

# New treatments for IBD

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# Disclosures

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# Organization

1. Randomized controlled trials.
2. How I like to classify IBD medications.
3. Lets talk new medications.
4. Changing routes of delivery.
5. New approaches to managing medications
6. The END!

# Clinical Trials + 'Phases'



**Phase 0 → Animals  
(pre-clinical)**

**Any evidence it works?**



**Phase 1 → Humans**

**Is it safe?**



**Phase 2 → Patients**

**What is the best dose?**

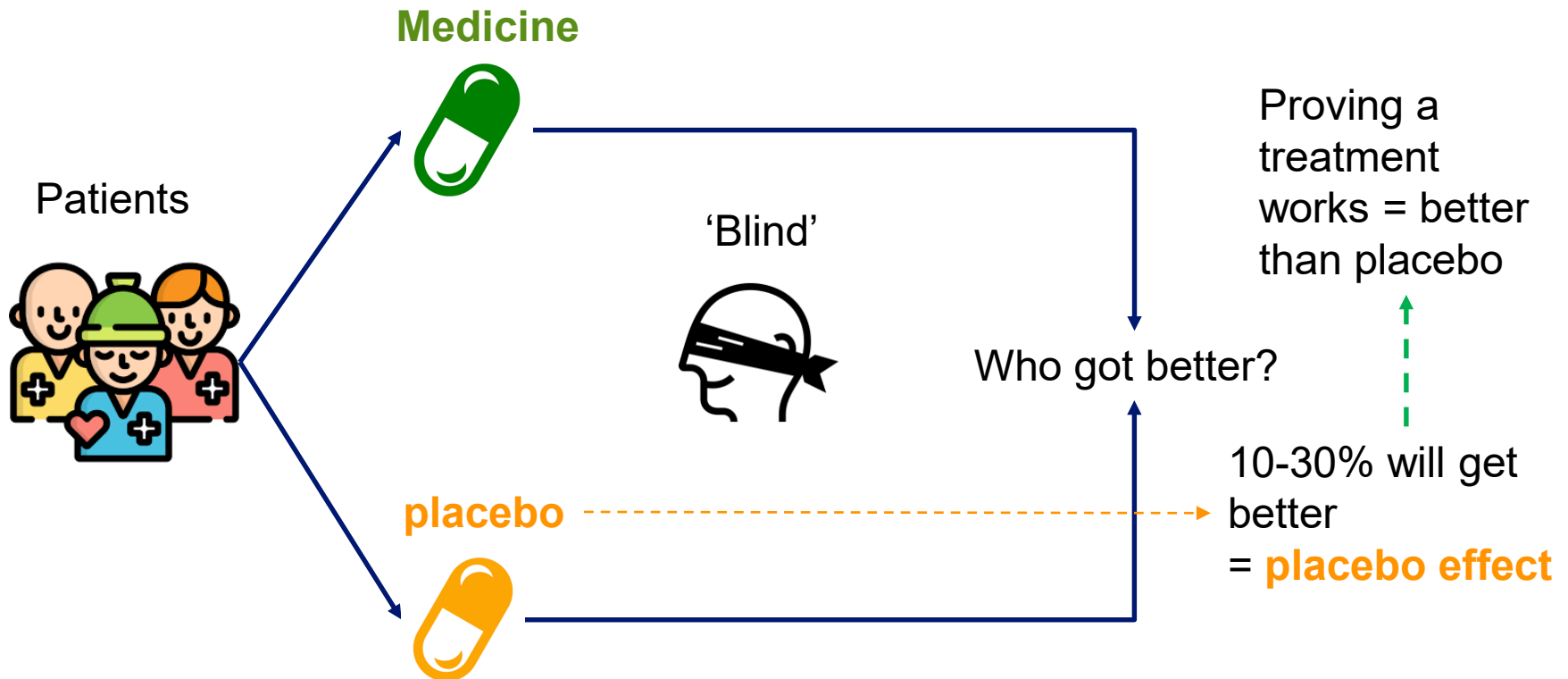


**Phase 3 → Lots of  
Patients (~500-700)**

**Does it work in IBD?**

# How do we 'prove' something works?

## Randomized Controlled Trial (RCT)

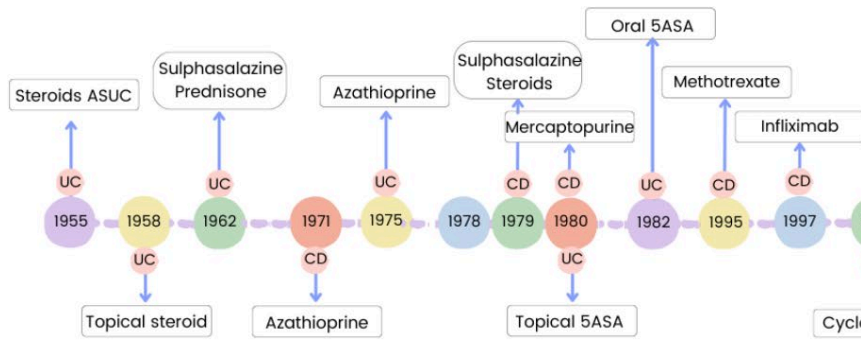


# Stop and Summarize.

- RCTs are critical.
- This is why providers are cautious about non-RCT approaches.
  - Alternative therapies.
  - Internet testimonials
- Some may work, but if they haven't gone through the proper studies, providers hesitate to give patients incorrect information.

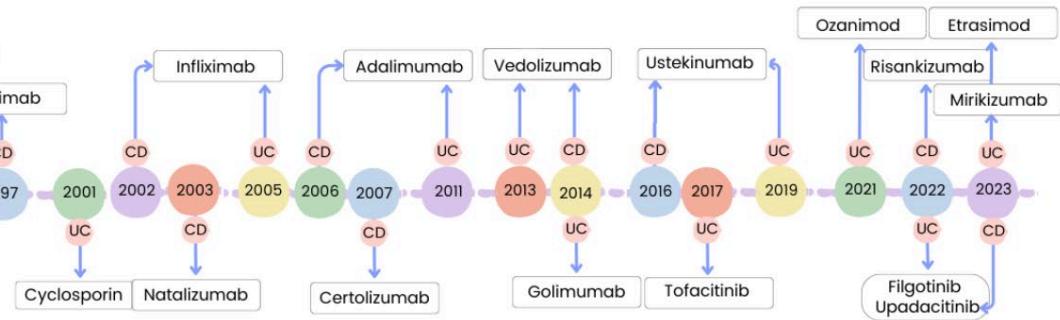
# More medications than EVER!!

## PRE BIOLOGIC ERA



Year of publication of the first trial showing positive results

## BIOLOGIC ERA



Year of publication of the phase III trial

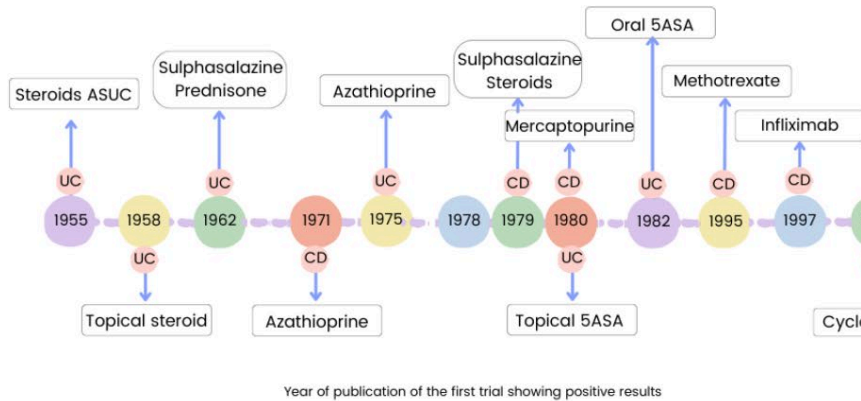


@Bealoquebea

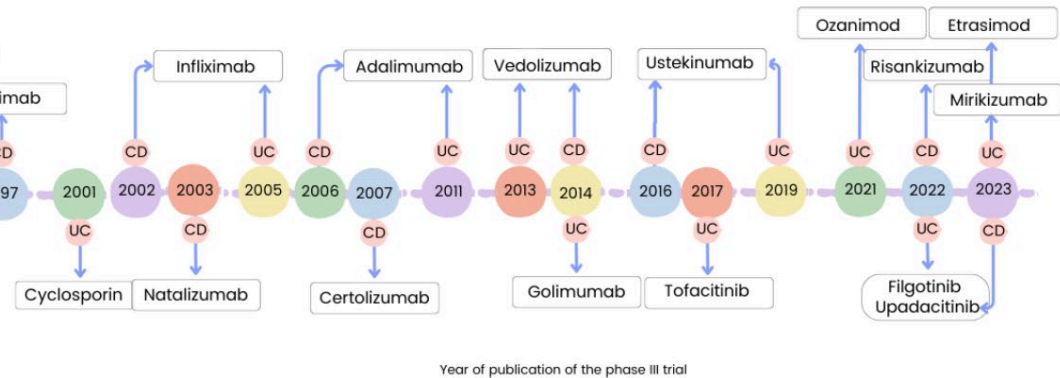
<https://ibd-eii.com/>

# Options are good!

## PRE BIOLOGIC ERA



## BIOLOGIC ERA



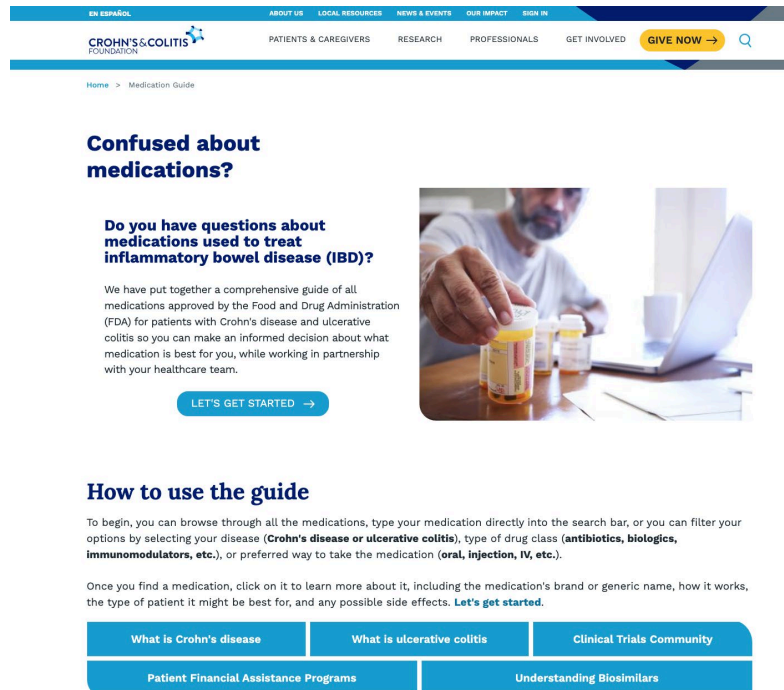
# But how can we keep track of them?

<https://ibd-eii.com/>



# Check out the Crohn's and Colitis Foundation website for more information.

<https://www.crohnscolitisfoundation.org/patientsandcaregivers/ibd-medication-guide>



The screenshot shows the website's navigation bar with links for 'EN ESPAÑOL', 'ABOUT US', 'LOCAL RESOURCES', 'NEWS & EVENTS', 'OUR IMPACT', and 'SIGN IN'. Below the navigation bar, there are links for 'PATIENTS & CAREGIVERS', 'RESEARCH', 'PROFESSIONALS', and 'GET INVOLVED', along with a 'GIVE NOW' button and a search icon. The breadcrumb trail reads 'Home > Medication Guide'. The main heading is 'Confused about medications?'. Below this is a sub-heading 'Do you have questions about medications used to treat inflammatory bowel disease (IBD)?' followed by a paragraph explaining the guide's purpose. A 'LET'S GET STARTED' button is present. An image shows a person's hands holding several pill bottles on a desk with a laptop. Below the image is the section 'How to use the guide', which provides instructions on how to navigate the guide. At the bottom, there are five blue buttons: 'What is Crohn's disease', 'What is ulcerative colitis', 'Clinical Trials Community', 'Patient Financial Assistance Programs', and 'Understanding Biosimilars'.

**Confused about medications?**

**Do you have questions about medications used to treat inflammatory bowel disease (IBD)?**

We have put together a comprehensive guide of all medications approved by the Food and Drug Administration (FDA) for patients with Crohn's disease and ulcerative colitis so you can make an informed decision about what medication is best for you, while working in partnership with your healthcare team.

[LET'S GET STARTED →](#)

**How to use the guide**

To begin, you can browse through all the medications, type your medication directly into the search bar, or you can filter your options by selecting your disease (**Crohn's disease or ulcerative colitis**), type of drug class (**antibiotics, biologics, immunomodulators, etc.**), or preferred way to take the medication (**oral, injection, IV, etc.**).

Once you find a medication, click on it to learn more about it, including the medication's brand or generic name, how it works, the type of patient it might be best for, and any possible side effects. **Let's get started.**

[What is Crohn's disease](#)   [What is ulcerative colitis](#)   [Clinical Trials Community](#)

[Patient Financial Assistance Programs](#)   [Understanding Biosimilars](#)

# Currently Approved Therapies for IBD

- **Ulcerative Colitis**

- Anti-TNFs: Remicade, Humira, Simponi
- Anti-Integrins: Entyvio
- S1Ps: Zeposia, Velsipity
- JAKi: Xeljanz, Rinvoq
- Anti-cytokine: Stelara, Omvoh

- **Crohn's Disease**

- Anti-TNFs: Remicade, Humira, Cimzia
- Anti-Integrins: Entyvio
- Anti-cytokine: Stelara, Skyrizi

# That's a lot, with a lot more medications coming.

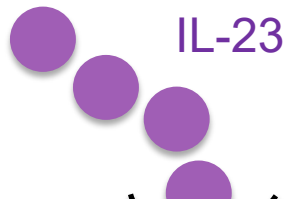
	Anti-TNF	Anti-adhesion molecules	JAK inhibitors	Anti-IL-12 and/or anti-IL-23	Immunosuppressants	S1P receptor modulators	Anti-cytokines (others)
Phase I and/or II		<ul style="list-style-type: none"> <li>• AJM347</li> </ul>	<ul style="list-style-type: none"> <li>• Peficitinib</li> <li>• TD-1473</li> <li>• Deucravacitinib</li> </ul>		<ul style="list-style-type: none"> <li>• Apremilast</li> <li>• GSK2831781</li> <li>• Ravagalimab</li> </ul>	<ul style="list-style-type: none"> <li>• Amiselimod</li> </ul>	<ul style="list-style-type: none"> <li>• Spesolimab</li> <li>• PF-06480605</li> </ul>
Phase III		<ul style="list-style-type: none"> <li>• AJM300</li> <li>• Ontalizumab</li> <li>• Etrolizumab</li> </ul>	<ul style="list-style-type: none"> <li>• Filgotinib</li> <li>• Upadacitinib</li> </ul>	<ul style="list-style-type: none"> <li>• Brazikumab</li> <li>• Risankizumab</li> <li>• Guselkumab</li> <li>• Mirikizumab</li> </ul>		<ul style="list-style-type: none"> <li>• Etrasimod</li> <li>• Ozanimod</li> </ul>	<ul style="list-style-type: none"> <li>• Spesolimab</li> </ul>
Launched	<ul style="list-style-type: none"> <li>• Adalimumab</li> <li>• Golimumab</li> <li>• Infliximab</li> </ul>	<ul style="list-style-type: none"> <li>• Vedolizumab</li> </ul>	<ul style="list-style-type: none"> <li>• Tofacitinib</li> </ul>	<ul style="list-style-type: none"> <li>• Ustekinumab</li> </ul>	<ul style="list-style-type: none"> <li>• Tacrolimus</li> <li>• Cyclosporine</li> </ul>		

- Oral administration
- Intravenous or subcutaneous

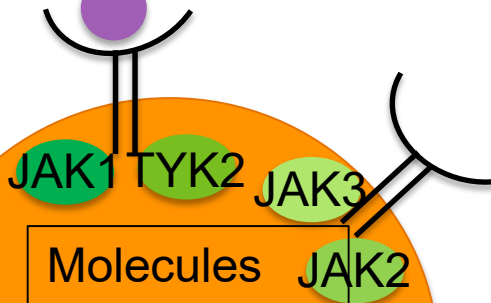
Kobayashi T, Nature reviews, Sept 2020

# Here is one way to think about IBD medications.

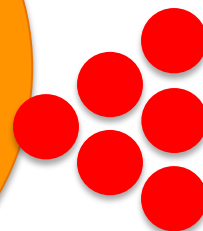
Molecules that help it grow



IL-23



Molecules that turn it on

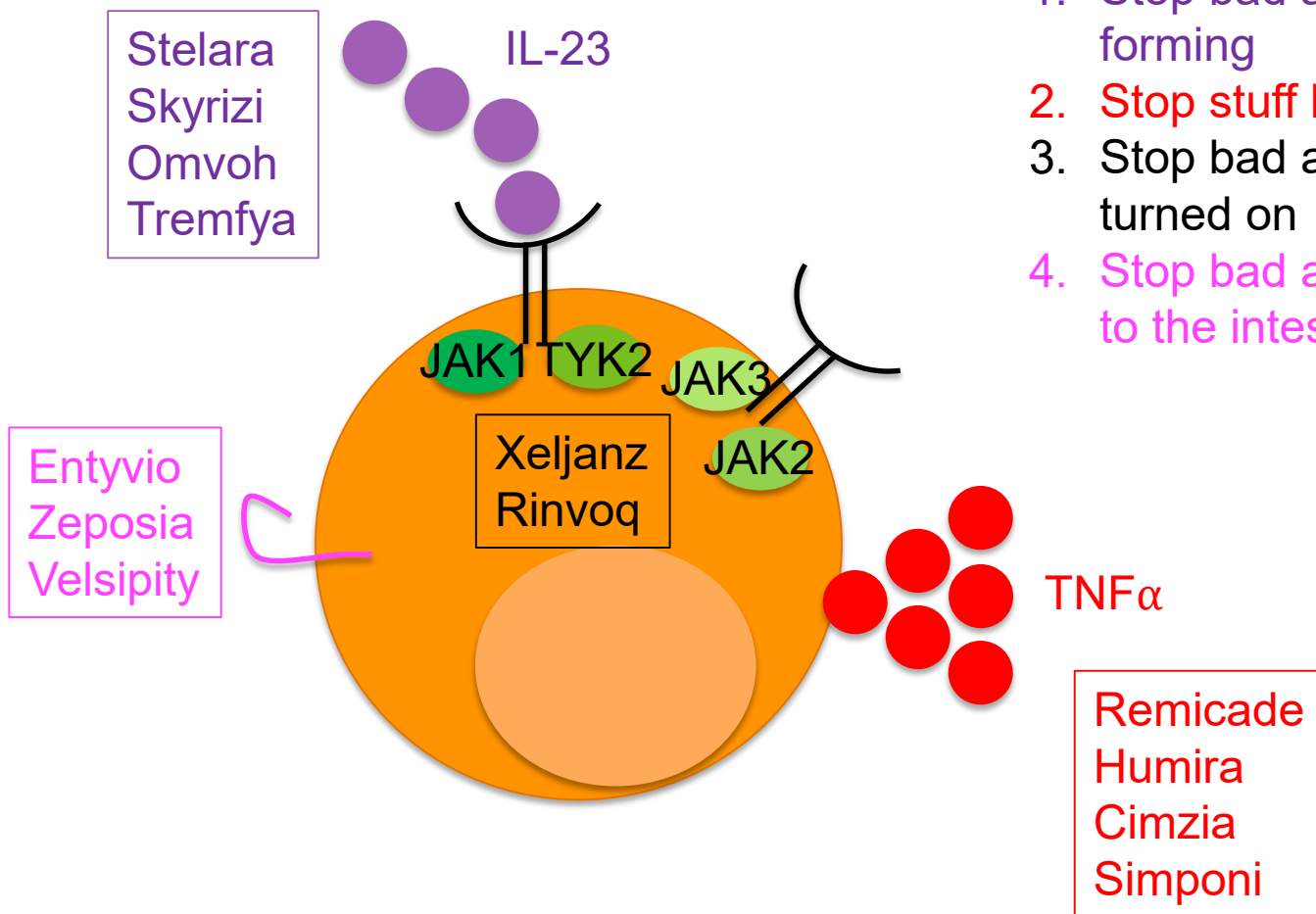


TNF $\alpha$

Molecules that help it get to the gut

Molecules that cause damage

# Meds fall into classes in that model.



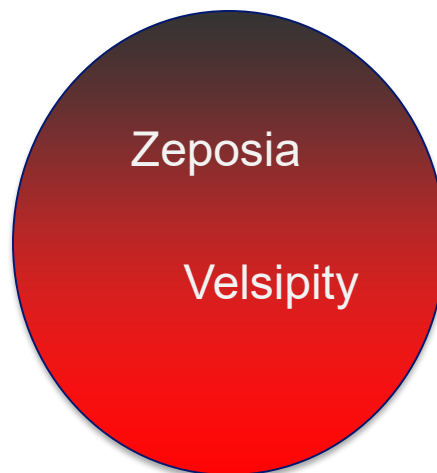
1. Stop bad actors from forming
2. Stop stuff bad actors make
3. Stop bad actors for being turned on
4. Stop bad actors from getting to the intestine

# Many new drugs. Lets talk about some recently approved ones.

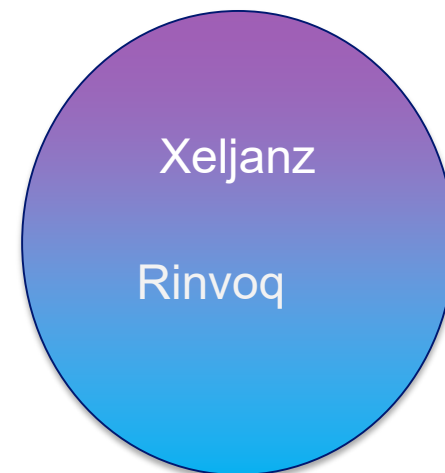
**anti-IL-23:** stop inflammatory cells from developing



**S1PR1:** stop inflammatory cells from getting to the gut



**JAKi:** stop inflammatory cells from activating



## Skyrizi Effectiveness

- Crohn's
- Anti-IL23 monoclonal – IV x 3, then SQ q 8 weeks
- 45% in remission by week 12
- 52% in remission by 1 year
  
- A recent, but unpublished study indicates it is more effective than Stelara

## Skyrizi Safety

- Infections – similar to placebo
- Rare shingles, no TB
- Some elevated liver enzymes, usually during IV infusions



## OmvoH Effectiveness

- Ulcerative Colitis
- Anti-IL23 monoclonal – IV x 3, then SQ q 4 weeks
- 24% in remission by week 12
- 50% in remission by week 40
  
- A recent, but unpublished study indicates it is equally effective as Stelara

## OmvoH Safety

- Infections –
- Shingles and Candida
- nasopharyngitis
- Several cancers (which are not likely to be related to OmvoH)

## Zeposia Effectiveness

- UC
- 18% in remission by week 10
- 37% in remission by week 52
- Oral pill, starter pack over 1 wk.
- Can require additional testing before (eye, EKG)

## Zeposia Safety

- Infection.
- Nasopharyngitis
- Serious infection in <2% over 52 weeks
- 2 cancers, probably unrelated to Zeposia
- Can lower heart rate and increase blood pressure, these are probably transient in most.
- Increased liver enzymes
- Drops white blood cell count in most.
- Should not use if untreated and severe sleep apnea or recent heart attack.

## Velsipity Effectiveness

- UC
- Treat-through design.
- 27% in remission by week 12
- 32% in remission by 1 yr
- Oral pill.
- Can require additional testing before (eye, EKG)

## Velsipity Safety

- Infection, but not different than placebo.
- Shingles
- UTIs
- Can lower heart rate and increase blood pressure, these are probably transient in most.
- Can reduce white blood cell count.
- Can increase liver labs.
- Should not use if recent heart attack.

## Rinvoq Effectiveness

- Crohn's and Ulcerative Colitis
- A JAKi (like tofa) - High effectiveness, fast
- UC – reduced bleeding on day 1, urgency day 3
  - 30% in remission by 8 weeks, 36% with endoscopic improvement.
  - 47% in remission at 1 year.
  - Comparable to infliximab, **better** than any other UC Rx
- CD – 50% in remission by week 12
  - Comparable to infliximab, **better** than any other CD Rx
- Once a day tablet

## Rinvoq Risks

- #1 is Shingles – in ~ 5% of patients per year if not vaccinated
- Get Shingrix vaccine!
- Elevated liver tests, CPK test, low neutrophils
- Nasopharyngitis, URIs
- Rare cancer, MI, VTE – not significant in trials > placebo, but occurred



# Bottom line

## 1. The Good

1. Lots of new drugs on the way
2. Many work in different ways than what we have now
3. Many will be oral or SQ shots (easier to use!)

## 1. Questions.

1. Long-term safety of new drugs

# New ways to deliver 'old' drugs

Entyvio → Infusion → Shot



Infliximab → Infusion → Shot



# LAST but NOT LEAST!!!

- IBD community is working on new ways to manage severe disease.
- Dual targeted therapy (DTTs) is on the horizon.
  
- DTTs – Give 2 medications at one time to better control disease.
- Lots of unanswered questions.
  - Who is the right patient?
  - What is the risk?
  - What are the right combinations? (fast acting/high risk medication with slower acting low risk medication?)
  - How long to treat with DTT?
  
- Probably some patients with more severe disease will benefit from DTT
  
- But many ?'s unclear.

# Main take home: The right drug for you highly individualized.

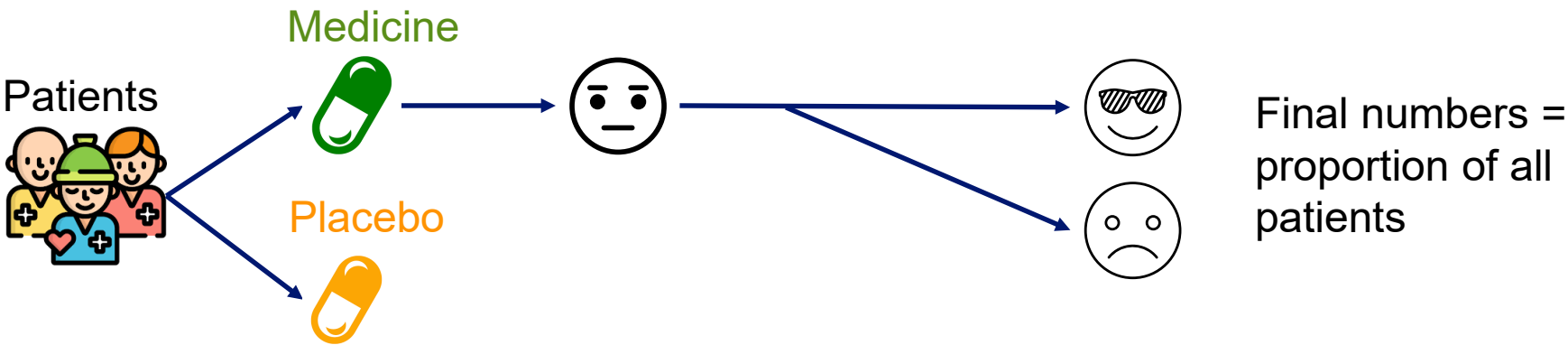
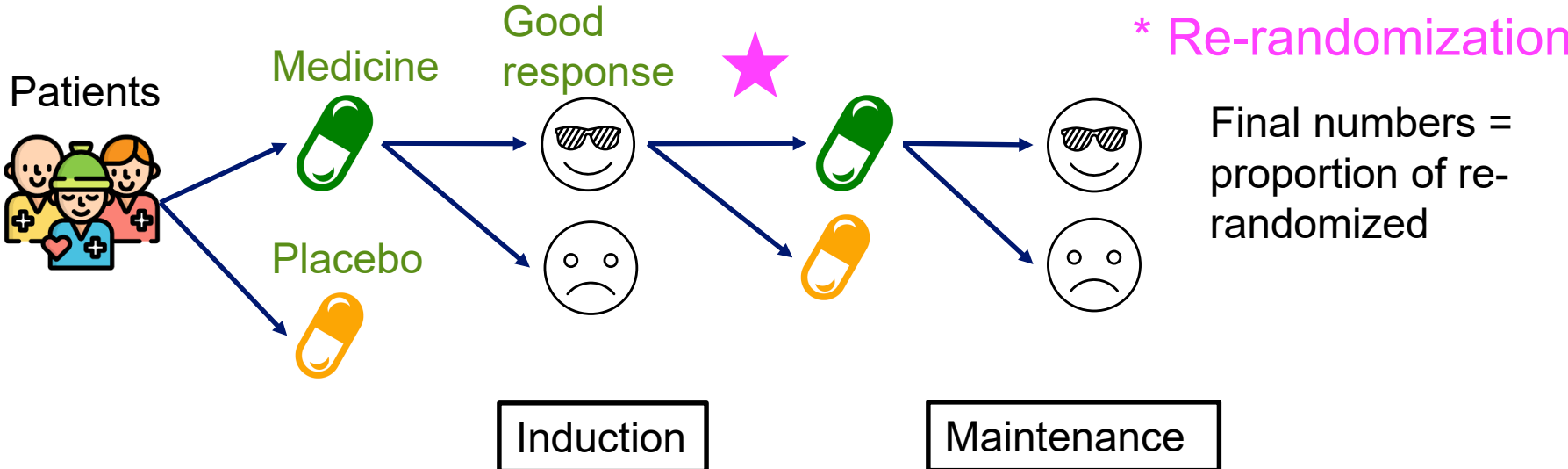
- The severity of your IBD.
- The medications you've been on before.
- Preference for oral, IV or shot.
- **INSURANCE!!!!**
- Your personal medical health (cardiovascular disease, age, medical conditions).
- Major positive with so many options. Better chance to find the right fit.

# The End!

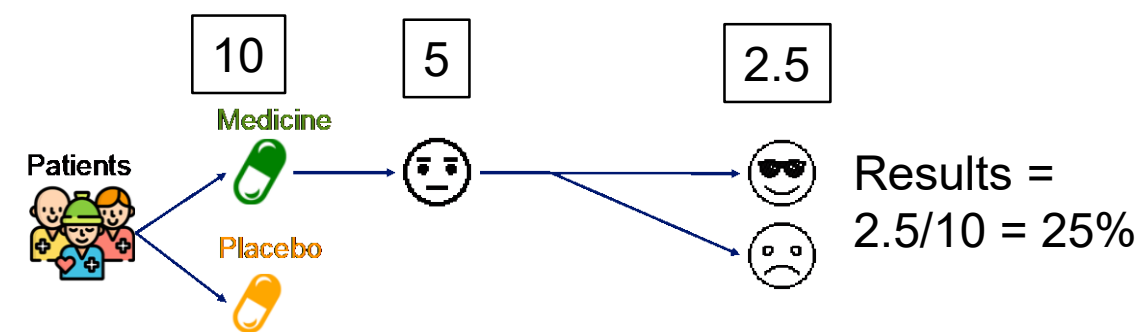
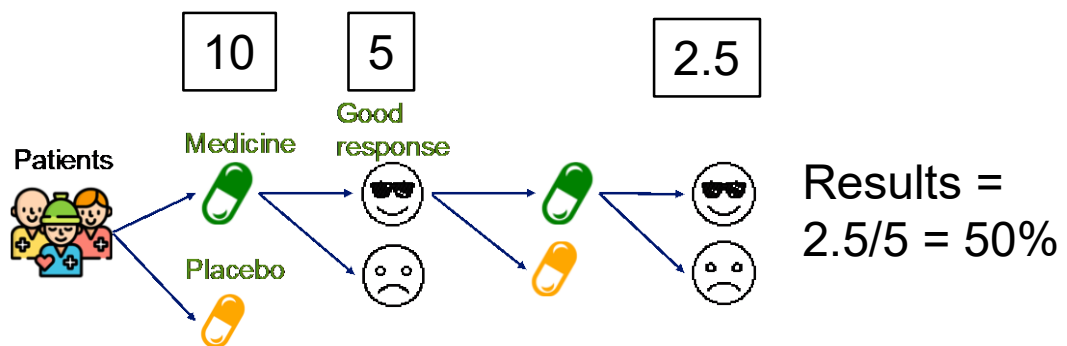
Thank you for your time and attention!

Questions ?

# Trial design and two ways to build RCTs



# Trial design and two ways to build RCTs



- Treat-through trial = lower response rates.
- Can't directly compare to re-randomization.
- Recent trials are treat-through.
- Lower TT rates does not always mean less effective.