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# Systematic Review and Meta-analysis of Briakinumab, a Fully Human Interleukin 12/23 Monoclonal Antibody, for the Treatment of Moderate to Severe Chronic Plaque Psoriasis

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## INTRODUCTION

- Psoriasis is a chronic autoimmune disease characterized by formation of red, itchy, scaly patches of abnormal skin.
- Psoriasis is estimated to affect 2-3% of population worldwide[1]
- Psoriasis has systemic manifestations as well
- Severe psoriasis may increase the risk for cardiovascular events such as acute myocardial infarction[2,3]
- Immune pathways mediated by a variety of cytokines appear to have an important role in psoriasis disease mechanisms
- Important cytokines believed to be involved in the pathogenesis of psoriasis include TNF-α, IFN-γ, IL-12, IL-23, IL-12, and IL-17[4]
- IL-23 in particular has been found to be highly expressed in psoriatic skin lesions[5]
- **Briakinumab** is a fully human anti-IL12/23 monoclonal antibody which has been shown to be efficacious in the treatment of moderate-to-severe psoriasis[4,6]

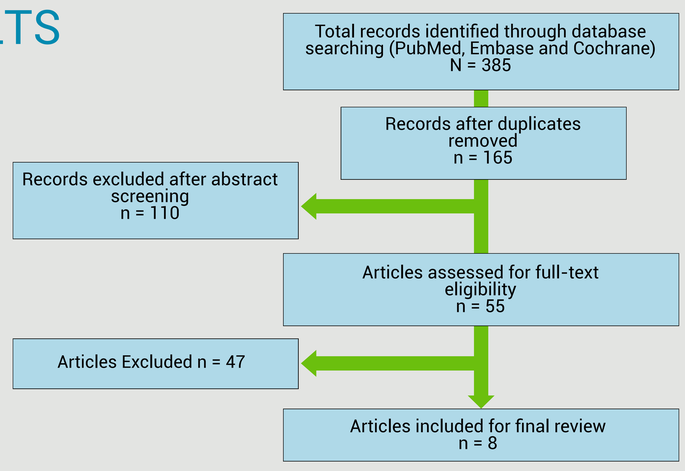
## OBJECTIVE

- To evaluate the efficacy and safety of Briakinumab, a fully human interleukin 12/23 monoclonal antibody, in the treatment of moderate-to-severe chronic plaque psoriasis (CPP)

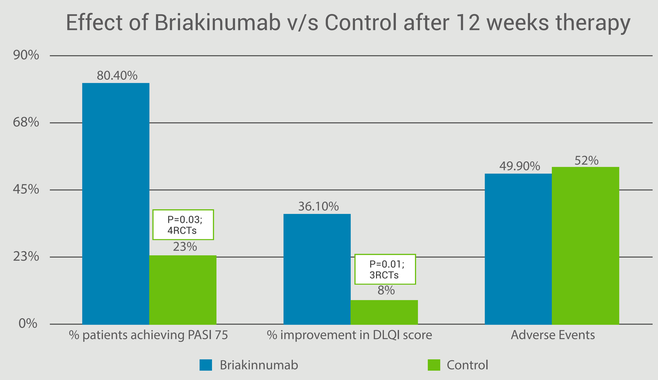
## MATERIALS AND METHODS

- Literature search was conducted in MEDLINE, EMBASE, Cochrane Library, and clinicaltrials.gov without any language or date restrictions
- In addition, references of the included studies were screened for additional studies.
- All RCTs examining the efficacy and safety of briakinumab in adult patients with moderate-to-severe chronic plaque psoriasis were included
- Study quality of included trials were assessed using the Cochrane Risk of Bias Tool.
- Two authors independently selected papers, extracted data and assessed quality.
- Our primary outcome was improvement in symptom severity assessed by Psoriasis Area Severity Index (PASI) score and Dynamic Global Physician Assessment (DGPA) score at 12 weeks.
- Secondary outcomes were quality of life, assessed using Dermatology Life Quality Index (DLQI) and adverse events.

## RESULTS




- A total of 8 RCTs with 2659 CPP patients were analysed
- After 12 weeks of therapy, patients receiving Briakinumab (in comparison with control) showed:
  - Better achievement of PASI 75
    - Risk ratio 3.21, 95% CI 1.09 to 9.45; P=0.03, four RCTs
  - Better improvement in symptom severity (DGPA)
    - Risk ratio 3.89, 95% CI 1.36 to 11.11, P=0.01, four RCTs
  - Better improvement in DLQI scores
    - Risk Ratio 3.99, 95% CI 0.78 to 20.36; P=0.01, three RCTs
  - Similar adverse event profile
  - Removal of Gordon 2012 study from analysis reduced the heterogeneity.




PASI: Psoriasis Area Severity Index
DLQI: Dermatology Life Quality Index

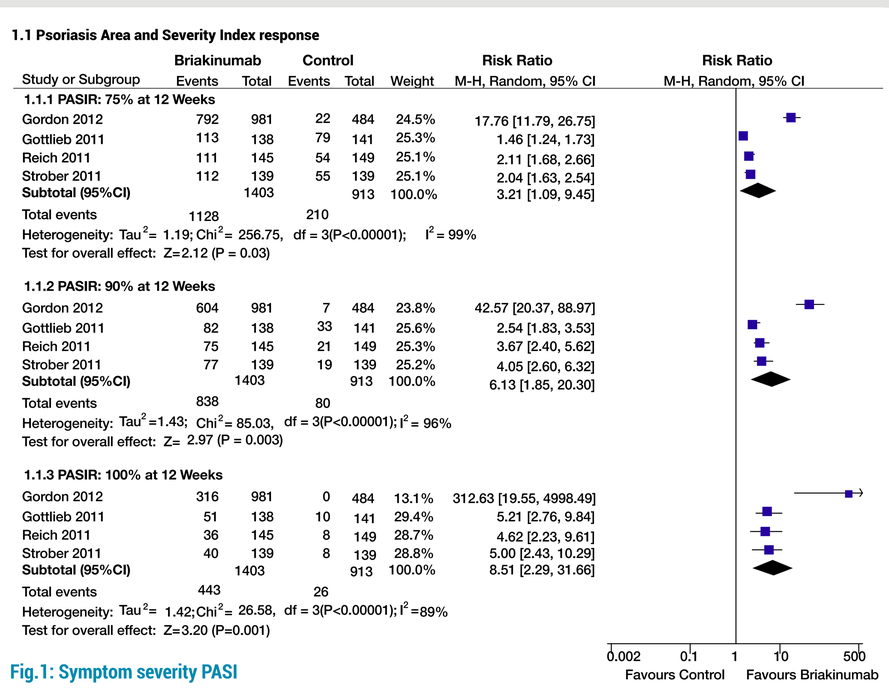



Fig.1: Symptom severity PASI

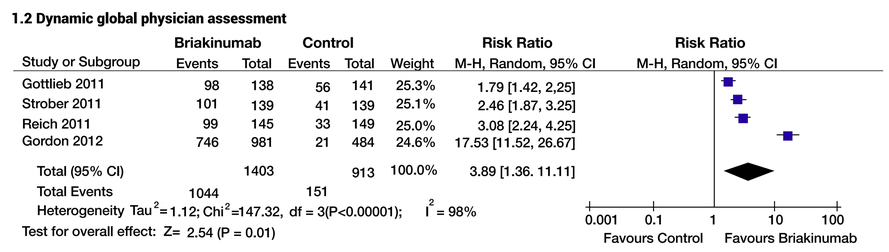



Fig.2: Symptom severity DGPA

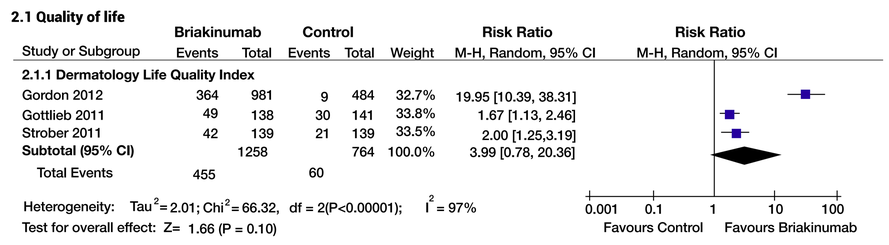



Fig.3: QOL DLQI

## DISCUSSION

- Current therapy of psoriasis includes:[1]
  - Topical agents such as Vit D, calcipotriol, corticosteroids, dithranol, and retinoids
  - Systemically used agents such as methotrexate and cyclosporine
  - Phototherapy includes UV-B, Psoralen plus ultraviolet A (PUVA) therapy, and excimer laser.
  - Biological therapy includes agents such as Denilukin diftitox, Efalizumab, Alefacept, Ustekinumab, Briakinumab, and Etanercept
- Disadvantages of biologics are their high cost and strictly parenteral route of administration[1]
- In developed countries, biologicals are being widely used for moderate-to-severe psoriasis[1]
- The pathogenesis of psoriasis involves activation of T cells and cytokines; Psoriasis is now recognized as one of the most common T cell-mediated disorders[7]
- Antigen-induced activation of T-cells leads to initiation of cellular cascade
- This leads to proliferation and differentiation of cutaneous T cells → keratinocyte alterations → psoriatic plaques[8]
- As part of this cellular cascade, many proinflammatory cytokines are released, including TNF-α and various interleukins[3]
- More recently, the role of the structurally related cytokines IL-12 and IL-23 in psoriasis has become apparent
- IL-12 and IL-23 are thought to be involved in controlling differentiation of T helper cells, during the psoriasis immune response[9]
- Briakinumab, a fully human anti-IL-12 /23p40 monoclonal antibody, has been shown to be highly effective and well tolerated in the treatment of psoriasis in many studies

## CONCLUSION

- Briakinumab associated with significant improvement in symptom severity compared to other treatments among patients with moderate to severe CPP.
- As the reported outcomes showing wide confidence intervals, results should be interpreted with some caution.

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