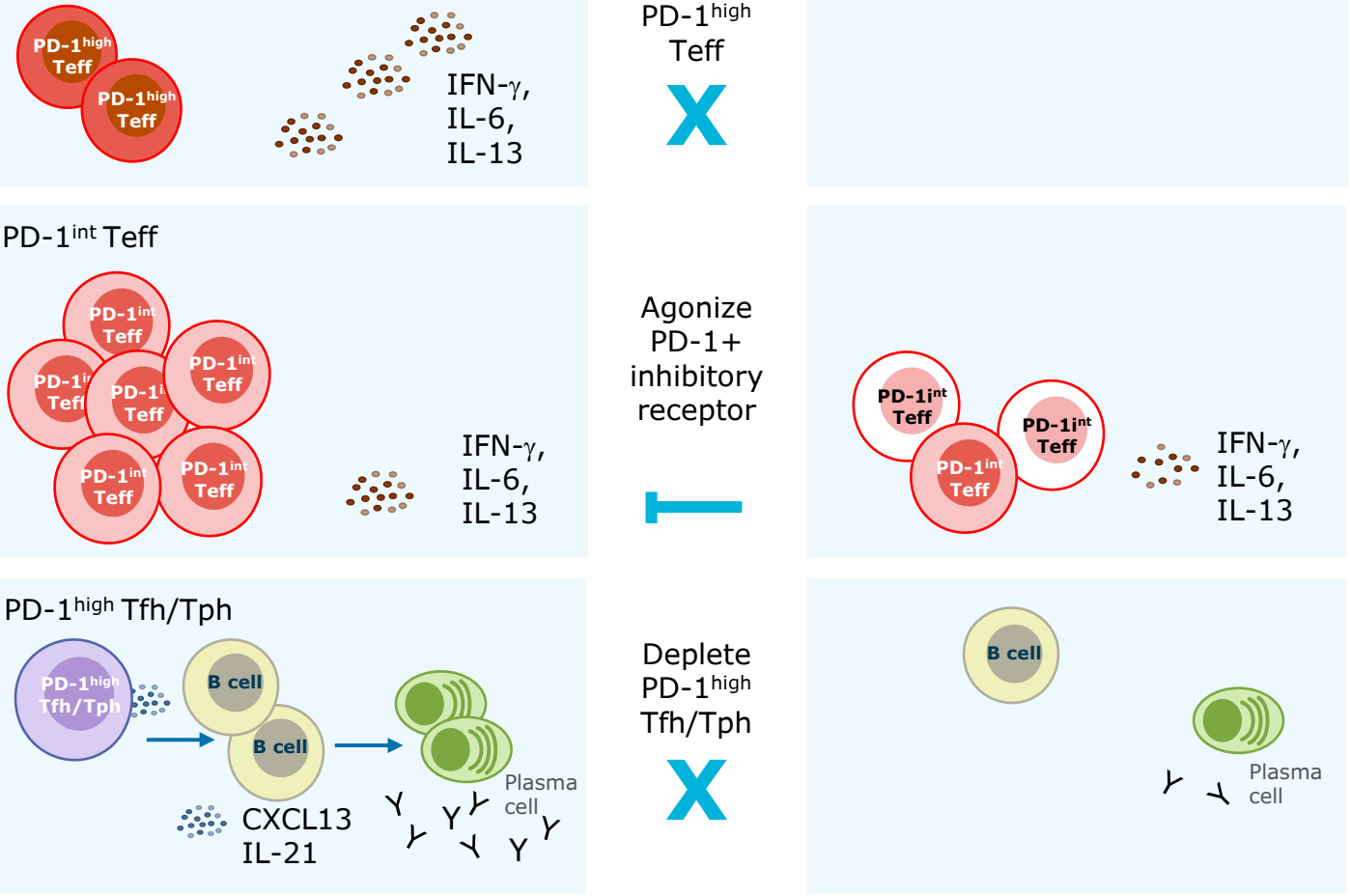


Lymphoid tissues → **Periphery** → **Inflamed tissue**

Adapted from Akiyama et al, Ann Rheum Dis, 2023.

Rosnilimab depletes and agonizes PD-1+ T cells targeting multiple drivers of disease pathogenesis

Pathogenic driver	MoA	Impact on T cells	Immunologic Outcome
PD-1^{high} Teff	Deplete PD-1^{high} Teff		**Reduce** T cell migration, proliferation and cytokine secretion
PD-1^{int} Teff	Agonize PD-1+ inhibitory receptor		
PD-1^{high} Tfh/Tph	Deplete PD-1^{high} Tfh/Tph		**Reduce** plasma cell generation and autoantibody levels



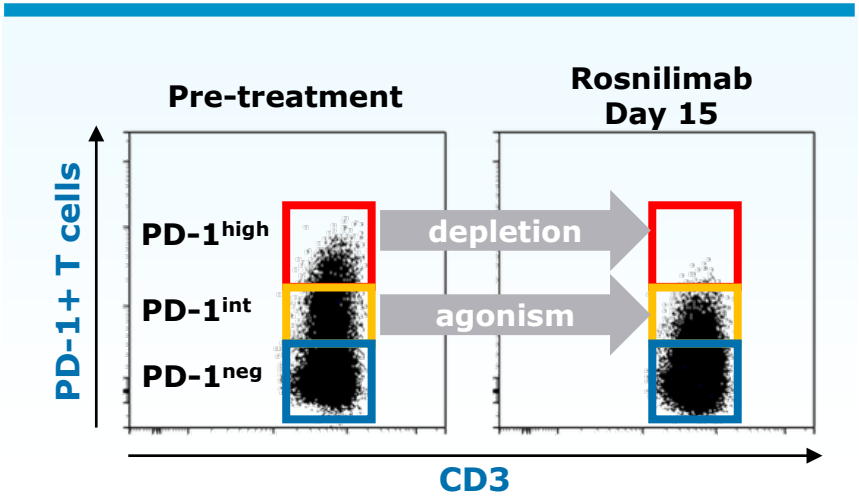
Rosnilimab restores immune balance bringing T cell composition to a less activated state

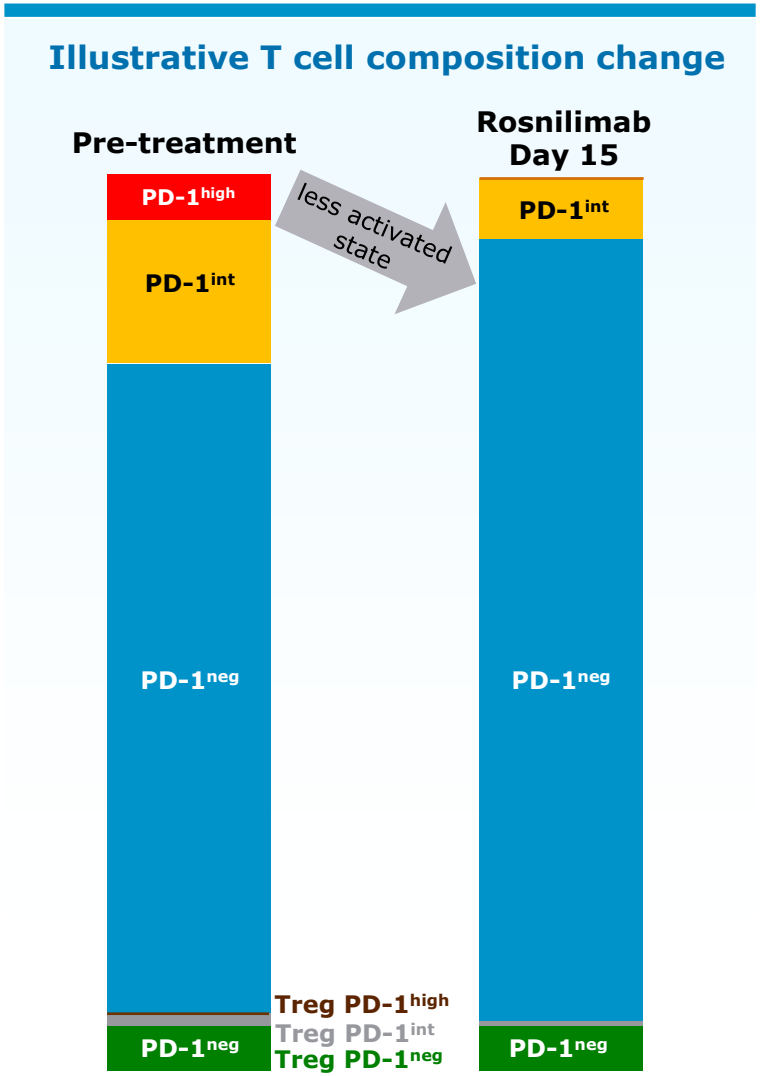
PD-1 expression on both CD4 and CD8 T cells correlates with activation state

Rosnilimab targets only a small proportion of T cells

In healthy volunteers:

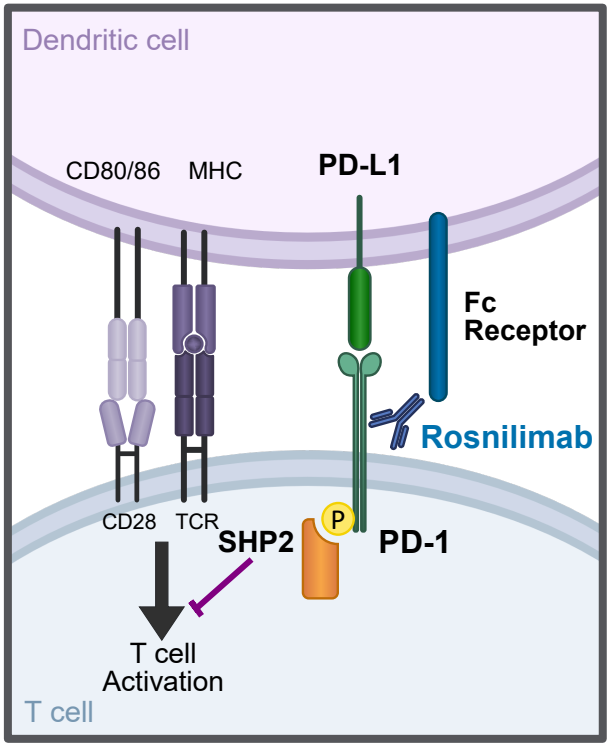
- Deplete PD-1^{high} T cells: ~5-8% of total T cells
- Agonize remaining PD-1^{int} T cells: ~15% of total T cells



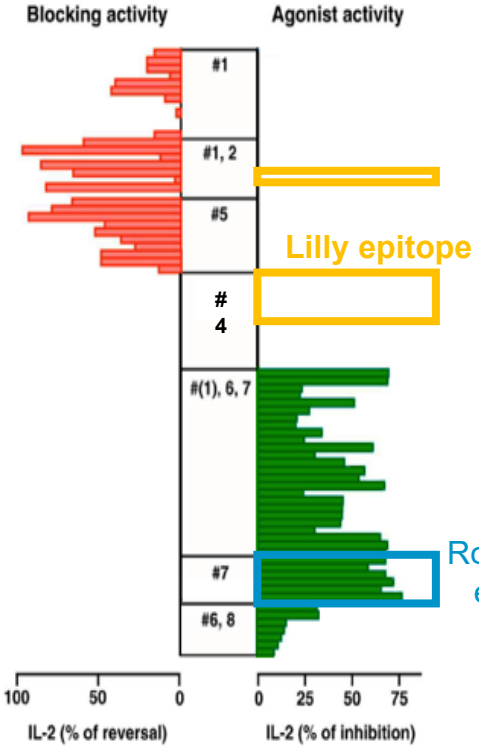


Data illustrative, based on Phase 1 data from healthy volunteer study. Data on file with Anaptys.

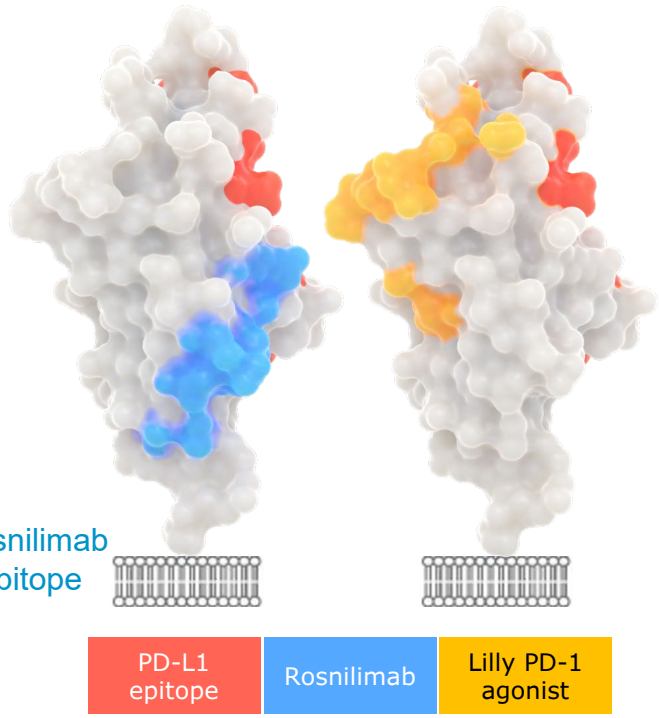
Rosnilimab optimizes PD-1+ T cell inhibitory signaling by enabling tight immune synapse formation



Functional assay of antagonism or agonism[1]



Rosnilimab **Lilly PD-1 agonist**



"A shared feature of agonist mAbs is recognition of the membrane-proximal extracellular region…" and "…activity depends on Fc receptor–supported crosslinking"

Suzuki, et al. 2023

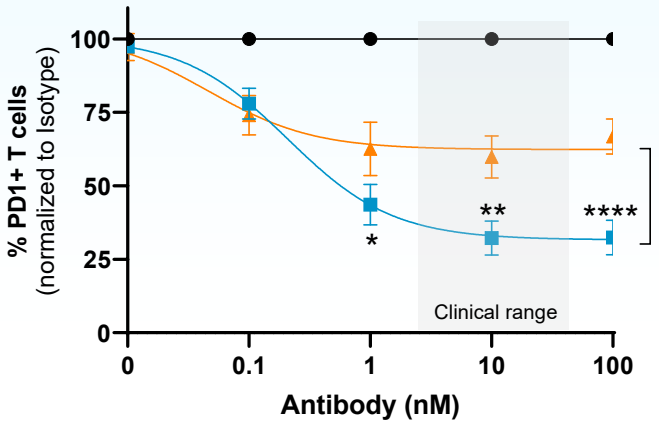
1.Adapted from Suzuki et al., Sci. Immunol. 8, eadd4947 (2023).

Rosnilimab's membrane-proximal binding epitope results in best-in-class potency vs. Lilly's PD-1 agonist

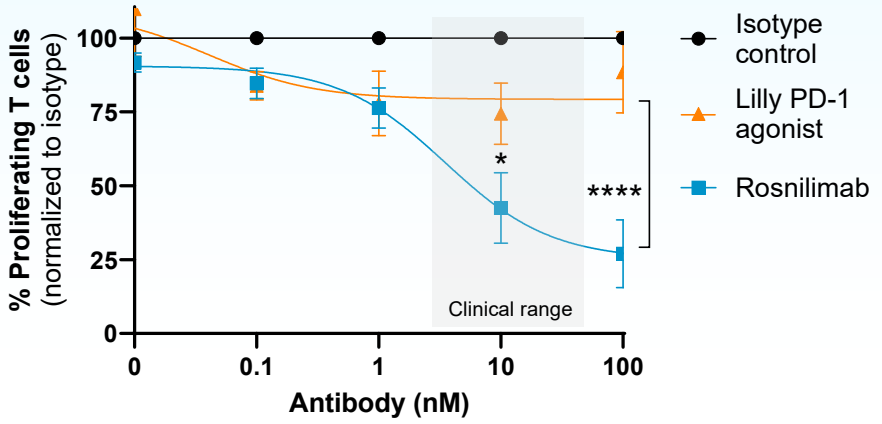
		Rosnilimab (IgG1k Fc)	Lilly (IgG1k Fc)
Structural characteristics	Membrane-proximal epitope	✓	✗
	PD-1 binding properties	✓	✓
	Fc receptor binding affinity	✓	✓
Functional outputs	Depletion ($PD\text{-}1^{high}$)	✓	Decreased
	Agonism ($PD\text{-}1^{int}$)	✓	Decreased

Rosnilimab demonstrates potent depletion and agonism at clinically relevant concentrations

Depletion (NK cell-mediated ADCC)[1]



Agonism (DCs + total T cells; no ADCC)[2]



[1] Healthy donor T cells + NK cells (1:5 ratio) + antibody in in-vitro ADCC assay, representative data from N=5 donors.

[2] Healthy donor purified DCs + autologous total T cells stimulated with anti-CD3, cultured for 3 days for assessment of T cell proliferation Two-way ANOVA. Tukey's multiple comparison test. ****P<0.0001, ***p<0.001, **p<0.01, *p<0.05.

Rosnilimab is optimized for two MOAs: depletion and agonism of PD-1+ T cells in both inflamed tissue and periphery

PD-1 expressed preferentially on activated Teff and Tfh/Tph cells mediating autoimmune and inflammatory pathology

Rosnilimab restores immune balance bringing T cell composition to a less activated state

Rosnilimab's membrane-proximal binding epitope and Fc receptor binding affinity enables formation of a tight immune synapse resulting in best-in-class potency

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RA Treatment Landscape 2023

JONATHAN GRAF, M.D.

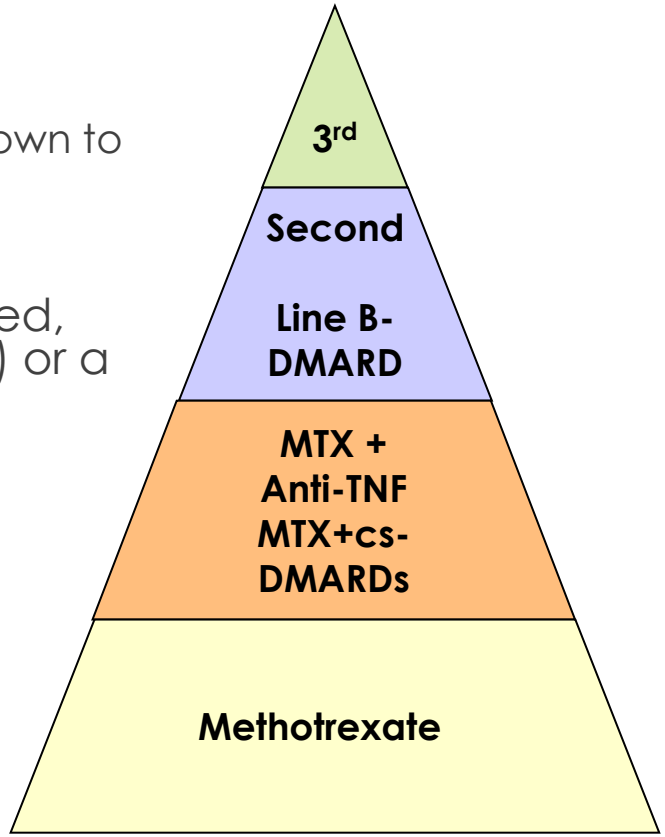
PROFESSOR OF MEDICINE, UCSF

DIRECTOR, UCSF RA COHORT

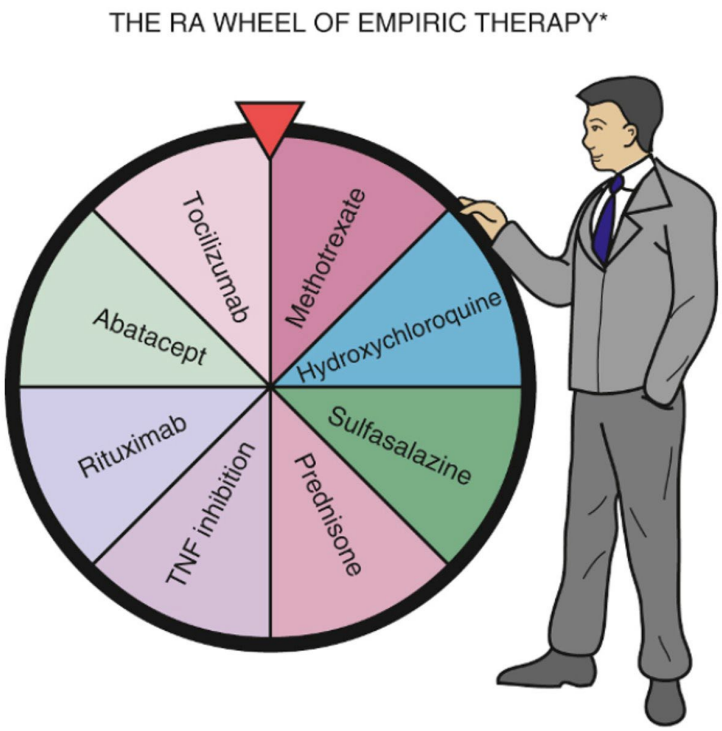
DIVISION OF RHEUMATOLOGY, ZUCKERBERG SAN FRANCISCO GENERAL

Treat to target approach for early RA: 2023

- Start methotrexate
  - Initiate long term therapy with an agent shown to retard radiographic progression
- If low disease activity target is not achieved, add an b-DMARD (usually anti-TNF agent) or a combination of cs-DMARDs
- If disease remains active, ascend the pyramid of therapies until at disease activity target
- Even with T2T strategy, goal of remission is achieved in less than 60% of RA patients



Choice of RA therapy: Not always obvious



RA is a heterogeneous disease

No standard biomarker to predict which therapy best for which patient

RA therapeutic landscape is often riddled with trial and error

Costly in terms of money, toxicity and delay in reaching T2T goals

(Courtesy James O'Dell, MD)

Rheumatoid Arthritis: The ideal treatment landscape

Cs-DMARDs:
MTX; LEFL

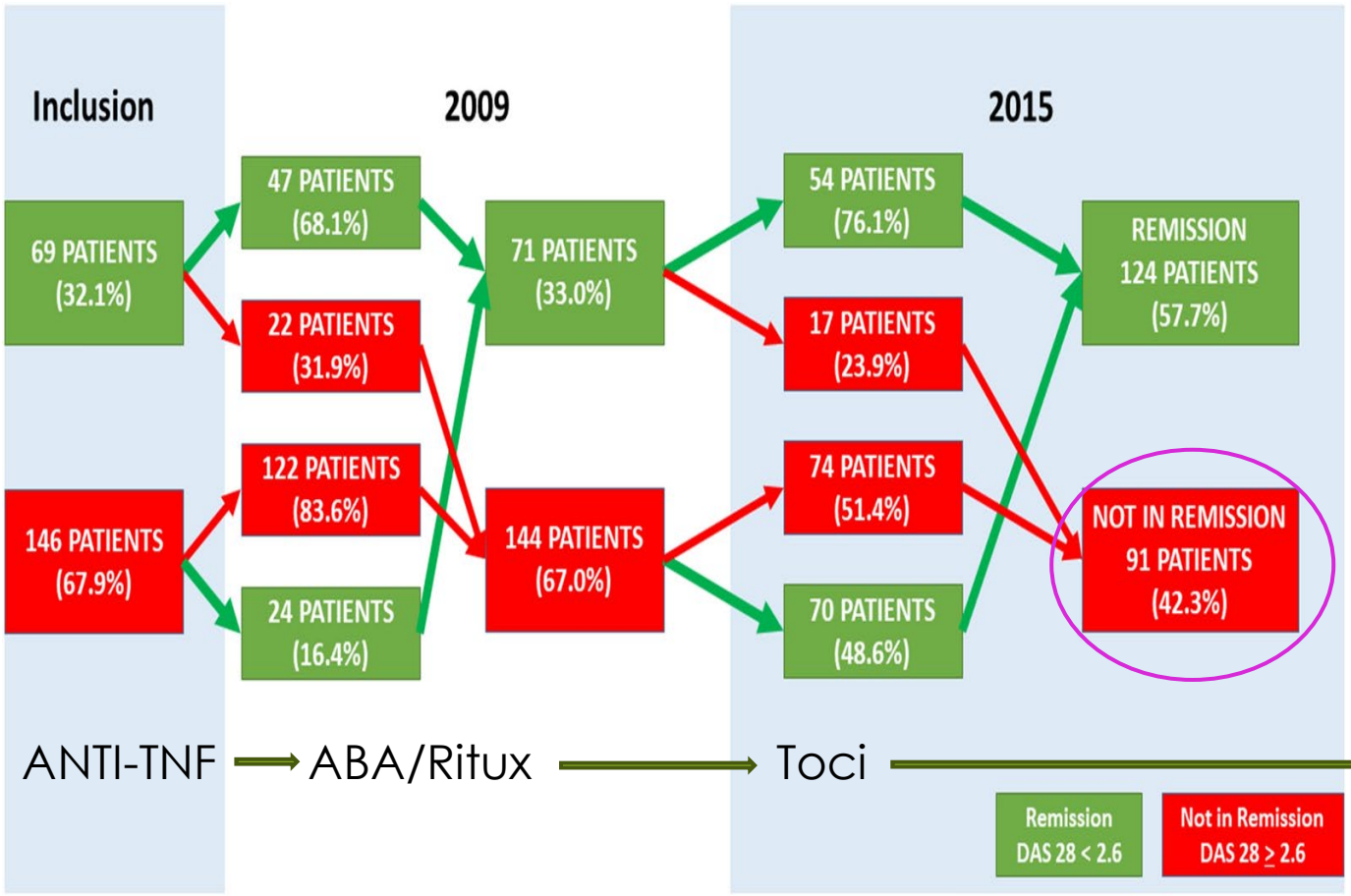
B-DMARDs:
Anti-TNFs
T-cell co-stim blockade
Anti-IL6R

B-DMARDs:
B-cell depleting therapies

Ts-DMARDs:
JAKibs

Actual treatment landscape: State of RA treatment in real-world cohort: Poitiers, France 2007-2015

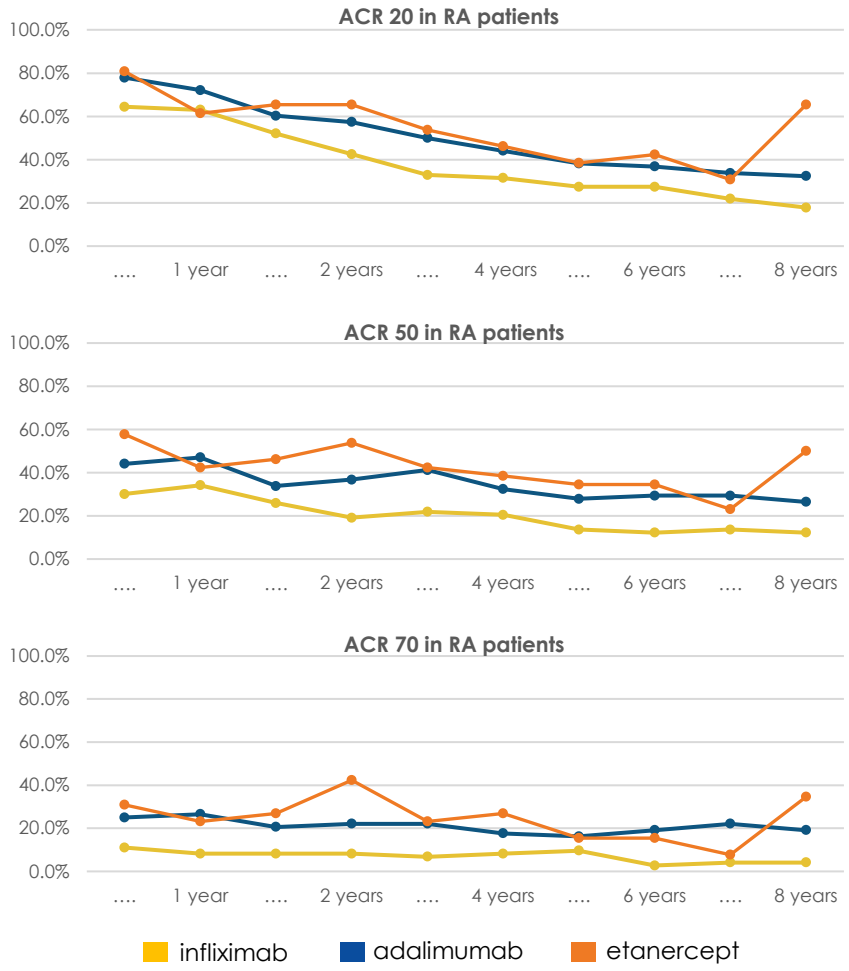
Larid et al.. Sci Rep 12, 2563 (2022).

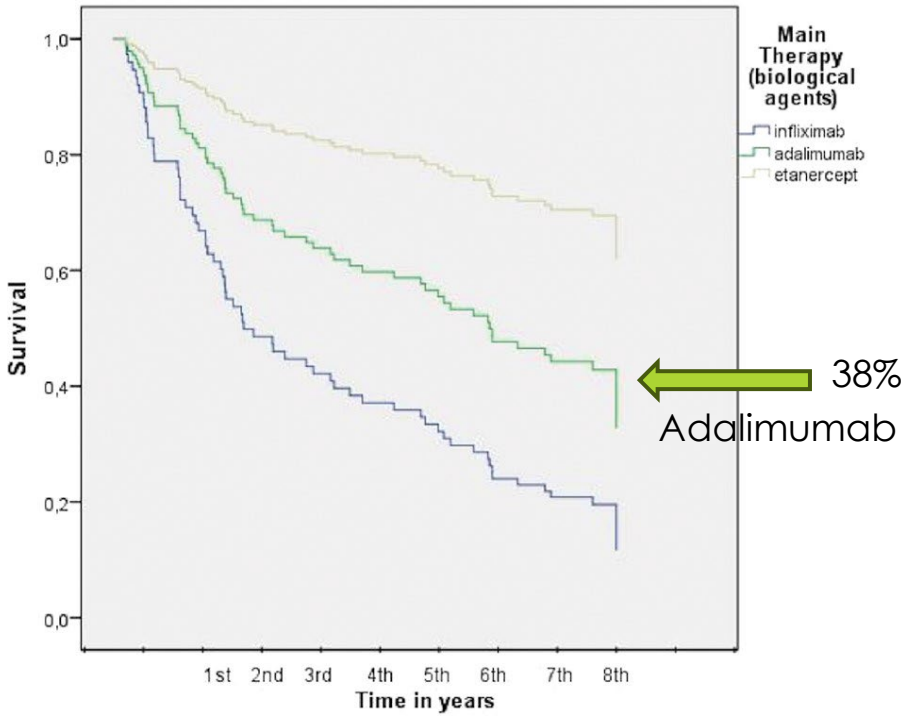


Objective: to evaluate the remission rate and the maintenance of remission in patients with RA after 7-years follow-up in "real life" conditions, during a period encompassing T2T emergence.

Real world 8-year survival rates: Anti-TNF therapy 2000-2015

Papadopoulos et al. Rheumatology Advances in Practice, Volume 3, Issue 1, 2019



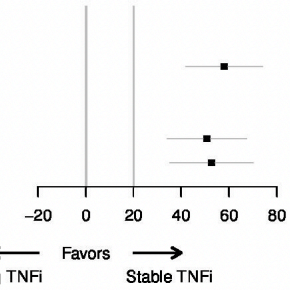


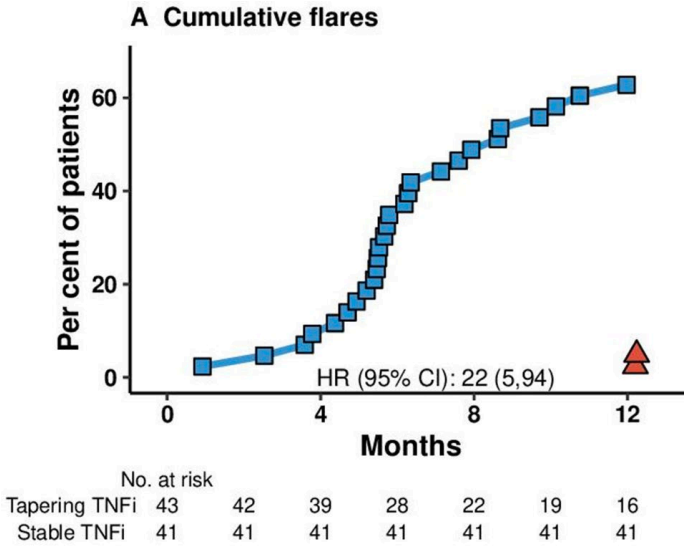
Real world is not a clinical trial: RA is a life-long disease

Current B-DMARDs do not cure RA: *Attempting to taper TNFis: The* ARCTIC REWIND TNFi Trial

Lillegraven S, et al. Ann Rheum Dis 2023;0:1–10. doi:10.1136/ard-2023-224476

	Tapering TNFi	Stable TNFi	Risk difference (95% CI)
Primary analysis[a]	27/43 (63%)	2/41 (5%)	58% (42%,74%)
Additional analyses of primary outcome			
Randomised and initiated therapy[b]	28/47 (60%)	4/45 (9%)	51% (34%,67%)
csDMARD comedication[c]	22/38 (58%)	2/38 (5%)	53% (35%,70%)





Rheumatoid arthritis

OPEN ACCESS

CLINICAL SCIENCE

Effect of tapered versus stable treatment with tumour necrosis factor inhibitors on disease flares in patients with rheumatoid arthritis in remission: a randomised, open label, non-inferiority trial

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Handling editor Josef S Smolen

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/ard-2023-224476).

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Check for updates

ABSTRACT

Objectives Many patients with rheumatoid arthritis (RA) require treatment with tumour necrosis factor inhibitor (TNFi) to reach remission. It is debated whether tapering of TNFi to discontinuation should be considered in sustained remission. The aim of ARCTIC REWIND TNFi was to assess the effect of tapering TNFi to withdrawal compared with stable treatment on the risk of disease activity flares in patients with RA in remission ≥1 year.

Methods This randomised, open-label, non-inferiority trial was undertaken at nine Norwegian rheumatology departments. Patients with RA in remission ≥12 months on stable TNFi therapy were allocated by computer-based block-randomisation to tapering to discontinuation of TNFi or stable TNFi. Conventional synthetic disease-modifying antirheumatic co-medication was unchanged. The primary endpoint was disease flare during the 12-month study period (non-inferiority margin 20%), assessed in the per-protocol population.

Results Between June 2013 and January 2019, 99 patients were enrolled and 92 received the allocated treatment strategy. Eighty-four patients were included in the per-protocol population. In the tapering TNFi group, 27/43 (63%) experienced a flare during 12 months, compared with 2/41 (5%) in the stable TNFi group; risk difference (95% CI) 58% (42% to 74%). The tapering strategy was not non-inferior to continued stable treatment. The number of total/serious adverse events was 49/3 in the tapering group, 57/2 in the stable group.

Conclusion In patients with RA in remission for more than 1 year while using TNFi, an increase in flare rate was reported in those who tapered TNFi to discontinuation. However, most regained remission after reinstatement of full-dose treatment.

Trial registration numbers EudraCT: 2012-005275-14 and clinicaltrials.gov: NCT01881308.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The treatment goal for most patients with rheumatoid arthritis (RA) is to reach and sustain remission, with prevention of structural joint damage and disability.
⇒ Several studies have assessed tapering or stopping of tumour necrosis factor inhibitor (TNFi) in patients with RA in low disease activity or who fulfil remission criteria based on Disease Activity Score calculated with 28 joints.
⇒ There are less data available for the clinically relevant group of patients who have been in prolonged remission and who do not show clinical signs of synovitis.

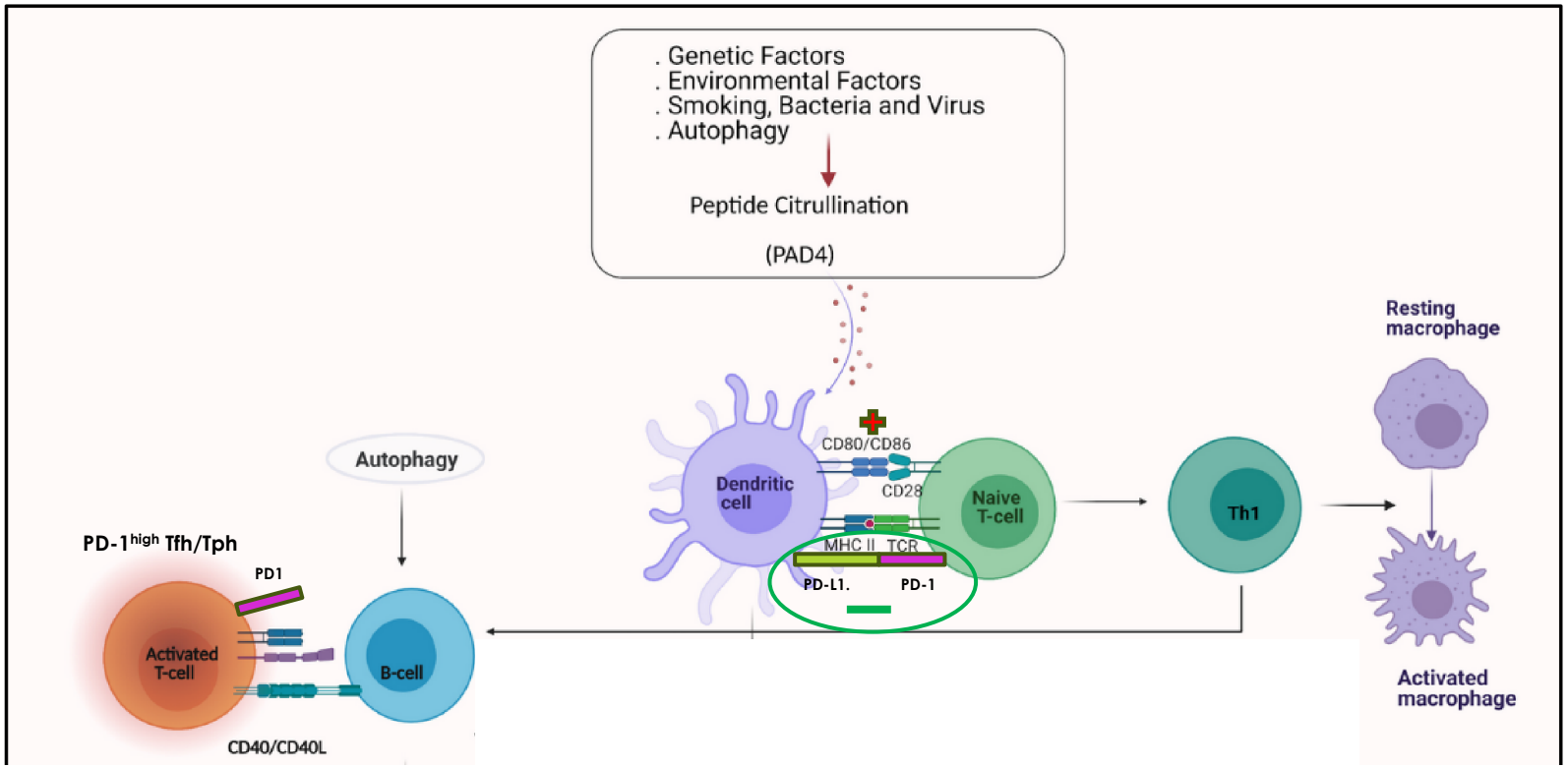
WHAT THIS STUDY ADDS

⇒ The ARCTIC REWIND Trial was conducted in patients with RA where remission had been sustained for at least 1 year on stable medication, and the patient had no swollen joints at inclusion.
⇒ Despite the stringent inclusion criteria, there was a large increase in frequency of disease activity flares in patients tapering TNFi to discontinuation versus continuation of stable TNFi dose.
⇒ The response to reinstatement of the initial TNFi dose was mostly good without any difference in radiographic joint damage progression.

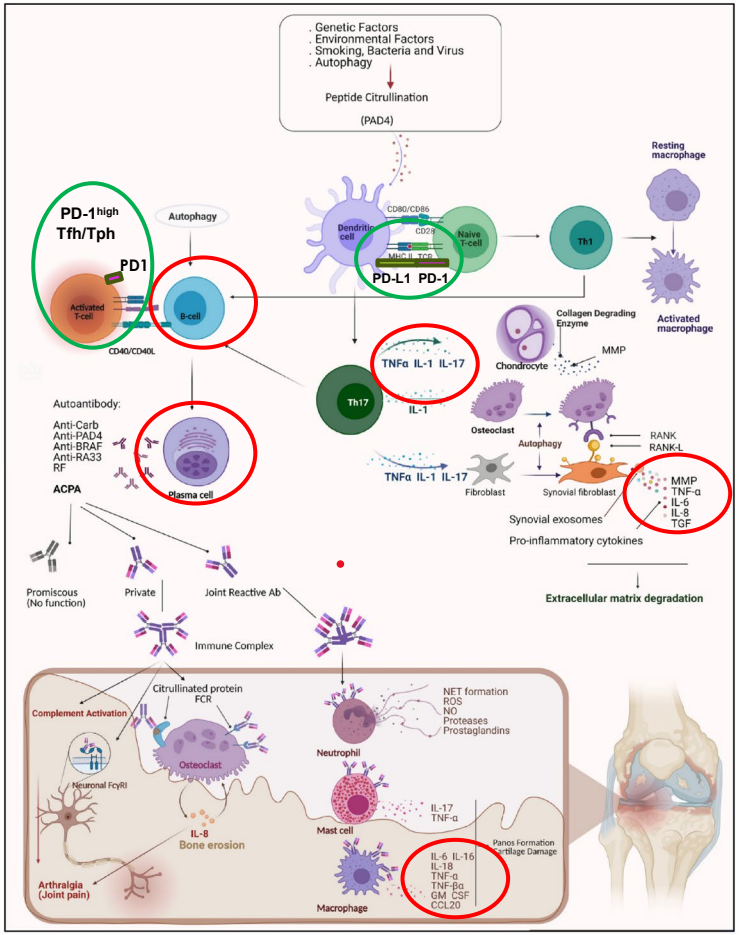
been in long-term remission using these medications has not been established.[1–4]

According to current recommendations, patients with RA will be treated with methotrexate monotherapy after disease onset. In cases of insufficient

PD-L1 is a central nodal point regulating T cell activity



Resetting the immunologic thermostat: Potential to down-regulate multiple pathways



Known targets of current therapeutics

TNF-a
IL-1

IL-6

B-cell activation
Plasma cell development

Other cytokines (GM-CSF) that use JAK-STAT signaling pathways

PD-1 agonist class has shown compelling POC

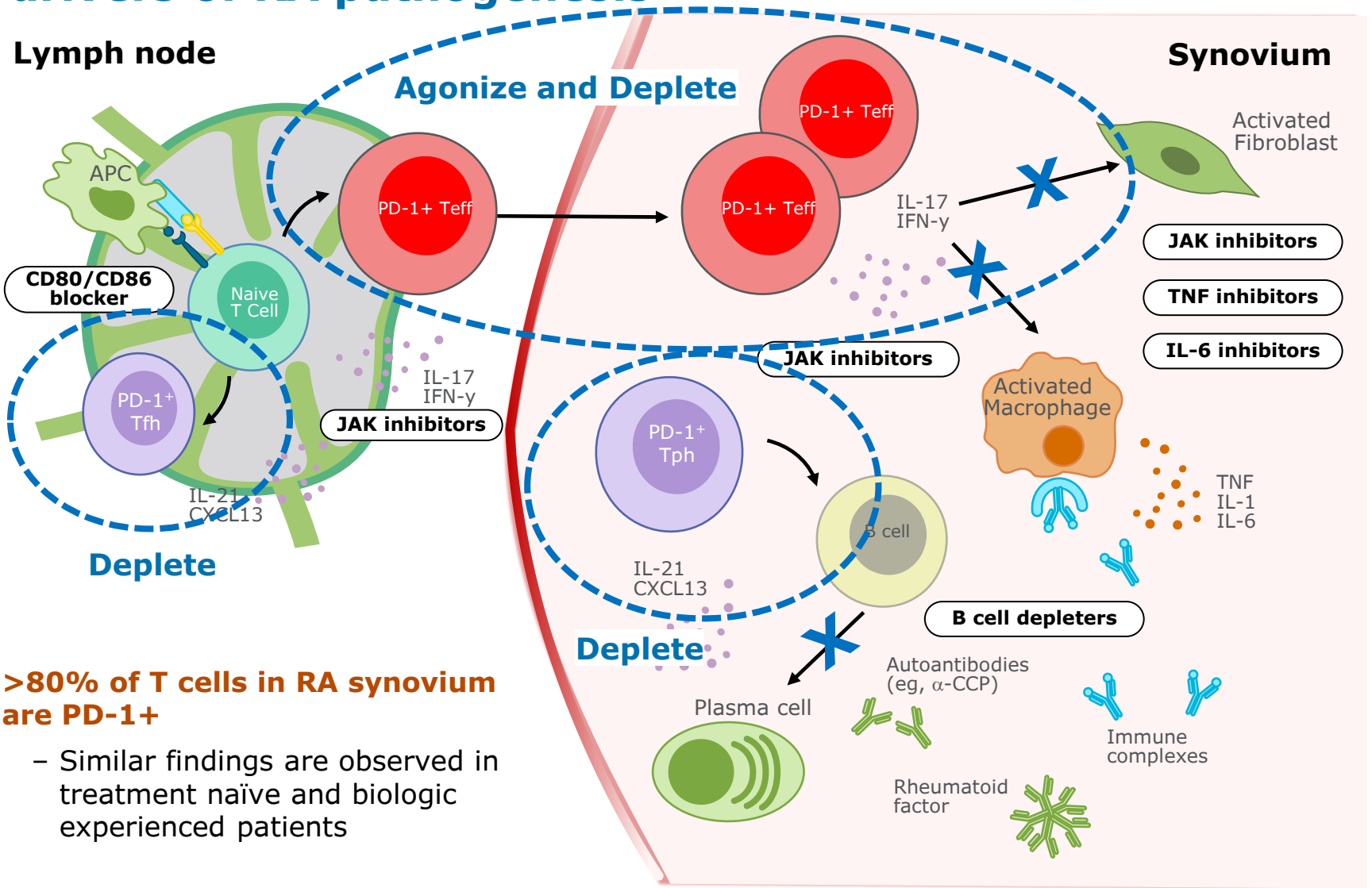
What are the unmet needs in RA?

- Sizeable number of patients not at RA disease activity targets
  - Especially targets that achieve remission (or better)
- Need to reset the immune system environment so that:
  - Treatment efficacy doesn't wane
  - Therapy will work in ALL RA patients regardless of disease heterogeneity
- Analogy: Think about the environment in which one lives
  - Phoenix: Keep the air conditioning running all summer to keep house cool. But if air-conditioning stops working, you're in trouble.
  - Move to San Diego: the climate outside controls the climate inside. Electricity bills will be much less because you won't need air conditioning.

Agenda

TOPIC	SPEAKER
Rosnilimab: a best-in-class PD-1 agonist	Dan Faga Chief Executive Officer
MOA and differentiation	Martin Dahl, Ph.D. Senior Vice President, Research
Rosnilimab in RA	
Unmet patient needs and opportunity for PD-1 agonists	Jonathan Graf, M.D. Professor, Medicine University of California, San Francisco
Targeting RA with rosnilimab and translational data	**Cailin Sibley, M.D., MHS, FACR** **Vice President, Translational Medicine**
Rosnilimab in UC	
Unmet patient needs, disease biology, and rationale for PD-1 agonist in UC	Bruce Sands, M.D., M.S. Professor and Chief, Gastroenterology Icahn School of Medicine, Mount Sinai
Targeting UC with rosnilimab and translational data	Martin Dahl, Ph.D.
PD-1 safety data and Phase 2 development plans in RA and UC	Paul Lizzul, M.D., Ph.D. Chief Medical Officer
Market opportunity and closing remarks	Dan Faga
Q&A	AnaptysBio

PD-1+ T cells broadly impact multiple clinically validated drivers of RA pathogenesis



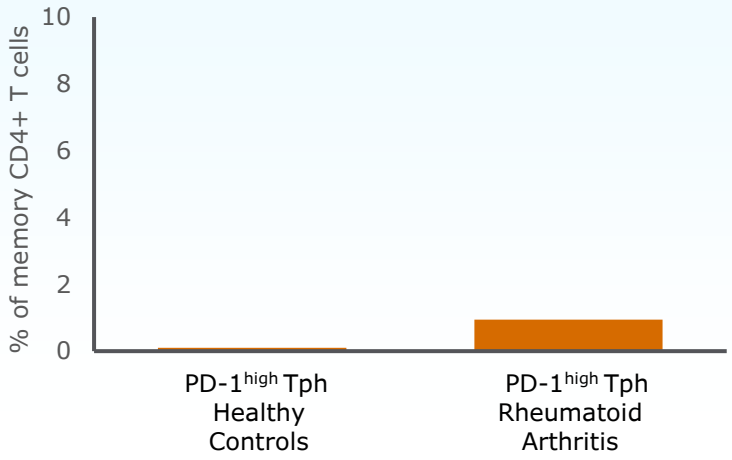
>80% of T cells in RA synovium are PD-1+

- Similar findings are observed in treatment naïve and biologic experienced patients

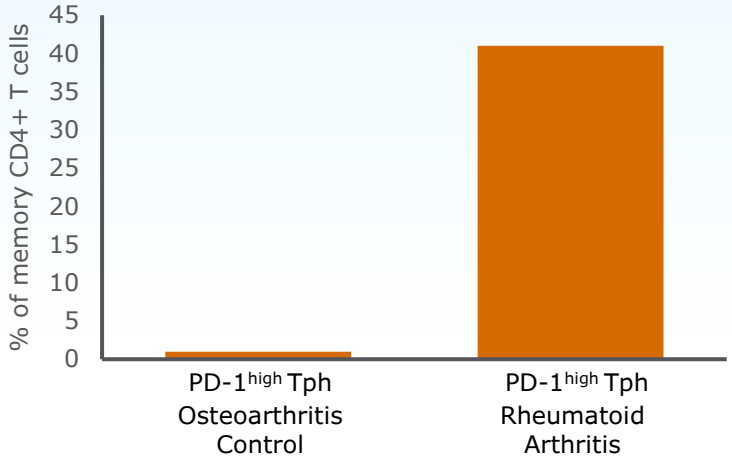
Adapted from Aletaha and Smolen, JAMA, 2018

PD-1^{high} Tph cells are elevated in RA synovium and secrete cytokines driving autoantibody production

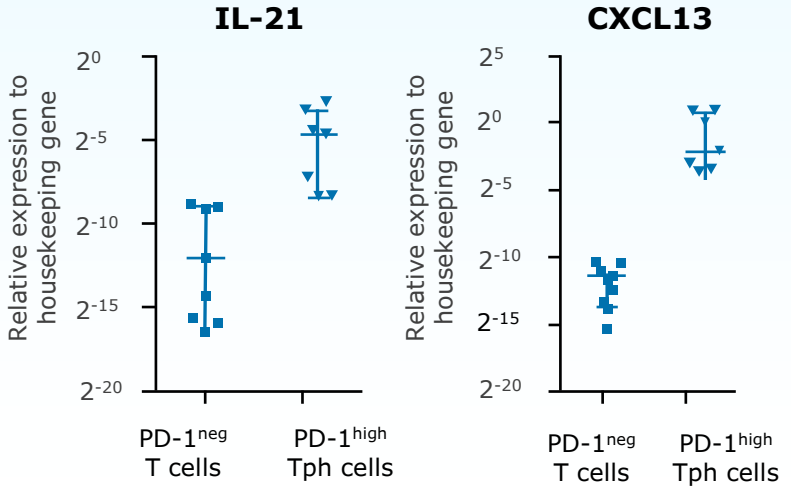
Peripheral blood[1]



Synovium[1]



Cytokine gene expression from synovial cells[2]



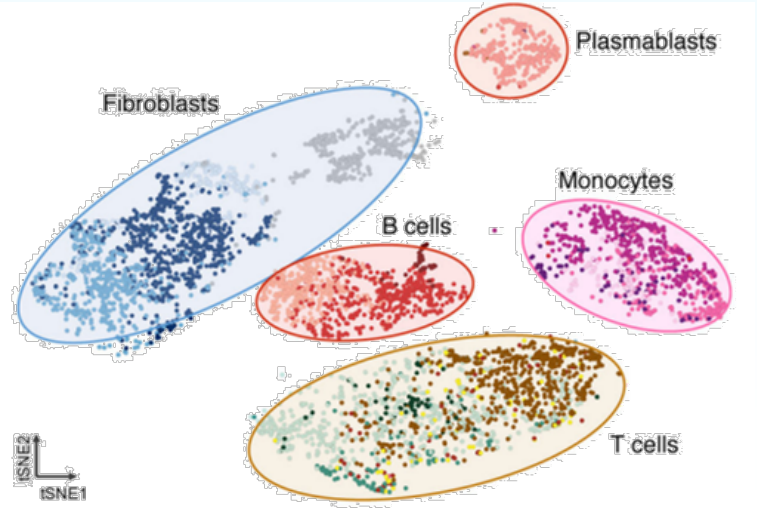
Reduction of plasma cell generation results in reduced autoantibody levels which contribute to synovial inflammation and damage

1. Adapted from Murray-Brown et al, RMC Open, 2022. 2.Adapted from Rao et al, Nature, 2017, p<0.001. RT-PCR data gene from isolated and sorted RA synovial cells normalized to RPL13A housekeeping gene

PD-1 agonism overcomes synovial heterogeneity challenges given broad overlap with key disease subtypes

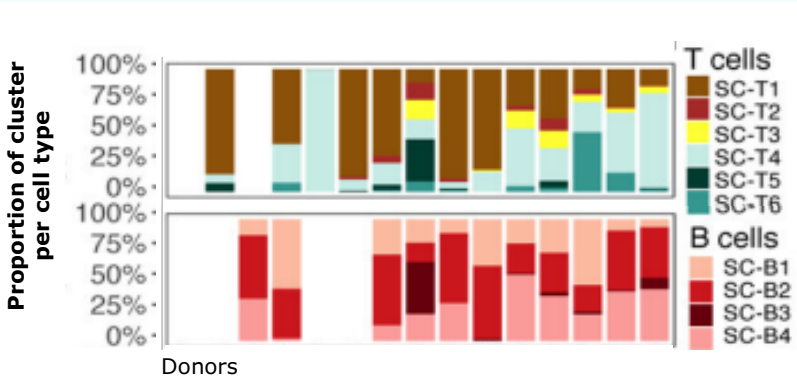
RA immune cells cluster into 18 different subtypes

Single cell RNA-Seq data from synovium



Individual patients differ in their composition of each cellular cluster

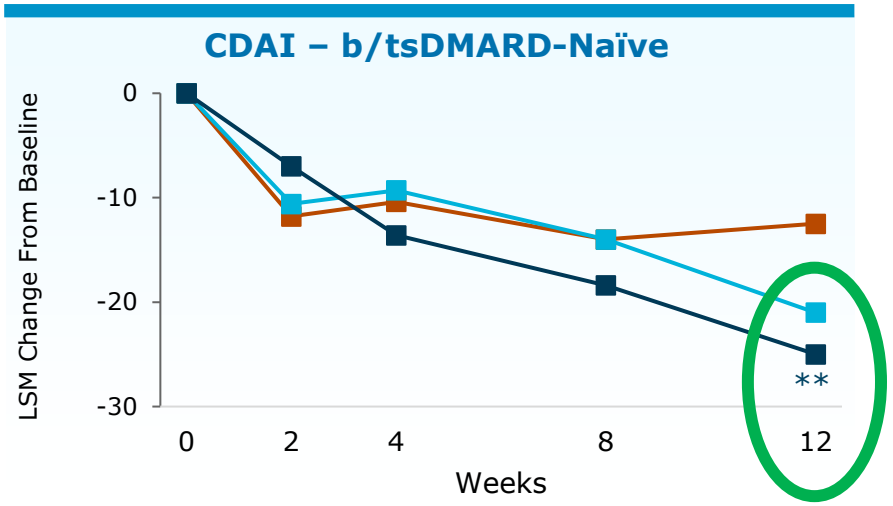
Leukocyte-rich RA

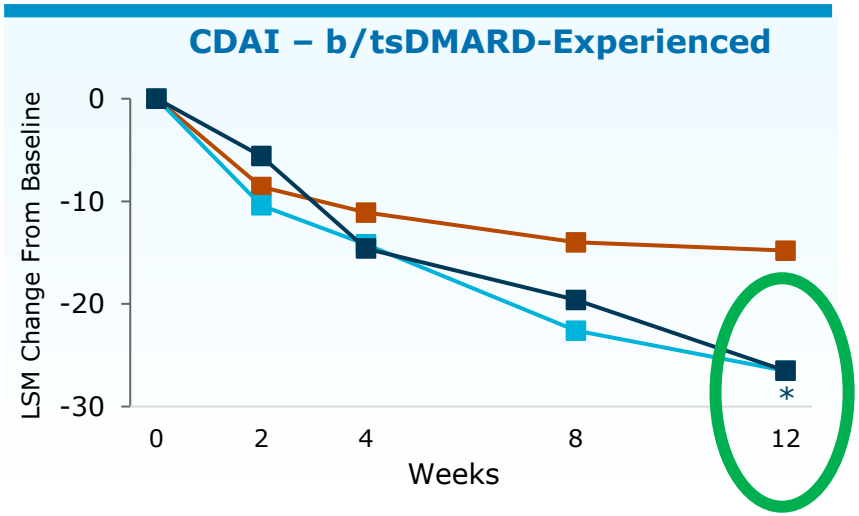


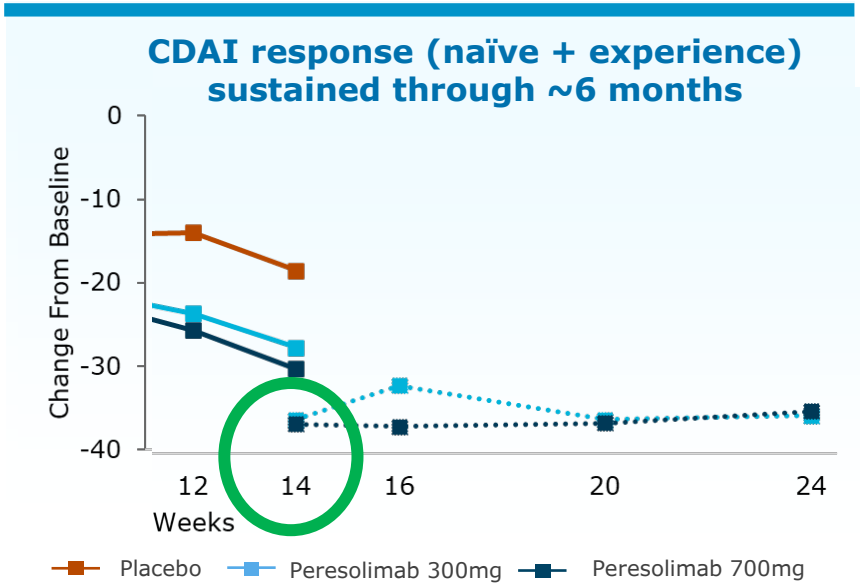
Therapeutics with more narrow mechanisms of action would not target most disease subtypes

From Accelerated Medicines Partnership (AMP) Consortium, Nat Immunol, 2019.

PD-1 agonist class is clinically validated in RA with compelling proof of mechanism







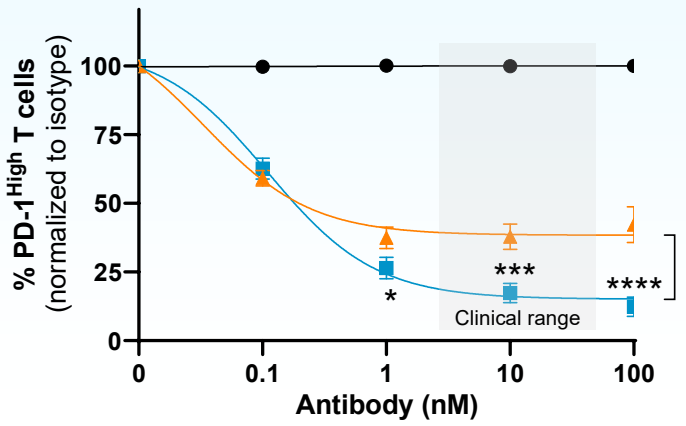
PD-1 agonist emerging profile: Peresolimab 98 patient placebo-controlled P2a study

- No safety signal
- Consistent efficacy across biologic-naïve and biologic-experienced patients
- Week 14 efficacy sustained through 6 months

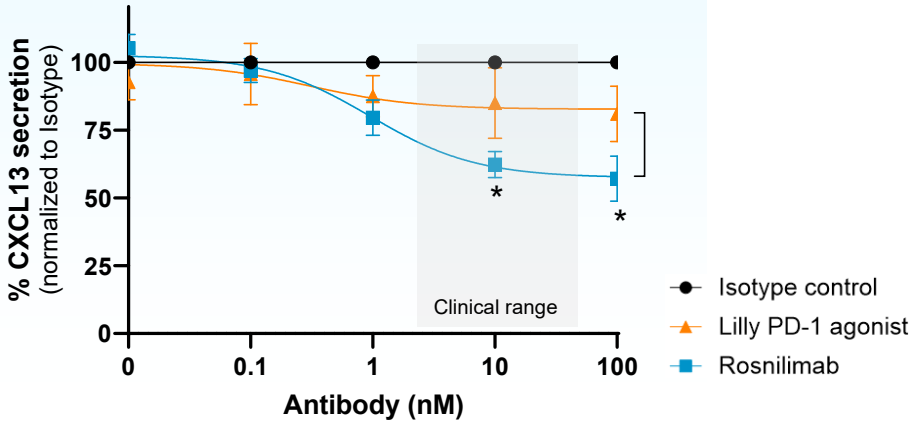
Tuttle, J. EULAR 2023, Week 14-Week 24 data estimated from peresolimab (PD-1 agonist) 2022 ACR presentation; CDAI=Clinical disease activity index. Sample size for top two charts: placebo n=24; peresolimab 300mg n=25 and peresolimab 700mg n=49. In bottom graph, placebo n=11, peresolimab 300mg n=12 and peresolimab 700mg n=18.

Rosnilimab's potent depletion and agonism reduces T cell proliferation and inflammatory cytokines that cause joint damage

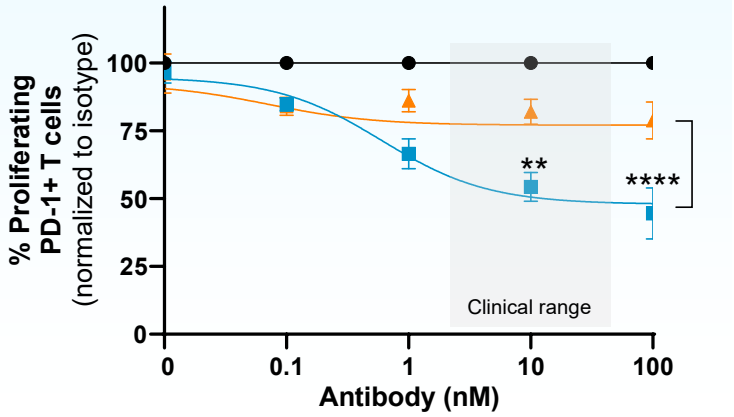
Depletion of PD-1^{high} T cells



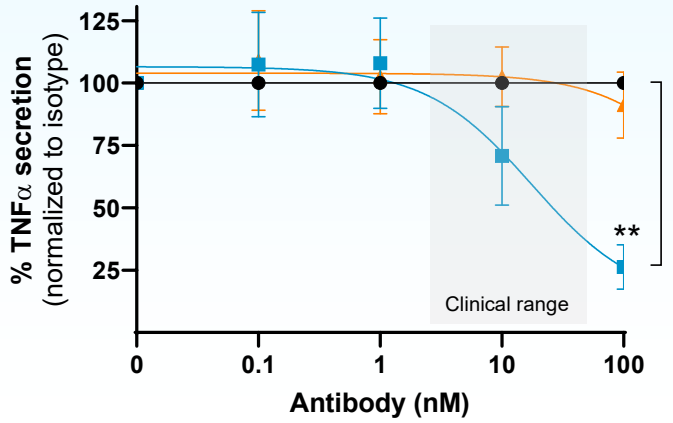
Inhibition of Tfh/Tph chemokine



Inhibition of T cell proliferation



Inhibition of inflammatory cytokine[1]



Anti-CD3+ anti-CD28 stimulation of RA patient PBMCs for assessment of depletion and agonism MOA, representative data from N=8 donors
Two-way ANOVA, Tukey's multiple comparison test. ****P<0.0001, ***p<0.001, **p<0.01, *p<0.05.

[1]TNFα secretion measured in anti-CD3+ anti-CD28 stimulation of purified DC+T cells from N=4 healthy donors.

Rosnilimab depletes and agonizes PD-1+ T cells broadly impacting multiple drivers of RA pathogenesis

PD-1 agonism overcomes synovial heterogeneity challenges given broad overlap with key disease subtypes

>80% of T cells in RA synovium are PD-1+, including PD-1^{high} Tph cells which secrete cytokines driving autoantibody production

PD-1 agonist class is clinically validated in RA with consistent efficacy across biologic-naïve and biologic-experienced patients sustained over 6 months

Preclinical data support rosnilimab's potent immunologic outcomes

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Ulcerative Colitis:
Disease pathogenesis, treatment landscape, unmet need

Bruce E. Sands, MD, MS
Chief of the Dr. Henry D. Janowitz Division of Gastroenterology
Dr. Burrill B. Crohn Professor of Medicine
Icahn School of Medicine at Mount Sinai
Mount Sinai Hospital
Mount Sinai Health System
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Disclosure of potential conflicts of interest

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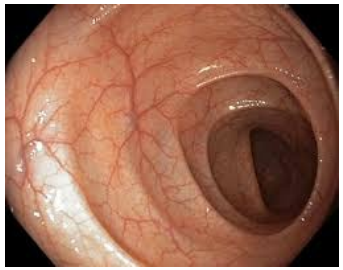
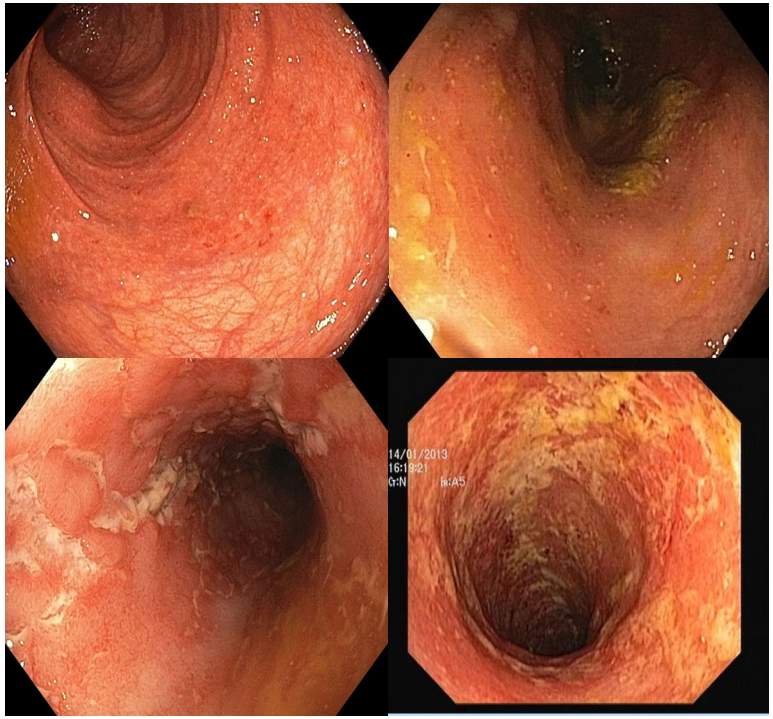
Stock and Stock Options	Ventyx Biosciences

Endoscopy findings of ulcerative colitis



Normal
Colon

Total Mayo Clinic Score =
SF + RB + MES + PGA



Stool Frequency (SF)
0 = Normal for the patient
1 = 1-2 stools/day in addition to the usual
2 = 3-4 stools/day in addition to the usual
3 = >5 stools/day beyond the usual

Rectal Bleeding (RB)
0 = No Blood
1 = Blood streaks in less the half of evacuations
2 = Evidence of fresh blood in most of the evacuations
3 = Bowel movements with fresh blood

Mayo Endoscopic Subscore (MES)
0 = Normal/inactive
1 = Mild disease (erythema, decreased vascular pattern)
2 = Moderate disease (marked erythema, loss of vascular pattern, erosions)
3 = Severe disease (spontaneous bleeding, ulcerations)

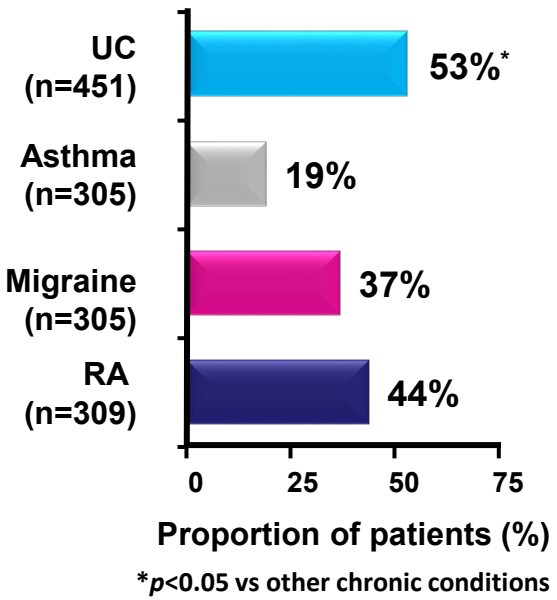
Physician's Global Assessment (PGA)
0 = Normal
1 = Mild disease
2 = Moderate disease
3 = Severe disease

Schroeder et al NEJM 1987
Images courtesy of Dr. Jerome Waye

UC has high impact on patient lives in U.S.

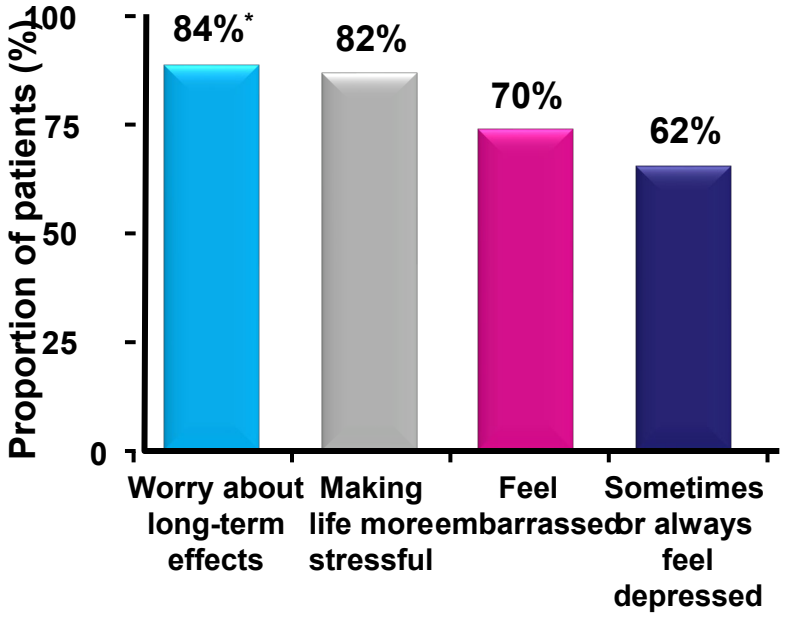
~1.5 million with UC in the U.S.

Proportion of patients who feel their condition was controlling their lives



*$p<0.05$ vs other chronic conditions

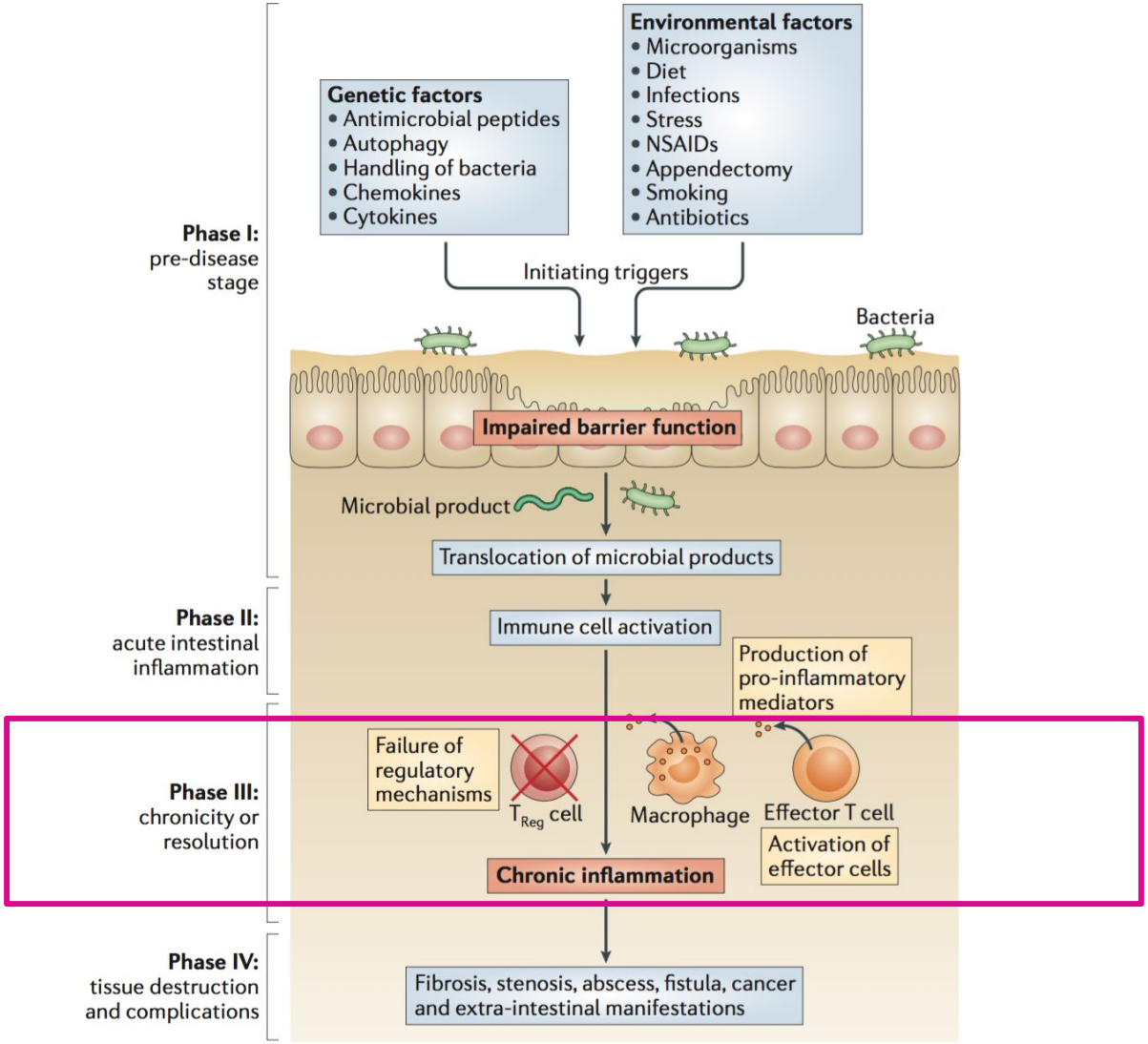
Psychological Impact of UC



Internet survey designed to assess a variety of disease impact indices

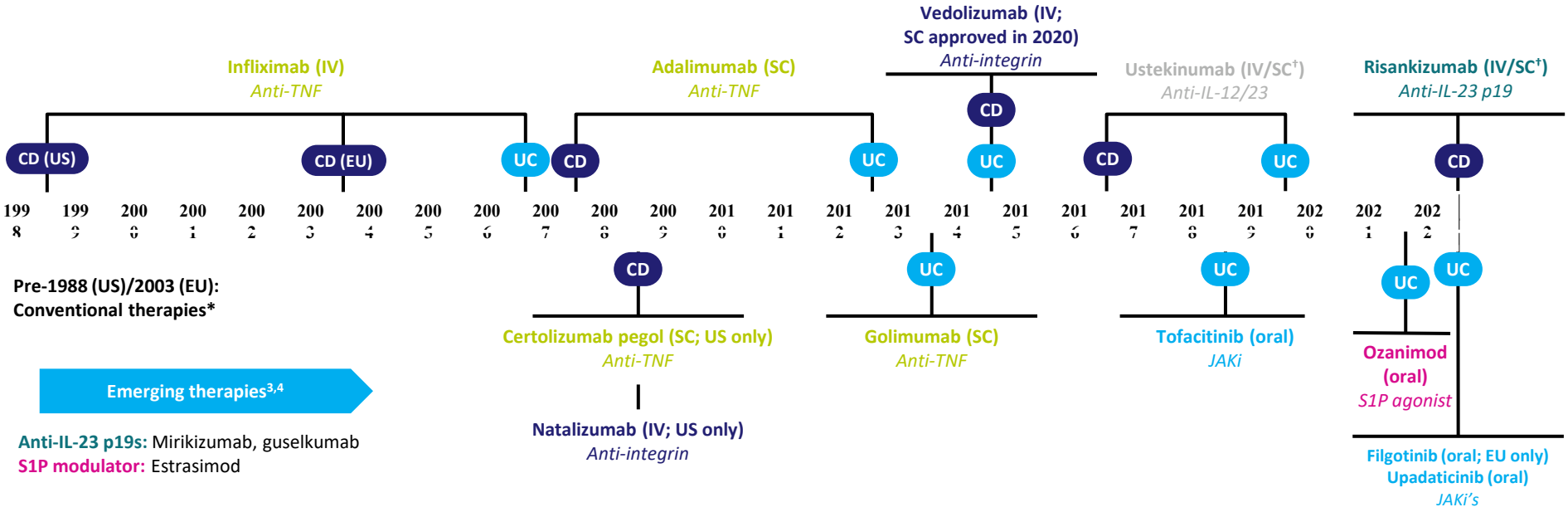
Rubin DT, et al Dig Dis Sci 2010

UC clinical presentation driven by activation of T effector cells, inflammatory cytokines and failure of regulatory mechanisms



Neurath, Nat Rev Immunol 2014

Increased understanding of IBD pathogenesis has led to the emergence of biologics and advanced therapies[1,2]

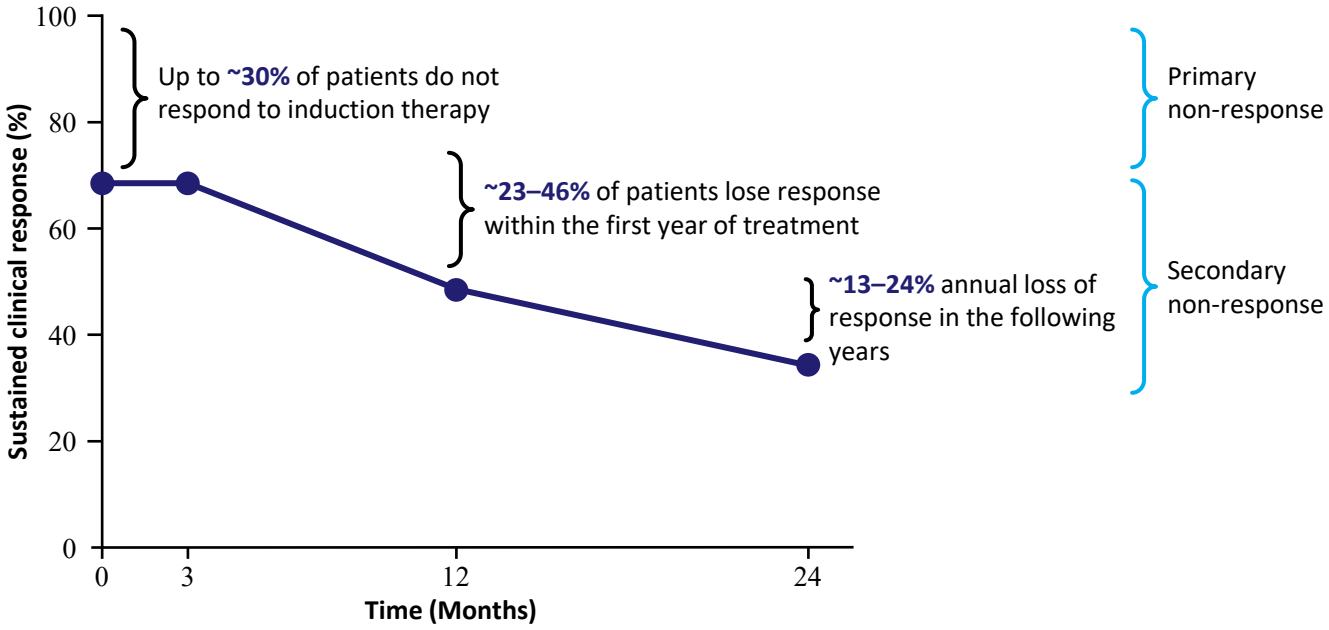


Last updated 16 December 2022. All approval dates reflect US Food and Drug Administration approval and European Medicines Agency/European Commission approval dates, unless otherwise stated.
*Conventional therapies include 5-aminosalicylic acid, steroids (prednisone/budesonide) and immunosuppressants ;†IV induction and SC maintenance
CD, Crohn's disease; IBD, inflammatory bowel disease; IL, interleukin; IV, intravenous; JAKi, janus kinase inhibitor; S1P, sphingosine 1-phosphate; SC, subcutaneous; TNF, tumour necrosis factor; UC, ulcerative colitis

1. Adegbola SO, et al. Int J Mol Sci 2018;19:2244; 2. Juillerat P, et al. Curr Res Pharmacol Drug Discov 2022;3:100104; 3. Vieujean S, et al. United European Gastroenterol J 2022; online ahead of print (doi: 10.1002/ueg2.12305); 4. Grossberg LB, et al. Aliment Pharmacol Ther 2022;55:789–804; see slide notes for references supporting drug approval dates

Anti-TNFs are considered the cornerstone of IBD treatment, including UC, but not all patients respond to treatment and many others lose response over time

Treatment response rates with infliximab and adalimumab in CD[1,2]



Data more limited for UC; however, in Phase 3 trials, primary non-response rates with infliximab were ~30–40%, and more than half of initial responders lost response to treatment in the first year[3]

CD, Crohn's disease; IBD, inflammatory bowel disease; TNF, tumour necrosis factor; UC, ulcerative colitis

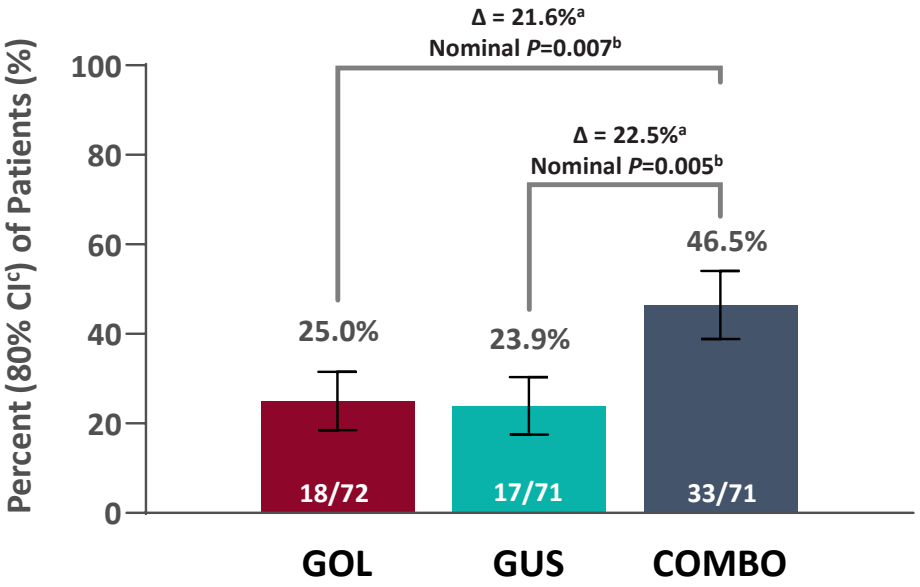
1. Roda G, et al. Clin Transl Gastroenterol 2016;7:e135; 2. Ben-Horin S, Chowers Y. Aliment Pharmacol Ther 2011;33:987–95; 3. Rutgeerts P, et al. N Engl J Med 2005;353:2462–77

Targeting multiple mechanisms provides opportunity to break through efficacy ceiling in moderate to severe UC

VEGA: Golimumab vs Guselkumab vs Combination

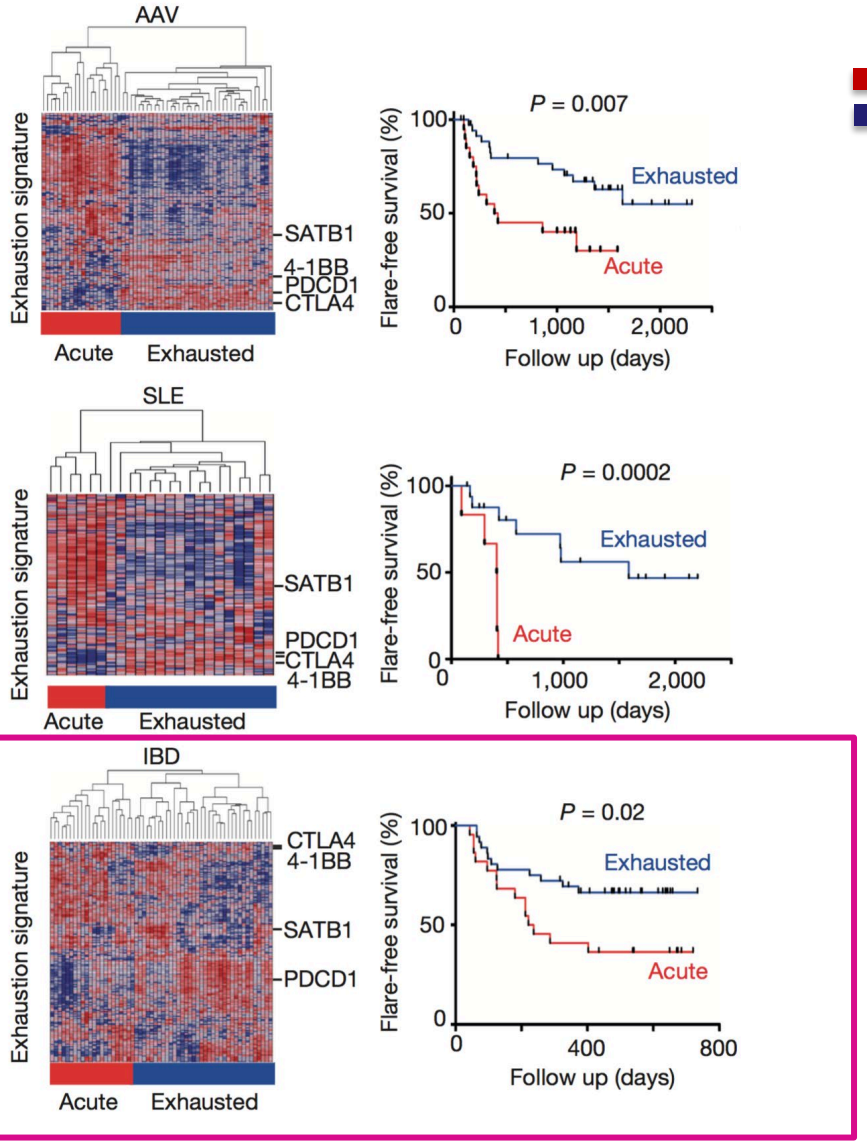
Clinical remission at Week 12

Mayo Stool Frequency Subscore of 0 or 1 and Not Increased from Baseline, a Rectal Bleeding Subscore of 0, and an Endoscopy Subscore of 0 or 1 with No Friability Present on the Endoscopy



Sands BE, et al. European Crohn's & Colitis Organization Congress; Feb 19, 2022; Virtual.

PD-1 mediated T cell exhaustion is associated with reduced flares in numerous autoimmune diseases



Reduced gene expression from baseline
Elevated gene expression from baseline

Exhaustion can be induced through agonism of PD-1 inhibitory receptor

McKinney et al, Nature 2015

Novel subset of T cells (T follicular helper cells) expanded in UC that may direct the B cell response

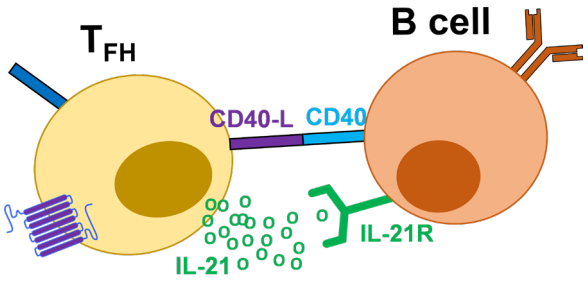
nature medicine
ARTICLES
https://doi.org/10.1038/s41591-022-01680-y
Check for updates

Ulcerative colitis is characterized by a plasmablast-skewed humoral response associated with disease activity

Mathieu Uzzan[1,2,3,26], Jerome C. Martin[2,4,5,26], Luka Mesin[6], Alexandra E. Livanos[1,2], Tomas Castro-Dopico[1,2,7], Ruiqi Huang[8,9], Francesca Petralia[9], Giuliana Magri[10], Shashi Kumar[11], Qing Zhao[12], Adam K. Rosenstein[1,2], Minami Tokuyama[1], Keshav Sharma[1,2], Ryan Ungaro[1], Roman Kosoy[9,13], Divya Jha[1,2], Jeremy Fischer[2], Harpriya Singh[1,2], Mary E. Keir[14], Nandhini Ramamoorthi[14], William E. O' Gorman[15], Benjamin L. Cohen[1], Adeeb Rahman[9,16,17], Francesca Cossarini[2], Akihiro Seki[1,2], Louise Leyre[1,2], Sonia Tejedor Vaquero[10], Sakteesh Gurunathan[1], Emilie K. Grasset[2,18], Bojan Losic[8,13], Marla Dubinsky[1], Alexander J. Greenstein[19], Zoe Gottlieb[1], Peter Legnani[1], James George[1], Haritz Irizar[9], Aleksandar Stojmirovic[20], Carrie Brodmerkel[20], Andrew Kasarkis[8,13,21], Bruce E. Sands[1], Glaucia Furtado[2], Sergio A. Lira[2], Zewen K. Tuong[7,22], Huaibin M. Ko[23], Andrea Cerutti[2,10,24], Charles O. Elson[12], Menna R. Clatworthy[7,22], Miriam Merad[2], Mayte Suárez-Fariñas[8,13], Carmen Argmann[8,13], Jason A. Hackney[25], Gabriel D. Victora[6], Gwendalyn J. Randolph[11], Ephraim Kenigsberg[2,9], Jean Frederic Colombel[1] and Saurabh Mehandru[1,2] ✉

A novel population of CXCL13+ Tfh-like cells is identified in the UC colon

A subset of T cells, T follicular helper cells (Tfh) 'help' with B cell responses



- Tfh/Tph cells significantly increased in active UC patients compared with stable remission UC patients and healthy controls
- Mayo Clinic Score, erythrocyte sedimentation rate, C-reactive protein all positively correlated with frequency of circulating Tfh cells in UC
- Tfh cells in germinal center increased in UC compared with controls
- Level of Tfh cells positively correlated with circulating new memory B cells, plasmablasts, serum IgG, IL-4, IL-21

Tfh/Tph cells express programmed death 1 (PD-1), CXC chemokine receptor 5 (CXCR5), inducible costimulatory molecule (ICOS), and B cell lymphoma 6 (BCL-6) and produce IL-21

Tfh/Tph = T follicular helper and T peripheral helper cells

Summary: Ulcerative Colitis

- High impact disease
  - High personal and economic impacts
  - Rising rates, globally
- Significant therapeutic limitations
  - Safety (anti-TNFs, JAK inhibitors)
  - Limited efficacy in achieving and maintaining remission
- Targeting multiple mechanisms provides opportunity to break through efficacy ceiling
- PD-1 pathway implicated in immune mediated disease, including UC
  - Therapies impacting T effector cells have been proven efficacious
  - PD-1+ Tfh/Tph cells expand in UC that may direct the B cell response
- PD-1 agonism has potential as a novel MOA for treatment of UC, with strong pre-clinical rationale

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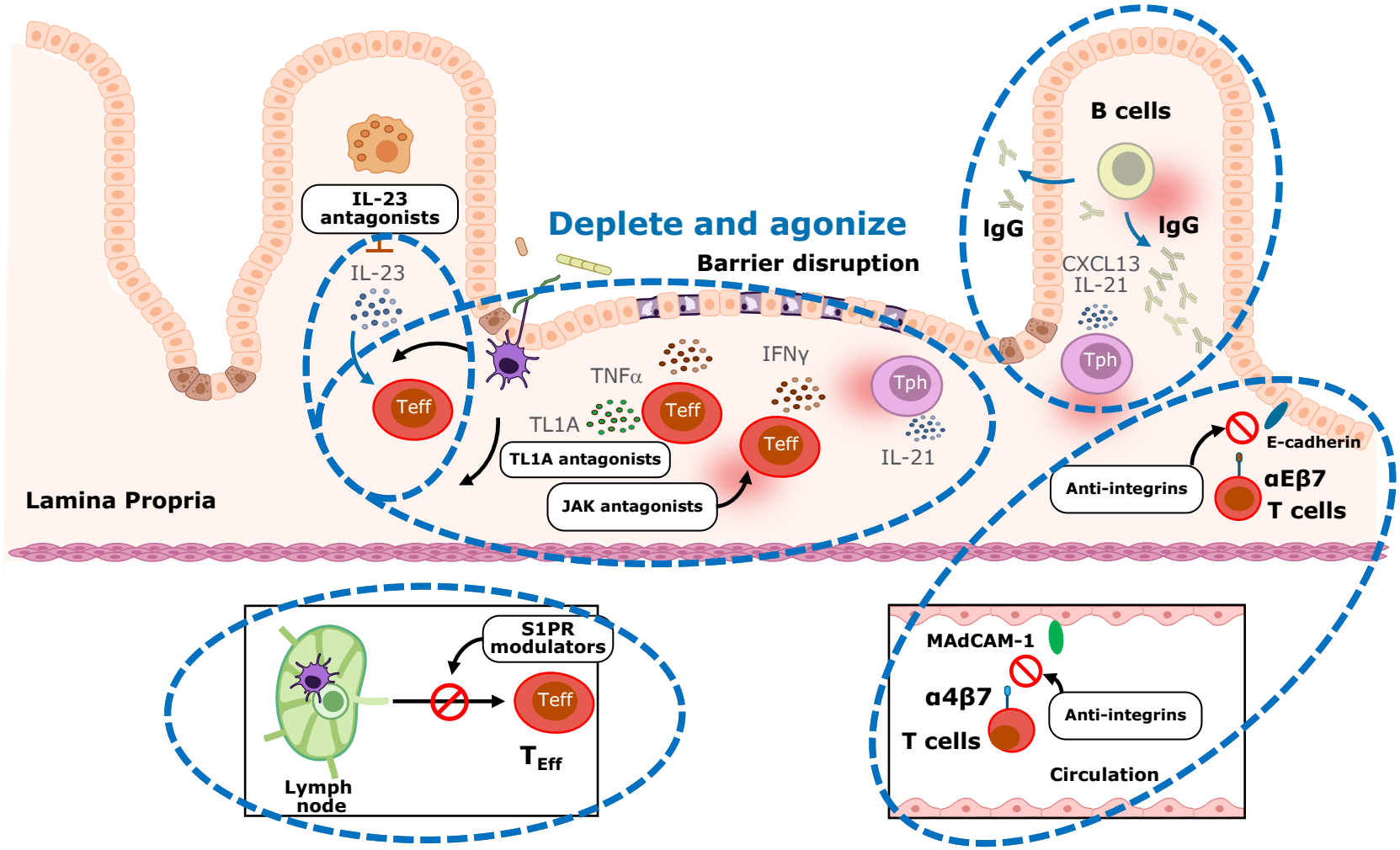
PD-1+ T cell activation broadly impacts multiple clinically validated drivers of UC pathogenesis

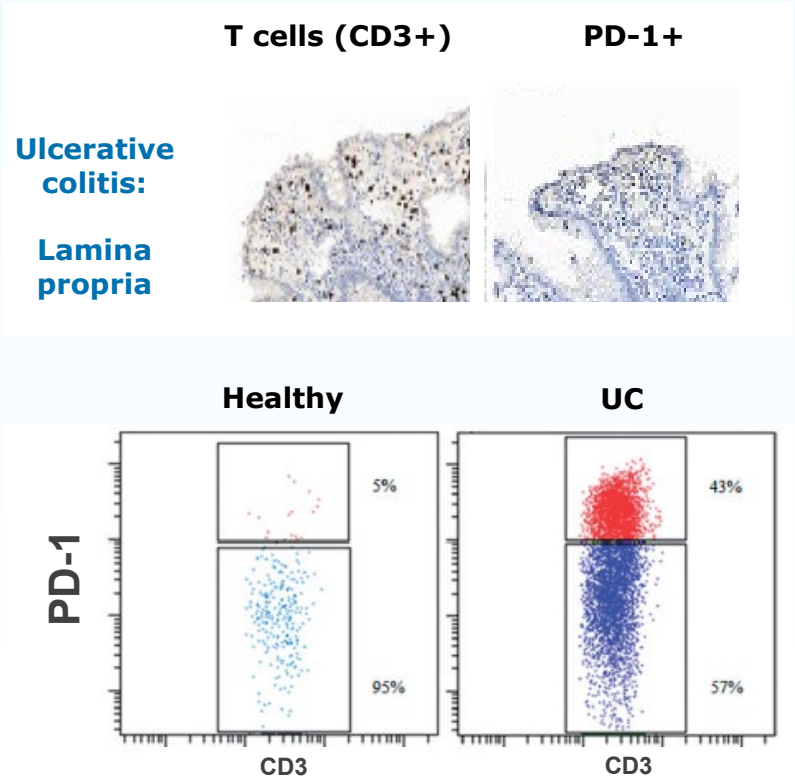
>40% of T cells in lamina propria in UC are PD-1+



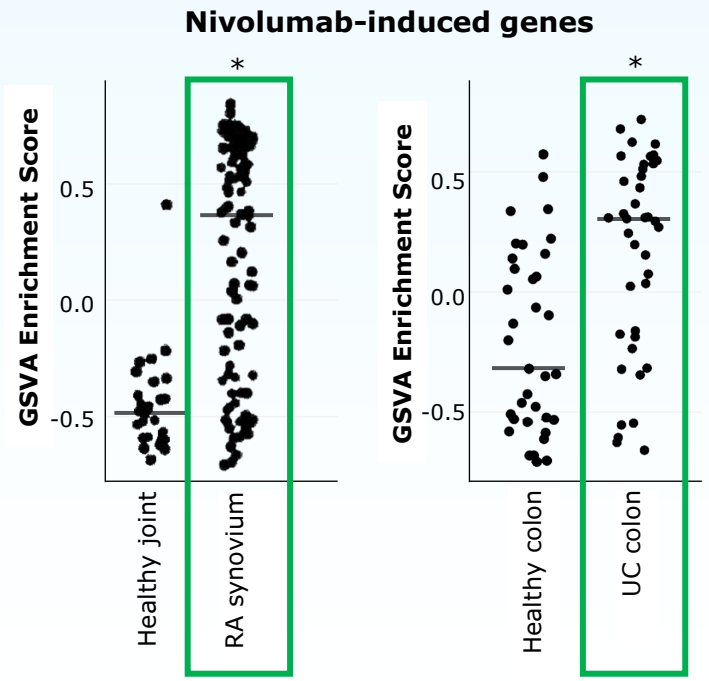
Adapted from Gastroenterology & Hepatology Volume 18, Issue 8 August 2022.

PD-1+ T cells are elevated and dysregulated in UC

~40% of T cells are PD-1+ in UC lamina propria



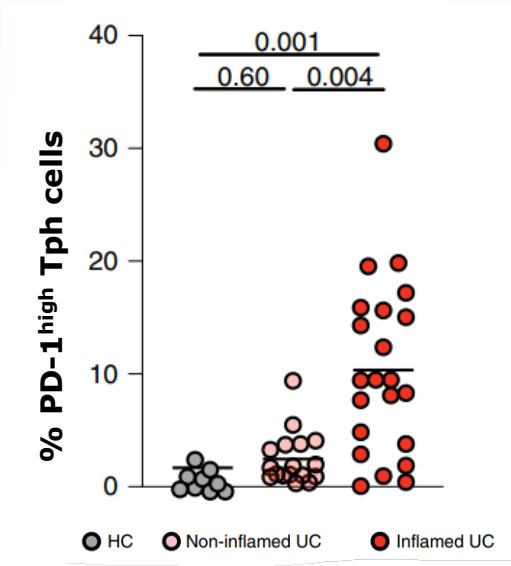
Similar dysregulation of PD-1 pathway genes between RA and UC



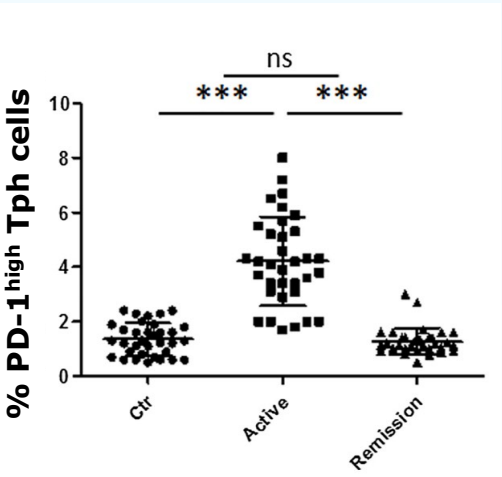
Guo et al, PLoS One. 2018; 13(2): e0192704; Nivolumab signature gene set containing ~100 genes induced by the anti-PD-1 antagonist therapeutic in TME of cancer patients was used for GSVA (gene set variation analysis) in synovial tissue biopsy samples of patients with RA. We performed the same analysis from UC biopsy tissue by utilizing available published data. * P<0.05

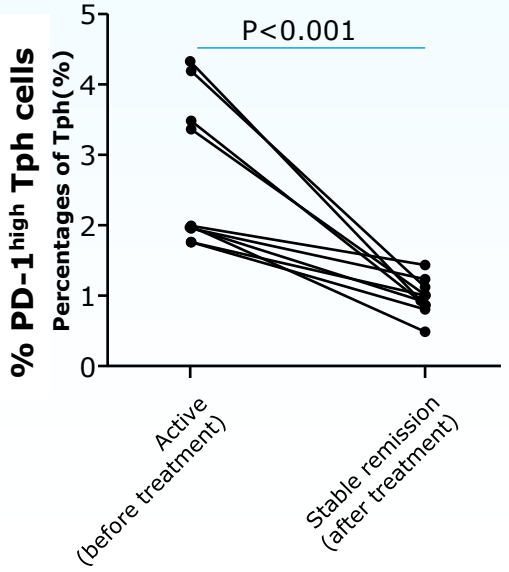
Reduction of elevated PD-1^{high} Tph cells in both UC colon and periphery correlates with remission

PD-1^{high} Tph cells are elevated



PD-1^{high} Tph cells are reduced with remission



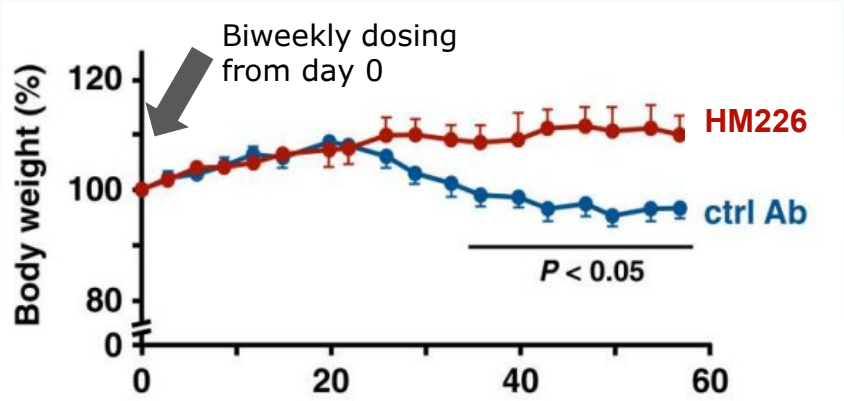


Reduction of plasma cell generation & autoantibody levels, including anti-microbial IgG antibodies contributing to colonic inflammation and barrier disruption

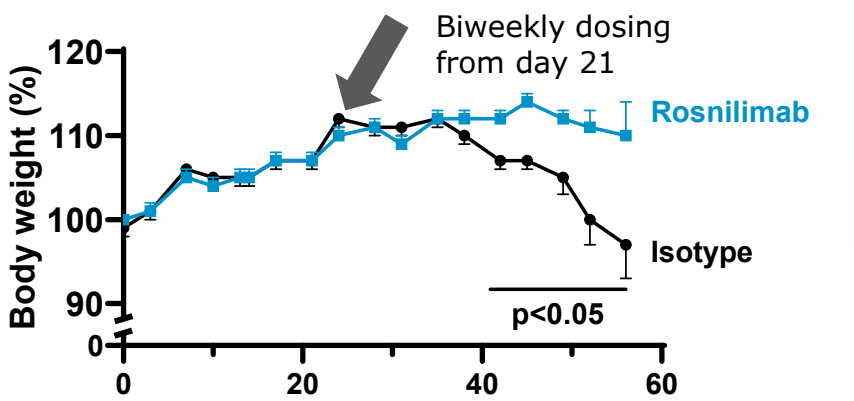
PD-1^{high} Tph cells defined by CD3+CD4+CD45RA-PD-1+TIGIT+ICOS+CXCR5-). Long et al, Immunology Letters 233 (2021) 2-10., Rao et al, Nature, 2017. *** p<0.001

Prophylactic or therapeutic dosing of PD-1 agonists induce and maintain remission in murine models

Prophylactic dosing of HM226 PD-1 agonist induce and maintain remission from colitis



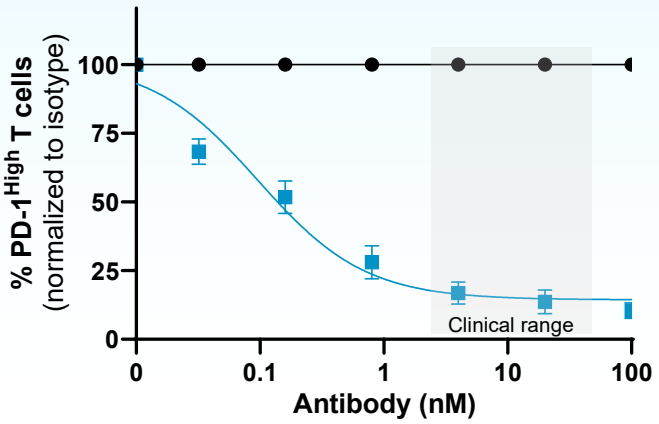
Therapeutic dosing of rosnilimab induce and maintain remission from colitis



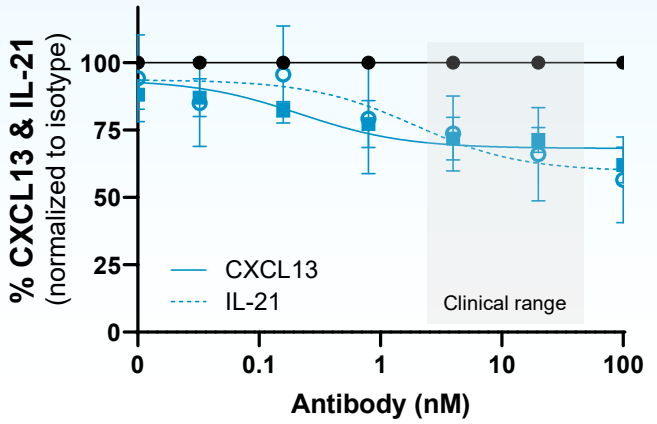
Rosnilimab and HM226 bind to the membrane proximal "epitope 7" of PD-1 that contributes to maximal PD-1 agonism. Rosnilimab formatted to mIgG2a to mediate effector function in mice. Suzuki et al., Sci. Immunol. 8, eadd4947 (2023).

Rosnilimab's potent depletion and agonism reduces T cell proliferation and inflammatory cytokines that disrupt barrier function

Depletion of PD-1^{high} T cells

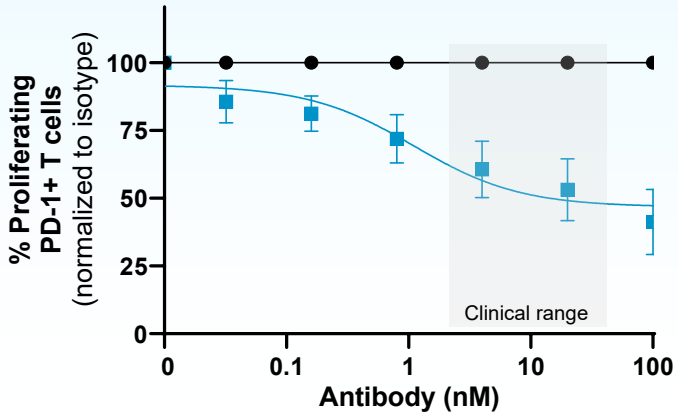


Inhibition of Tfh/Tph cytokine

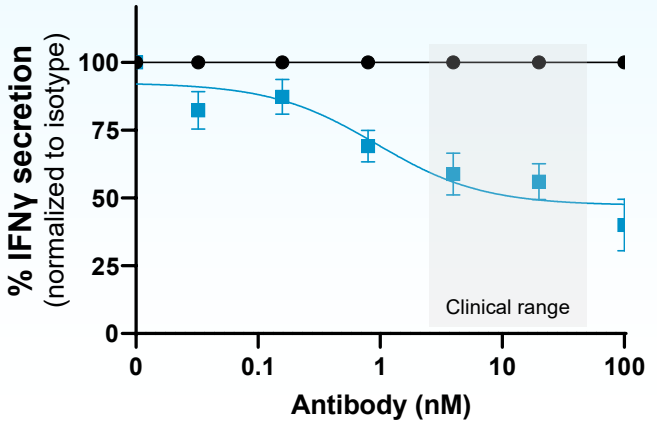


Isotype control
Rosnilimab
(N=6 UC patients)

Inhibition of T cell proliferation



Inhibition of inflammatory cytokine



Anti-CD3 + anti-CD28 stimulation of UC patient PBMCs for assessment of depletion and agonism MOA, representative data from N=6 donors.

Rosnilimab depletes and agonizes PD-1+ T cells broadly impacting multiple drivers of UC pathogenesis

>40% of T cells in UC lamina propria are PD-1+, including PD-1^{high} Tph cells which inversely correlate with disease remission

PD-1 agonists induce and maintain remission from colitis in murine models

Preclinical data support rosnilimab's potent immunologic outcomes

Agenda

TOPIC	SPEAKER
Rosnilimab: a best-in-class PD-1 agonist	Dan Faga Chief Executive Officer
MOA and differentiation	Martin Dahl, Ph.D. Senior Vice President, Research
Rosnilimab in RA	
Unmet patient needs and opportunity for PD-1 agonists	Jonathan Graf, M.D. Professor, Medicine University of California, San Francisco
Targeting RA with rosnilimab and translational data	Cailin Sibley, M.D., MHS, FACR Vice President, Translational Medicine
Rosnilimab in UC	
Unmet patient needs, disease biology, and rationale for PD-1 agonist in UC	Bruce Sands, M.D., M.S. Professor and Chief, Gastroenterology Icahn School of Medicine, Mount Sinai
Targeting UC with rosnilimab and translational data	Martin Dahl, Ph.D.
PD-1 safety data and Phase 2 development plans in RA and UC	**Paul Lizzul, M.D., Ph.D. Chief Medical Officer**
Market opportunity and closing remarks	Dan Faga
Q&A	AnaptysBio

Rosnilimab, and overall PD-1 agonist class, well-tolerated with no dose limiting tox observed to date

Rosnilimab Phase 1: 144 healthy volunteers (HV) in SAD and MAD cohorts

- Supports monthly SC dosing
- Favorable safety and tolerability
  - No SAEs related to rosnilimab[1]
  - No carcinogenic events observed
  - No infection risk signal

PD-1 agonist class: consistent tolerability profile to date

- Competitor PD-1 programs no carcinogenic events or infection risk signal
- >100+ RA patients treated with Lilly PD-1 agonist (highest dose of 700 mg IV over 6 months) showed tolerable profile[2]

Abatacept, targeting all T cells, has not shown clinically relevant carcinogenic increases in decades of commercial use

SAD=Single ascending dose; MAD=Multiple ascending doses; RO=Receptor occupancy; PK=Pharmakokinetics, SC = subcutaneous.

1. MAD cohort no SAEs; SAD cohorts 2 SAEs unrelated to rosnilimab as follows: Obstructive pancreatitis occurred in a placebo subject and Coronavirus infection occurred in drug 400 mg SC cohort on Day 24 until Day 31; participant recovered and discontinued from the study, and AE was deemed unrelated to rosnilimab.

2. Lilly peresolimab Phase 2 data in RA, published in NEJM (A Phase 2 Trial of Peresolimab for Adults with Rheumatoid Arthritis | NEJM).

Rosnilimab P2a in alopecia areata (AA) for Q4W SC dosing for 6 months was well tolerated with no significant safety signals

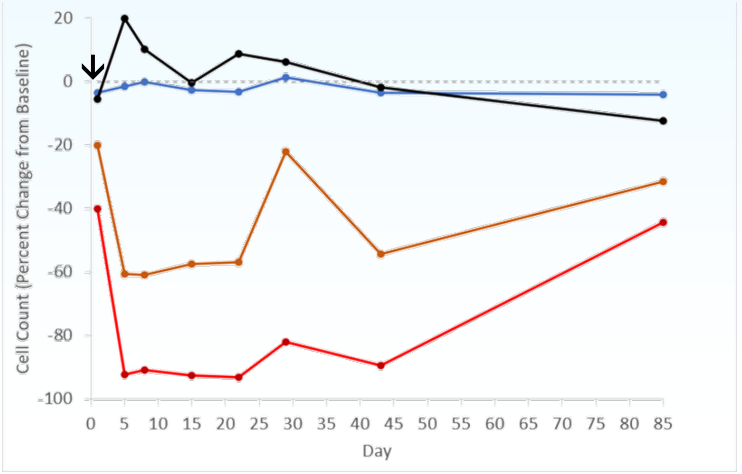
TEAE summary	Rosnilimab 400 mg (N=33)	Placebo (N=18)	All participants (N=51)
Participant with at least one TEAE	21 (63.6)	12 (66.7)	33 (64.7)
Related	6 (18.2)	3 (16.7)	9 (17.6)
Participant with at least one serious TEAE	1 (3.0)	1 (5.6)	2 (3.9)
Related	0	0	0
TEAE leading to treatment discontinuation	0	0	0
TEAE leading to study withdrawal	0	0	0
TEAE leading to death	0	0	0
Participant with at least one severe TEAE	1 (3.0)	0	1 (2.0)
Related	0	0	0

Top five TEAEs in more than 1 participant	Rosnilimab 400 mg (N=33)	Placebo (N=18)	All participants (N=51)
Infections (SOC)	12 (36.4)	11 (61.1)	23 (45.1)
COVID-19	7 (21.2)	2 (11.1)	9 (17.6)
Urinary tract infection	1 (3.0)	4 (22.2)	5 (9.8)
Arthralgia	2 (6.1)	1 (5.6)	3 (5.9)
Localized infection	1 (3.0)	2 (11.1)	3 (5.9)
Nasopharyngitis	1 (3.0)	2 (11.1)	3 (5.9)

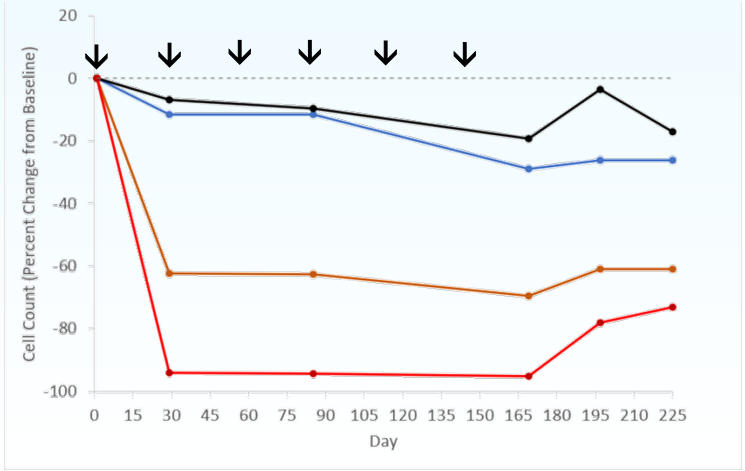
TEAE=Treatment emergent adverse event. Serious TEAEs: SAE for Placebo (n=1) of intestinal obstruction (designated unrelated); SAE for Rosnilimab (n=1) patient reported an unconfirmed MI (designated unrelated) and same event was designated severe AE.

Potent and sustained reduction in peripheral PD-1+ T cells for >30 days across P1 HV and P2a AA studies

Rosnilimab P1 healthy volunteers



Rosnilimab P2a AA patients



Consistent PD-1+ T cell effect

- >90% reduction of PD-1^{high} T cells
- >50% reduction of PD-1+ T cells

Overall T cell composition in less activated state

- Positive bias to Treg ratio

AA patients are in a low systemic inflammatory state

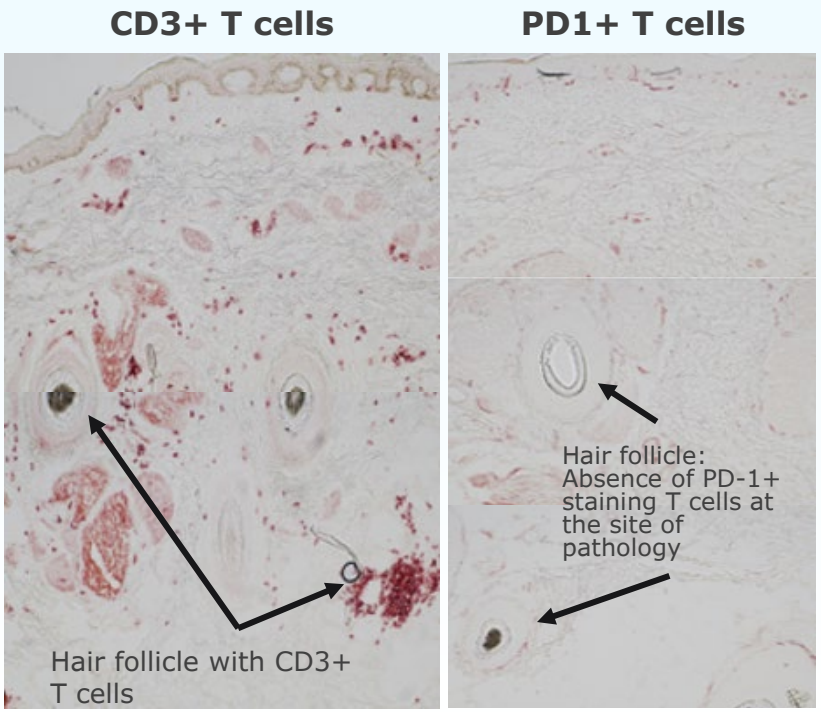
- Represented by no significant increase in peripheral PD-1+ T cells relative to healthy controls

Treg
Total T cells
PD-1+ T cells
PD-1^{high} T cells
↓ Dosing

AA=Alopecia Areata; Results shown from 400mg subcutaneous dose (single dose in healthy and monthly dose in AA).

PD-1 agonist MOA is not the right approach to treat AA given essentially undetectable PD-1+ cells at hair follicle

Representative IHC staining of scalp biopsy samples at baseline[1]



PD-1+ cells undetectable at hair follicle (site of clinical pathology)

- Only ~10-15% of T cells were PD-1+ in skin overall
- Non-localized and scattered throughout layers of skin

Rosnilimab "proof of mechanism" observed in skin

- Reduction in PD-1+ T cells
- Reduction in T cell activation markers and increase in Tregs

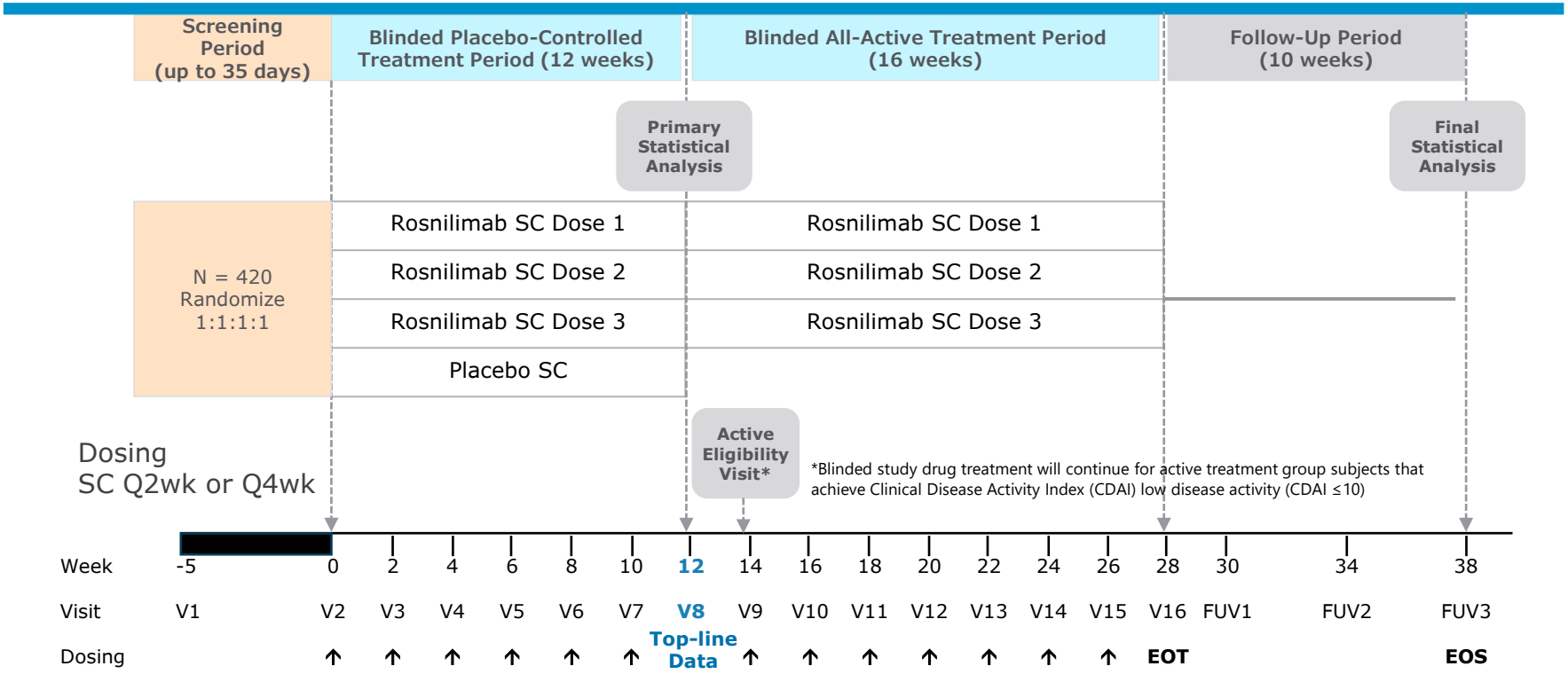
Targeting PD-1+ cells is not the right therapeutic approach for AA

- Re-entry of hair into the anagen growth phase may also be independent of inflammation

1.Panels are generally representative of all biopsies. Red coloring represents CD3+ or PD-1+ T cells. While T cell infiltrate was seen at selected hair follicles, these cells were not PD-1+. When seen, the "rare" PD-1+ cells were scattered at dermal-epidermal junction away from site of disease pathology.

Rosnilimab Phase 2b in moderate-to-severe RA

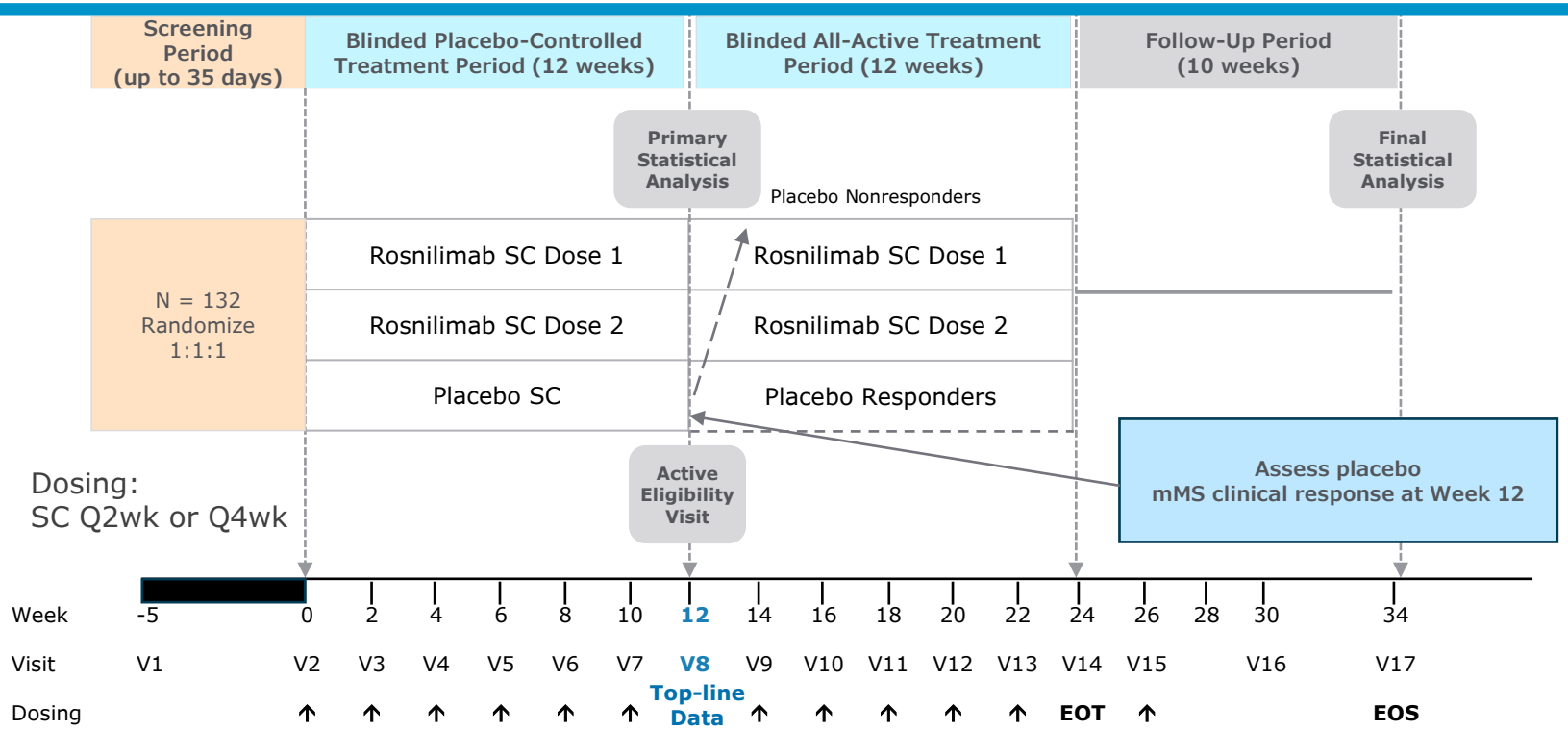
Initiated Q3 2023; Top-line data mid-2025



Patient population		• Adults with moderate-to-severe rheumatoid arthritis, >=6 TJC and SJC • Positive RF or CCP • Includes both MTX-IR and b/tsDMARD experienced patients (~50% b/tsDMARD experienced) • IR or intolerance to < 3 classes of b/ts DMARD
Endpoints	Primary	• Mean change from Baseline in DAS28-CRP at Week 12
	Secondary	• ACR20/50/70 • CDAI ≤ 10 (low disease) and ≤ 2.8 (remission) • DAS28-CRP ≤ 3.2 (low disease); DAS28-CRP ≤ 2.6 (remission)
Exploratory endpoints		• Mean change from Baseline in synovial and peripheral biomarkers

Rosnilimab Phase 2 in moderate-to-severe UC

Initiating Q4 2023; Top-line data H1 2026

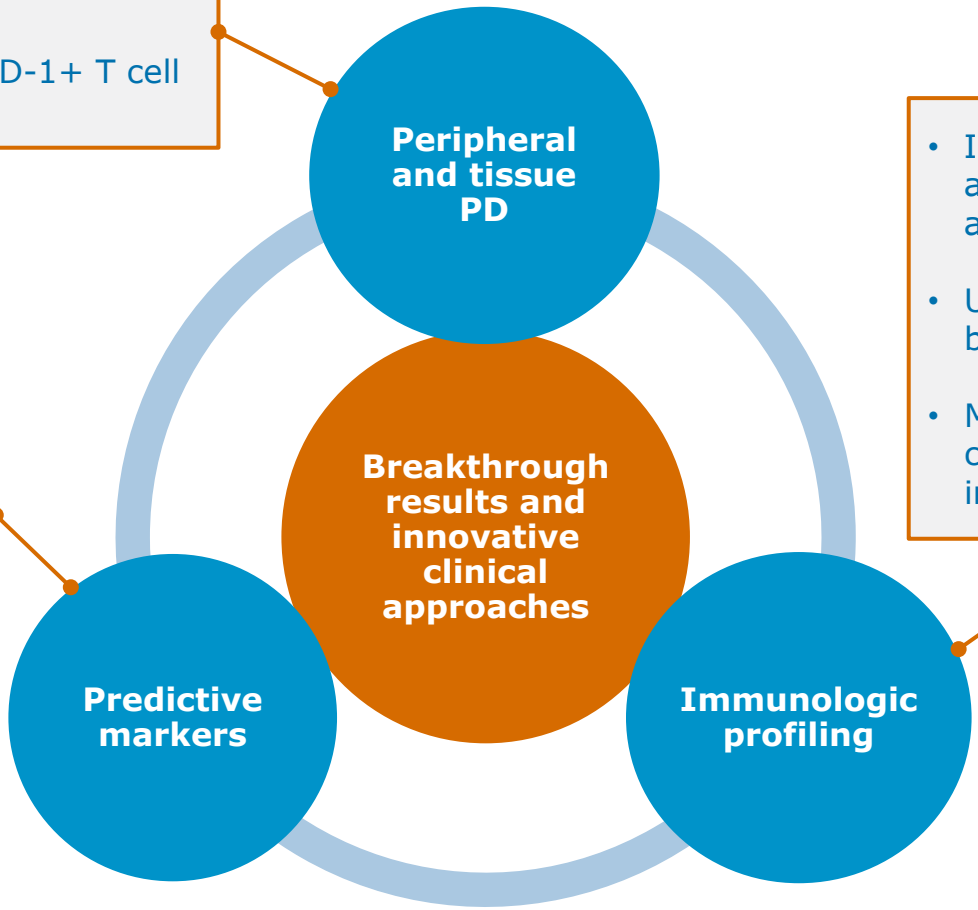


Patient population		• Adults with moderate-to-severe ulcerative colitis • Inadequate response to, loss of response to, or intolerance to as least 1 conventional or advanced UC therapy (~50% advanced UC therapy experienced)
Endpoints	Primary	• Mean change from Baseline in modified Mayo Score (mMS) at Week 12
	Secondary	• Clinical remission on mMS • Clinical response on mMS • Endoscopic remission • Mucosal healing
Exploratory endpoints		• Mean change from Baseline in colonic tissue and peripheral biomarkers

Robust translational plans explore predictive markers of treatment response in RA and UC and inform future indications

- Profile agonism and depletion mechanisms
- Tissue vs peripheral PD-1+ T cell depletion

- Precision medicine approaches



- Impact on immune activation and agonism markers
- UC and RA disease biomarkers
- Map immune changes to future indications

Rosnilimab is potential best-in-class in RA and first-in-class in UC

Rosnilimab was well tolerated in clinical studies with no significant safety signals while demonstrating potent and sustained reduction in peripheral PD-1+ T cells for >30 days

PD-1+ T cells are elevated in inflamed tissue and periphery in RA and UC

Global Phase 2b trial initiated in moderate-to-severe RA with top-line data expected mid:25

Global Phase 2 trial in moderate-to-severe UC initiating Q4:23 with top-line data expected 1H:26

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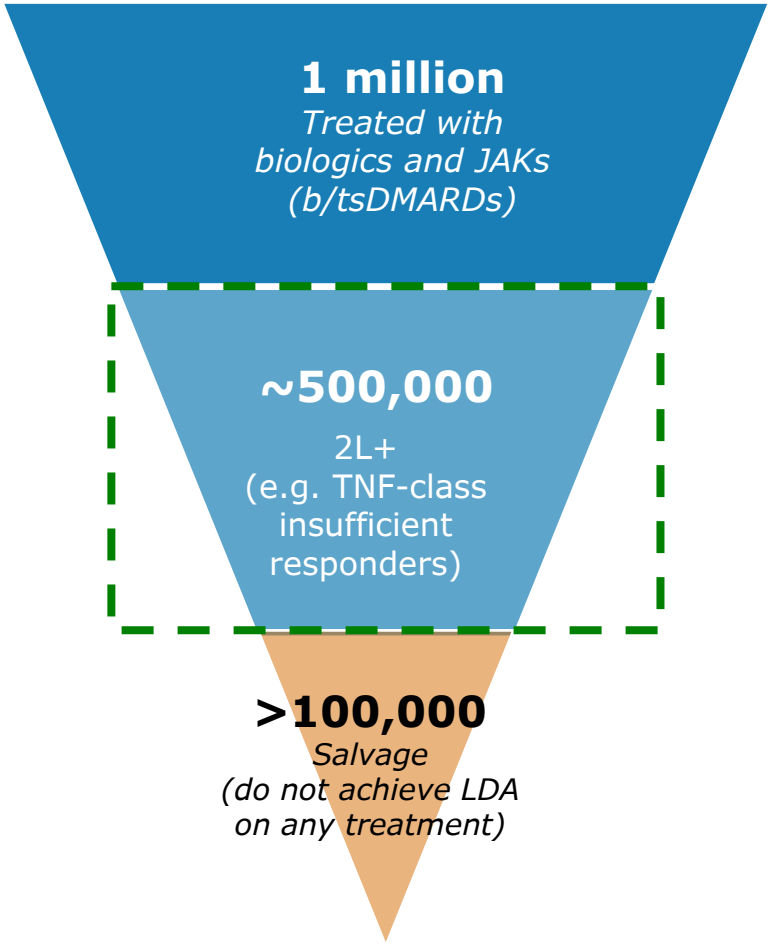
Market opportunity and closing remarks	**Dan Faga**
Q&A	AnaptysBio

Substantial opportunity for new class of biologics with differentiated outcomes in RA

U.S. "biologic experienced" RA prevalence[1,3,4]



>$10bn U.S. sales in "post TNF" market (2021)[2]

Fragmented market

- Lack of established SOC
- No new therapeutic class launched since 2012 *(JAK inhibitors: Xeljanz)*

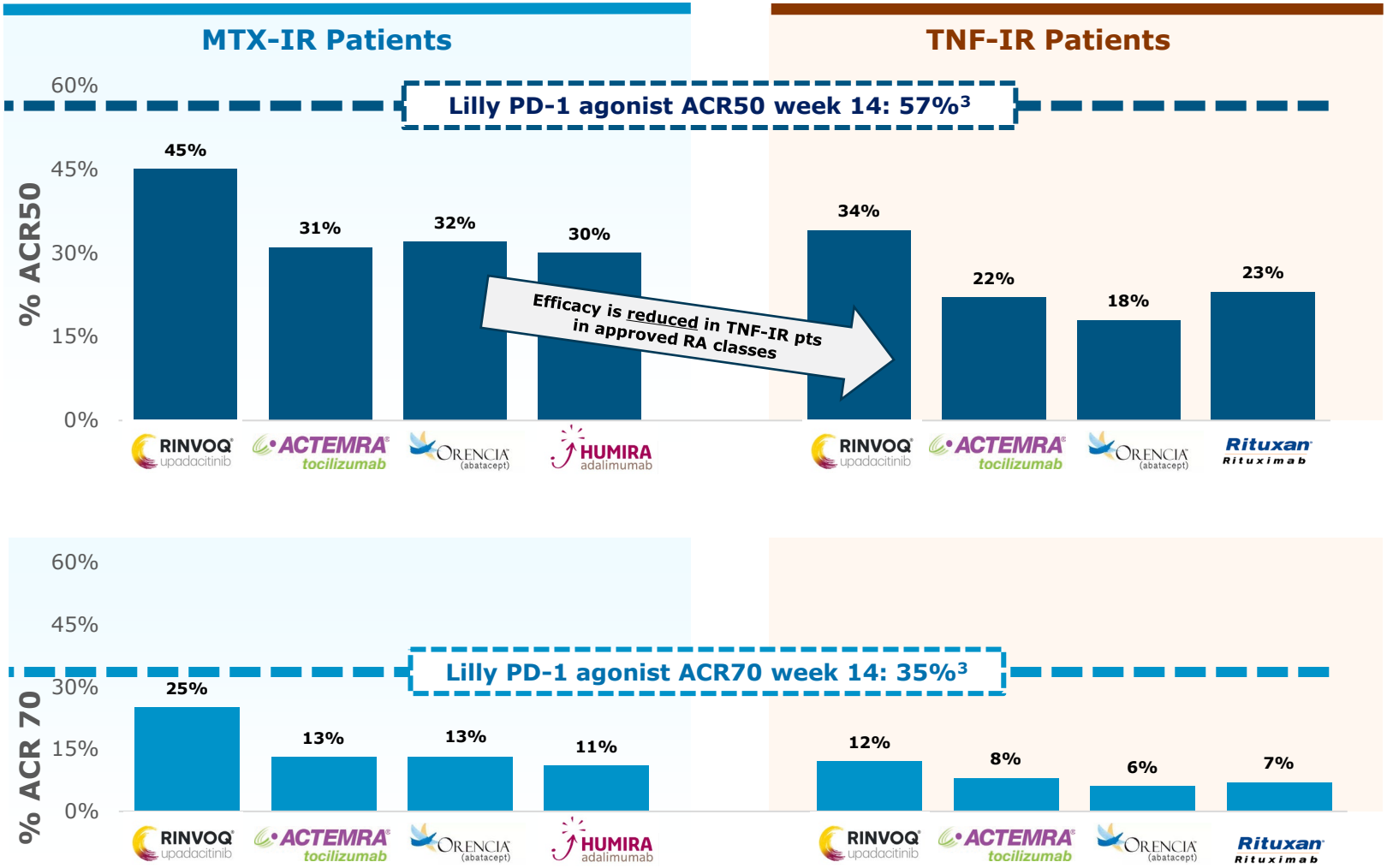
PD-1 agonist: Significant potential to differentiate from insufficient SOC

- Deeper responses
- Broader patient population: consistent response across lines of therapy
- Restore immune balance
- Emerging profile allows potential for combinations in future

1. Claims analysis to determine market size based on 5 years of claims history; 2. Evaluate Pharma; 3. b/tsDMARD – biologic/targeted synthetic disease modifying antirheumatic drug, 2L – 2nd line; 4. Anaptys market research 2022

PD-1 agonist class has shown commercially meaningful outcomes (ACR50 and ACR70) regardless of prior treatment

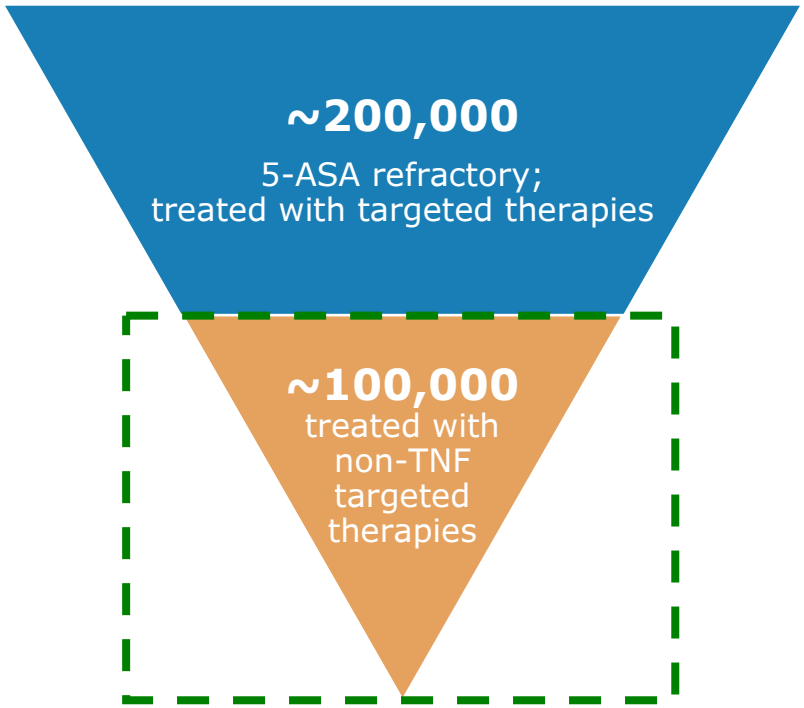
Absolute scores at Week 12[1,2]



1. Phase 3 registrational data from product labels; 15mg dose for upadacitinib in STUDY V 2. Tocilizumab (8mg/kg dose); Smolen J (2008) The Lancet Vol 371: 987-997; Emery, P. (2008) ARD 67(11): 1516-1523; Adalimumab; Keystone E (2004) Arthritis & Rheumatism Vol 50 #5:1400-1411; Rituximab; Cohen S (2006) Arthritis & Rheumatism Vol 54 #9: 2793-2806 3. Tuttle, J. (2023) NEJM;388:1853-62. Note patient population is 63% MTX-IR, 37% b/tsDMARD-IR; Similar efficacy was observed regardless of prior b/tsDMARD use.

Substantial opportunity for new class of biologics with differentiated outcomes in moderate and severe UC

U.S. moderate-to-severe UC prevalence[1]



>$6.5bn US sales in "non-TNF" market (2028)[2]

- UC prevalence growing faster than population

Fragmented market

- Severe: No clear choice after TNF failure
- Moderate: balance convenience and safety

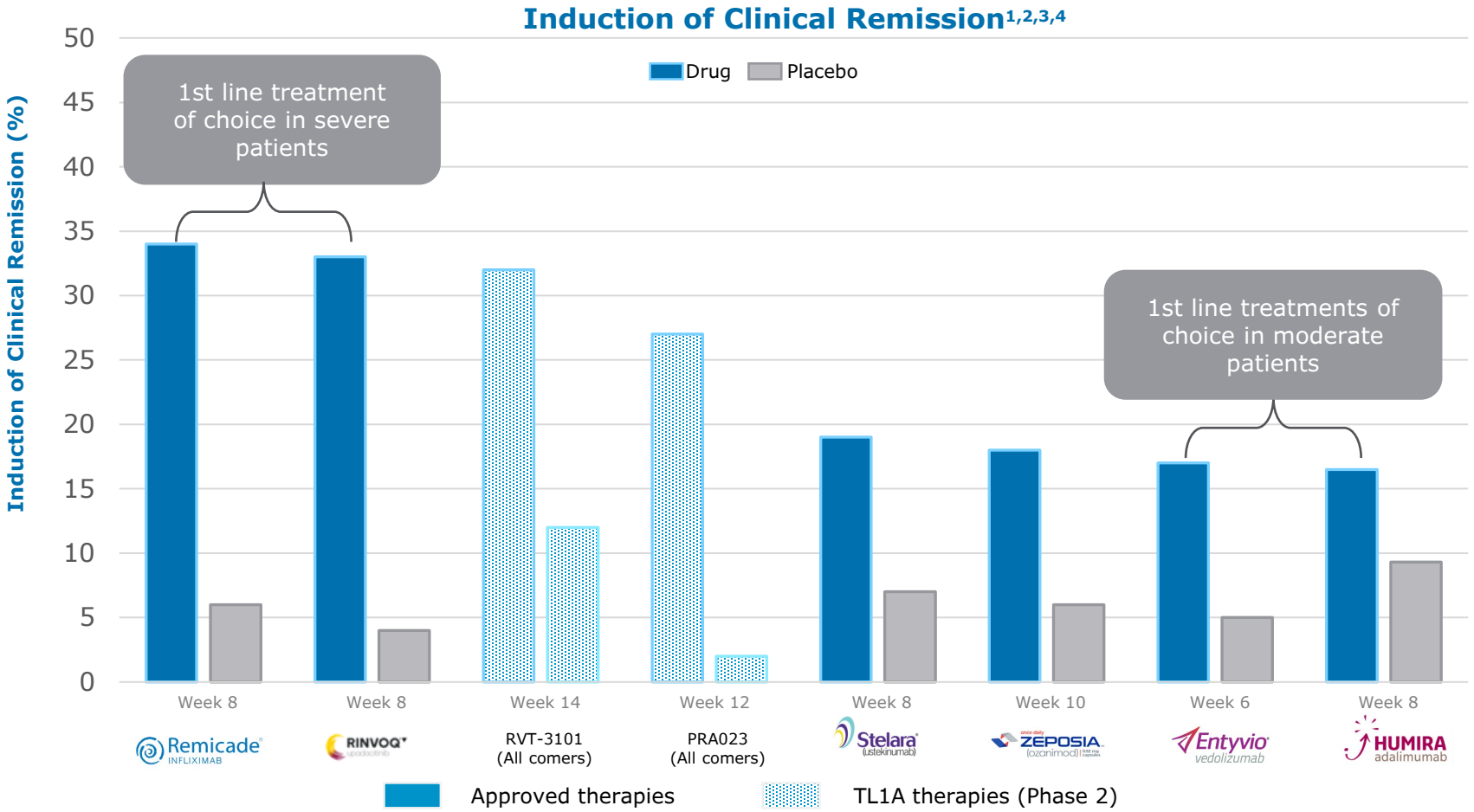
PD-1 agonist: Significant potential to differentiate from insufficient SOC

- Deeper responses: induction and/or maintenance
- Broader patient population: TNF-refractory
- Restore immune balance
- Emerging profile allows potential for combinations in future

1. Yu H (2018) Aliment Pharmacol Ther. 2018 Feb;47(3):364-370. doi: 10.1111/apt.14430; 2. Evaluate Pharma;
Note: Targeted therapy – biologic/targeted small molecule drug, 2L – 2nd line

UC lacks highly effective treatment options to induce and maintain clinical remission

Following remission on induction therapy, one third to one half of patients relapse within 1 year



1. Phase 3 registrational data from product labels; 2 Prometheus Bioscience corp. presentation Mar 2023; 3. Roivant corp presentation Jan 2023: 4. Remission measured using modified Mayo Score, except for Remicade, Humira and Entyvio which used full Mayo Score

Rosnilimab targets PD-1+ T cells broadly impacting pathogenic drivers of autoimmune & inflammatory diseases

PD-1 agonists deplete and agonize PD-1+ T cells, in both inflamed tissue and the periphery

Rosnilimab, a best-in-class PD-1 agonist, reduces T cell migration, proliferation & cytokine secretion and reduces plasma cell generation & autoantibody levels

Translational and clinical data support rosnilimab's potential for deep responses across heterogenous patient populations while restoring immune balance in RA and UC

RA: global Phase 2b trial initiated Q3:23 with top-line data mid:25
UC: global Phase 2 trial initiating Q4:23 with top-line data H1:26