Rheumatologists may one day be able to test in advance which patients with rheumatoid arthritis will benefit from expensive biological response modifier TNF-antagonist drugs — or biologics — and which will not. A new study has indicated that RA patients with the most elevated type 1 interferon levels tend to be those who responded most favorably to TNF-antagonist drugs.

Physician-in-Chief Mary K. Crow, MD, led this initial study for HSS, in conjunction with University of Southern California. Going into the research, the team knew that levels of IFN-beta, a protein that can limit cell division, is present in the joint tissue of some patients with rheumatoid arthritis. The researchers wondered if variable levels of this protein could play a role in how patients respond to TNF-antagonist drugs.

To test this hypothesis, the investigators set out to determine the relationship between levels of type 1 interferon activity in the blood prior to beginning therapy and the ability of the drug to control rheumatoid arthritis in patients. They studied the role of IFN-beta, and because they knew that IFN-beta induces interleukin-1 receptor antagonist (IL-1Ra), another protein, they also tested levels of IL-1Ra.

“Treatment with these drugs is very expensive; the drugs can cost $16,000 or so per year. If you are going to use them, you would like to know that they are likely to work in your patient.”

- Mary K. Crow, MD
Lower Type 1 Interferon, Lower Response

A 35-patient sample was divided into three groups: RA patients who received a TNF-antagonist drug, RA patients who got no drug, and healthy volunteers. Using the Disease Activity Score in 28 joints, the patients were treated, then evaluated to determine whether they had a moderate, good, or no response to the drug. Comparing the three groups, higher levels of type 1 interferon prior to treatment were found in the blood of patients who benefited most. Lower levels were associated with lower response.

More Good Response Indicators

Patients who had an increased IFN-beta/alpha ratio – meaning they had more IFN-beta – were also more likely to respond to TNF-antagonist therapy. Another indication of good response was significantly higher baseline levels of IL-1 receptor antagonist in plasma samples when compared with nonresponsive or moderate responders.

If wider studies prove consistent with these promising early findings, the results could represent a new tool for improved management of patients with rheumatoid arthritis. While TNF-antagonist drugs have substantial clinical efficacy for some patients, they do not provide the same benefits for an estimated 30 to 50% of patients with RA. The drugs can also carry some risk of toxicity.

Knowing whether a TNF-antagonist biologic will help a patient’s rheumatoid arthritis can save time, money, and patients investing emotionally in the possibility of relief. As Dr. Crow adds, “For those who demonstrate low levels of blood interferon activity, that information might be useful to guide patients to alternative treatments that might be more likely to work for them.

Methodology Included:

- RA patients (n = 35), from a single center were evaluated before and after initiation of TNF-antagonist therapy. 12 RA patients from the same center who were not treated with a TNF-antagonist were studied as controls.
- Plasma type I IFN activity was measured using a reporter cell assay and disease status was assessed using the Disease Activity Score in 28 joints (DAS28).
- Levels of interleukin-1 receptor antagonist (IL-1Ra) were determined in baseline plasma samples using a commercial enzyme-linked immunosorbent assay.
- The clinical response was classified according to the European League Against Rheumatism criteria for improvement in RA.

Findings Included:

- The plasma type I IFN activity, the IFNβ/α ratio, and the IL-1Ra level were predictive of the therapeutic response in TNF-antagonist–treated RA patients, indicating that these parameters might define clinically meaningful subgroups of RA patients with distinct responses to therapeutic agents.
- Plasma type I IFN activity at baseline was significantly associated with clinical response (odds ratio 1.36 [95% confidence interval 1.05–1.76], P = 0.020), with high baseline IFN activity associated with a good response.
- Changes in DAS28 scores were greater among patients with a baseline plasma IFNβ/α ratio >0.8 (indicating elevated plasma IFNβ levels).
- Consistent with the capacity of IFNβ to induce IL-1Ra, elevated baseline IL-1Ra levels were associated with better therapeutic outcomes (odds ratio 1.82 [95% confidence interval 1.1–3.29], P = 0.027).