

Guidelines

Use of rituximab for the treatment of rheumatoid arthritis: the Latin American context

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Executive summary

Scope and purpose of the guidelines

GLADAR (Grupo Latino Americano de Estudio de Artritis Reumatoide) is a large group of Latin American (LA) rheumatologists experienced in the diagnosis and treatment of RA. In 2006, PANLAR and GLADAR published the first LA position paper on the pharmacological treatment of RA [1]. Since then, new therapies have emerged to help achieve the ultimate goal to preserve the patient's ability to function independently with an optimal quality of life.

The current guidelines provide evidence-based advice on the use of rituximab for physicians and rheumatologists treating RA in LA. A recent consensus publication has emanated from a group of European investigators [2]; however, as opposed to their work, our consensus document deals with the particulars of the use of rituximab in LA and it represents the work of GLADAR having been endorsed by all GLADAR centres.

This is a short summary of the whole guideline. The full guideline is available on the journal website.

Guidelines for the use of rituximab in RA in LA

GLADAR agreed on 21 evidence-based recommendations (from A to D) [3], and an algorithm on the use of rituximab in RA patients (Fig. 1).

Indications for rituximab

- (1) Rituximab may be used in patients with active [disease activity score (DAS) $28 \geq 3.2$] RF-positive RA, who have had an incomplete response or intolerance to an adequate course with TNF inhibitors [4] as previously defined (A) [1].
- (2) Rituximab may also be used in patients with an inadequate response or intolerance to more than one conventional DMARD, who cannot receive TNF inhibitors (A) [5, 6].
- (3) There is no strong evidence to recommend rituximab to RF-negative RA patients [4, 6]; GLADAR, however, recommends that RF-negative patients be considered for treatment if they fulfil treatment failure criteria (B).

Who should administer rituximab?

- (4) A rheumatologist with experience in the diagnosis, evaluation and treatment of patients with RA should be the one managing this treatment. Treatment should be administered in an experienced infusion unit, with immediately available emergency care (D).

How should patients be screened before initiating rituximab?

- (5) A complete physical examination and detailed history searching especially for comorbid conditions and recurrent infections should be performed (D).
- (6) A chest radiograph is not mandatory but it is advisable (D).
- (7) Routine laboratory testing including CBC with differential should be included in the initial screening (D).
- (8) Baseline as well as prior to each infusion immunoglobulin levels (IgA, G, M) should be determined; if decreased levels are observed, it is advisable to infuse patients with immunoglobulins before initiating rituximab (D).
- (9) Hepatitis B, C and HIV serologies are recommended prior to treatment initiation. Patients with hepatitis B should not be treated with rituximab (D). Patients with hepatitis C could be treated with rituximab (D); however, before this is done, viral load needs to be assessed and proper anti-viral treatment should be given (D).

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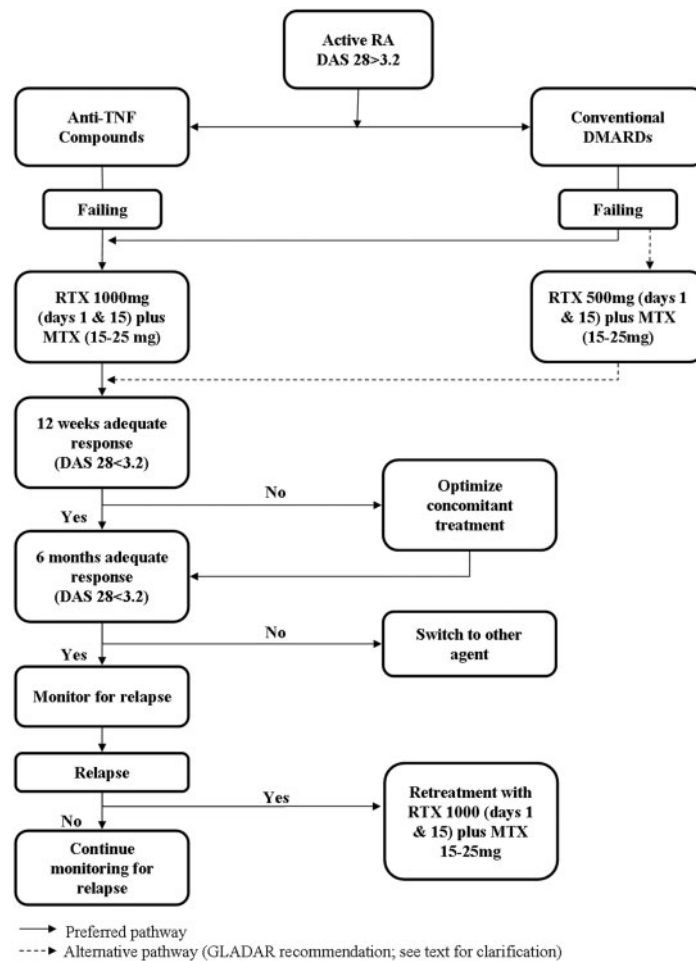


FIG. 1. Algorithm for use of rituximab in patients with RA. Broken line presents an alternative pathway; RTX: rituximab; MTX: methotrexate; pathway recommended: continues line; alternative pathway: broken line.

- (10) Vaccines with inactivated pathogens (hepatitis B, pneumococcus, influenza) should be administered at least 4 weeks prior to the administration of rituximab (D).

How patients should be treated?

- (11) Patients who have already received anti-TNF therapy should receive a starting dose of 1000 mg per infusion on days 1 and 15 (A) [4].
- (12) GLADAR recommends that a dose of 2×1000 mg should be considered initially in most cases (Fig. 1; left side of the algorithm) (A), but 2×500 mg could be considered particularly in patients with prior inadequate response to traditional DMARDs (Fig. 1; right side of the algorithm) who have not received anti-TNF therapy (A) [6].
- (13) Rituximab should be administered in conjunction with methotrexate at adequate doses (A).
- (14) The decision to use other DMARDs or rituximab monotherapy for those patients who cannot tolerate methotrexate is left to the treating rheumatologist. Concomitant treatment with cyclophosphamide is not recommended (D).
- (15) The use of i.v. methylprednisolone (100 mg) prior to each rituximab infusion is recommended to reduce the frequency and severity of infusion reactions (A).
- (16) Repeated treatment should be considered in those patients who relapse ($DAS\ 28 \geq 3.2$) after initial response but only after 6 months have elapsed (C). Those patients with a good

clinical response as per the defined criteria do not need to receive repeated treatment until they relapse (C) [7].

How should patients be evaluated?

- (17) Patients should be assessed before treatment initiation and at least every 3 months thereafter. Although any composite activity index can be used, GLADAR strongly recommends the use of the DAS 28 because of its simplicity, friendliness and feasibility in daily clinical practice (D). A patient should be considered a responder if she/he achieves a DAS 28 score < 3.2 at week 24. For patients who do not experience clinical improvement by week 12, GLADAR recommends optimizing the doses of concomitant therapies (e.g. increasing methotrexate or prednisolone doses, or administering intra-articular glucocorticoid injections) (D).
- (18) Measurement of human antichimeric antibodies (HACAs) antibodies is not required as part of the follow-up of patients treated with rituximab (A).

Contraindications

- (19) Rituximab should not be administered to children, pregnant women and during lactation, to patients allergic or hypersensitive to rituximab or any other chimerical and/or humanized antibodies (D).

- (20) Rituximab is contraindicated in the presence of active and recurrent infections and severe heart failure (New York Heart Association Class IV) (A).

Switching anti-TNF or giving rituximab

- (21) As there are no head-to-head studies comparing the efficacy and tolerance of the diverse biologic treatments available, whether to switch to another TNF inhibitor or start a new biologic agent is a decision best left to the experience of the treating rheumatologist and to the patient's preference (D) [8, 9].

There are still some unresolved issues related to the use of rituximab that require further studies (long-term safety, retreatment and concomitant medications, etc.). When new information appears, an update of this consensus statement will be considered.

These recommendations and guidelines are intended to help physicians and rheumatologists on the use of rituximab, but the ultimate decision of what is best for the individual patient should rest on the treating physician in close communication with the patient.

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