Dr Bernard Chin, Gastroenterologist

IBD Update, Part 2

For mild to moderate IBD which does not remit despite high doses of 5ASA agents and required multiple courses of high dose steroids in a year, Immunomodulators such as the Thioguanines and Methotrexate are the next step. It is important to look for risk factors of suboptimal response to 5ASA.

Crohns Disease (CD)

5ASA are poor agents for CD anyway. It is important to check that the patient has stopped, and continues to abstain from smoking. That is probably the single biggest environmental risk factor for CD.

Terminal ileitis in an ATSI patient should alert the clinician to the possibility of tuberculosis. Immunosuppression in this setting could be catastrophic.

Ulcerative Colitis (UC)

5ASA work very well for most cases of mild to moderate UC. Check for ongoing use of NSAIDS, which have been shown to precipitate flares of UC.

Immunomodulators

Thioguanines

Thioguanines are the preferred agents when an Immunomodulator is selected. I prefer 6MP as this is the active metabolite of Azathioprine (AZA). Starting doses are 6MP 1 to 1.5mg/kg versus AZA which is 2 to 2.5mg/kg.

It is a good idea to check Thiopurine Methyltransferase (TPMT) activity with phenotype testing prior to starting Thiopurines. We do not use Thiopurines if TPMT activity is low or absent (bone marrow toxicity). In intermediate TPMP activity, we start at half the usual dose and watch the lymphocyte count carefully.

It normally takes 1 to 3 months for a clinical response. We often use a tapering dose of steroids (see Part 1 of this series for our IBD steroid regime: *https://www.cairnsprivate.com.au/For-GPs/Digital-GP-Updates)*, over this period if we want to achieve remission during a difficult flare.

We watch the lymphocyte count fortnightly for 2 months to ensure the dose is not high enough to cause lymphopenia. We are aiming for a lymphocyte count of around 1.0.

Although not mandatory, I routinely check Thiopurine Metabolites (Therapeutic Drug Monitoring or TDM), to ensure there are no toxic by-products that are not detected early. We are aiming for a **6-TG level between 230 and 450 picomoles/8 X 10^8 erythrocytes**. Anything lower is suggestive of non-compliance, suboptimal Thiopurine dosing or preferential metabolism to 6-MMP instead of to 6-TG (“shunters” or Thiopurine resistance).

6-TG levels above 450 have been associated with bone marrow suppression.

6-MMP levels above 5700 increases the risk of hepatoxicity.

Thiopurine resistance

In patients where escalating doses of thiopurines result in low 6-TG and high 6-MMP, we would use Allopurinol to shift the metabolism of drugs towards 6-TG. We would use a quarter of the highest dose of Thiopurine achieved in the patients in addition to Allopurinol 100mg daily. We would then repeat TDM to ensure the metabolities are in the desired zones. Pharmacists get quite alarmed at the combination of a Thiopurine and Allopurinol and should be reassured that this is deliberate should you receive a panicked call from pharmacist!

Methotrexate (MTX)

In patients who are intolerant to Thioguanines, Methotrexate should be considered.

We would start MTX at 25mg weekly IM (unreliable oral bioavailability), until the patient is in remission. We would then convert the patient to MTX 25mg oral weekly and adjust the dose depending on disease activity and lymphocyte count. At these levels, the risk of long term liver toxicity is very low.

Routine monitoring

Once patients are on a stable dose and in remission, I would routinely check FBC and LFTS twice a year. Immunomodulators tend to slightly increase the risk of solid cancers, particularly skin cancers in FNQ. Patients should undergo routine screening tests for breast and cervical (females) and skin cancers, regardless of their age. Patients who have had CD and pan-colitis UC for more than 8 years should have 3 yearly colonoscopies for dysplasia surveillance.

Immunomodulators and pregnancy

Thiopurines are safe during conception and the entire term of pregnancy. Patients who wish to cease their Thiopurine (particularly if they have a history of difficult to control IBD), should weigh up the risk of a flare during pregnancy, causing obstetric complications such as miscarriages, and the higher risk of infertility with active IBD.

MTX is contraindicated 3 months prior to conception and during the pregnancy due to teratogenicity.

5ASA agents are safe throughout pregnancy although it can reduce sperm motility in males and, hence, affect fertility.

Next Episode: The old and new biologic agents and their role in the current management of IBD

About Dr Bernard Chin

Dr Chin graduated from the University of Adelaide and completed his Gastroenterology training in Sydney. He has an interest in the latest endoscopic obesity treatments and bowel cancer screening. He is the founder and principal of Cairns Gastroenterology since 2007, operating at both Cairns Private Hospital and Cairns Day Surgery.

Contact

Cairns Gastroenterology
Suite 3, Level 3, 120 Bunda Street
Cairns QLD 4870

Ph: 07 4041 2877
Fax: 07 4041 6135