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Risk of Eczema Herpeticum in atopic dermatitis patients receiving JAK inhibitors, biologics or other systemic therapy.

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 October 2023 and was last updated on 20 October 2023.

INTRODUCTION

Review question / Objective To estimate the association of Janus Kinase (JAK)inhibitors with the incidence of eczema herpeticum compared with placebo, Dupilumab, cyclosporine, methotrexate and other systemic therapy used in atopic dermatitis.

Rationale It is unclear if there is increased risk of eczema herpeticum in atopic dermatitis receiving JAK inhibitors and if the risk is similar or higher compared to other forms of systemic treatment for atopic dermatitis.

Condition being studied Atopic dermatitis is the most common inflammatory skin disease in developed countries and is characterised by an impaired epidermal barrier and immune dysregulation. Reactivation and super-infection of human herpes simplex virus is a known complication to occur in AD, and this superinfection is known as eczema herpeticum. It is unclear if the risk of eczema herpeticum is increased in individuals receiving systemic / immunosuppressive agents for AD.

METHODS

Search strategy Literature search will be conducted using MEDLINE, Embase and Cochrane databases to identify RCTs and long term extension studies of JAK inhibitors, biologics, immunosuppressive agents in atopic dermatitis. Search terms would include eczema, Dermatitis, Atopic, Cyclosporine, Azathioprine, JAK inhibitors, Abrocitinib, Upadacitinib, Baricitinib, Prednisolone, corticosteroids, mycophenolate mofetil, lebrikizumab, tralokinumab, dupilumab.
Search will be performed in accordance with PRISMA requirements.

Participant or population adult atopic dermatitis.

Intervention JAK inhibitors including upadacitinib, abrocitinib, baricitinib.

Comparator Dupilumab, tralokinumab, lebrikizumab, prednisolone, corticosteroid, methotrexate, mycophenolate mofetil, cyclosporine.

Study designs to be included Randomised controlled trials and long term extension studies.

Eligibility criteria adult > 18 years; diagnosis of atopic dermatitis.

Information sources Midline, embase, cochrane, trial registers (ISRCTN), ClinicalTrials.Gov.

Main outcome(s) Risk of eczema herpeticum.

Data management Records and data will be stored on an electronic repository.

Quality assessment / Risk of bias analysis Risk of bias will be analysed using Cochrane Risk of Bias tool.

Strategy of data synthesis Meta-analysis will be performed to estimate the risk of eczema herpeticum between JAK inhibitors and comparators. Incidence rate ratios for pooled phase II/III/IV RCT and for combined phase II/III/IV RCT and LTE data. In LTE studies without. long-term comparator data, comparator data from the original RCTs will be included for comparison. Meta analysis will also be performed to estimate the effect of JAK I medications on the risk of eczema herpeticum relative to placebo.

Subgroup analysis The various types of JAK inhibitors (Abrocitinib, Upadacitinib and Baricitinib) will be analysed separately.
To analysis low dose versus high dose JAK inhibitors. (Low dose : Abrocitnib 100mg, Upadacitinib 15 mg, Baricitinib 2mg; High dose: Abrocitinib 200mg, Upadacitinib 30mg, Baricitinib 4mg).

Sensitivity analysis "leave-one-out" meta analysis to investigate the influence of individual studies on pooled estimates.

Language restriction English.

Country(ies) involved Singapore.

Keywords Eczema herpeticum, herpes simplex, atopic dermatitis, JAK inhibitors, cyclosporine, Dupilumab.

Dissemination plans Will be published.

Contributions of each author

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