Thrombocytosis in rheumatoid arthritis patients receiving Baricitinib and concomitant conventional synthetic disease modifying antirheumatic drugs (csDMARDs)

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INTRODUCTION

Baricitinib is an orally administered Janus Kinase (JAK) 1/2 selective inhibitor used in patients with moderate to severe rheumatoid arthritis (RA). Previous studies demonstrated 1) acceptable overall safety and efficacy profiles 2) mild to modest thrombocytosis among some patients receiving JAK inhibitors. Clonal thrombocytosis is associated with increased risk of complications (such as bleeding, ischaemia and thrombosis) as opposed to reactive thrombocytosis.

AIM

To identify any presence of thrombocytosis, determine 1) its' severity/clinical significance and 2) the type of conventional synthetic disease modifying antirheumatic drugs (csDMARD) most at risk to cause it in RA patients receiving combination of Baricitinib and csDMARD.

METHODS

A retrospective review of medical records and blood parameters were performed for identification and characterization of all RA patients on Baricitinib and csDMARD combination therapy who were actively attending the rheumatology service at University Hospital Kerry. This was further classified to a specific subset receiving Baricitinib and Leflunamide combination therapy group (as there were no thrombocytosis observed in other combination groups (Table 1).

Table 1: Demographic of patients on Baricitinib-Leflunamide combination therapy

Female (n)	5
Male (n)	1
Age (Median)	53
On prednisolone (n)	1
Platelet (Baseline)/ Mean	313.5
Platelet (3 months of starting Baricitinib)/Mean	425.5
Duration on Baricitinib (Months/Mean)	11.6

RESULTS

6 patients were identified (5 female, 1 male; median age 53) on both Baricitinib and csDMARD. All 6 were seropositive (6 patients positive for RF; 5 for anti-CCP); none had baseline primary thrombocythaemia or splenectomy. Platelet elevation was observed in all 6 patients (3 remained within normal platelet range) after commencement of Baricitinib (mean increase of $112x10^9$/L). 3 patients developed persistent thrombocytosis (mean of $543x10^9$/L; mean increase of $149.3x10^9$/L) (all on Baricitinib-Leflunamide combination. Reduced but persistent thrombocytosis were still observed after Baricitinib dose reduction in all patients (from 4mg to 2mg). CRP was reduced in all patients to within normal limits (≤3mg/dL) in all 6 patients post treatment with Baricitinib. So far, none of the patients with thrombocytosis developed or had documented venous thromboembolism episodes (VTE)

The three patients with persistent Thrombocytosis were females and sero positive RA, and after reducing their Baricitinib from 4mg to 2mg, eventually 2 of them were switched to Abatacept.

CASES

Case 1

59 years old female with seropositive RA started Arava July 2017, and Baricitinib in September 2019. Her baseline platelet was ($393x10^9$) .and 12 weeks after commencing on combination therapy with Baricitinib was noted to have moderate thrombocytosis ($504x10^9$). This remained persistent for 11 months despite dose reduction of Baricitinib and despite no VTEs during the 11 months, she was eventually switched to Abatacept with normalization of her blood parameters.

Case 2

52 years old female with seropositive RA started Arava in November 2015, and Baricitinib in August 2019. Her baseline platelet was($371x10^9$) and 12 weeks after commencing on combination therapy eventually with Baricitinib was noted to have moderate Thrombocytosis ($550x10^9$).This remind persistent for 12 months despite dose reduction of Baricitinib and despite no VTEs during the 12 months, she was eventually switched to Abatacept with normalization of her blood parameters.

Case 3

54 years old female with seropositive RA started Arava July 2017, and Baricitinib in August 2019, Her baseline platelet was ($418x10^9$) .and 12 weeks after commencing on combination therapy with Baricitinib was noted to have moderate thrombocytosis ($507x10^9$). This remained persistent for 12 months despite dose reduction of Baricitinib and despite no VTEs during the 12 months. Then Baricitinib was decreased to 2 mg daily with normalization of her blood parameters.

CONCLUSION

1)Our report highlights the need to regularly monitor blood counts in RA patients receiving Baricitinib and concomitant csDMARD

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2) We would recommend that caution should be used when Baricitinib and Leflunamide are given concomitantly. Well suppressed CRP in these patients (despite the thrombocytosis) points toward a clonal rather than reactive cause.

3)However, more investigations would be required while the relevance and possible complications of the thrombocytosis remains unknown.

References

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