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Crohn's and Colitis Canada
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De-escalation of Therapy
In IBD

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Objectives

• Understand the reasons why clinicians would/should consider a de-escalation in IBD therapies
• Recognize which patients might be suitable for de-escalation in treatment
• Review the current evidence on de-escalation of treatments for IBD
Why de-escalate?

- Risk of infections
- Risk of neoplasm
- Pregnancy
- Social Economic/Patient preference
Concerns regarding combination therapy

**Infection**

**TREAT REGISTRY**

- 6273 CD on IFX
- Long term safety of IFX in large cohort
  - Moderate to severe disease activity
  - Narcotic
  - Prednisone
  - IFX
Infections

Corticosteroids → Candida species
Thiopurines → Viral illness
anti/-TNF → Fungi and mycobacteria
Infections

- Corticosteroids → Candida species
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3x increased risk of infection
Cancer

TREAT Registry

Independent association with malignancy
- Baseline age
- Disease duration
- Smoking

No increased risk with mono or combo therapy
Economic Issues

In some countries, economic issues are limited patients access to anti-TNF where clinicians are encouraged to de-escalate does and/or to withdraw anti-TNF when possible.
What’s the target?

- Mucosal healing
- Clinical symptoms
- Biomarkers
What’s the target?

- Mucosal healing
  - Deep Remission
- Clinical symptoms
  - Sustained >1 year
- Biomarkers
  - FCal, CRP, Hgb, WBC
Show me the…

IS + anti-TNF vs. anti-TNF monotherapy

SONIC
Patients receiving IFX + AZA had significantly higher rates of CS-free clinical remission and mucosal healing as compared to those receiving either treatment alone.
What about those patients who are refractory to conventional IS?

Should we continue both?

- Reduced disease activity
- Less risk of needing to switch to another anti-TNF
- Greater ano-fistula closure
De-escalation strategies

Corticosteroids
Ineffective as maintenance/minimize expose

Immunosuppressives
Immunogenicity MTX/Thiopurines

Anti-TNF
Dose optimization Increase/decrease interval
De-escalation strategies from two to one drug...

Combination IS & anti-TNF

IS Discontinuation

Van Assche et al. 81 pts/ remission x6months

Open-label, randomized, controlled study

Dose optimization = Discontinuation
De-escalation strategies from two to one drug...

Combination IS & anti-TNF

Anti-TNF Discontinuation
Rheumatology Saleem et al. 2010

47 patients in clinical remission on MTX/IFX
Main predictor of successful withdrawal was time to treatment from diagnosis
So what about IBD?

2 Prospective Trials

GETAID
2008
- 115 CS dependent CD patients
- IFX 0,2,6 vs placebo then AZA
- At week 12, 75% IFX pts in remission off CS

STORI
2012
- 115 CD/CS remission x6m IFX/AZA x1y
- 44 relapses at 12m
- 7 more at 24m
- 15% relapse within 1year with 2 or<

Risk for relapse
- Male
- No prior surgery
- WBC
- CRP
- FeCal
- Hgb
Summary

• Patients exposed to a combination of IS and anti-TNF have an increased risk of infection
• No clear signal for associated cancers compared to single therapy
• IS alone relapse rates at 12 months following IS cessation is close to 20% CD & 30% UC
• No IBD studies examined anti-TNF withdrawal in scheduled monotherapy
Summary

- In patients receiving IS & IFX for at least 6 months, relapse rate of IFX failure following IS cessation is near 20% at 24 months and seems to be similar to those who continued combo therapy.
- Anti-TNF cessation in CD on combo-therapy shows a relapse rate close to 40% and 50% over 1 and 2 years respectively.
- Special populations: young male, pregnancy and the elderly require special consideration.
De-escalation treatment strategy should be mainly considered in patients with high risk of severe adverse events and low relapse risk (patients in deep remission) after drug withdrawal.
Thank-you