RISK OF SERIOUS INFECTIONS IN PATIENTS WITH PSORIASIS ON BIOLOGIC THERAPIES

A Systematic Review and Meta-Analysis

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WHY IS THIS STUDY NEEDED?

1. Evidence gap for patients with psoriasis; current evidence extrapolated from rheumatoid arthritis
2. New biologic therapies approved for psoriasis since last systematic review – ustekinumab, secukinumab
3. Inform guideline development and decision making

METHODS

- **Population** – patients with primarily psoriasis
- **Intervention** – adalimumab, etanercept, infliximab, ustekinumab, secukinumab
- **Comparator** – any above biologic, placebo, other systemics
- **Outcome** – serious infection (SI; investigator defined)
- Study design – systematic reviews; randomised controlled trials (RCTs); prospective cohort studies
- Key exclusions – n < 50; indirect populations (e.g. patients with rheumatoid arthritis)
- Search conducted in PubMed, Medline, Embase, Cochrane, inception to 29/09/2015
- Two assessors screened title/abstracts
- National Clinical Guideline Centre (NCGC) data extraction tool
- National Institute for Health and Care Excellence (NICE) risk of bias checklists
- Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria for quality of evidence
- Meta-analysis – pooled Peto's odds ratio (OR); I^2 test for heterogeneity

RESULTS

6987 references

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204 full-text articles assessed for eligibility

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30 RCTs (32 studies), 1 cohort study

13359 RCT participants
4993 cohort study participants

54 serious infections in RCTs
323 serious infections in cohort study

13 RCTs excluded patients with history of serious infections

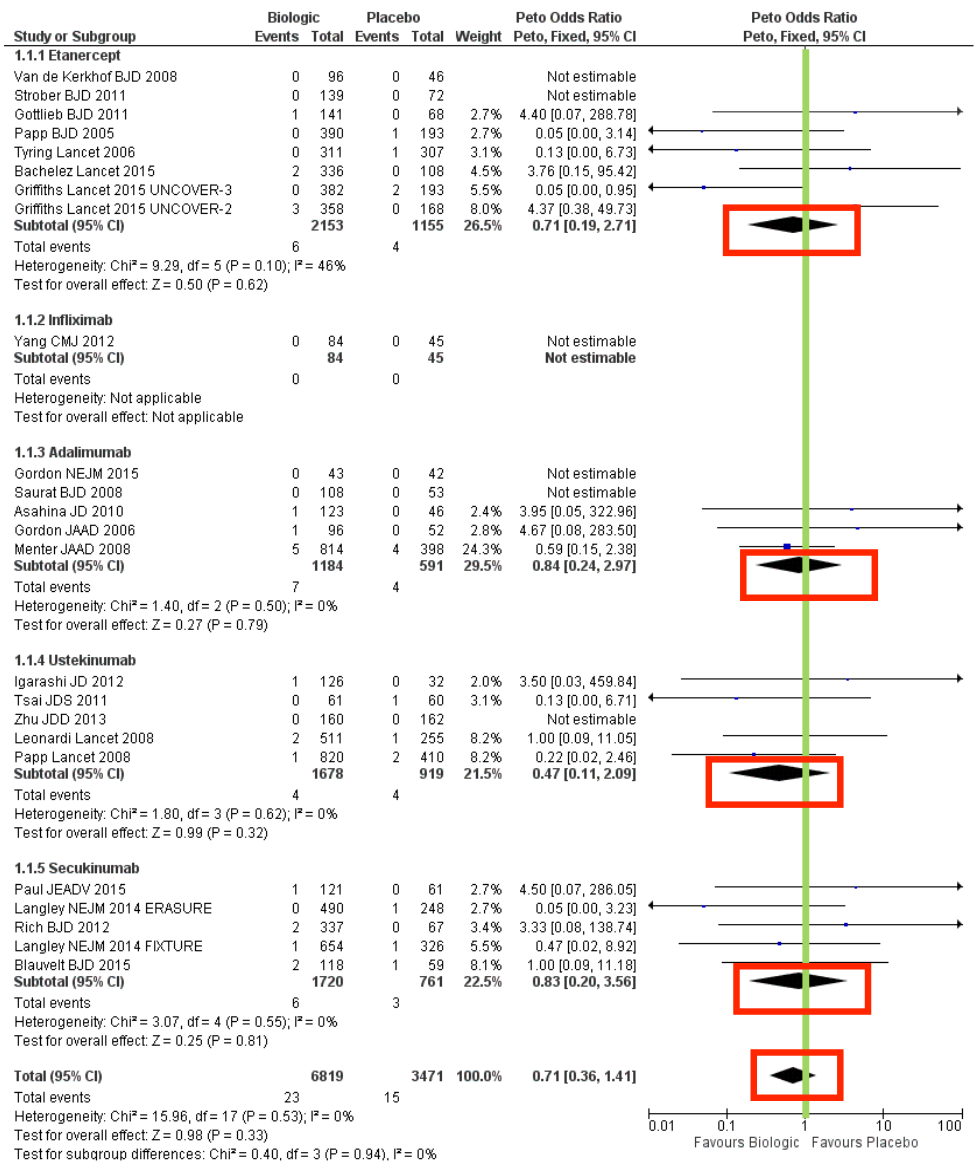
RISK OF BIAS AND QUALITY OF EVIDENCE

1. 26 (83.9%) low risk of selection bias; 26 (83.9%) low risk of performance bias; 27 (87.1%) no clear reporting of investigator blinding (information bias), 1 open-label RCT, 29 (93.5%) low risk of attrition bias; no clear publication bias from funnel plot
2. Overall quality (GRADE) low – very low due to very serious imprecision / serious risk of bias
3. 3 out of 33 studies reported their definition of SI outcome

Forest plot for dose-independent comparison between biologic therapies and placebo at week 12-16, adults, RCT

NO DIFFERENCE IN RISK OF SI

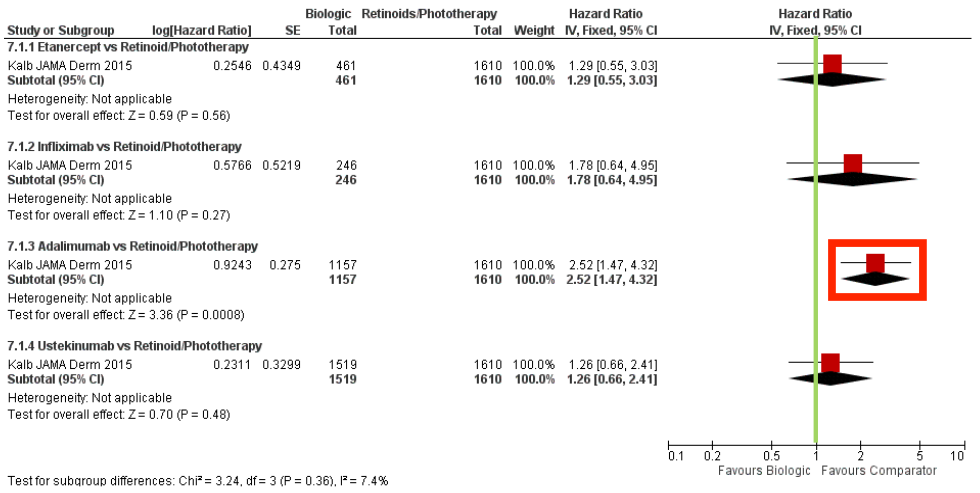
GRADE quality
Low – etanercept, secukinumab
Very low – /, adalimumab, ustekinumab



Forest plot for dose-independent comparison between biologic therapies and acitretin/phototherapy, adults, cohort study

ADALIMUMAB 2.5x RISK OF SI

GRADE quality
Low – adalimumab
Very low – infliximab, adalimumab, ustekinumab



KEY LIMITATIONS

1. Lack of long-term data for RCTs
2. Study population for the RCTs different from target population in real-world settings
3. Definitions of adverse events outcome (SI) not clearly reported

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SUMMARY

1. **No increased short-term risk of serious infection from RCT data for any biologic used in patients with psoriasis**
2. **Adalimumab 2.5x risk of SIs as compared to acitretin/ phototherapy cohort**
3. **Further well designed observational studies needed to clarify risk of SI in patients with psoriasis on biologic therapies**

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British Association of Dermatologists – healthy skin for all
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