AJRCCM Articles in Press. Published on 30-March-2017 as 10.1164/rccm.201703-0552LE

Questioning the Effectiveness of Baricitinib for Pulmonary Manifestations of Rheumatoid Arthritis

By

Jason Chertoff, MD, MPH *

Ali Ataya, MD *

*University of Florida College of Medicine - Division of Pulmonary, Critical Care, and Sleep Medicine

Corresponding Author

Jason Chertoff MD, MPH

917-232-0297

jason.chertoff@medicine.ufl.edu

University of Florida College of Medicine

1600 SW Archer Road; Gainesville, FL; 32608

To the editor:

As you are almost certainly aware, baricitinib recently showed promising results in patients with rheumatoid arthritis (RA) (1). Indeed it was encouraging to learn about the morbidity and radiographic progression benefit of baricitinib when compared to adalimumab or placebo in patients with rheumatoid arthritis. In addition to these positive results, I was also intrigued by the absence of any mention to baricitinib's role – if any – in treating the pulmonary manifestations of rheumatoid arthritis (RA) like interstitial lung disease (ILD). Pulmonary involvement culminating in ILD occurs in approximately 10% of patients with RA and is responsible for significant morbidity and 10-20% of all mortality associated with the disease (2, 3). Moreover, while 80-90% of patients with RA present with typical articular symptoms, as many as 10% of RA patients can present with pulmonary involvement as their presenting symptom. In fact, when compared to those RA patients without ILD, those with ILD have an estimated standardized mortality ratio of 2.5 to 5.0 (4, 5).

Although disease modifying antirheumatic drugs (DMARDS) and certain biologic therapies have greatly reduced RA's extra-articular manifestations, their benefit in RA-ILD remains obscure (4, 5). Currently, the optimal treatment for RA-ILD is largely ambiguous and consists of smoking cessation, chronic glucocorticoids, and immunosuppressive agents like azathioprine, mycophenolate, and cyclophosphamide; the efficacy of biologic agents like etanercept and adalimumab continues to be unproven (4, 5). Thus, there is much room for improvement in the RA-ILD arena, which is why the findings of baricitinib's efficacy are so compelling.

I am eager to learn whether baricitinib has any benefit on symptoms and radiographic progression in patients with RA-ILD. If possible, I implore researchers closely involved with

AJRCCM Articles in Press. Published on 30-March-2017 as 10.1164/rccm.201703-0552LE

this drug to conduct post-hoc analyses or prospective trials to analyze the effectiveness of baricitinib in patients with RA-ILD. I believe that these investigations, whether significant or not, would add invaluable knowledge to the stagnated field of treatments for RA-ILD.

In conclusion, the recent report of baricitinib's efficacy in RA is encouraging, and demonstrates that it has potential to benefit millions of patients with RA. My hope is that researchers heed my suggestion and investigate whether this therapy is capable of benefitting patients with RA-ILD. By doing this, these researchers are uniquely empowered to improve outcomes in patients with RA-ILD - a lung disease where treatments have been predominantly suboptimal.

References

1. Taylor PC, Keystone EC, van der Heijde D, Weinblatt ME, Del Carmen Morales L, Reyes Gonzaga J, et al. Baricitinib versus Placebo or Adalimumab in Rheumatoid Arthritis. N Engl J Med. 2017;376(7):652-62.
2. Kim EJ, Elicker BM, Maldonado F, Webb WR, Ryu JH, Van Uden JH, et al. Usual interstitial pneumonia in rheumatoid arthritis-associated interstitial lung disease. Eur Respir J. 2010;35(6):1322-8.
3. Olson AL, Swigris JJ, Sprunger DB, Fischer A, Fernandez-Perez ER, Solomon J, et al. Rheumatoid arthritis-interstitial lung disease-associated mortality. Am J Respir Crit Care Med. 2011;183(3):372-8.
4. Solomon JJ, Ryu JH, Tazelaar HD, Myers JL, Tuder R, Cool CD, et al. Fibrosing interstitial pneumonia predicts survival in patients with rheumatoid arthritis-associated interstitial lung disease (RA-ILD). Respir Med. 2013;107(8):1247-52.
5. Vij R, Strek ME**.** Diagnosis and treatment of connective tissue disease-associated interstitial lung disease. Chest. 2013;143(3):814-24.