Rheumatology MCN Practice Nurse Update

DMARD Monitoring Near Patient Testing Guidance

- Significant change to NPT guidance in 2018
- Updated in line with the British Society for Rheumatology guidance
  - https://academic.oup.com/rheumatology/article/56/6/865/3053478
- Advantages
  - Allowed reduced monitoring for stable patients on the most frequent DMARDs (Methotrexate and sulphasalazine)
  - Advantages to patients and to Primary care with less frequent monitoring
- Disadvantages
  - Addition of assessment of renal function and eosinophils has led to significant increase in queries and unnecessary withholding of DMARDs

Changes in DMARD monitoring due to Covid

- Early in Covid outbreak – concerns from Primary care that blood monitoring would need to stop and therefore patients would need to stop DMARDs.
- Advice from BSR, EULAR and ACR – that patients SHOULD continue DMARDs and biologic treatments
- Modified guidance for a temporary time period was issues.
  - Was reviewed end of June – Rheumatology MCN agreed to continue and review again before end of October
  - Modified guidance currently being reviewed ADTC.

Modified DMARD guidance

- BSR Covid guidance suggested that most patients could have 3 monthly monitoring and some less frequently.
- Other health boards (Forth Valley) had already moved onto modified guidance.
- As also it is patient specific and higher risk patients will need to have a more frequent schedule

DMARDs

- **Methotrexate**
- **Sulphasalazine**
- **Hydroxychloroquine** (No blood monitoring)
- **Leflunomide**
- Azathioprine
- Penicillamine

Covid DMARD monitoring- Methotrexate

- Baseline
  - U+E, FBC
  - AST, ALT and albumin
  - CXR(carried out at rheumatology clinic)
- 2 weekly until dose if stable for 6 weeks then monthly for 3 months then 12 weekly
- Dose increase 2 weekly until on stable dose for 6 weeks then previous schedule
- Always monthly if co-prescribed Leflunomide

DMARD monitoring- sulphasalazine

- FBC, U+E, AST and or ALT and albumin at baseline
- 2 weekly until dose stable for 6 weeks, then monthly for 3 months then 3 monthly
- If after 1 years bloods are stable- monitoring can be discontinued
- Abnormal bloods as per MTX

DMARD- monitoring Leflunomide

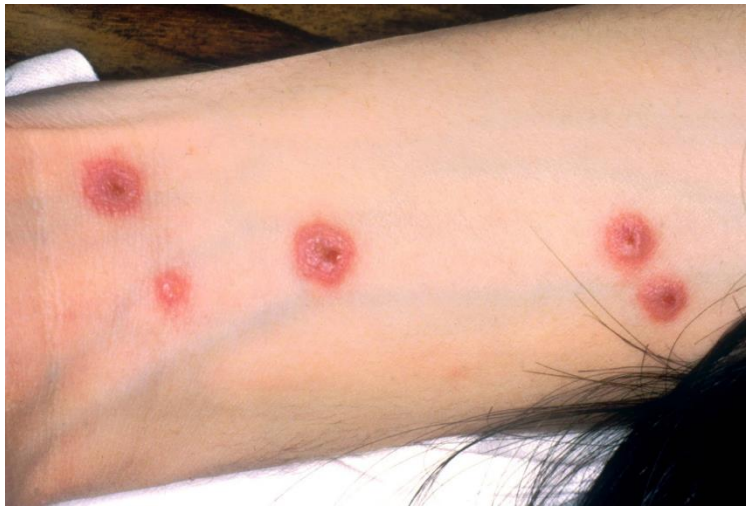
- Also need to check BP
  - One of the most common reasons for stopping Leflunomide
- Need to stay on more frequent LFT monitoring if also on MTX
- If serious side effects- needs a wash out with cholestyramine as has a very long half life

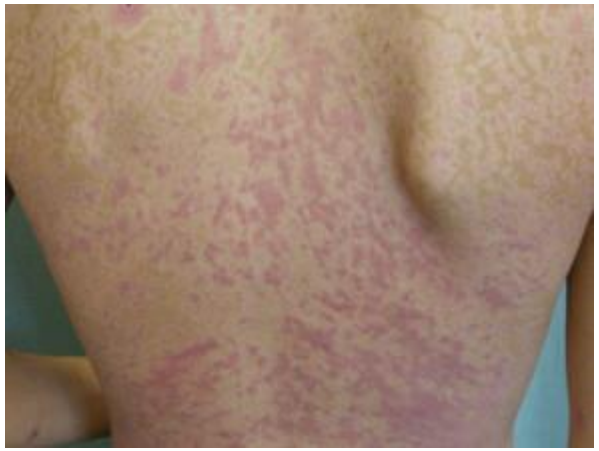
Methotrexate monitoring

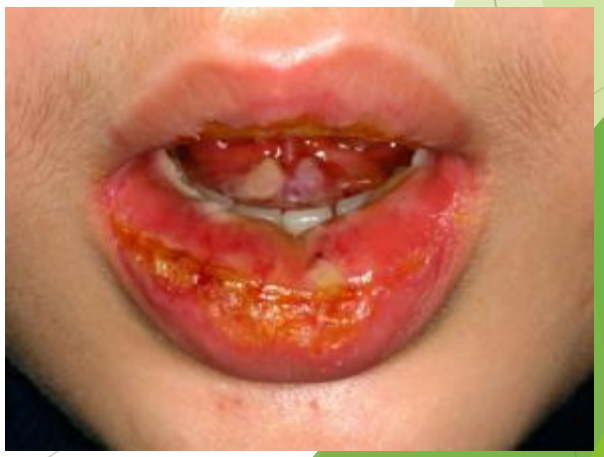
- FBC
  - Total white cell count <3.5
  - Neutrophils <1.6
  - Platelets <140
- Minor changes - ask for advice and keep on treatment. If significant change ask to withhold and seek advice.
- LFT
  - AST and or ALT >100 or unexplained albumin <30g/l
  - Prompt discussion and possibly withholding if a delay in advice

When to be concerned

- Sore throat, easy bruising – prompt to check FBC –may be an early sign of FBC abnormalities
- Rash – Sulphasalazine and hydroxychloroquine can be associated with Stevens-Johnson Syndrome and Toxic epidermal necrolysis







When to be concerned

- Mouth ulcers
  - Check folate, B12
  - May need to reduce dose or change to subcutaneous MTX
- Nausea
  - Common
  - Prochlorperazine can be helpful
  - Reducing dose, dividing dose
  - Changing to METOJET

When to be concerned

- Shortness of breath
  - Methotrexate very rarely can cause an acute pneumonitis –usually soon after commencing drug
  - Can predispose to chest infection
  - Slow development of pulmonary fibrosis is usually due to underlying Rheumatoid arthritis and not methotrexate.
- Stop if developed chest infection, sudden unexplained new shortness of breath

Temporary Covid monitoring

- FBC, U+E, AST and or ALT and albumin
- 2 weeks after start of treatment, 6 weeks after start of treatment, 3 months after start of treatment
- Then once every 6 months if stable
- If co-prescribed leflunomide then no less than 2 monthly

MCV

- Rise in MCV can be a sign of early bone marrow suppression related to DMARDs and can occur before any other changes
- Common causes of high MCV
  - B12, folate deficient
  - Alcohol excess
  - Hypothyroidism
- Haematology also suggest checking Immunoglobulins and electrophoresis.
- If MCV high but stable –continue to monitor
- If rising MCV and otherwise normal FBC continue DMARD and seek advice
- If rising MCV and change in FBC (lowering of platelets, white cell count) – stop DMARD and seek advice

Eosinophilia

- New addition to DMARD monitoring
- Rise in eosinophils can be a feature of toxicity to sulphasalazine and hydroxychloroquine and could prompt discontinuation of the medication
- Mild eosinophilia seen in asthma, hay fever and other allergic conditions.
- Very high eosinophils can be a sign of other disease (e.g. above 5)
- If high significant change in eosinophils occurs on starting new medication – ask patient about rash - and if present stop.

Renal function

- New guidance on NPT 2018
  - Creatinine clearance <30% or a decrease in eGFR to <60ml/min
  - Suggests withholding and discussing with Rheumatology team

- Small changes in renal function unlikely to necessitate a change in DMARDs but significant changes could increase toxicity of medication and a dose change may be necessary (especially methotrexate)
- Change in renal function may indicate a new health problems or a deterioration in health that may require a review of the most appropriate treatment for that patients.

When should monitoring frequency be altered

- Recent hospital admission
- Frequent intercurrent infections
- Significant co-morbidities-e.g. renal or cardiac disease
- Alcohol excess
- Abnormal tests of monitoring
- Co-prescribed leflunomide
- Increased frequency should be specified by Rheumatology team but please ask if feel in frequent monitoring is not appropriate for your patient
- This is not an exhaustive list!

DMARDs – Renal impairment

All information based taken from Renal Drug Database

Accessed online 01/09/2020

Sulphasalazine

Dose in normal renal function:

Rheumatoid arthritis: 0.5 g daily, increased to 1.5 g twice daily

Dose in Renal impairment:

GFR (mL/min): 20–50
Dose as in normal renal function. Use with caution.

GFR (mL/min): 10–20
Dose as in normal renal function. Use with caution.

GFR (mL/min): <10
Start at very low dose and monitor. Use with caution.

Methotrexate

Dose in normal renal function:

Rheumatoid arthritis:

- Oral: 7.5–20 mg once weekly
- IM, IV, SC: 7.5–25 mg once weekly

Dose in Renal impairment:

GFR (mL/min): 20–50

50% of normal dose

GFR (mL/min): 10–20

50% of normal dose

GFR (mL/min): <10

Contraindicated.

Leflunomide

Dose in normal renal function:

- Rheumatoid arthritis: 100 mg daily for 3 days then 10–20 mg daily
- Psoriatic arthritis: 100 mg daily for 3 days then 20 mg daily

Dose in Renal impairment:

GFR (mL/min): 20–50

Dose as in normal renal function.

GFR (mL/min): 10–20

Use with caution.

GFR (mL/min): <10

Use with caution.

N.B Contraindicated in moderate to severe renal impairment by UK manufacturer due to insufficient evidence.

Azathioprine

Dose in normal renal function:

- For Autoimmune conditions - 1–5 mg/kg/day

Dose in Renal impairment:

GFR (mL/min): 20–50

Dose as in normal renal function.

GFR (mL/min): 10–20

75–100% of usual dose

GFR (mL/min): <10

50–100%

Penicillamine

Dose in normal renal function:

Rheumatoid arthritis: 125–250 mg daily for first month; increase by same amount every 4–12 weeks until remission occurs. Maintenance dose: usually 500–750 mg daily in divided doses. Maximum 1.5 g daily

Dose in Renal Impairment

GFR (mL/min): 20–50

Avoid if possible or reduce dose. 125 mg for first 12 weeks. Increase by same amount every 12 weeks.

GFR (mL/min): 10–20

Avoid – nephrotoxic.

GFR (mL/min): <10

Avoid – nephrotoxic.

Biologics

Guidelines

doi:10.1093/rheumatology/key208

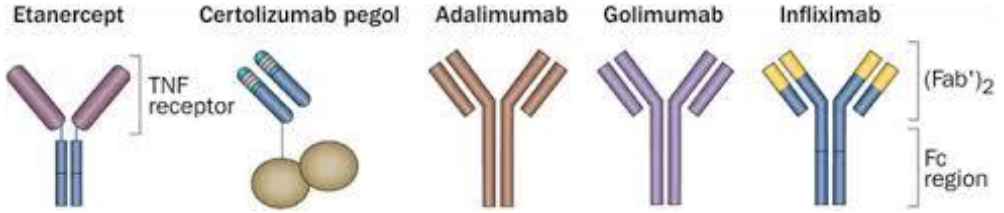
British Society for Rheumatology

The British Society for Rheumatology biologic DMARD safety guidelines in inflammatory arthritis

Christopher R. Holroyd[1], Rakhi Seth[1], Marwan Bukhari[2], Anshuman Malaviya[3], Claire Holmes[1], Elizabeth Curtis[4], Christopher Chan[1], Mohammed A. Yusuf[3], Anna Litwic[4,5], Susan Smolen[3], Joanne Topliffe[3], Sarah Bennett[1], Jennifer Humphreys[6], Muriel Green[7] and Jo Ledingham[8] for the British Society for Rheumatology Standards, Guidelines and Audit Working Group

Key words: rheumatoid arthritis, psoriatic arthritis, psoriatic arthritis, ankylosing spondylitis, biologic, Anti-TNF, safety

Biologics



- Anti-TNF
  - Etanercept, infliximab, adalimumab, golimumab, certolizumab

  Risks/contraindications: TB, Infection risk, MS, CHF

- Anti-CD20
  - Rituximab

  Risks: Infection, PML, Hypogammaglobulinaemia

- Anti-IL6
  - Tocilizumab, Sarilumab

  Risks: Minimal CRP, infections, high lipids,

Biologics

- CTLA4-Ig
  - Abatcept

  Risks: Infections,

- Other Interlukin blockers
  - Secukinumab (IL-17), Ustekinumab (IL12/23)

  Risks: Infections

- JAK inhibitors
  - Tofacitinib, Baricitinib, Upadacitinib

  Risks: High lipids, infections esp VZV, reduced CRP

Biologics

- Infections
  - Higher rates of infections
  - Highest in first 6 months
  - Reduced thereafter but remains above risk with conventional DMARDs
  - Examples:
    - TB, Varicella zoster, opportunistic infections, intracellular organisms (e.g. Listeria, Salmonella)

- Vaccines
  - Determine vaccine status before starting biologics
  - Ideally should get vaccinated against influenza and pneumonoccal as per vaccination schedule
  - Vaccines can be given during therapy with anti-TNF, IL6, CTLA4-Ig; ideally before RTX administered
  - **Avoid** live vaccines
  - Response to vaccinations attenuated in patients on csDMARDs and biologics

Biologics in practice

- Monitoring is carried out by acute team in Rheumatology
- Only patients on biologic + DMARD will get bloods check routinely at practice
- Important to note that biologics not always added to electronic prescription record = RISK
- ACTION POINT: If see a biologic on clinic letter flag to GP/Practice to get added to ECS

Contacting rheum departments

- Best contact for GP surgeries are the clinical nurse specialists
- All rheumatology departments have an advice/helpline number and this is the most common way to get in touch for advice
- Some are answering machines and the patients leave a message and some are answered by an administrator - patient is then added to a clinic list for a call back
- Some departments have a generic email address to contact for advice
- Alternative contact is department secretaries
- At GGH patients are given a card with all the relevant numbers on them

Patient education

- Patients are talked through all aspects of the medications including dosage, side effects, administration and blood monitoring prior to starting, but we do advise that it is a lot of info to take in and to call the helpline if they need any further advice.
- Methotrexate patients are advised re stopping meds if they develop an infection

ASSESS/TREAT FLARES

- Flares can be transient or persistent
- Initial advice could include rest, ice/heat packs, maximising analgesia (review anti-inflammatories; advise re paracetamol/cocodamol; consider topical pain relief such as lidocaine patches
- If persistent refer patient to the dept helpline for review where we would assess for synovitis, administer 80mg IM Kenalog for symptom relief and review meds, if required

Inflammatory markers

- ESR and CRP are useful to evaluate disease activity and to assess how medications are working by looking at trends in results. However we look at that together with other factors
- In RA disease activity score is made up of number of swollen joints, number of tender joints, patient global score - patient assessment of their disease activity from 0 (low disease activity) to 10 (high disease activity) and ESR.

For any other Information Rheumatology MCN Contacts

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