Inflammatory Bowel Disease Medical Management - Update

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Conventional treatment for IBD

- 5 ASA
- Corticosteroids
- Thiopurines

- Anti TNF treatment
 - Infliximab 1998 for CD & 2008 for UC
 - Adalimumab 2007 for CD & 2015 for UC
 - Golimumab 2015 for UC
- Primary and secondary treatment failures
- Adverse effects

- Cellular Signalling
 - IL 12 & IL 23 Ustekinumab, Rizankizumab, Mirikizumab
 - JAK inhibitors
 - intracellular tyrosine protein kinases
 - 4 members JAK 1, JAK 2, JAK 3 and Tyrosine Kinase
 - Small molecules rapid action
 - First IBD therapy administered orally
 - affect multiple cytokine-dependent immune pathways
 - Tofacitinib nonselective
 - Filgotinib, Upadacitinib JAK 1 selective

- Leucocyte Trafficking
 - Anti Integrin Vedolizumab
 - Sphingosine 1 Phosphate (S1P) modulators Ozanimod

- Vedolizumab humanized monoclonal antibody against $\alpha 4\beta 7$ integrin
 - UC & Crohns Disease (2015)
- Tofacitinib (2018) JAK Inhibitor non selective
 - UC
 - Failed or intolerant to conventional therapies and Anti TNF
- Ustekinumab Monoclonal antibody IL12 & IL 23
 - Crohns Disease (2017)
 - UC (2020)
 - Failed conventional therapy or Anti TNF

- Filgotinib (2022)
 - Selective JAK1 inhibitor maximise efficacy and minimise side effects
 - UC only NOT for CD
- Ozanimod (2022)
 - S1P modulator
 - UC only
 - Conventional and Anti TNF failure

- Upadacitinib (2023)
 - Second generation selective JAK1 inhibitor
 - Only small molecule for UC and CD 2023.
 - UC failure of conventional therapy or anti TNF
 - CD must have had previous biologics exposure.
- Risankizumab (2023)
 - Humanized monoclonal antibody
 - IL 23
 - CD only must have previous biologics exposure

- Mirikizumab (2023)
 - Monoclonal antibody IL23
 - UC Only 2023
 - Unable to tolerate conventional or anti TNF
 - Lost response to anti TNF

Ulcerative Colitis & Crohns disease	Ulcerative Colitis ONLY	Crohns ONLY
Infliximab Adalimumab Vedolizumab Ustekinumab Upadacitinib	Mirikizumab Tofacitinib Filgotinib	Rizankizumab

Anti TNF

- Infusion reactions
- Opportunistic Infections
- Malignancies

Vedolizumab

- Nasopharyngitis
- Headache
- Jointpain
- No serious and opportunistic infections compared to Placebo
- No PML
- No increased malignancy

Ustekinumab & IL therapies

- No difference compared to placebo
 - No serious AE, serious Infections
 - No opportunistic infections
 - No malignancies

Managing potential adverse events of JAK inhibition.

no suitable treatment alternatives.

NMSC have been reported with JAKI.

Advise sun protection and periodic skin

examination, particularly those at high risk.

MACE

Increased risk of MACE. Avoid in smokers and patients with other CV risk factors for IHD or CVD, unless no suitable treatment alternatives.

LIVER IMPAIRMENT

Hepatic metabolism for JAKI; tofacitinib> upadacitinib> filgotinib. Avoid in Child-Pugh C cirrhosis. Risk of transaminitis – regular LFT monitoring.

RENAL IMPAIRMENT

Dose reduction required if creatinine clearance <30ml/min for upadacitinib and tofacitinib and <60ml/min for filgotinib. Avoid in all patients with ESRF.

VTE

VTE have been associated with JAKI use in clinical trials. Use with caution in patients with risk factors for VTE, including oestrogen containing hormonal treatment

CANCER DIABETES MELLITUS

Increased risk of cancer. Avoid in Increased risk of serious infection and patients with cancer risk factors, unless MACE. Use with caution.

Treatment interruption until infection

resolves. Administer antiviral drugs at

onset. Consider shingles vaccination.



OVER 65s

Increased risk of serious infection. Avoid in patients ≥65 years unless no suitable treatment alternatives.

PREGNANCY & BREASTFEEDING

JAKI are small molecules that cross the placenta and have demonstrated teratogenicity in pre-clinical studies. JAKI pass into breast milk. Family planning discussion prior to initiation.

DYSLIPIDAEMIA

Associated dose-dependent increase in lipid parameters. Check lipid profile at baseline and post-induction and manage elevation according to local guidelines.

CYTOPENIA

JAKI should not be initiated /treatment should be suspended if; haemoglobin <80g/dL neutrophil (ANC) <1 x 10⁹ cells/L lymphocyte (ALC) <0.5 x 10⁹ cells/L

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Ozanimod

- Bradycardia
- Herpes Zoster
- Upper respiratory infections

Personalising Patient Treatment – IBD MDT

- Disease duration, phenotype, extraintestinal manifestations
- Previous drug exposure & treatment response
- Comorbidities, age, gender, BMI, muscle mass
- Safety profile
- Patient preferences
- Patient risk of future complications

Thank you Questions