

Title of Research

Influence of Demographic and Environmental Factors on Anti-TNF Efficacy in Rheumatoid Arthritis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials (PROSPERO number CRD42018071079)

Lead Researcher

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Summary of Research

Rheumatoid arthritis (RA) is a chronic autoimmune disease that affects small joints and causes systemic inflammation with a prevalence of 3 to 8/1,000 patients. This disease is associated with significant morbidity mortality, disability and socioeconomic costs. Drugs that target inflammation pathways, such as tumor necrosis factor (TNF) antagonists, have improved treatment options in RA. However, primary or secondary failure is still a problem for one in three patients treated with these therapies. Increased understanding of the factors determining treatment response is therefore essential.

This study focuses on infliximab and placebo only.

Study Design

A systematic review and meta-analysis have been performed to examine the influence of demographics and disease-related factors on anti-TNF drugs' efficacy in randomized controlled trials (RCTs) involving RA. These factors have been included: age; sex; disease duration; the disease activity score, DAS28; C-reactive protein (CRP) level; rheumatoid factor (RF); anti-citrullinated protein antibodies (ACPA); smoking status; body mass index (BMI); and physical activity. The following has also been noted: author, year of publication, study acronym, journal, PMID, NCT or clinical trial registry number, anti-TNF evaluated and type of control, number of patients included, main outcome, time for main outcome, duration, extension, sponsor.

Eligible studies have been selected by title and abstract on the CENTRAL database, by searching for RCTs evaluating the efficacy of an anti-TNF compared to placebo or disease modifying anti-rheumatic drugs (DMARD) in RA. After reviewing the full text of eligible studies, studies that report data of efficacy in subgroups of interest have been included. Assessment of risk of bias following the Cochrane tool of risk of bias for RCTs has been evaluated in duplicate.

Study Population

The study population comprises adults (≥ 18 years of age) with RA according to American College of Rheumatology (ACR) 1987 or ACR/European League Against Rheumatism (EULAR) 2010 criteria. Only infliximab and placebo will be studied. Inclusion criteria: RCTs of infliximab and placebo in RA patients and reported efficacy data by subgroups of demographic and disease related factors of interest. Exclusion criteria: non-randomized controlled trials, observational studies, randomized trials comparing 2 anti-TNF drugs without a control group.

Funding Source of Research

None

Requested Study

IM101-043 (NCT00095147): Abatacept and Infliximab in Combination With Methotrexate in Subjects With Rheumatoid Arthritis

Statistical Analysis Plan

A meta-analysis of aggregate data will be performed, following appropriate methods (relative risks or standardized mean difference) depending of the nature of the outcome considered. A fixed effect model will be performed first, with addition of a random effect model in case of significant heterogeneity. Heterogeneity will be considered significant if the m-value of the heterogeneity test is <0.10 or I^2 is higher than 50%.