Effect of tight control of inflammation in early psoriatic arthritis (TICOPA): a multicentre, open-label, randomised controlled trial

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Abstract

Background Tight control of inflammation with a prespecified target optimises outcome and is now considered standard of care in rheumatoid arthritis but has never been evaluated in psoriatic arthritis. We aimed to assess the effect of tight control on early psoriatic arthritis using a treat-to-target approach.

Methods In a UK multicentre, open-label, parallel group, randomised, controlled trial in eight rheumatology secondary care centres in the UK, adults with early psoriatic arthritis were randomly assigned (central telephone randomisation, 1:1 ratio, with treatment groups balanced for randomising centre and pattern of arthritis [oligo *vs* polyarticular]) either to tight control with a step up regimen aiming for minimal disease activity using methotrexate, combination disease-modifying anti-rheumatic drugs (DMARDs) and anti-tumour necrosis factor drugs as required or to standard care. Patients were required to be over 18 years of age, have active disease at screening (duration of symptoms <24 months), and no previous treatment for articular disease with DMARDs. All patients were assessed by a masked assessor, but patients and treating physicians were not masked to treatment. Primary outcome was the proportion of patients achieving an American College of Rheumatology (ACR) 20 response at 48 weeks. Multivariate logistic regression was used to compare treatment arms with adjustment for arthritis classification and randomising centre. Data were analysed by intention to treat (ITT). Missing component data for primary and key secondary outcomes were imputed with multiple imputation for ITT analyses. Ethics and governance approval for this study was obtained from Northern and Yorkshire Research Ethics Committee and Leeds Teaching Hospitals Trust. Written informed consent was obtained from all patients before participation in the trial. The trial is registered with ClinicalTrials.gov, number NCT01106079; and with Current Controlled Trials, number ISRCTN 30147736.

Findings 206 patients (median age 45 years, IQR 37·9–53·4, 52% male) were recruited from 2008 to 2012. 101 patients were randomised to tight control and 105 to standard care. By week 48, 12 patients had withdrawn (five tight control, seven standard care) and 12 were lost to follow-up (six from each group). 146 patients (71%) presented with polyarthritis and these characteristics were similar across treatment groups. In the ITT population, the odds of achieving an ACR20 at 48 weeks were greater in the tight control group than in the standard control group (odds ratio [OR] 1·91, 95% CI 1·03–3·55; p=0·0392). In complete case analysis 55 (61·8%) of 89 patients in the tight control group showed ACR20 response compared with 37 (44·6%) of 83 patients receiving standard care (χ^2 5·11, p=0·02). The most commonly reported adverse events were nausea, liver abnormalities, and infections (common cold). Adverse events were reported in 179 (86·9%) of 206 patients (97% [98/101] tight control *vs* 77·1% [81/105] standard control). 33 serious adverse events were reported in 20 patients (25 in 14 patients on tight control, eight in six patients on standard care). Ten serious adverse events were thought to be related to drug therapy, eight in the tight control arm and two in standard care. There were no unexpected serious adverse events or deaths.

Interpretation This study is the first to our knowledge to show that tight control of disease activity, in which a treat-to-target approach is used, significantly improves joint outcomes for patients newly diagnosed with psoriatic arthritis. Although there were more adverse events and serious adverse events in the group assigned to tight control no unexpected serious adverse events were seen.

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Contributors
LC, SB, PE, PC, and PH were responsible for the study design. LC, AM, HC, and NNC collected the data. LMcP, SB, SRB, and NC did the analysis. All authors wrote the abstract.

Conflicts of interest
LC, PE, PC, and PH have received research funding, honoraria, or both from Pfizer. All other authors declare that they have no conflicts of interest.