An Updated Systematic Review and Network Meta-Analysis on Risks of Respiratory Tract Infections with Biologic and Targeted Synthetic Antirheumatic Agents in Psoriatic Arthritis

Chang SH[1], Liu YS[2], Bilal J[3], Bhattacharjee S[4], Kwoh CK[3]
[1]University of Florida, Gainesville, FL, USA, [2]The University of Texas at Austin, Austin, TX, USA,
[3]University of Arizona, Tucson, AZ, USA, [4]Bayer US, Whippany, NJ, USA

Background

- Biologic and targeted synthetic disease modifying antirheumatic agents have been widely used among patients with psoriatic arthritis (PsA)
- Current evidence on head-to-head comparative risk of respiratory tract infections (RTIs) is unclear

Objective

- To compare the risk of RTIs associated with individual agents and their respective drug classes in PsA based on randomized controlled trials (RCTs)

Method

- **Systematic Review**
  - Data reception-Oct 2023 (updated review started from March 2021)
  - Medline, PubMed, Embase, Scopus, Cochrane Central, and clinicaltrials.gov

Inclusion criteria	Exclusion criteria
○ Phase III or IV RCTs ○ Patients ≥18 years ○ Studies report outcomes of RTIs	○ Studies on investigational drugs ○ Studies that only presented the subgroup and post hoc analyses of the initial RCT

  - Outcome of interest
    - RTIs
    - The period of outcome identification was limited to time within the placebo-controlled period
- **Network Meta-analysis**
  - **Main analysis**
    - Combined with previous search result
    - 32 RCTs; 14,643 participants; 15 treatment options; 9 classes
  - **Bayesian network** meta-analysis with **random-effects** model using **R**
  - Pair-wise comparisons between **individual treatment effect** and **class effect** were presented by odds ratio (OR) and 95% confidence intervals (CIs)
  - The surface under the cumulative ranking curve (**SUCRA**) were used to report the relative ranking of each treatment and class*

*Class categories of included treatments	
Class	**Individual treatment**
classical disease-modifying antirheumatic drugs **(cDMARDs)**	MTX
Interleukin 12/Interleukin 23 **(IL12/IL23)**	Usketinumab
Interleukin 17A **(IL-17A)**	Bimekizumab, Ixekizumab, Secukinumab
Interleukin 23 **(IL23)**	Guselkumab, Risankizumab
Janus kinase inhibitors **(JAKi)**	Tofacitinib, Upadacitinib
Phosphodiesterase-4 inhibitor **(PDE4i)**	Apremilast
Selective Co-stimulation Modulators **(SCM)**	Abatacept
Tumor Necrosis Factor inhibitors **(TNFi)**	Adalimumab, Certolizumab Pegol, Etanercept, Golimumab, Infliximab

  - **Subgroup analysis**
    - Individual drug effect and class effect for upper RTI
  - **Quality assessment**
    - Cochrane risk-of-bias tool was used to evaluate the risk of bias in randomized trials

Result

- **Main analysis (RTIs)**
  - Table 1 shows the characteristics of primary network
  - The networks for comparisons of individual treatments and classes were displayed in Figure 1A and Figure 1B, respectively

Table 1. characteristics of primary network

Characteristics	Individual	Class
Number of interventions	17	9
Number of studies	40	40
Total number of patients in network	18897	18897
Total possible pairwise comparisons	136	36
Total number of direct pairwise comparisons	21	10

Network of included trials based on

Figure 1A. Individual treatments

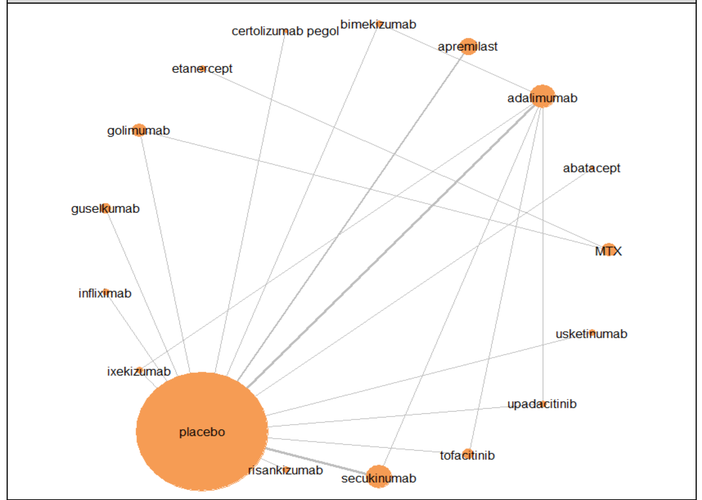
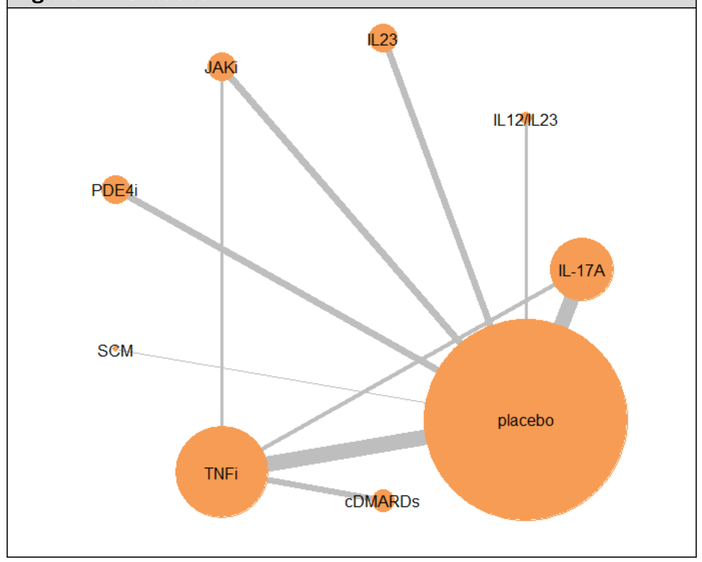


Figure 1B. Classes



Result

- Relative ranking SUCRA value ranked **abatacept** (SUCRA 0.94) as the best treatment with the lowest risk of RTIs occurrence, while **certolizumab pegol** (SUCRA 0.12) was ranked as the worst in terms of RTIs risk
- For the class-level comparison, **SCM** (SUCRA 0.97) was associated with the lowest risk of RTIs, while **PDE4i** (SUCRA 0.16) was associated with the highest risk of RTI
- League tables (Table 2 and 3) show the similar result for individual-level and class-level comparison, respectively

Table 2. Head-to-head comparisons for the risk of RTIs between individual treatments

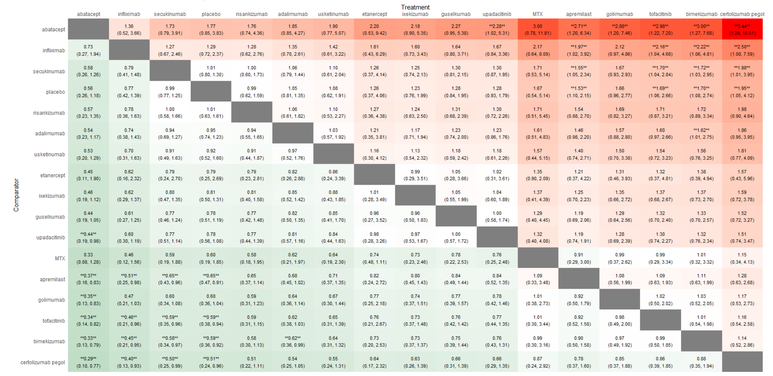
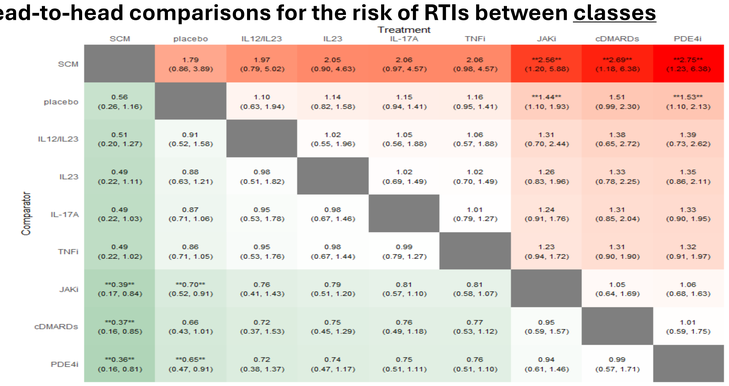


Table 3. Head-to-head comparisons for the risk of RTIs between classes



- **Subgroup analysis (upper RTIs)**
  - All 40 studies in the main analysis reported upper RTIs
  - The network of induvial-level and class-level was same as figure 1A and 1B, respectively
  - In the network meta-analysis
    - Individual-level: Consistent to main findings, **abatacept** (SUCRA 0.94) was ranked as the best treatment with the lowest risk of RTIs occurrence, while **certolizumab pegol** (SUCRA 0.16) was ranked as the worst in terms of RTIs risk
    - Class-level: The ranking of classes for risk of upper RTIs remained unchanged as the primary analysis (**SCM** [SUCRA 0.97], **IL12/IL23**, **IL23**, **IL-17A**, **TNFi** , **JAKi** , **cDMARDs** and **PDE4i** [SUCRA 0.16])
- **Quality assessment**
  - The overall risk of bias was low. 2 studies were found to have some concern in the process of randomization

Conclusion

- Our findings suggest that **abatacept** (individual treatment effect) and **SCM** (class effect) were least likely to be associated with occurrence of RTIs. However, more analyses are needed to evaluate the severity and type of RTIs associated with current treatments