Study protocol

Adverse events in patients receiving placebo in phase III trials of biologics for psoriasis: a systematic review and meta-analysis

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Aim

The aim of this meta-analysis is to determine 1) the prevalence of common adverse events (AEs) 2) the prevalence of AEs of interest in patients receiving placebo in phase III trials of biologics for psoriasis.

Study design

Systematic review and meta-analysis

Eligibility criteria

Published studies in English language, from any year and any healthcare setting are eligible to be included. The studies must be phase 3 and must be randomized placebo controlled clinical trials. To qualify for inclusion, studies must be original and must report the number of patients and/or prevalence of AEs in placebo treated patients.

Literature search

Two authors will independently screen three databases (Pubmed, Embase, and Web of Science). We will search the databases from inception through April 2019 using the search terms: “Psoriasis AND (phase III OR phase 3)”.

Selection of studies and data extraction

Records will be screened according to title and abstract and duplicates will be removed. Studies that meet the inclusion criteria will be selected for full text screening as well as studies where eligibility is unclear based on title or abstract. Any disagreement between the two reviewers will be resolved through debate and the resulting decision must be unanimous. In the case that a study population is included in more than one publication, the newer publication will be included.

The literature selection and the reasons for study exclusion will be documented in a PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analysis) flow diagram.
The following data will, where applicable, be retrieved from each publication: first author’s name, year of publication, study name or NCT number, dosing schedule, week of evaluation, number and gender of patients, mean or median age, number of: AEs, serious AEs (SAE), discontinuation due to AE, death, and common AEs/SAEs or of interest including: Major adverse cardiovascular events (MACE), tuberculosis, inflammatory bowel diseases (IBD), candida infections, upper respiratory tract infection (URTI), depression, infections, serious infectious episodes (SIE), injection site reactions (ISR), malignancies, malignancies excluding non-melanoma skin cancer (NMSC), nasopharyngitis, and arthralgia.

Data synthesis

Data synthesis will be conducted using StatsDirect version 3 (StatsDirect Ltd., Cheshire, UK). Proportion meta-analysis will be performed to obtain pooled prevalence. Heterogeneity of studies will be assessed with Cochran’s Q-test, using a significance level of 0.05, and I² statistic. Estimates will be conducted using random effects model (Der Simonian and Laird). Should studies present substantial heterogeneity, then additional sensitivity analyses will be performed. Publication bias will be assessed with funnel plots and Egger test. The PRISMA guidelines will be followed when reporting results of this study.