CSRO
Coalition of State Rheumatology Organizations

BOARD OF DIRECTORS

Madelaine A. Feldman, MD, FACR
President

Gary Feldman, MD
Vice President

Michael Saitta, MD, MBA
Treasurer

Michael S. Brooks, MD, FACP, FACR
Secretary

Leyka M. Barbosa, MD, FACR
Director

Kostas Botsoglou, MD
Director

Mark Box, MD
Director

Aaron Broadwell, MD
Director

Adrienne Burford Foggs, MD
Director

Amish J. Dave, MD, MPH
Director

Sarah Doaty, MD
Director

Harry Gewanter, MD, FAAP, MACR
Director

Adrienne R. Hollander, MD
Director

Firas Kassab, MD, FACR
Director

Robert W. Levin, MD
Director

Amar Majjhoo, MD
Director

Gregory W. Niemer, MD
Director

Joshua Stolow, MD
Director

HEADQUARTER OFFICE

Ann Marie Moss
Executive Director

555 E. Wells Street, Suite 1100
Milwaukee, WI 53202-3823
Phone: 414-918-9825
Email: info@csro.info
Website: www.csro.info

January 31, 2022

Gabriel Bien-Willner, MD
Angella Charnot-Katsikas, MD
MolDX Program
Palmetto GBA
17 Technology Circle
Columbia, SC 29202

Re: Predictive Testing to Guide Targeted Therapy Selection in Rheumatoid Arthritis Contractor Advisory Committee (CAC)

Dear Drs. Bien-Willner and Charnot-Katsikas,

The Coalition of State Rheumatology Organizations (CSRO) is comprised of over 40 state and regional professional rheumatology societies whose mission is to advocate for excellence in the field of rheumatology, ensuring access to the highest quality of care for the management of rheumatologic and musculoskeletal disease. Our coalition serves the practicing rheumatologist.

Today, we write in support of local coverage for new predictive testing tools that would enable rheumatologists to more efficiently treat patients with rheumatoid arthritis (RA). We concur with the sentiment expressed by your subject matter experts (SMEs) at the recent multi-jurisdictional CAC meeting: ***predictive testing to guide therapy selection would improve clinical outcomes and lower Medicare and beneficiary costs by steering beneficiaries away from therapies that will not meaningfully improve their RA.***

RA is a complex, progressive disease that leads to loss of function in untreated or undermanaged patients. In fact, one panelist likened it to a "kitchen fire," emphasizing the need to smother the flames before the house is engulfed: *"You've got to be aggressive with [RA] early…or you're going to get…a poor result."*

Unfortunately, the process of identifying the most effective treatment to slow disease progression can be lengthy and inefficient. Rheumatologists adhere to the American College of Rheumatology (ACR) Guideline for the Treatment of Rheumatoid Arthritis, which allows rheumatologists to choose between a growing array of medication therapies, referred to as Disease Modifying Anti-Rheumatic Drugs (DMARDs). In most circumstances, rheumatologists will first prescribe a conventional, non-biologic DMARD (e.g., methotrexate, hydroxychloroquin). If treatment goals are not reached or the patient cannot tolerate the medication, rheumatologists will prescribe a targeted therapy, such as a biologic DMARD. Biologic DMARDs include an array of drug classes, including tumor necrosis factor inhibitors (TNFis) (e.g. adalimumab, etanercept). At present, there are no published studies to suggest the optimal sequence of different therapies following non-biologic DMARDs, leaving rheumatologists and their patients to employ a "try-and-fail" approach to identify an effective biologic therapy.

Currently, rheumatologists consider a multitude of factors such as disease activity and severity, comorbidies, patient values and preferences, safety and efficacy data, clinican comfortability, and payer requirements.

In the vast majority of cases, TNFis are the most frequent first-line biologic DMARD prescribed.[1, 2, 3] This is in part due to rheumatologists' experience with the TNFi drug class. However, one of the most frequent reasons cited by our members, is formulary construction by payers, including Medicare Advantage (MA) plans, which overwhelmingly favors the highly rebated TNFi class.

Yet despite being the most prevalent first-line targeted therapy, approximately 30-40% of patients do not achieve clinical improvement when prescribed a TNFi.[4] More concerning, patients are often unable to access a different class of therapies (e.g., janus kinase inhibitors (JAK), interleukin-6 inhibitors (IL-6)) without first attempting dose escalation (i.e., increasing the amount or frequency of the current TNFi therapy) and/or cycling through other TNFi therapies. Most plans, including MA, require dose escalation and cycling as part of their utilization management protocols. In other words, if the TNFi does not work, the current payer strategy amounts to simply making patients take more of it. This "fail first" and "fail harder" approach means patients may spend a year or more on a therapy that will not work for them, leading to increased disease severity, disability, and pain.

Absent clinical evidence to support initiating treatment with one biologic DMARD over another, beneficiary access to alternative therapies will remain challenged. This is why precision medicine tools to "rule out" certain therapies would be immensely helpful. As explained by one SME panelist, *"…we're almost on a clock when we're treating [RA] patients…if you're able to at least [eliminate] one of the biologic classes from the get-go, then that could save you a lot of time and it could greatly benefit the patient long-term.*"

Our organizations support objective, science-based approaches to identifying appropriate medication therapies for RA treatment and management. And, if there were coverage for such tools, including predictive testing to guide targeted therapy selection in RA, clinicians would employ those tools to narrow decision-making on therapy prescribing. As noted by one SME panelist, *"[i]t would be nice to cut down the amount of time that I spent telling patients that we're doing this by trial and error, going from TNF to T-cell blocker to IL-6 blocker, if we could go straight to one,"* because, as noted by another SME panelist, *"...it's imperative to try to get patients on the best treatment for them as soon as possible…"*

In addition, absent literature to the contrary, we would agree with the SME panelists that restrictions on when to use predictive testing should be avoided at the outset. This would include limiting the use of predictive testing to certain patients or requiring the use of certain disease activity indices beyond what is standard practice. As one SME panelist noted, "*I don't think that the data would really dictate where you would kind of pigeonhole this type of marker's use.*" Further, it is our understanding is that predictive drug response testing is generally a "one-time" event; however, with evolving science this could change.

---

[1] Dierckx, S., Sokolova, T., Lauwerys, B.R. et al. Tapering of biological antirheumatic drugs in rheumatoid arthritis patients is achievable and cost-effective in daily clinical practice: data from the Brussels UCLouvain RA Cohort. Arthritis Res Ther 22, 96 (2020). https://doi.org/10.1186/s13075-020-02165-4

[2] Jin Y, Desai RJ, Liu J, Choi NK, Kim SC. Factors associated with initial or subsequent choice of biologic disease-modifying antirheumatic drugs for treatment of rheumatoid arthritis. Arthritis Res Ther. 2017;19(1):159. Published 2017 Jul 5. https://doi:10.1186/s13075-017-1366-1

[3] Curtis JR, Zhang J, Xie F, et al. Use of oral and subcutaneous methotrexate in rheumatoid arthritis patients in the United States. *Arthritis Care Res (Hoboken)*. 2014;66(11):1604-1611. doi:10.1002/acr.22383

[4] Wijbrandts CA, Tak PP. Prediction of Response to Targeted Treatment in Rheumatoid Arthritis. *Mayo Clin Proc*. 2017;92(7):1129-1143. doi:10.1016/j.mayocp.2017.05.009

For these reasons, ***our organizations recommend that you establish a local coverage policy for the use of predicitive testing to guide targeted therapy selection with the following caveats.***

- ***The ordering and interpretation of predictive testing in rheumatoid arthritis should be at the sole discretion of the treating rheumatologist.***

- ***Predictive testing should not be used by payers to switch stable patients to a different medication or deny coverage of the stabilizing medication based on the results of said test.***

Thank you for considering the feedback of practicing rheumatologists. Should you have any questions, please contact me at mfeldman@csro.info.

Sincerely,

Madelaine A. Feldman, MD, FACR
President, Coalition of State Rheumatology Organizations (CSRO)