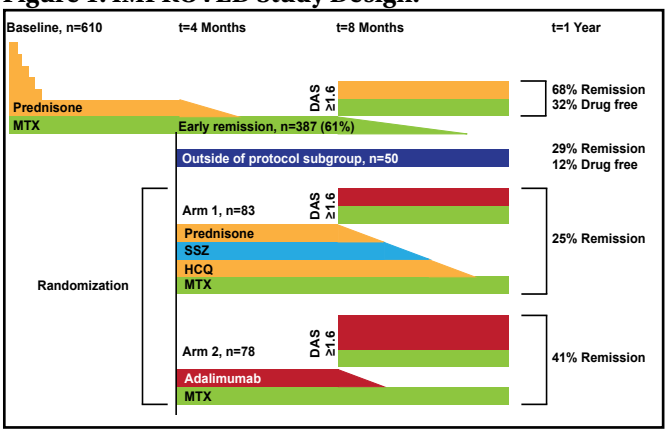
Figure 1. IMPROVED Study Design.



DAS=Disease Activity Score; HCQ=hydroxychloroquine; MTX=methotrexate; SSZ=sulfasalazine. Reproduced with permission from L Heimans, MD.

Short- and Long-Term Efficacy of Tofacitinib in the Treatment of Patients with RA and an Inadequate Response to TNF Inhibitors

Written by Maria Vinall

Treatment with the oral Janus kinase (JAK) inhibitor tofacitinib was associated with an improvement in the signs and symptoms of rheumatoid arthritis (RA), physical function, and patient reported outcomes in RA patients with an inadequate response to tumor necrosis factor inhibitors (TNFi). The improved response was maintained over 24 months. Data from 11 studies [Monotherapy: NCT00550446, NCT00687193, NCT00814307; background DMARD: NCT00413660, NCT00603512, NCT00960440, NCT00847613, NCT00856544, NCT00853385; LTE: NCT00413699, NCT00661661] were pooled and Gerd R. Burmester, MD, Charité University Hospital, Berlin, Germany, presented the results.

In a prior study, tofacitinib improved the signs and symptoms of RA in 399 TNFi treatment refractory patients over 6 months [Burmester G-R et al. *Arthritis Rheum* 2011]. The purpose of this analysis was to provide additional short- and long-term data concerning the effect of tofacitinib on the signs and symptoms of RA, physical function, pain, and fatigue compared with placebo in this patient population and to further characterize the activity of tofacitinib by number of failed TNFi, by reason for failure (adverse event vs lack of efficacy). In the newer study, data from 9 randomized Phase 2 and 3 studies (n=614) and 2 open-label long-term extension studies (n=510) were analyzed. Patients were treated with tofacitinib (5 or 10 mg BID) either as monotherapy or on a background of nonbiologic disease-modifying antirheumatic drugs (DMARDs), or, in Phase 2 and 3 studies, with placebo.

Efficacy in reducing the signs and symptoms of RA was assessed by changes in American College of Rheumatology improvement response criteria (ACR20/50/70) and 28-joint Disease Activity Score (DAS28)-4 erythrocyte sedimentation rate (ESR) scores. Physical function was assessed by mean change from baseline in Health Assessment Questionnaire Disability Index (HAQ-DI). Pain and fatigue were assessed using change from baseline on the Short Form-36 Bodily Pain item and the Functional Assessment of Chronic Illness Therapy-Fatigue item. More than 60% of the patients had failed at least one TNFi in all groups.

At Month 3, significantly greater ACR20/50/70 responder rates were seen with tofacitinib compared with placebo ($p<0.0001$, $p<0.0001$, $p<0.05$, respectively). This pattern was consistent regardless of 1 or 2 prior TNFi failures. Tofacitinib also improved mean DAS28-4 ESR scores, values for HAQ-DI, and body pain and fatigue at 3 months and over 24 months. No new safety signals were detected in the previously presented randomized controlled trial in TNFi inadequate response patients treated with tofacitinib [Burmester GR et al. *Arthritis Rheum* 2011].

The investigators concluded that tofacitinib may offer a benefit in difficult-to-treat patients resistant to standard DMARDs.

SC Tocilizumab Reduces RA Disease Activity When Used with DMARDs

Written by Wayne Kuznar

When used in combination with traditional disease-modifying antirheumatic drugs (DMARDs), response rates were significantly superior with a subcutaneous (SC) form of tocilizumab compared with placebo in a 24-week Phase 3 study of patients with moderate to severe rheumatoid arthritis (RA).

A SC form of tocilizumab gives patients the opportunity to self-administer treatment, reported Alan Kivitz, MD, Altoona Center for Clinical Research, Duncansville, Pennsylvania, USA. 656 patients with moderately to severely active RA of at least 6 months duration and an inadequate response to 1 or more DMARDs (20% had prior treatment with anti-TNF) were randomized in a 2:1 ratio to treatment with SC tocilizumab (n=437; 162 mg every 2 weeks) or SC placebo (n=219) with continuation of DMARDs [Kivitz AJ et al. ACR 2012 Poster L8]. Oral corticosteroids and nonsteroidal anti-inflammatory drugs were permitted if patients were on stable dosages for at least 4 weeks prior to baseline.