SUPPLEMENTARY METHODS

Choice of reference category for medication exposure

Regarding the choice of the reference category for disease-modifying antirheumatic drugs (DMARDs), the most populated categories and therefore possible choices were TNF inhibitors (TNFi), methotrexate, and absence of DMARD therapy. While the TNFi group was the largest group overall, patients receiving TNFi were younger, had less comorbidities, smoked less, took steroids less often, and had better disease control than the overall average, and therefore this group was felt to be inappropriate as a reference group. The proportion of patients receiving methotrexate, on the other hand, was much higher among psoriatic arthritis (PsA) patients compared to patients with axial spondyloarthritis (axSpA) or psoriasis without arthritis (PsO). Moreover, in spondyloarthritis patients with purely axial disease, conventional synthetic DMARDs like methotrexate are ineffective and rarely prescribed. Thus, absence of DMARD therapy was adopted as the medication reference group for DMARDs.

Assumptions of the proportional odds model

In the proportional odds model, the odds ratio for the events “hospitalized or deceased” vs. “neither hospitalized nor deceased” is assumed to be equal to the odds ratio for the events “deceased” vs. “not deceased (hospitalized or not hospitalized)”. This is the odds ratio reported as results for the model. Potential deviations from this assumption were assessed graphically by plotting the stratified means for the levels of the ordinal outcome together with the expected values given that the proportional odds assumption holds,[1] without detecting deviations of concern overall (data not shown).

Statistical interactions

Four two-way interactions were modeled in an additive sense[2]:

1. Between hypertension and cardiovascular disease (CVD): hypertension alone, CVD alone, hypertension combined with CVD; vs. no hypertension and no CVD.
2. Between obesity and diabetes: obesity alone, diabetes alone, obesity combined with diabetes; vs. no obesity and no diabetes.
3. Between smoking status and cancer: cancer and known smoking habits, cancer unknown smoking habits, no cancer and ever smoked or unknown smoking habits; vs. no cancer and never smoked. The interaction between smoking status and cancer was modelled in a non-standard way due to the group of patients

with missing information on smoking habits presenting an OR exceeding the ORs for patients that had never or ever smoked in preliminary analyses, suggesting it was more appropriate to consider it as a separate subgroup within the interaction.

4. Between disease activity and prednisolone-equivalent glucocorticoid (GC) use: remission/low disease activity and GC use, moderate/high disease activity and no GC use, moderate/high disease activity and GC use; vs. remission/low disease activity and no GC use.

Patients excluded and handling of missing data

Patients under the age of 18, patients with missing primary outcome as well as missing values for age, sex, pandemic time period, DMARD exposure, patients treated with more than one biological DMARD, patients treated with DMARDs not typically used or licensed for PsO, PsA or axSpA, PsA (abatacept, B-cell inhibitors, IL-1 and IL-6 inhibitors), and patients diagnosed with multiple inflammatory rheumatic diseases (except for Sjögren's syndrome, and if not receiving B-cell therapies, azathioprine, mycophenolate, ciclosporin, cyclophosphamide or tacrolimus) were excluded from the analysis (529 patients excluded in total).

Further, for some analyses, medications without patients at all or medications with all patients falling into the same outcome category had to be excluded for statistical reasons in some of the secondary and sensitivity analyses (leflunomide, cyclosporine, IL-23 inhibitors, and apremilast, for the analyses focusing on patients with axSpA; antimalarials, leflunomide, sulfasalazine, cyclosporine, JAK inhibitors, and glucocorticoids in the presence of moderate/high disease activity, for the analysis focusing on patients with PsO; antimalarials and cyclosporine, for the analysis using the binary outcome mortality). Missing values for comorbidities, glucocorticoid therapy, disease activity and NSAIDs were derived by multiple imputation using full conditional specification.[3]

References

1. Harrell F. Regression Modeling Strategies: With Applications to Linear Models, Logistic Regression, and Survival Analysis. Chapter 5: Resampling, Validating, and Simplifying the Model. 2001 01/01; 3:88-103.

2. Rothman KJ. Modern epidemiology: Little, Brown & Co, Boston, 1986.

3. van Buuren S. Multiple imputation of discrete and continuous data by fully conditional specification. Stat Methods Med Res 2007;16:219–42.