

Inflammatory Bowel Disease: New Insights into Therapy and Treatment Goal

Alallam Alallam, MBBCh, ABIM, FRCPC
Staff Gastroenterologist, TBRHSC
Assistant Professor, NOSM

Objectives

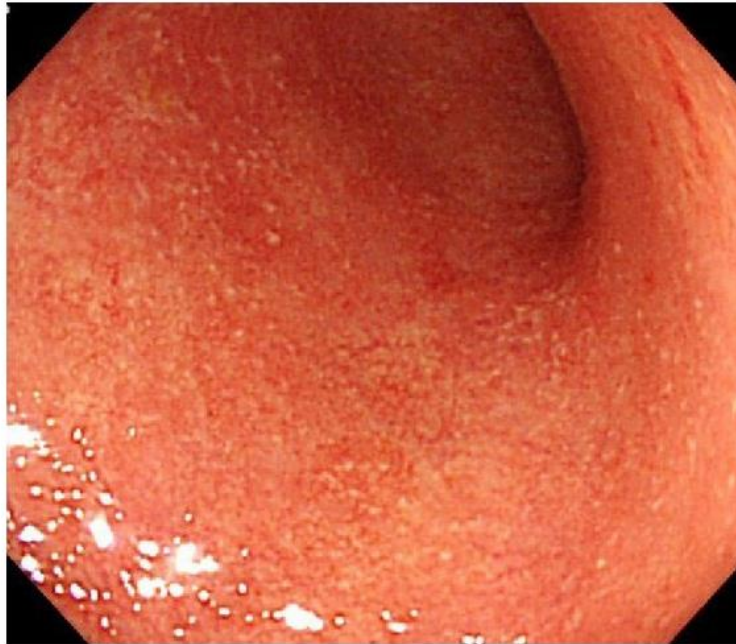
- Overview of treatment options
- Role of primary care providers in managing IBD patients
- Caring for a patient on biologics

Case 1

- 23-year-old male with 6 months history of 2-3 soft bowel movements, occasional rectal bleeding, tenesmus
- Otherwise healthy, no meds
- O/E: unremarkable
- BW: normal CBC, CRP and Albumin

Case 1

- Colonoscopy: mild proctitis

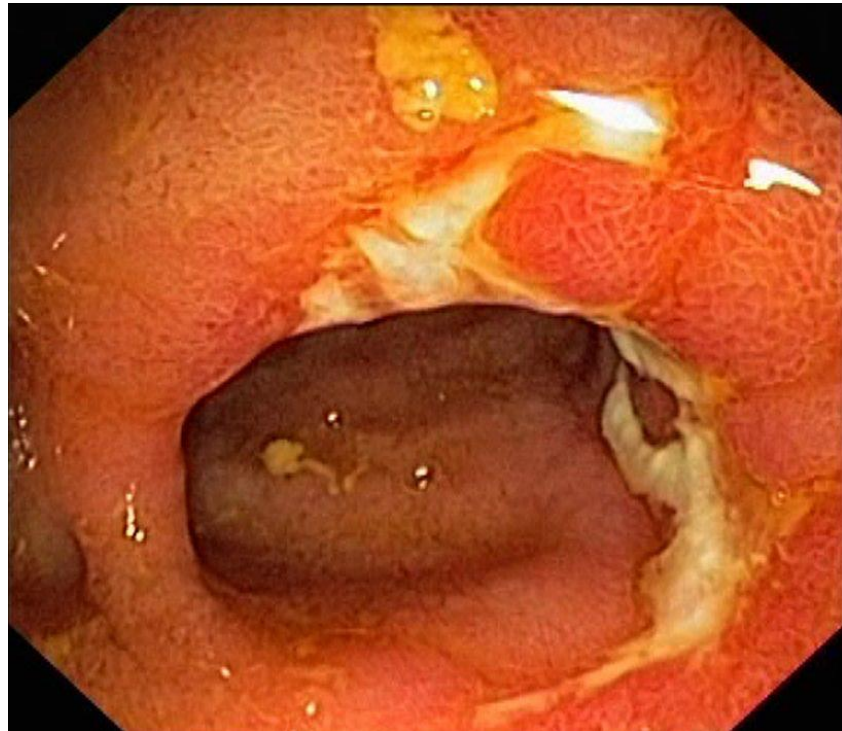


Case 2

- 19-year-old female with few months history of abdominal pain, wt loss and non-bloody diarrhea, along with anal pain
- O/E: tenderness in RLQ, perianal fistula
- BW: Hb 115, MCV 75, CRP 20, Albumin 35

Case 2

- Colonoscopy: terminal ileum ulceration, deep ulcers in the rectum

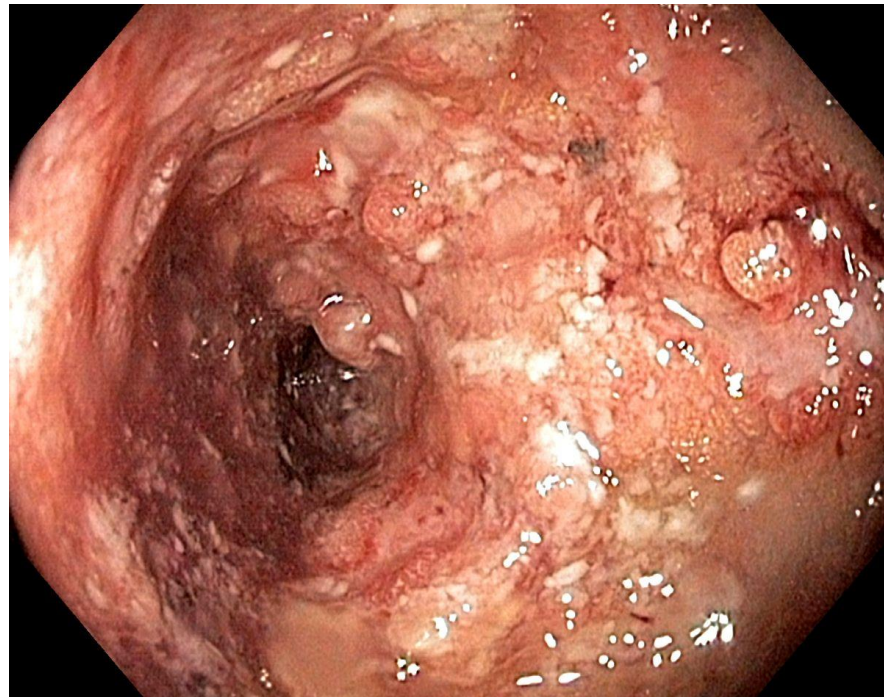


Case 3

- 31-year-old male with 1 month history of bloody diarrhea, Abdominal cramps, feeling unwell
- Recently quite smoking
- O/E: a febrile, HR 105, abdominal tenderness
- BW: Hb 105, CRP 45, Albumin 32

Case 3

- Sigmoidoscopy: severe colitis



Some thoughts about the cases

- Severity of disease
- Urgency of the consultation, scope, therapy

Treatment Goal(s)

- **“Old” goal**
 - Clinical symptoms control (Patient feeling better)
- **Ultimate goal of IBD management**
 - Complete disease control
 - Stop disease progression
 - Altering the natural course of IBD

New Therapeutic Outcomes

- Clinical remission (Steroid-free remission)
- Biological remission (e.g. normal CRP)
- Endoscopic remission(mucosal healing)

Treatment phases

- Induction of remission
- Maintenance of remission

Response

Treatment Options

5-ASA & Sulfasalazine

Mesalamine

Steroids

Prednisone, budesonide

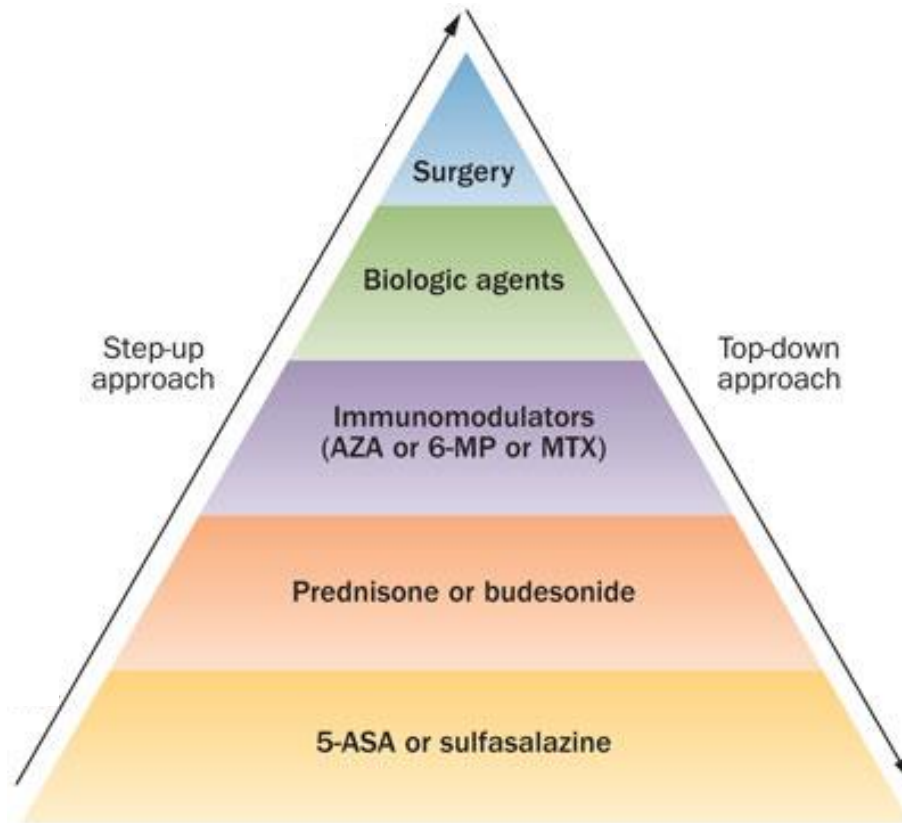
Immunomodulators

6-MP, AZA, MTX

Biologics

Anti-TNF α

IBD Treatment Pyramid



5-ASA

- Mesalamines
 - Salofalk, Asacol, Pentasa, Mezavant
- Ulcerative colitis
 - Induction and maintenance
- Crohn's
 - Induction: ? Modest effect for mild to moderate disease
 - Maintenance: ? post op

Corticosteroids

- Commonly used steroids
 - Prednisone
 - Budesonide (Entocort)
 - Mainly for Rt side Crohn's disease
 - Methylprednisolone
- Very effective for induction
- Not for maintenance

Immunomodulators

- Thiopurines
 - Azathioprine (Imuran)
 - 6 mercaptopurine (6-MP)
- Methotrexate
- Induction: not effective, mechanism of action
- Maintenance: yes, especially as steroid sparing

Biologics

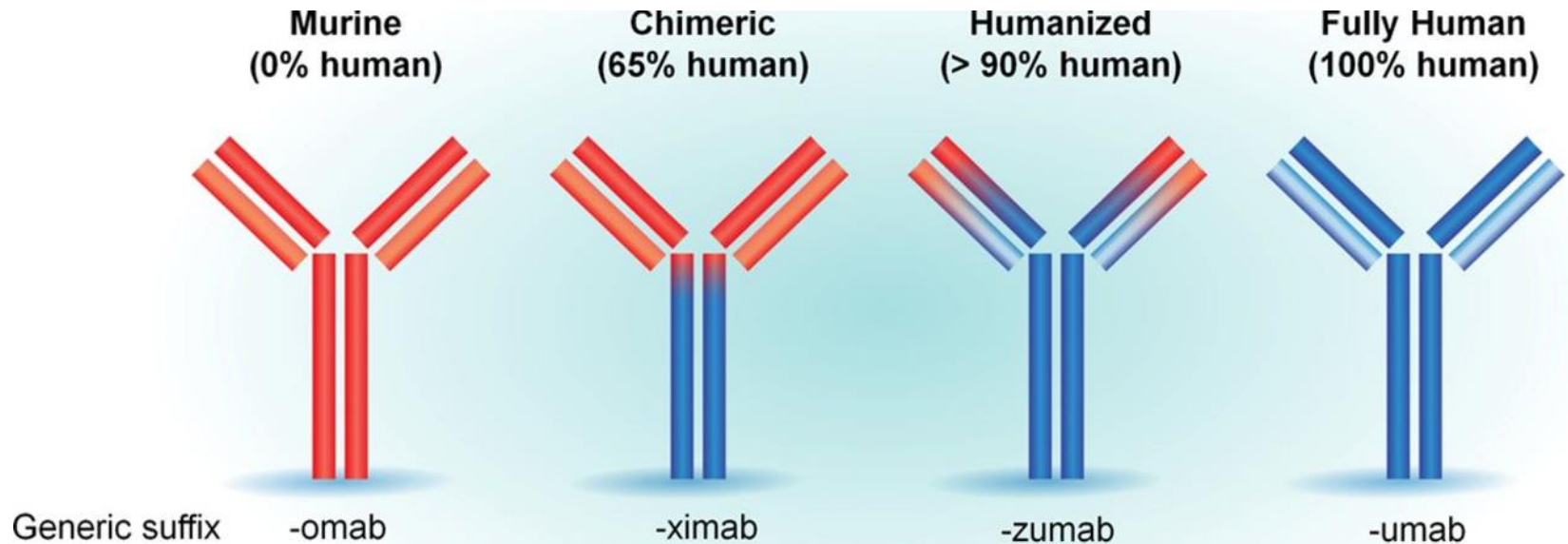
Immunology 101

- T helper cell :
 - Th1, Th2
- Th1(proinflammatory cell) , produce cytokines: eg
 - TNF (tumor necrosis factor)
 - IL 12 (interleukin)

Immunology 101

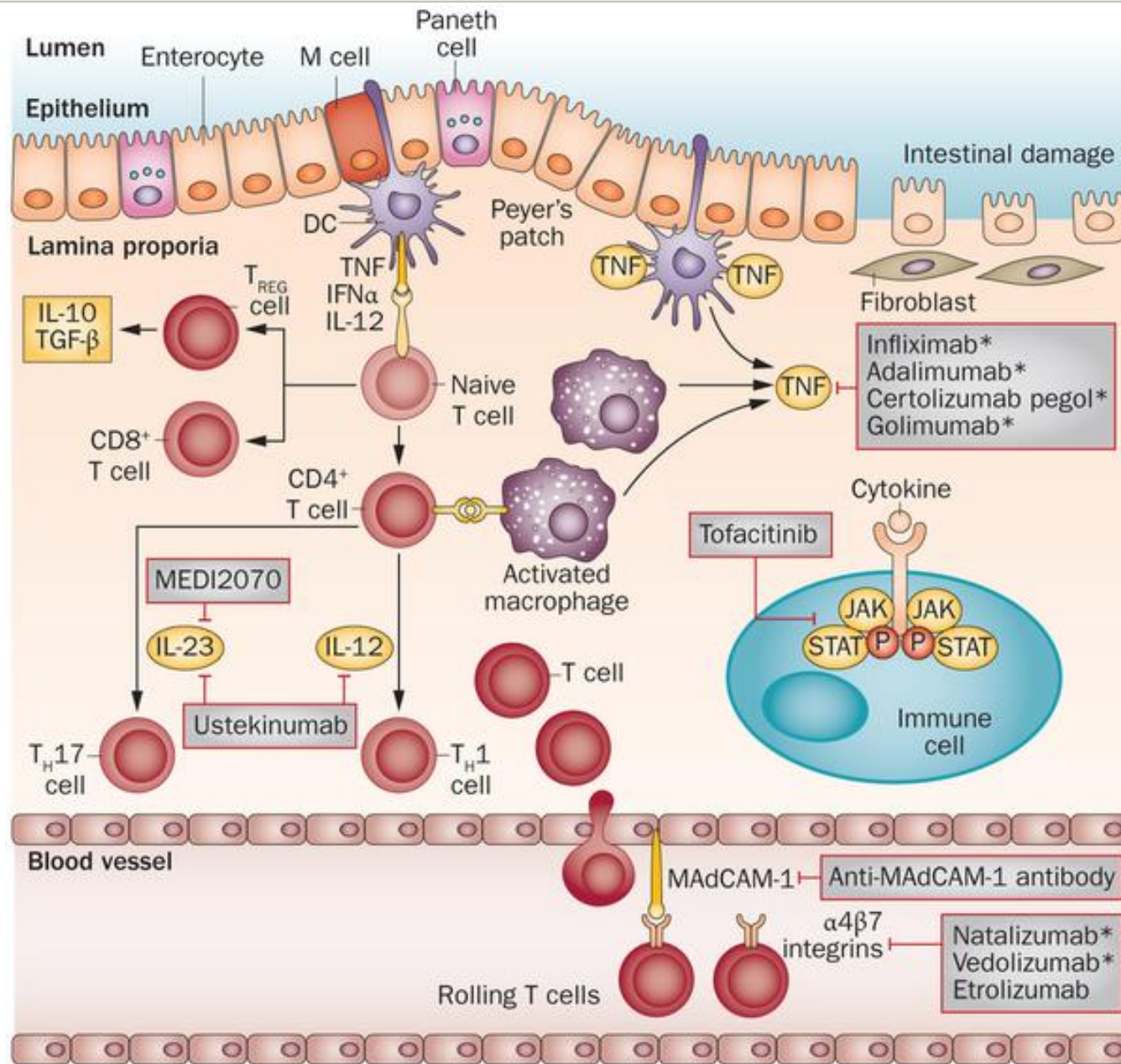
- Principle of therapy
 - Down regulate Th1
 - Inhibit the effector functions of the cytokines
 - Monoclonal antibodies
- Nomenclature
 - ‘-mab’ indicates a monoclonal antibody (mAb)
 - ‘-ximab’ indicates a chimeric mAb
 - ‘-zumab” indicates a humanized mAb

Monoclonal Antibodies (mAb)



IBD-Biologics

Anti-TNF α therapies	Anti-integrin antibodies	IL 12 & IL23 inhibitors
Neutralize TNF α	Block leukocyte migration to the sites of inflammation	Block IL12&IL23 receptors on Th
Examples:	Examples:	Example:
Infliximab (Remicade) Adalimumab (Humira) Golimumab (Simponi) Certolizumab (Cimzia)	Natalizumab (Tysabri) Vedolizumab (Entyvio)	Ustekinumab (Stelara)



Biologics

- Anti-TNF α
 - Infliximab (Remicade)
 - Adalimumab (Humira)
 - Golimumab (Simponi)
- Anti-Integrin (new)
 - Entyvio (Vedolizumab)
- Effective for both induction and maintenance

When to use Biologics

- Examples:
 - Refractory disease (to conventional therapy)
 - Severe disease (acute severe UC)
 - Steroid dependent
 - High disease burden
 - Fistulizing Crohn's

Dosing and regimen

	Remicade	Humira	Simponi	Entyvio
Route of administration	IV infusion	S/C	S/C	IV infusion
Induction dose	5 mg/kg @ 0,2,6 wks	160 mg @0 80mg @2	200mg @0 100mg @2	300mg @ 0,2,6 wks
Maintenance dose	5mg/kg q 8 wks	40mg q2wks	50 mg q4wks	300mg q8wks

Cautions/ Adverse events

- Infection
- Reactivation of HBV infection
- Reactivation of Tuberculosis
- Demyelinating disease
- Autoimmune disease : lupus like
- Psoriasis like
- Worsening severe CHF

Anti-TNF and Malignancy

- ? Malignancies
- ? Lymphoma
- Hepatosplenic T cell lymphoma
 - Rare
 - Fatal
 - Young male
 - Concomitant use of thiopurines

Things to do before starting biologics

- Check for Hepatitis B virus (HbsAg)
- T.B skin test
- Chest x-ray

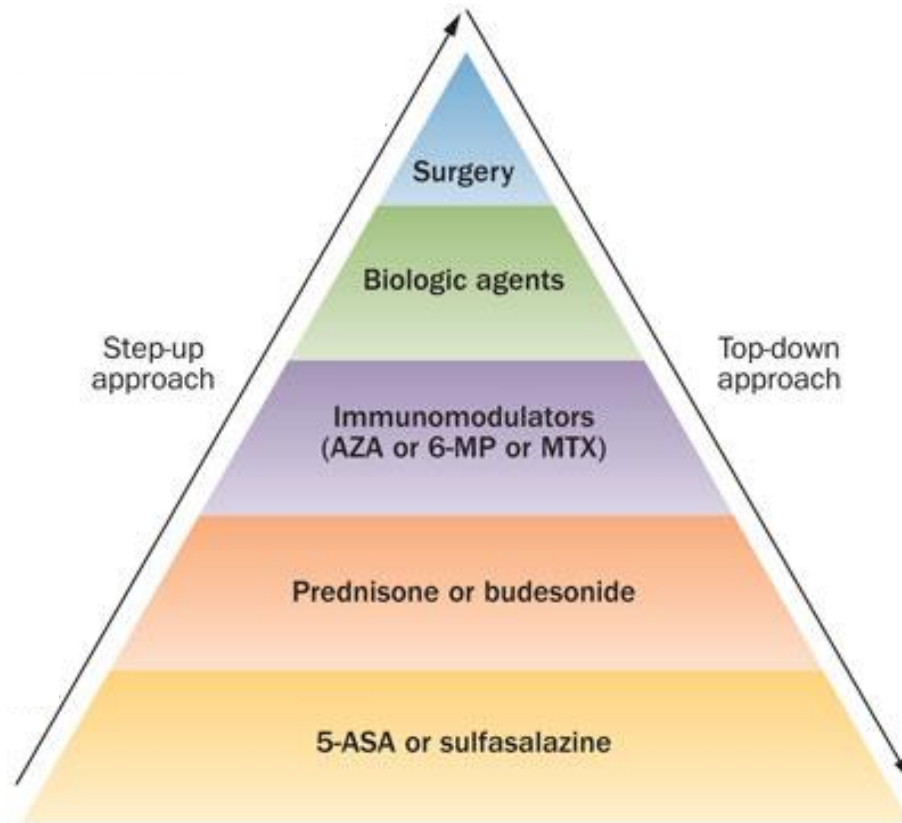
Immunosuppression & Vaccination

- Routine inactivated vaccines should be brought up to date
 - Including HAV, HBV, HPV
- Pneumococcal polysaccharide vaccine
- Live Vaccines are contraindicated once started high-level immunosuppression
 - (varicella, measles, rubella, yellow fever)
 - Check VZV immunity, give Zoster vaccine 4 wks before starting therapy if older than 50

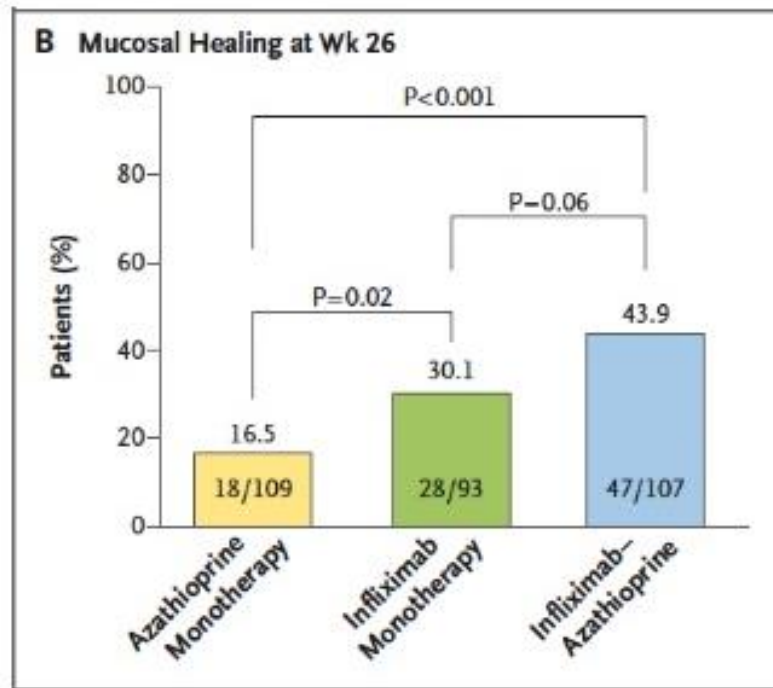
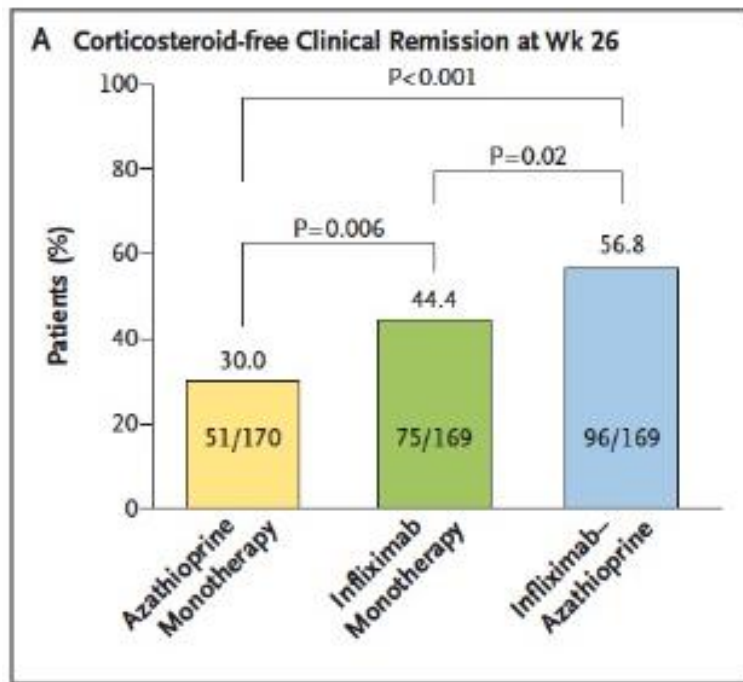
Monitoring IBD patient

- Clinically
 - Remission , general well being , psychology, quality of life
- Examine: skin ? annually
- Blood work
 - No routine tests for pts on biologics
 - CRP
 - Routine CBC/ liver profile if on thiopurines or MTX
- Need for: Vit D, Ca, Vit B12, Iron

IBD Treatment Pyramid



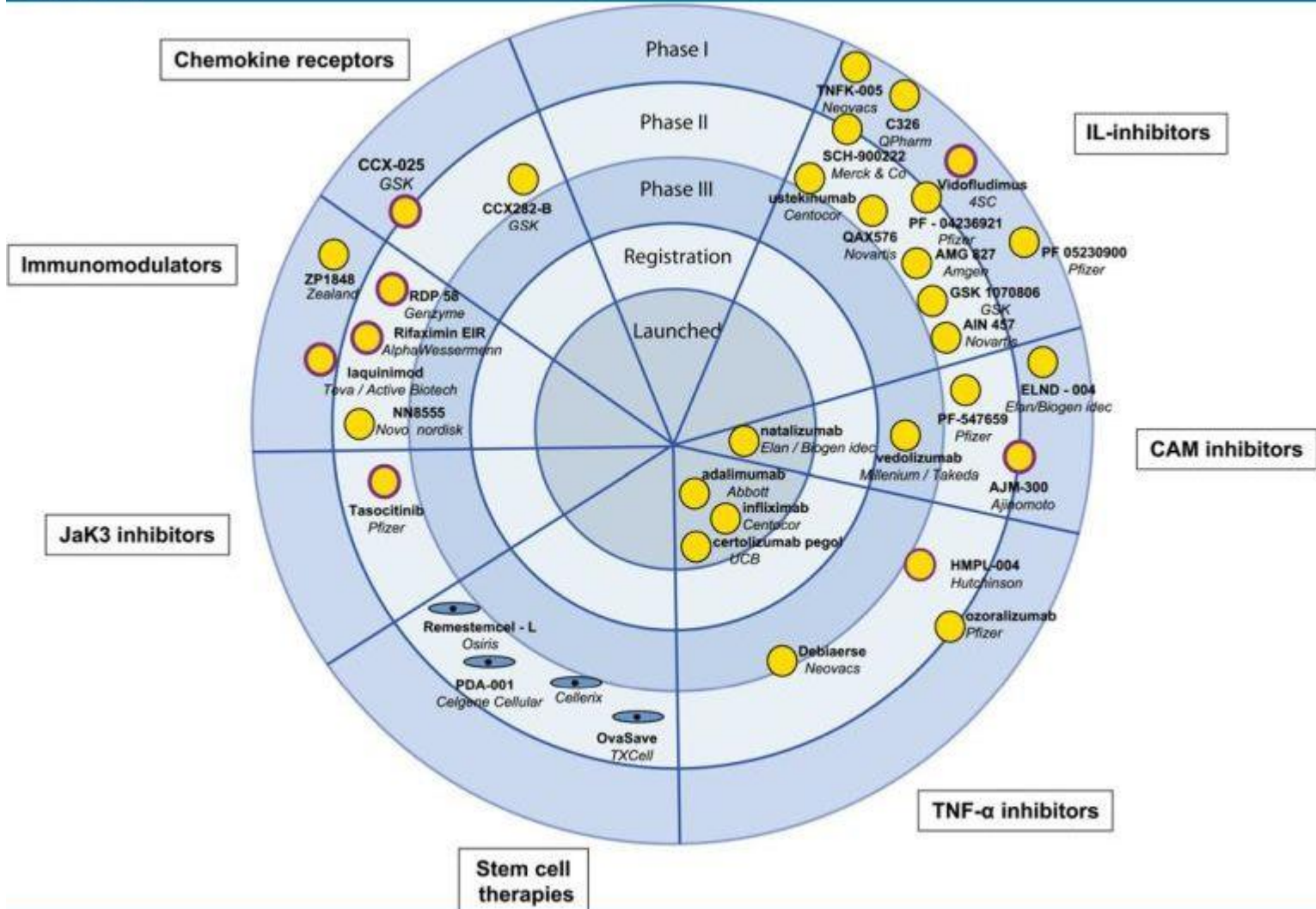
Combo therapy



SONIC trial. Colombel JF. N Engl J Med 2010;362:1383-95.

Points to mention

- Antibody formation against mAb
- Therapeutic drug monitoring
- Dose escalation
- Pregnancy
- New drugs are in the pipe line



Conclusion

- IBD have wide spectrum of presentation.
- New treatment goals including mucosal healing.
- Biologics have changed the natural history of IBD.
- Primary care providers play integral role in managing IBD patients.
- Future is brighter for IBD patients.