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Centre, Stellenbosch



Conventional therapy in IBD

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Anti-inflammatory drugs

Aminosalicylates

5-ASA active moiety

inhibit proinflammatory cytokine production

first line in UC

dose-dependent efficacy and adverse events

oral

topical

Corticosteroids

natural hormones or their derivatives

potent non-specific anti-inflammatory effect

multiple side effects

oral (high or low systemic bioavailability)

intravenous

topical



Conventional immunomodulators

Thiopurines

interfere with nucleic acid synthesis/ cell division and growth

Methotrexate

interfere with nucleic acid and protein synthesis / cell division

promotes cells apoptosis (death)

Calcineurin inhibitors

lower the activity of T lymphocytes and their immune response

Induction of remission

Ulcerative colitis

+
+
+/- (few data)
+/- (few data)
+
+
+

Aminosalicylates
Corticosteroids
Thiopurines
Methotrexate
Calcineurin inhibitors
Anti-TNF agents
Anti-integrin agents

Crohn's disease

+/- (colon)

+
-
+
?
+
+

Maintenance of remission

Ulcerative colitis

+

-

+

?

-

+

+

Aminosalicylates

Corticosteroids

Thiopurine

Methotrexate

Calcineurin inhibitors

Anti-TNF agents

Anti-integrin agents

Crohn's disease

+/- (post-op)

-

+

+

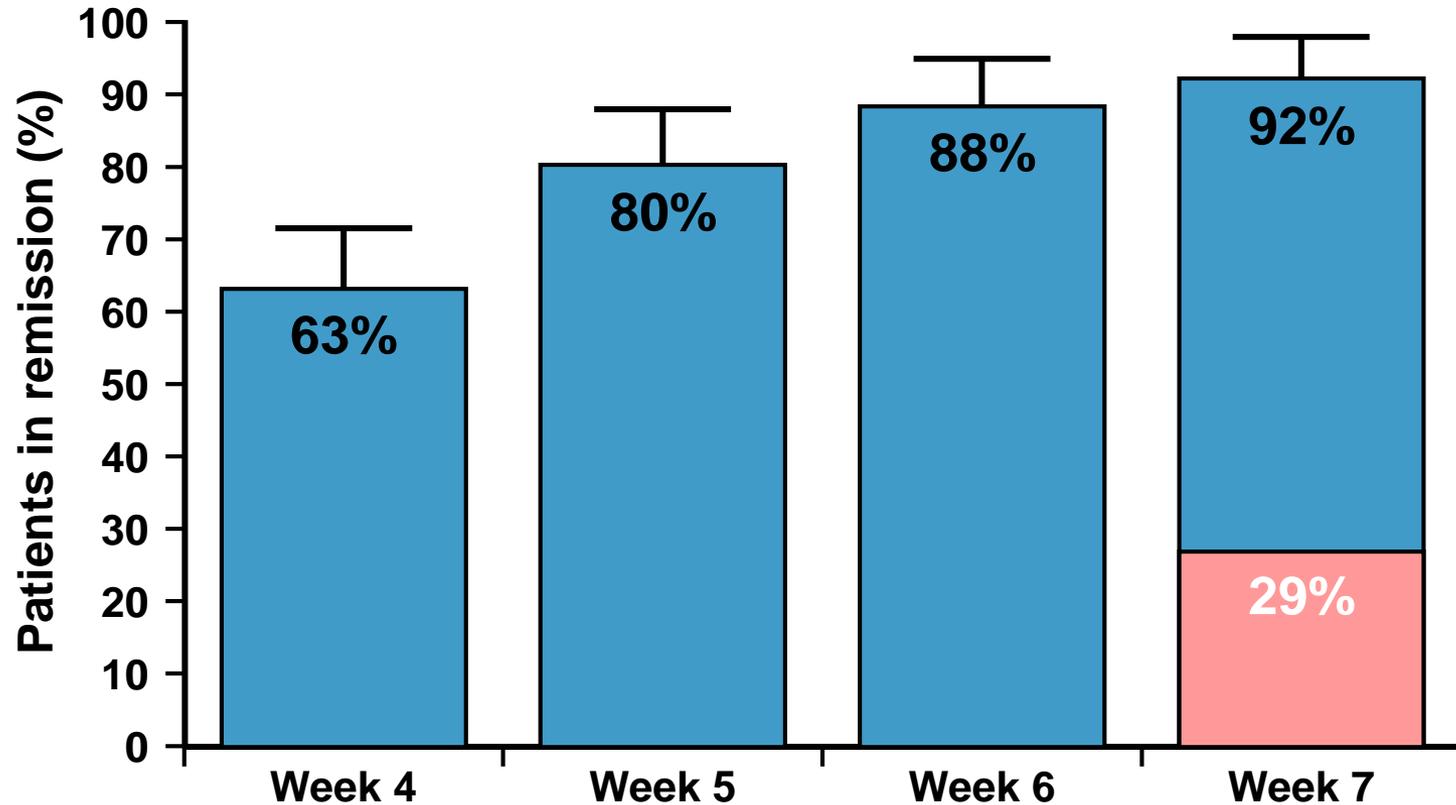
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+

+

92% in remission at 7 weeks with prednisolone

Prednisolone 1mg/kg until in clinical remission



Induction of remission in UC

Mesalazine: strong effect

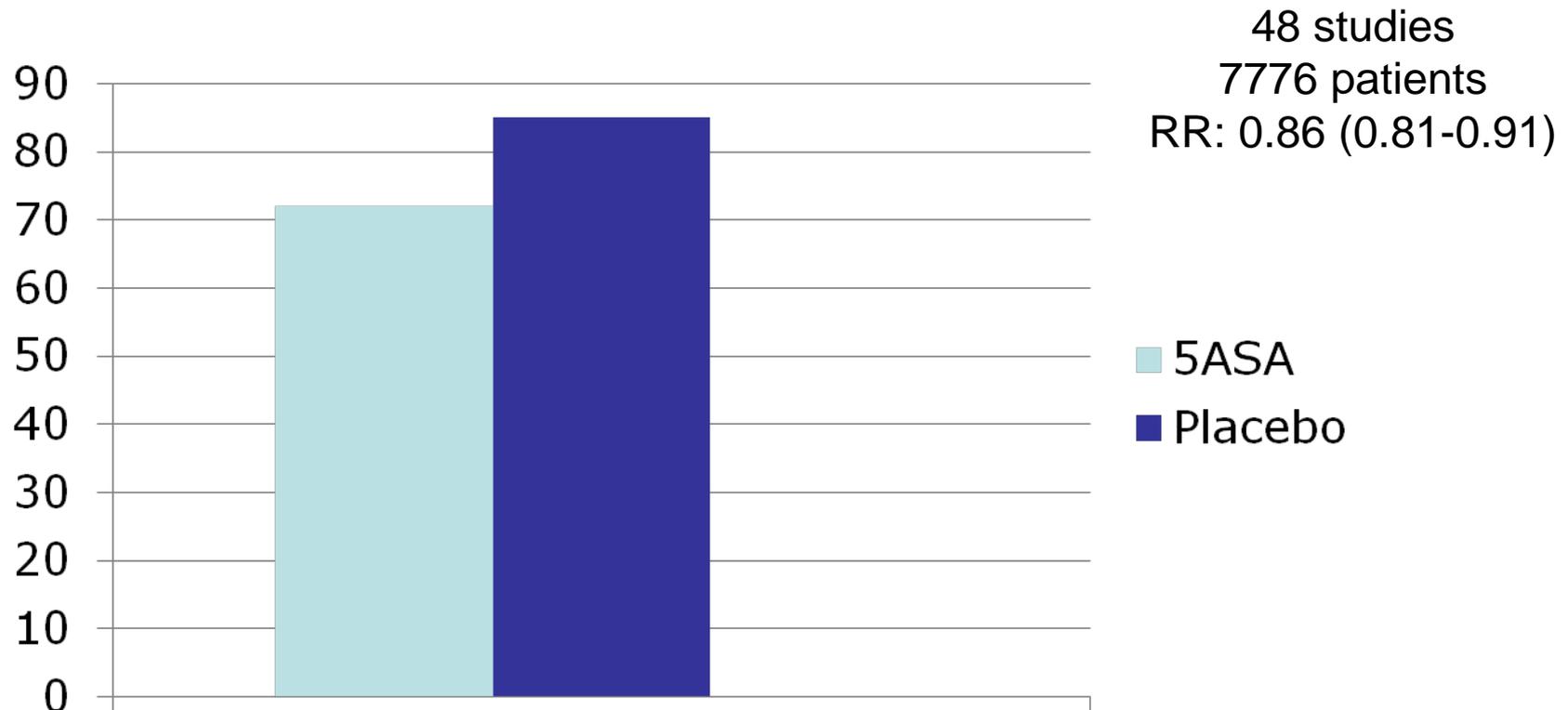
Steroids: strong effect (systemic or topical steroids)

Cyclosporin: strong effect in acute severe colitis



Meta-analysis of mesalazine for induction of remission in UC

Remission failure rate



Maintenance of remission in Crohn

No treatment in mild cases

Mesalazine in mild cases

Purines:

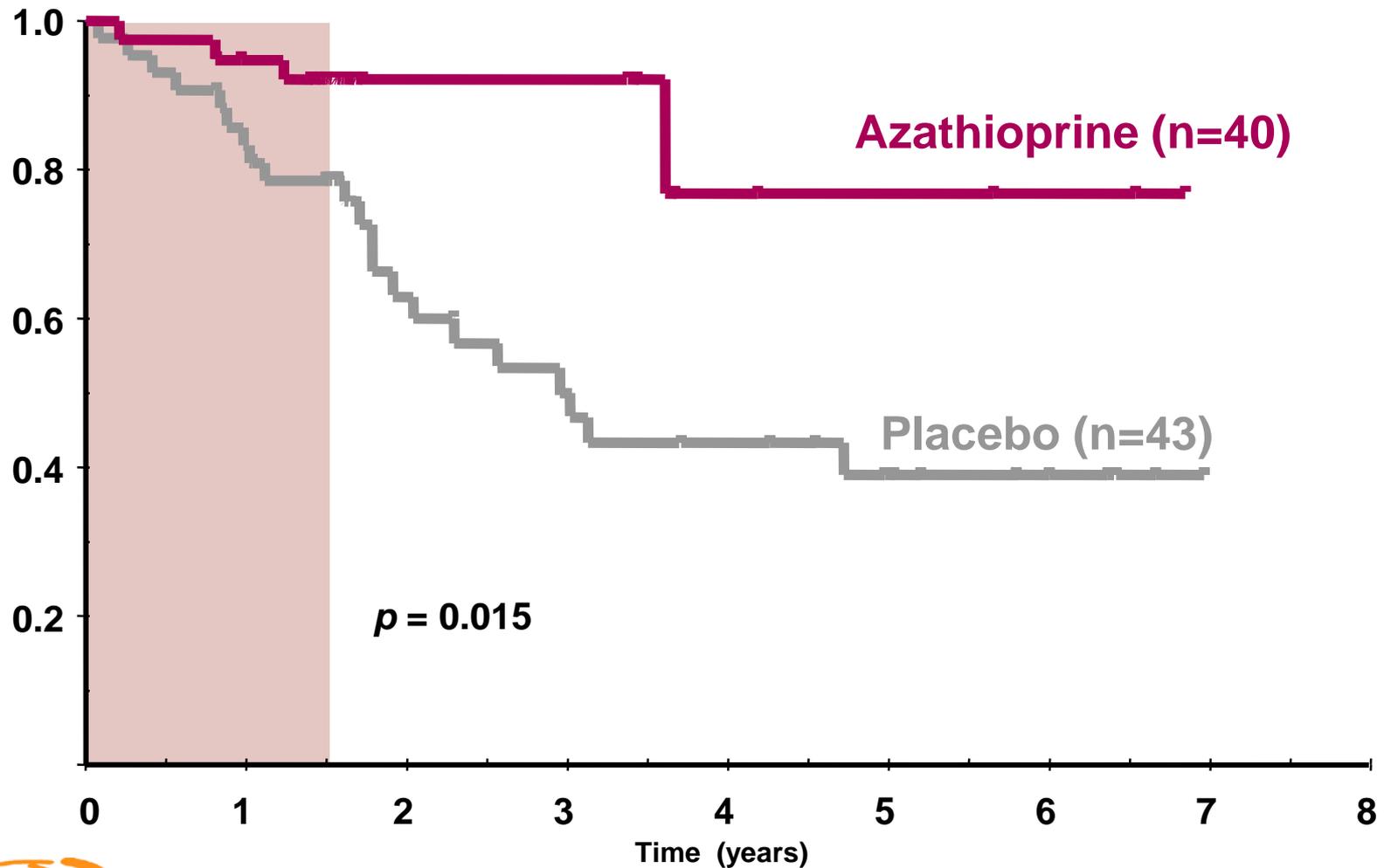
- Tolerated by 80% of patients
- Steroid sparing in 50% of patients
- Remission without steroids in 25%
- Tissue healing in 20%
- Safety issues (lymphoma, skin cancers, liver toxicity)

Methotrexate:

- Similar to purines (but less data and finally apparently less toxicity)



Azathioprine withdrawal trial in CD



Maintenance of remission in UC

Mesalazine: strong effect

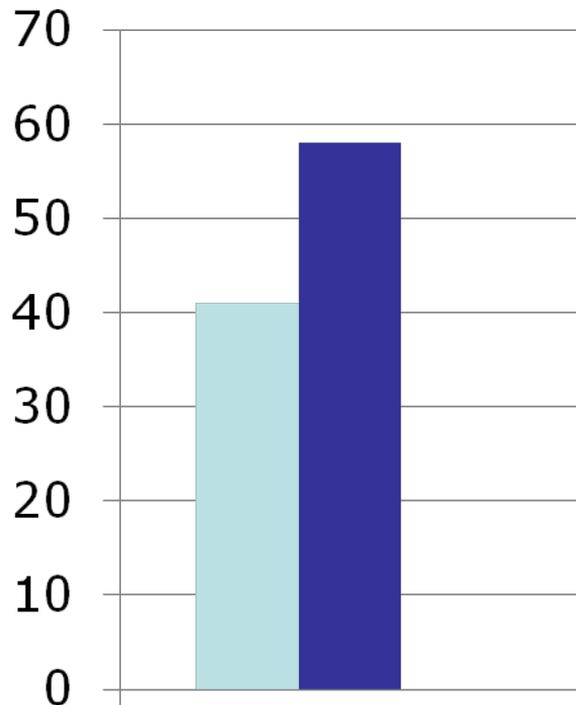
Purine: probably similar to Crohn (but less data)

Methotrexate:?

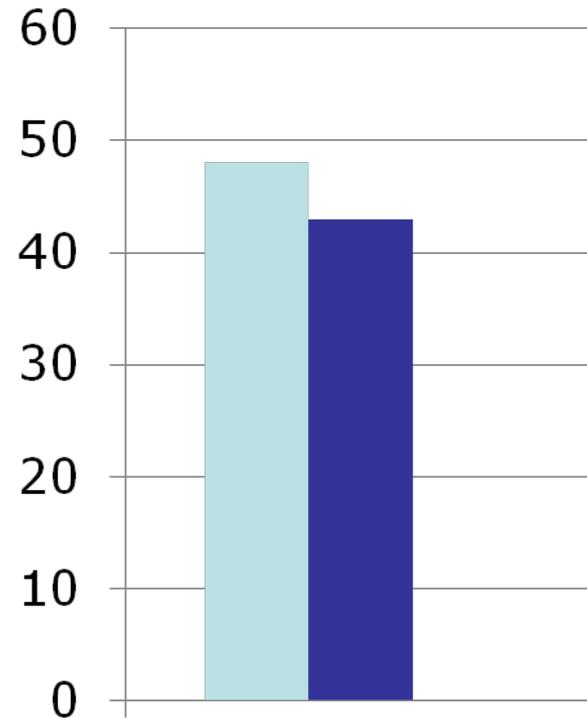


Meta-analysis of mesalazine for maintenance of UC

Relapse rate



7 studies
1298 patients
RR: 0.69 (0.62-0.77)



12 studies
1655 patients
RR: 1.14 (1.03-1.27)



Crohn: surgery is not always bad... and should be part of the strategy in some cases

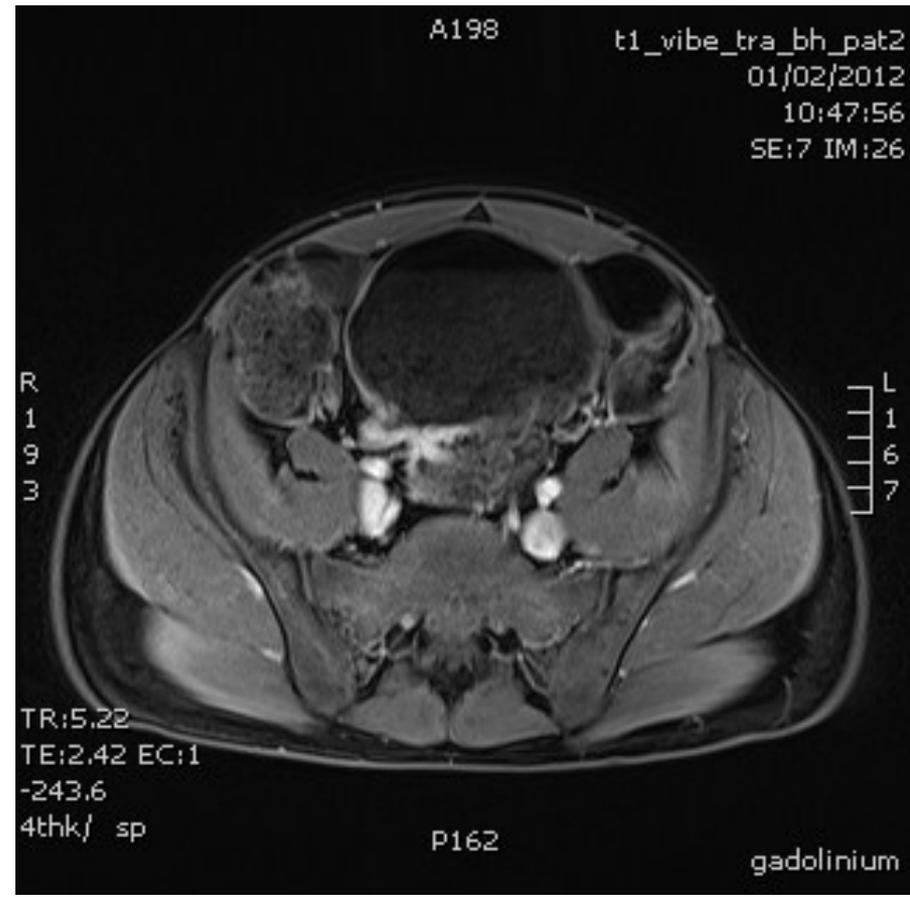
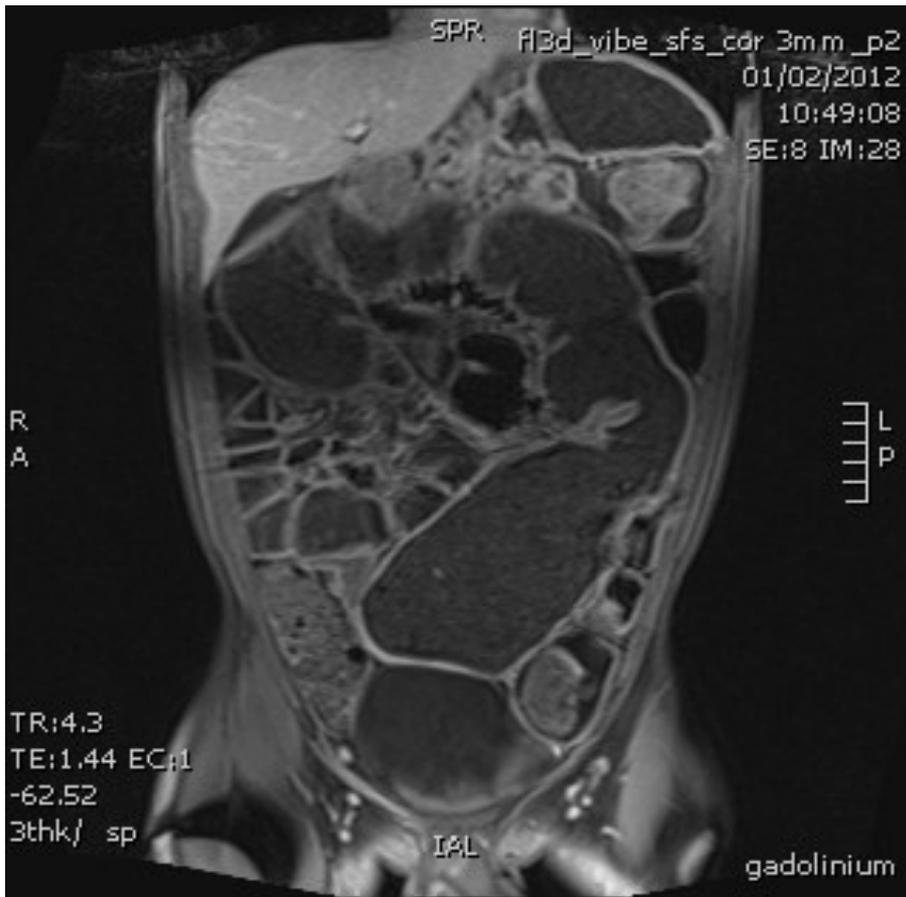
Sometimes best option for very damaged tissue (fibrosis-fistula-abcesses)

Must be limited in extent and number (short resection) and should preserve intestinal function

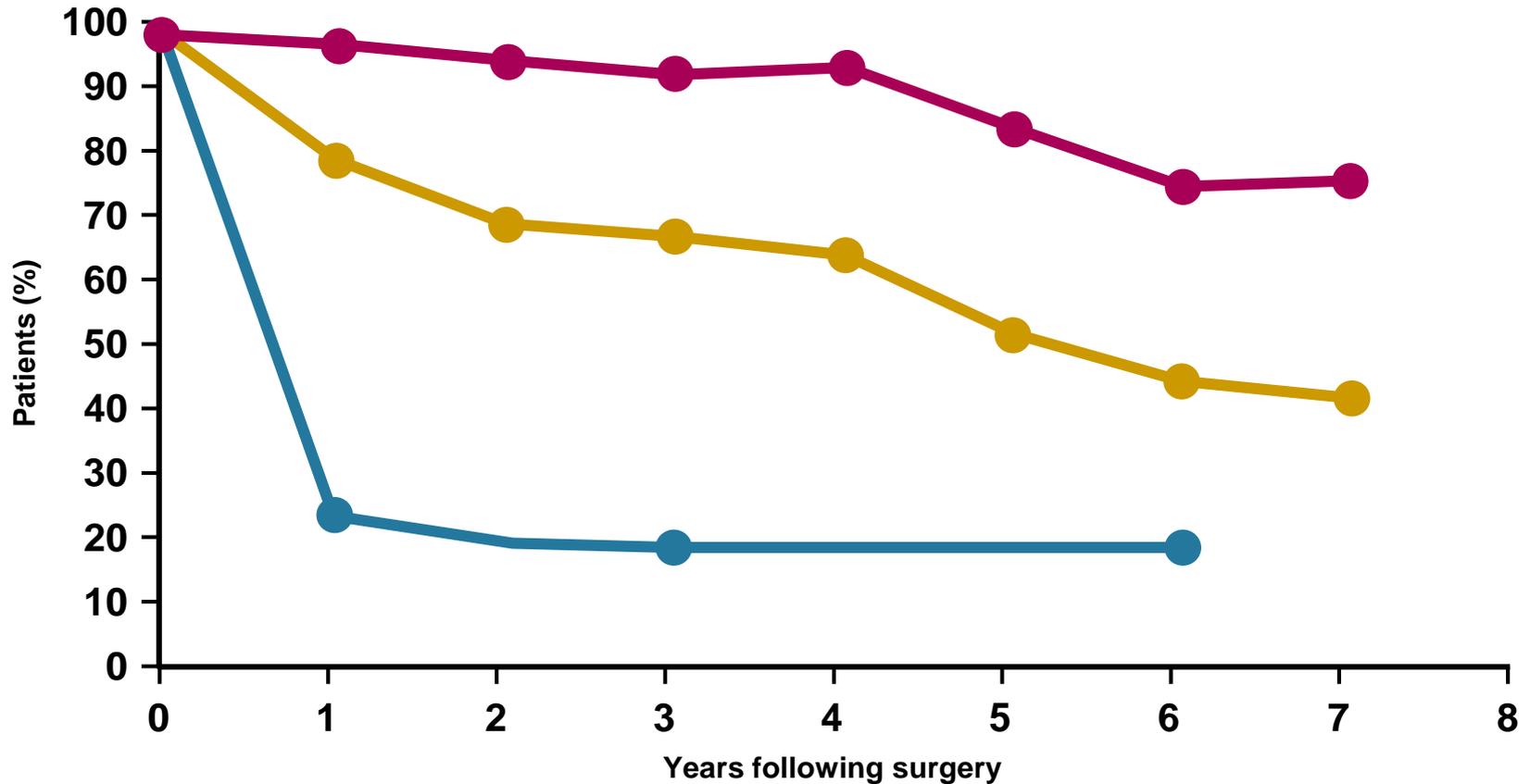
Allows to « restart on a clean base » with optimal treatment strategy and monitoring



How would you treat this?



Surgery may induce longstanding remission



- Survival without surgery
- Survival without symptoms
- Survival without endoscopic lesions

UC: surgery is sometimes the best option... but should not be seen as a cure.

Best option in:

- Refractory acute severe colitis (potentially lethal disease)
- Chronic untractable disease (situation should be compared to the predicted results of surgery and also integrate potential new drugs)

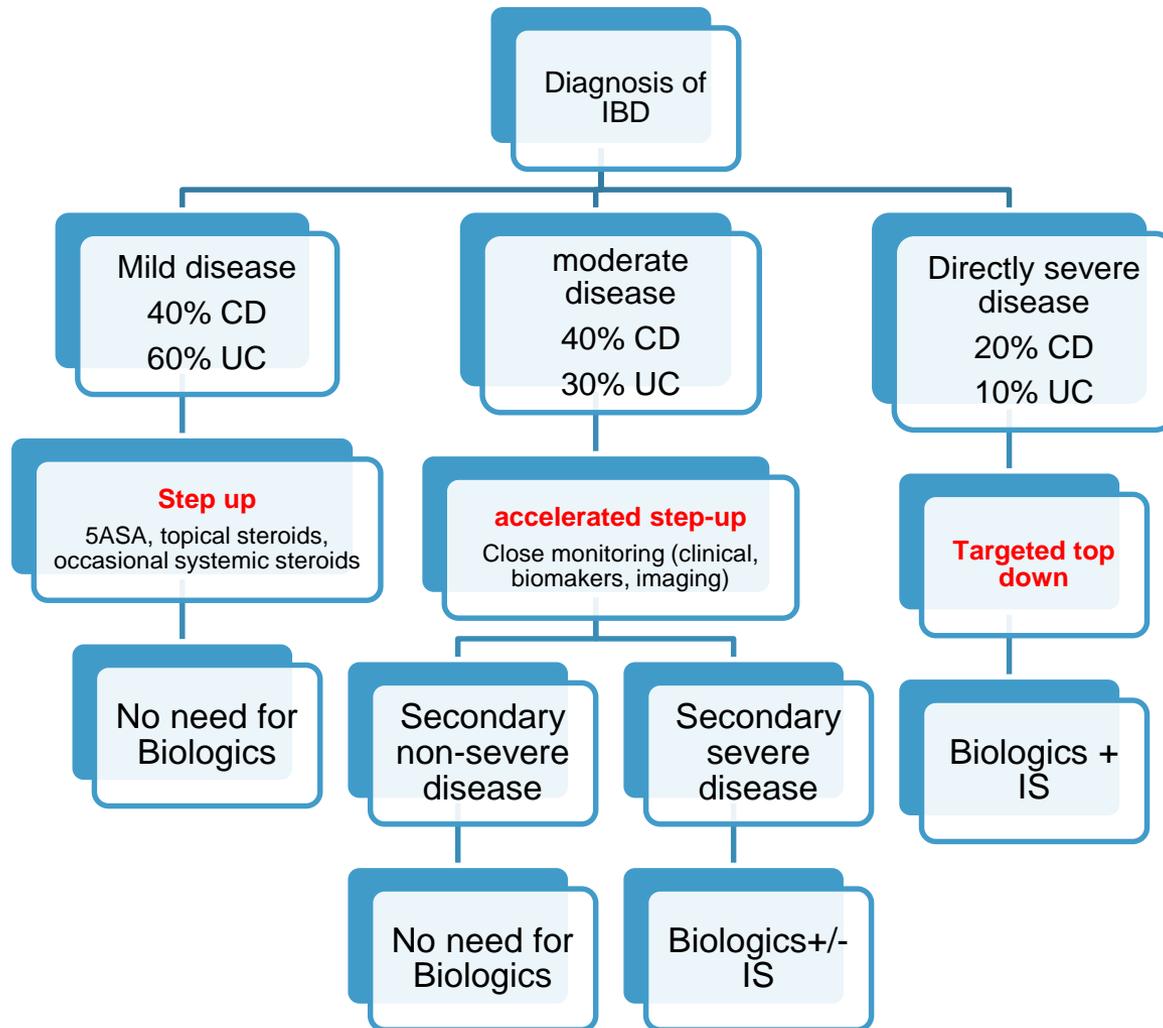
Average function includes:

- 5-6 stools/d including 1 at night
- Some incontinence episodes

Risk of pouchitis is significant (10-15% of chronic inflammation)



Tailored therapeutic algorithm for IBD



Numbers give in this slides represent an approximate estimation from several cohorts and population-based data.

Solberg et al. Scand J Gastroenterol 2009;44:431-40. Langholz E et al. Scand J Gastroenterol 1996 ; 31 : 260-6. Hoie O et al Gastroenterology 2007 ; 132 : 507-15.

Munkholm P et al. Scand J Gastroenterol 1995 ; 30 : 699-706. Solberg IC et al. Clin Gastroenterol Hepatol 2007 ; 5 : 1430-8. Thia KT et al. Gastroenterology 2010 Oct;139:1147-55.



Thank you for your attention



head-to-head studies

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