

SARAA GUIDELINES FOR BIOLOGIC THERAPY

February 2010

General information

Aims of the SARAA biologics registry:

- The prospective collection of data of patients on biologic DMARD therapy especially focusing on tuberculosis as this is endemic in South Africa.
- To facilitate the funding of biologic therapies by assessing the eligibility for use and ongoing safety of the use of biologics.
- To collect data about biologic use in South Africa.

Instructions for application for the use of a biologic patient

- Patient demographic and clinical information must be submitted to the SARAA biologics registry for all patients.
- Forms are available on the SARAA website.
- The prescribing of biologic therapies is restricted to registered rheumatologists.
- Tuberculosis test results must accompany all applications. Latent tuberculosis must be treated according to SARAA recommendations before treatment is commenced. The following must accompany the SARAA registry form:
 - Report of chest x-rays not older than 3 months at time of application
 - Results of PPD skin test
- Testing for chronic hepatitis B and C is advised before commencing biologic treatment.

Entry criteria for use of biologic DMARD therapy in patients with rheumatoid arthritis

1. Patients must have active rheumatoid arthritis
2. All patients must have a history of use of at least 3 DMARDs used serially or in combination over a 6-month period at maximum tolerated doses.
 - a. Methotrexate should be one of the DMARDs unless contraindicated at a dose of preferably 20mg weekly.
 - b. Leflunamide should be used if appropriate.
3. High disease activity: SDAI > 26 **or**
4. Moderately active disease: SDAI score $\geq 11 - 26$ if 3 or more additional poor prognostic features are present
 - a. A strongly positive rheumatoid factor
 - b. HAQ ≥ 1.5

- c. Radiographic erosion within first 2 years of disease
 - d. Extra-articular disease such as nodules, episcleritis or vasculitis
5. A motivation should accompany the application for any patient with an SDAI score lower than 26.

The Simplified Disease Activity Index (SDAI) scoring system is to be used to measure and monitor disease activity (Clin Exp Rheumatol 2005;23:S100-8). Please note the CRP is in mg/dL, this means the local CRP score must be divided by 10.

- Disease activity will be defined according to Aletaha *et al* (Arth Rheum 2005; 52; 2625-2636)
 - Low disease state: SDAI \leq 11 (previously 20)
 - High disease state :SDAI \geq 26 (previously 40)

The registry must be notified of any changes in biologic therapy or adverse events during the course of treatment.

12 monthly clinical updates are to be added to the registry.

Exclusions from treatment

- Women who are pregnant or breastfeeding
- Serious active infection or susceptibility to recurrent infection, such as bronchiectasis
- Septic arthritis of a native joint within the last 12 months
- Sepsis of a prosthetic joint within the last 12 months or indefinitely if the joint remains in situ.
- New York Heart Association grade 3/4 congestive cardiac failure for infliximab and etanercept
- Clear history of demyelinating disease
- Current malignancy. Caution advised in previous malignancy

More information about safety of the biologics is contained in the accompanying articles.

Exit criteria:

It is encouraged to stop biologic therapy in the following circumstances:

- Failure to achieve adequate improvement in SDAI score; defined as an improvement of ≥ 7 SDAI points from entry score, after 3 months of anti-TNF therapy.

- Failure to achieve a low disease state; defined as a SDAI score \leq 11 or a major SDAI response of \geq 17 points after 6 months of treatment.
- Intolerance to therapy.

Treatment regimes:

- The dosing should be based on manufacturer's recommendations for the treatment of RA
- Once a consistent response had been achieved, treatment should be reviewed periodically to assess the need for continued treatment, the dose of the drug to be used and the intervals between dosing to ensure that patients receive the minimum effective treatment
- Biologics should be used in rheumatoid arthritis in combination with methotrexate. Where the patient is intolerant of methotrexate or methotrexate is inappropriate, etanercept or adalimumab can be given as monotherapy.

References:

1. Assessment of rheumatoid arthritis activity in clinical trials and clinical practise. J.Smolen and D.Aletaha: Arthritis and Rheum 2006. Up to date.
2. The definition and measurement of disease modification in inflammatory rheumatic diseases. Aletaha d, Smolen J: Rheum Dis Clin of North Am 2006;32:9-44.
3. Remission and active disease in rheumatoid arthritis: defining criteria for disease activity states. Aletaha D. Arthritis Rheum 2005;52:2625-2636.

SARAA guidelines on TNF- α blocker switching

SARAA follows the European (EULAR) guidelines and wishes to place no restriction on switching between TNF- α blockers.

Switches should be based on:

- Lack of efficacy:
 - SDAI score improvement of $<$ 7 points from entry score, after 3 months of TNF- α blocker use.
 - Failure to achieve a low disease state after 6 months of treatment: SDAI score \geq 11

- Failure to achieve major SDAI response of ≥ 17 points after 6 months of treatment.
- Intolerance to current TNF- α blocker
- Affordability and practicality (change in patient circumstances).

Switching between etanercept, adalimumab or infliximab or vice versa is clinically appropriate.

Reference: Ann Rheum Dis 2005;64:iv2-iv14.

SARAA guidelines on the use of rituximab

Rheumatoid arthritis patients are eligible for rituximab treatment with:

- SDAI score improvement of <7 points from entry score at 3 months of TNF- α blocker use
- Failed to achieve a low disease state SDAI ≤ 11 at 6 months use of a TNF- α blocker
- Failed to show a ≥ 17 point SDAI improvement after 6 months of TNF- α blocker treatment.
- Failed a TNF – α blocker due to intolerance
- Patient ineligible for use of TNF – α on clinical grounds:
 - RA vasculitis
 - Previous TB
 - Sepsis, bronchiectasis, chronic leg ulcers
 - Malignancy, lymphoma
 - Interstitial lung disease
 - Any history of demyelination
 - Overlap syndrome
 - Drug induced auto-immunity (TNF blockers)

Repeated treatments of rituximab should only be considered after 24 weeks if good improvement of 7 -17 points in SDAI scores was seen at 16 weeks after the last treatment.

Reference: Consensus statement on the use of rituximab in patients with rheumatoid arthritis. Smolen J. Ann Rheum Dis 2007;66,2: p143-150.

SARAA guidelines on TNF- α blockers in ankylosing spondylitis

Eligibility for treatment with TNF-blocking drugs:

Treatment with TNF blocking agents may be appropriate if:

- The patient has a definite diagnosis of ankylosing spondylitis
- Active ankylosing spondylitis:
 - BASDAI at least 4cm
 - Spinal pain VAS (in last week) at least 4cm
- Failure of conventional treatment with 2 or more NSAIDs each taken sequentially at maximum tolerated/recommended dose for 4 weeks for patients with predominantly axial disease
- Failure to respond to DMARD therapy of 6 months of sulphasalazine and/or methotrexate at adequate doses for patients with significant peripheral disease

Exclusions from treatment

- Women who are pregnant or breastfeeding
- Significant, active infection or susceptible to recurrent infection such as bronchiectasis
- Septic arthritis of a native joint within the last 12 months
- Sepsis of a prosthetic joint within the last 12 months or indefinitely if the joint remains in situ.
- New York Heart Association grade 3/4 CHF for infliximab
- Clear history of demyelinating disease

Treatment regimes

- These should be according to the manufacturer's recommendations for the treatment of AS
- Once a consistent response had been achieved, treatment should be reviewed periodically to assess the need for continued treatment, the dose of the drug to be used and the intervals between dosing to ensure that patients receive the minimum effective treatment

Definition of response to treatment

- Reduction of BASDAI to 50% of the pre-treatment value or a fall of at least 2 units
- Reduction of the spinal pain VAS (last One week) by at least 2cm on VAS

Assessment of response should be carried out at 12 weeks. Treatment should not be stopped because of ineffectiveness within 12 weeks

Criteria for withdrawal of therapy

- Development of severe adverse effects
- Inefficacy at 3 months treatment:
 - BASDAI improvement < 50% < 2 units
 - Spinal pain reduction < 2 cm on VAS

Reference: Ann Rheum Dis 2006;65:316-320.

Guidelines on the use of TNF- α blockers in psoriatic arthritis.

SARAA wishes to comply with the guidelines for psoriatic arthritis treatment as published by the British Society for Rheumatologists.

The full guidelines can be viewed on the BSR website:
<http://rheumatology.org.uk>

These guidelines are extensive, but SARAA encourages you to follow them.