Bridging the gap between 2024 EULAR/PreS Recommendations for Still's Disease and practice: the need for awareness of biomarkers and timely use of IL-1/ IL-6 inhibition

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Submitted: 24/01/2025

Accepted: 13/03/2025

Dear Editor,

In a recent issue of Annals of the Rheumatic Diseases (ARD), Fautrel and colleagues published the "EULAR/PReS recommendations for the diagnosis and management of Still's disease, comprising systemic juvenile idiopathic arthritis and adult-onset Still's disease."[1]

To assess current clinical practice regarding Still's disease (SD), we applied a questionnaire to Portuguese clinicians managing this condition. We obtained 52 responses, mostly from rheumatologists (96%), with 78% treating adults only, and 22% treating children as well. Two pediatricians subspecialised in pediatric Rheumatology also participated. The majority (85%) of respondents managed fewer than five SD cases annually.

Regarding diagnosis, 56% primarily use Yamaguchi criteria, while 18% rely on clinical experience. Only 35% utilize IL-18 or S100 proteins and approximately 40% of respondents indicated a lack of access to IL-18 and S100 testing. This limitation is primarily due to the absence of these tests in their clinical institutions, highlighting a significant barrier in adopting new biomarkers in routine clinical practice. Nearly one-third were unfamiliar with these biomarkers, and 4% considered them irrelevant in clinical practice.

Concerning the timing of patient reassessment, 62% reevaluate the patient after one week, 92% after one month, and 85% at month 3 and 6. Time constraints were the main reason for deviations.

In refractory cases, 35% adjust therapy after one week, 31% after two weeks, and 29% after four weeks. Half of the respondents expect to achieve clinically inactive disease (CID) with low-dose glucocorticoids after three months, but only 39% aim for CID without glucocorticoids by month 6.

Nearly half (48%) do not use diagnostic scores for macrophage activation syndrome (MAS), mostly due to their complexity, while 38% use the HScore. New biomarkers for MAS remain underutilized: S100 proteins are used by 27%, soluble IL-2 receptor by 13%, and activated CD8 T-lymphocytes, IL-18 and CXCL-9 by less than 10%. Although pulmonary involvement in SD is a recent concern, 70% actively investigate respiratory signs.

Glucocorticoids are part of first-line therapy for 95% of respondents, and 37% do not initially include IL-1 or IL-6 inhibitors, mainly because they prefer options considered to have a better benefit-cost or due to access issues. If CID is not achieved within three months of IL-1/IL-6 inhibitors and low dose glucocorticoids, 76% switch to another IL-1/IL-6 inhibitor. Most (57%) begin reducing biologics after 12 months of CID without glucocorticoids, while only 16% do so after six months.

Approximately half of respondents believe the recommendations will at least moderately influence their practice. Our sample size does not allow an in-depth comparison of specific subgroups, but our findings highlight the variability in diagnostic and treatment approaches. This aligns with a care pathway analysis among European AOSD experts, which found consistency in the overall pathway but differences in diagnostic criteria, sequencing of biologics, treatment preferences, and laboratory tests employed[2].

As the EULAR/PReS recommendations were recently released, their implementation will depend on access to biologic therapies and biomarkers across healthcare systems. The role of conventional DMARDs in SD treatment remains debated. In 2022, German guidelines included methotrexate and calcineurin inhibitors as first-line glucocorticoid-sparing agents in mild disease, while in England, biologics are a third-line option after two conventional DMARD failures[3,4]. The omission of conventional DMARDs in EULAR/PReS recommendations has been questioned[5].

While many clinicians recognize the recommendations' potential impact and highly agree with them (Figure 1), underuse of recent biomarkers and biologic therapies highlights gaps in resource availability and familiarity with emerging tools. We hope broader adoption will enhance access to IL-1/IL-6 inhibitors and recent biomarkers, ultimately improving SD patient outcomes.

Tables and Figures

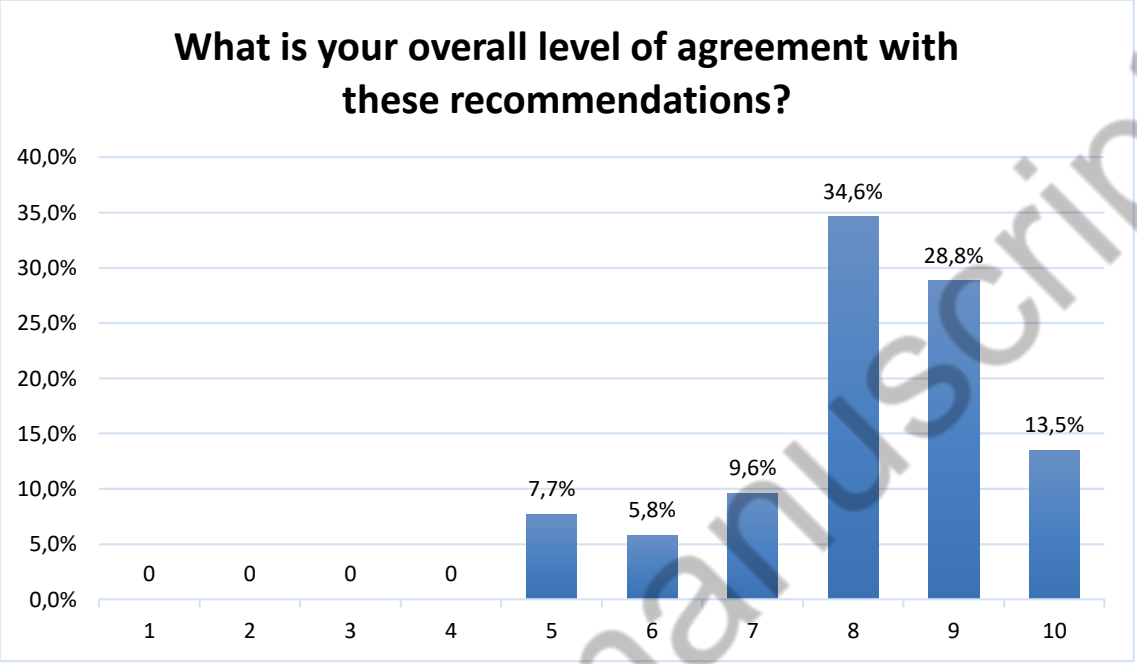

Figure 1- Graphic representation of the level of agreement (0-10) with the 2024 EULAR/PReS Still's Disease recommendations.

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