Time to address the challenge of difficult to treat psoriatic arthritis: results from an international survey

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Psoriatic arthritis (PsA) is a highly heterogeneous disease with involvement of multiple tissues, underpinned by complex pathogenesis. Despite major improvements in the range and availability of efficacious treatment options, including biological and targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs),1 significant clinical unmet needs remain, with overall low rates of achievement of disease remission.2 Furthermore, a divergence of response is often seen between tissues, particularly skin and joints, or poor response in the presence of comorbidities, including mental health and other factors, leading to a growing number of patients having ongoing symptoms and apparent difficult to treat or manage PsA. Similar to rheumatoid arthritis (RA), a proportion of PsA patients exhibit disease which is refractory or resistant to more than one class of b/tsDMARD.3 4 The European Alliance of Associations for Rheumatology has recently proposed a definition for 'difficult-to-treat (D2T) RA' now used in clinical practice and research.5 6 In the absence of a similar definition in PsA, which has a more heterogeneous phenotype and b/tsDMARD options beyond those in RA, we launched a survey of rheumatologists globally to gather emerging perceptions on the possible terminology, definition and scope of D2T PsA. The survey, consisting of 19 questions (see online supplemental material), was designed by the authors following expert review and discussion and circulated electronically and via social media between 1 June 2023 and 31 July 2023. Categorical/ordinal survey data variables were analysed using R Studio 2023.06.0+421. In addition, three qualitative, free-text response questions were added to identify the most popular themes/answers to capture the breadth of opinion and consensus on each topic. A total of 244

responses were obtained with a larger representation from rheumatologists based in Europe (79.4% from Europe, 11.5% South America, 3.7% Asia, 3.3% North America and 0.8% Australia). Most respondents were aged 30–69 (96.2%), representing a broad spectrum of clinical experience from junior registrars to senior consultants. The majority (72.5%) worked in academic or teaching hospital settings. Despite the significant number of patients managed in individual centres (37.7% with >300 PsA patients), only 20.5% of clinicians worked in a combined rheumatology/dermatology service. The majority of respondents (34.8%) favoured a definition of D2T PsA to include failure of at least 2 classes of b/tsDMARDs with a pragmatic definition of truly 'refractory PsA' 'failing all available classes of b/tsDMARDs' being preferred (74.3%). Two-thirds (68%) felt that failure to ≥1 conventional synthetic DMARD should also be considered. Reflecting the complexity of PsA, there was wide variation on what disease activity outcomes should be used with 40.6% of respondents favouring the use of composite measures, and 38.1% stating that any individual clinical manifestation or symptom score would suffice. When asked about treatment targets in the context of D2T PsA, 86.5% of respondents favoured 'low disease activity' as a more feasible target to achieve than 'remission'. Beyond previous treatments and routine clinical parameters, five additional areas were highlighted as important for consideration in the definition of D2T PsA: radiographic progression and structural changes, axial disease, functional limitations, comorbidities and extramusculoskeletal manifestations. Interestingly, disagreement was seen regarding the most appropriate terminology for so-called 'D2T' disease with 56.6% favouring the term D2T PsA vs 41% preferring 'difficult-to-manage PsA' reflecting a wider spectrum beyond drug non-response. In conclusion, these results highlight the diversity of opinions among specialist rheumatologists on how to define D2T PsA. This survey acts as a springboard to call for the development of a consensus definition to facilitate clinical research and the development of treatment pathways for DT2 PsA. This effort will require input from patients and international experts, including representation from allied specialties such as dermatology, in order to comprehensively address the complex needs of this challenging PsA population.