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PG Forum

International publications of interest from India

1. **Rathi M, Goyal A, Jaryal A, Sharma A, Gupta PK, Ramachandran R, Kumar V, Kohli HS, Sakhuja V, Jha V, Gupta KL. Comparison of low-dose intravenous cyclophosphamide with oral mycophenolate mofetil in the treatment of lupus nephritis. Kidney Int. 2015 Oct 21. doi: 10.1038/ki.2015.318. [Epub ahead of print]**

   The authors recruited patients with lupus nephritis (LN) (class III, IV, or V) and randomized them to receive either low-dose cyclophosphamide (CYC) or oral mycophenolate mofetil (MMF). Those with crescentic LN, a serum creatinine over 265 μmol/l, and neurological or pulmonary lupus were excluded. MMF was prescribed at daily doses of 1.5–3 g for 24 weeks, while CYC was administered as six fortnightly infusions of 500 mg each. All patients received three methylprednisolone injections, followed by oral corticosteroids. Maintenance therapy with azathioprine and low-dose corticosteroid was started at end of induction therapy. The primary end point was treatment response at 24 weeks, while secondary end points were complete remission, systemic lupus erythematosus disease activity index and adverse events. Hundred patients were randomized to each group. At 24 weeks, 37 patients in each group achieved the primary end point. The complete remission rate was 50% in CYC and 54% in MMF group. Gastrointestinal symptoms were significantly more frequent in patients receiving MMF (52% vs. 4%). However, other adverse events were similar. This first of its kind comparison showed that MMF and low dose cyclophosphamide are equivalent as induction therapies in lupus nephritis.

2. **Sengupta S, Ray J, Ghosh B. Quality of life and clinical response to on-demand maintenance doses of infliximab in patients with ankylosing spondylitis. J Clin Rheumatol. 2015;21:355–8.**

   The authors assessed the effect of modified maintenance doses (MDs) of infliximab on the quality of life (QoL) of patients with ankylosing spondylitis (AS) over a period of 3 years. Medical records of patients with AS ($n = 25$) who received a normal induction dose but modified MDs as required were analyzed retrospectively. After induction dose and the first MD, patients were followed up every month and were treated with infliximab whenever Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score was 4 or greater. The study end points were the percentage of responders defined as reduction of 40% or greater in BASDAI score and improvement in QoL defined by mean change in SF-36 Physical Component Summary score, SF-36 Mental Component Summary score, and Ankylosing Spondylitis Quality of Life (ASQoL) values at week 6 and after the last MD (i.e., at the end of 3 years) compared with baseline. There were 20 men and the mean age was 40.6 years. At the end of 6 weeks and after the last MD, BASDAI 40 scores were achieved in 100% and 92% of the patients, respectively. From baseline, the mean change in BASDAI score at the end of 6 weeks and after the last MD was −3.56 and −3.40, respectively. The overall mean change in scores (BASDAI, SF-36 Physical and Mental Component Summary, and ASQoL) versus baseline, at 6 weeks, and after the last MD was statistically significant. This study shows that the use of on-demand rather than time scheduled infliximab produces significant improvement in outcome measures like BADAI and QoL. These findings lend support to the use of this expensive drug in an on-demand manner thereby substantially reducing costs.

3. **Lau CS, Chia F, Harrison A, Hsieh TY, Jain R, Jung SM, Kishimoto M, Kumar A, Leong KP, Li Z, Lichauco JJ, Louthrenoo W, Luo SF, Nash P, Ng CT, Park SH, Suryana BP, Suwannalai P, Wijaya LK, Yamamoto K, Yang, Yeap SS. APLAR rheumatoid arthritis treatment recommendations. Int J Rheum Dis. 2015 Sep;18:685–713.**

   The Asia Pacific League of Associations for Rheumatology has published guidelines on the management of rheumatoid arthritis based on experience with patients in the Asia-Pacific region. A Steering Committee for this purpose was established in 2013. The AGREE II instrument and the ADAPTE Collaboration framework were applied to systematically identify, appraise, synthesize, and adapt international rheumatoid arthritis guidelines for use in the Asia-Pacific region. Forty rheumatoid arthritis treatment recommendations, based on evidence and expert opinion, were drafted and are presented in this report. This welcome initiative addresses many of the concerns of rheumatologists and patients with RA in a geographical context specific manner.

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0973-3698/

4. **Furie RA, Leon G, Thomas M, Petri MA, Chu AD, Hislop C, Martin RS, Scheinberg MA; PEARL-SC Study. A phase 2, randomised, placebo-controlled clinical trial of blisibimod, an inhibitor of B cell activating factor, in patients with moderate-to-severe systemic lupus erythematosus, the PEARL-SC study. Ann Rheum Dis. 2015 Sep;74:1667–75.**

This multicentre dose-ranging phase 2b study evaluated the efficacy and safety of subcutaneous blisibimod, an inhibitor of B cell activating factor, in patients with systemic lupus erythematosus (SLE). 547 patients with SLE with anti-double stranded DNA or antinuclear antibodies and Safety of Estrogens in Lupus Erythematosus National Assessment-SLE Disease Activity Index (SELENA-SLEDAI) score ≥6 at baseline were randomised to receive placebo or blisibimod at one of 3 dose levels. The primary end point, measured at Week 24, was the SLE Responder Index-5 (SRI-5). SRI-5 response rates were not significantly improved in the pooled blisibimod groups compared with placebo but were higher in subjects randomised to the highest dose of blisibimod (200 mg once-weekly (QW)) compared with pooled placebo, from Week 16 to Week 24. SRI response rates compared with placebo were higher still in subjects who attained SELENA-SLEDAI improvements of ≥8, and in a subgroup of patients with severe disease (SELENA-SLEDAI ≥10 and receiving corticosteroids at baseline). No excess of serious adverse events, infections, malignancies or death was seen in the blisibimod group. These encouraging results could herald a new therapeutic agent for lupus and phase 3 trials are eagerly awaited.

5. **Kianifard T, Kianyfard T, Chopra A. Validation and relevance of Rheumatoid Arthritis Pain Scale (RAPS) in Indian (Asian) patients suffering from rheumatoid arthritis. Clin Rheumatol. 2015 Sep 12. [Epub ahead of print]**

The authors validated an Indian version of the Rheumatoid Arthritis Pain Scale (RAPS). Post translation (contextual), RAPS was administered (by face to face interview) to 172 consenting patients with moderately severe RA (mean pain visual analogue scale (VAS) 5.4 cm). RAPS contained 24 questions (numeric score, anchored at 0 (never) and 6 (always); range 0–144). Fifty-seven cohort patients on supervised rheumatology care were followed for 16 weeks. RAPS showed good face and content validity (consensus). Construct/criterion validity was demonstrated for subclass domains and total RAPS. Fair to modest correlation was seen with swollen joint count, Indian health assessment questionnaire, medical outcome short form (SF) 36 physical score, SF 36 mental score and C-reactive protein but not with pain VAS. Similar results were shown for subclass domains (physiologic, affective, sensory, cognitive). Age, disease duration and SF 36 were significant predictors (linear regression). RAPS was found to be a valid and clinically relevant instrument for measuring pain in Indian patients suffering from RA.

6. **Sharma A, Pinto B, Dogra S, Sharma K, Goyal P, Sagar V, Dhir V, Sharma S, Singh S. A case series and review of Poncet's disease, and the utility of current diagnostic criteria. Int J Rheum Dis. 2015 Sep 10. doi: 10.1111/1756-185X.12726. [Epub ahead of print]**

The authors report 23 patients with Poncet's disease. Thirteen patients had oligoarthritis and the remaining had polyarthritis with the ankle joint being most commonly involved. The duration of joint symptoms varied from 3 days to 6 years. All patients had non-erosive and non-deforming arthritis. Systemic symptoms were absent in 48% of patients. Mantoux test was positive in most cases (81%). Tuberculosis was most often extrapulmonary with lymph node tuberculosis being the commonest. All patients had complete resolution of joint symptoms with anti-tubercular treatment. Based on their findings, the authors propose a diagnostic criteria set with two essential, two major and three minor criteria. According to these criteria 19 patients had definite and three had probable Poncet's disease. This large case series highlights the clinical features of Poncet's disease and the diagnostic criteria proposed by the authors may prove useful in making a diagnosis.

7. **Malaviya AN. Has the possible inclusion of nonradiographic axial spondyloarthritis been factored into the ABILITY-2 study? Comment on the article by Mease et al. Arthritis Rheumatol. 2015;67:2793.**

The author comments on the recently published ABILITY-2 study. This is the first therapeutic trial of adalimumab in patients with non-psoriatic peripheral spondarthritis. The comment raises concerns regarding the inclusion of patients with non-radiographic axial spondyloarthritis in this trial, which would represent inclusion of some patients who had MRI proven sacroiliitis thus diluting the aim of the study. The authors in their reply clarified that they did not screen all patients with MRI and thus patients with non-radiographic axial SpA may have been included in this trial.

8. **Kansal A, Tripathi D, Rai MK, Agarwal V. Persistent expression and function of P-glycoprotein on peripheral blood lymphocytes identifies corticosteroid resistance in patients with systemic lupus erythematosus. Clin Rheumatol. 2015 Sep 29. [Epub ahead of print]**

Overexpression of P-glycoprotein (P-gp) on peripheral blood lymphocytes (PBL) may lead to resistance to corticosteroids in patients with SLE. The authors evaluated the role of P-gp protein on PBLs in patients with SLE and its relationship to response to corticosteroid (CS) therapy. SLE patients ($n = 42$) who were naïve to CS and immunosuppressive drugs were enrolled. Disease activity was assessed using SLE disease activity index (SLEDAI) and expression, and function of P-gp was evaluated by flow cytometry at baseline and after 3 months of therapy with CS. At 3 months, patients with SLEDAI >4 and SLEDAI ≤4 were grouped as nonresponders and responders, respectively. P-gp expression was significantly increased on PBLs of SLE patients as compared to healthy controls ($p < 0.001$). P-gp expression and function correlated with SLEDAI. P-gp expression and function were not different in responders and nonresponders at baseline. However, at 3 months of CS therapy, P-gp expression and function decreased in responders whereas it remained unchanged in nonresponders. These results suggest that overexpression of P-gp may be an important mechanism for corticosteroid resistance in patients with SLE.

9. **Misra DP, Agarwal V. Innate immune cells in the pathogenesis of primary systemic vasculitis. Rheumatol Int. 2015 Sep 24. [Epub ahead of print]**