SPEAKER DISCLOSURE

- Relationships with commercial interests:
  - **Grants/Research Support: Takeda**
  - **Speakers Bureau/Honoraria: Takeda, Janssen, Abbvie**
  - **Consulting Fees:** none
  - **Other: none**

DISCLAIMER

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These slides are intended for educational purposes only.

Takeda Canada does not recommend the use of ENTYVIO® in any other indication than as described in the Canadian Product Monograph.

INDICATIONS AND CLINICAL USE

ENTYVIO® (vedolizumab) is indicated for:

Ulcerative Colitis (Adults ≥ 18 years)

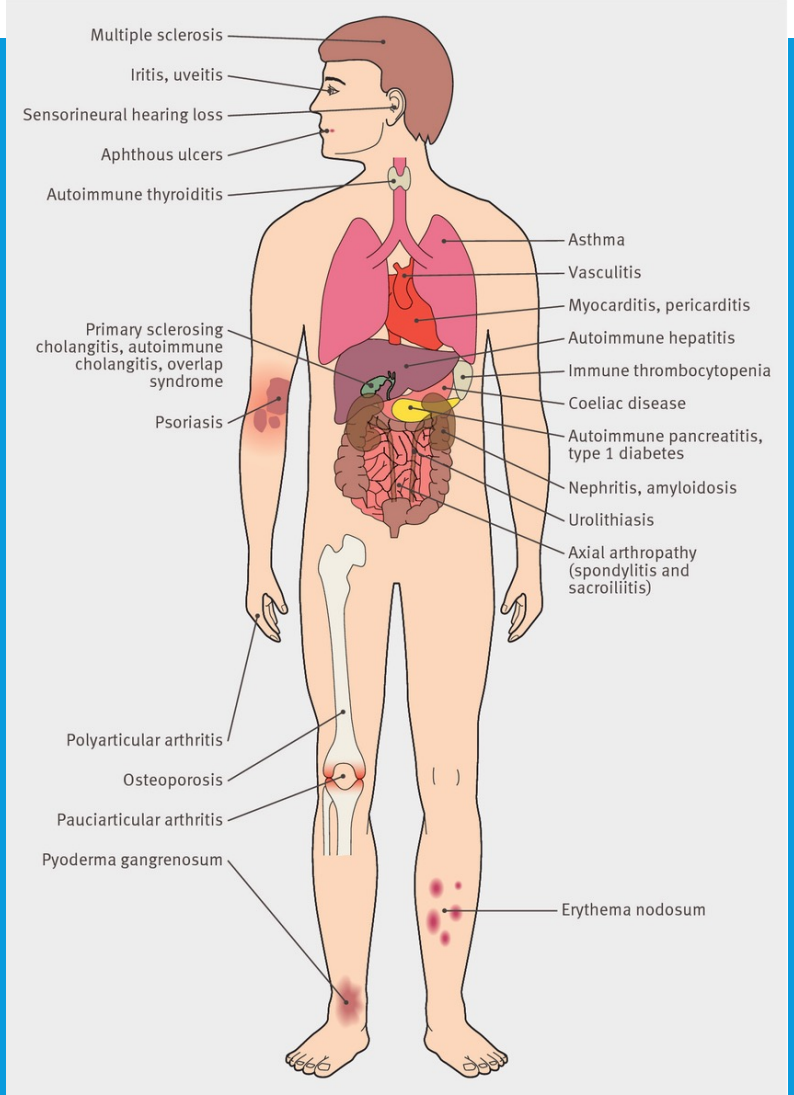
- the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response, loss of response to, or were intolerant to either conventional therapy or infliximab, a TNFα antagonist.

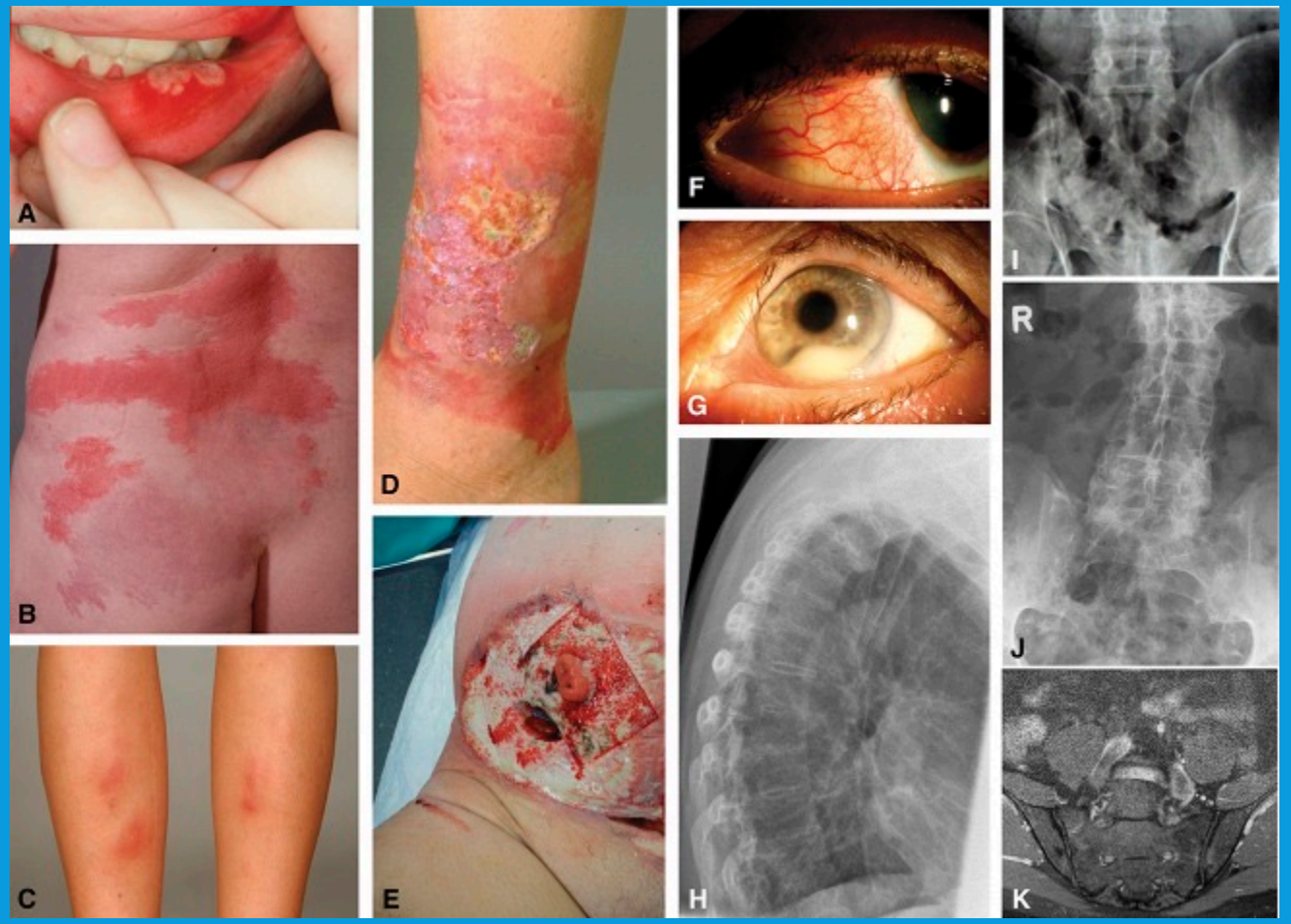
Crohn's Disease (Adults ≥ 18 years)

- the treatment of adult patients with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to immunomodulators or a tumor necrosis factor-alpha (TNFα) antagonist; or have had an inadequate response, intolerance, or demonstrated dependence on corticosteroids.

ENTYVIO® [Product Monograph]. Takeda Canada Inc July 2022

EXTRA INTESTINAL MANIFESTATIONS OF IBD

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OAG Gamification
BLINDSIDE

DISCLOSURES

- I made these slides
- No company input
- Been paid by every Pharma company, I think.
- Takeda is paying me, I think.
- No conflict of interest (?).
- I was PI and NEJM co-author for landmark Vedo studies: Gemini 1 and 2
- Millenium then, not Takeda.

MOCOMP ROLES

- I am not an expert
- I just have a lot of clinical experience in IBD for over 40 years.

"You can observe a lot, just by watching".

Yogi Berra

New York Yankee catcher, coach, manager

DR JEFF AXLER

- GP to GI
- Community based for 40 years at EGH
- Heavy based IBD practice: > 50%
- Sometime U of T lecturer
- CPSO site inspector/peer assessor
- OAG (president x 3 yrs) (2006-2009)
- Medcan OHP
- Is it better now: ITS WAY BETTER!!
- Clinical Research in IBD x 25 years: what's happened to the EIM's???

EIM'S OF IBD: A DIFFERENT VIEW

- Historically these were very common in GI practice
- As common as 30% of patients with IBD in community setting
- Incidence dropping as disease is diagnosed earlier,
- Treatment is now earlier
- Treatment is more effective for advanced disease
- More treatment options.

WHY IT HAPPENED?

- Disease changed?
- Treatment changed?
- Ability to diagnose and treat earlier?
- Treatment became more accessible, moving from university to community
- Clinical care moved to the community
- Clinical research moved to the community

OVERALL THEMES OF EIM'S

- Unknown causes
- Diffuse organ systems
- Unpredictable, not always related to IBD disease course
- Rare to "uncommon"
- Treatments vary from steroids to biologics to surgery
- No "good" studies: most are retrospective, or meta analysis

BEST AND MOST UP TO DATE REVIEW:

- ECCO Guidelines on EIM in IBD

Gordon et al (19 members)

Journal of Crohn's and Colitis, 2023 XX 1-37

- Reviews in Basic and Clinical Gastroenterology and Hepatology:

Extraintestinal Manifestations of IBD: Current Concepts, Treatment, and Implications for Disease Management.

Gastroenterology 2021; 161: 1118-1132

Rogler,(Zurich), Singh,(California) Kavanaugh (California)and David Rubin, (Chicago).

EIM OF IBD: A DOGS BREAKFAST

Classic EIM

- Uveitis, Scleritis, Episcleritis
- Oral manifestations
- Liver: PSC and AIH
- SpondyloArthopathy: Axial/non-axial
- Erythema Nodosum, Pyoderma Gangrenosum, Sweet Syndrome,
- ?Fistulas (not mentioned or included by ECCO!)

EIM'S: MORE BREAKFAST

Associations and Complications

- MS,CVA
- ILD, Bronchiectasis
- Myocarditis, CAD
- Fatigue
- Anemia
- Osteoporosis

EIM: END OF BREAKFAST

Treatments

- **Pancreatitis**
- **Osteoporosis**
- **Rashes**

AS FOR THE REST – MY ADVICE

- Share the load with your GI colleagues – ask their opinions.
- Refer to Neurologists, Dermatologist, Opthalmologist, Hepatologist
- Hematologist, Nephrologist
- Chat groups will replace expensive meetings to gather information and provide consensus when data is limited and individual experiences are limited
- May not be as "scientific" but information will be gathered faster and from a wide audience

PEARLS

- Oral lesions, EN, peripheral arthropathy: often follows the gut disease
- Axial arthropathy, PSC, pyoderma tend to act independently not with gut activity
- PSC: no benefit to Urso, Antibiotics, Vedo or anti-TNF
- AIH: use Imuran for maintenance
- NSAID's: no evidence of an association between NSAID use and UC flare.
- Axial Spondyloarthropathy: use anti-TNF, not Vedo or Stelara
- Non Axial: anti-TNF, MTX, and Salazopyrine, but enough info to say Vedo or Tofa
- Erythema Nodosa: control the IBD,
- Pyoderma: may be parallel or independent of IBD, use anti-TNF, steroid.
- HS: use anti-TNF, esp adalimumab at HIGH DOSE (160 mg weekly!)

It’s tough to make predictions, especially about the future.

The future isn’t what it used to be.

Yogi Berra
famous NY gastroenterologist

EIM'S FUTURE?

- Rarity
- Form part of spectrum of IBD that is not classic
- Failed treatments, multiple relapse, non responders:
- A different disease(s)
- Will be able to cycle through different treatments with different MOA till right selection
- Which is the right Rx? Guidelines, understanding pathophysiology
- Why do these EIM's happen. And why then, and why there?

- There lots to learn in this vast area of EIM
- More information to come.
- Its not over

- It ain’t over till its over
- And its not over.

WHAT ABOUT THE FUTURE OF IBD?

- Etiology
- Treatments
- Information
- Your roles: as guides and advisors is crucial to your patients.
- Things are looking UP!

HOW DID THAT HAPPEN

- 1. There was an "unmet need" – problems with no quick easy solutions
- 2. beginning of understanding underlying inflammatory mechanism: CYTOKINE
- 3. No access to advanced medical therapy thru the universities
- Thus: there was the "push" to try something
- 4. There was the inquisitiveness to try new things (just post new PPI)
- 5. There was interest in early and new ways to advance clinical trials
- 6. New models of cooperative care emerged: ECCO was prime example
- There was now a "pull" to a different way of treating complicated IBD

HOW DID I GET PUBLISHED IN NEJM

- Chance or pure luck
- There was the push and pull vectors
- We were just starting IBD clinical trials
- At a meeting, on a ski hill: What do you do? I make a new drug for IBD
- Me: I have lots of people who could use that
- Him: we think we have something really good.
- Me: I could be your best customer
- That was the start of start up Millenium connecting with TDDA
- We turned out to be the #1 contributor to the initial IBD studies on Vedo

- Gemini I and Gemini II
- It worked!
- It really put us on the map of IBD research
- I got published in NEJM
- We learned how to manage IBD research, how to select studies