Disease progression in patients with essential thrombocythaemia receiving anagrelide within a single institution

Nicki Gray*, Cheuk-kie Jackie Cheung[1], Abdullah Khalil[1], Jennifer O'Sullivan and Bethan Psaila[1],
[1]Haematology, Oxford University Hospitals NHS foundation trust, Oxford, United Kingdom

Introduction: Anagrelide is currently used as a second-line treatment to lower platelet counts in essential thrombocythaemia (ET). Since the PT1 study[1], there has been increased interest in the potential risk of accelerated myelofibrotic transformation in ET patients treated with anagrelide. Current BSH guidelines advocate monitoring bone marrow trephines at 3 yearly intervals for those treated with anagrelide to monitor for signs of emerging fibrosis[2].

Aim: To identify clinical features and outcomes of ET patients who received anagrelide in our local centre.

Methods: A retrospective chart review was performed to identify all patients prescribed anagrelide between January 2012 to December 2018 from pharmacy records. Clinical data was collated from electronic patient records.

Results: During the 6-year period (2012 to 2018), our institution treated 37 patients for a minimum of 2 consecutive months on anagrelide. The average duration of treatment was 43 months (range 3 – 132 months). Of those prescribed anagrelide during this period, 57% discontinued for either disease transformation, lack of adequate response or side effects. For those who discontinued for transformed disease (AML or MF), the average treatment duration was 34.2 months. Of those that discontinued for non-disease transformation indications, 70% stopped due to cardiac toxicity. 16 (43%) patients remained on anagrelide at the end of the study period (average treatment duration >62 months).

27% of patients (10/37) transformed to myelofibrosis and 3% (1/37) developed AML. Of those that transformed to myelofibrosis, 80% had the *JAK2V617F* mutation. In comparison, a similar study at our institution reviewing the outcome of 27 patients taking hydroxycarbamide over a similar time window identified 7% of patients progressing to myelofibrosis and 7% developing AML. Therefore the rate of myelofibrotic transformation was significantly higher in patients treated with anagrelide with a Chi squared value of 3.9 and P value of 0.047.

	Anagrelide	Hydroxycarbamide
Myelofibrosis	10 (6.94) [1.35]	2 (5.06) [1.85]
No myelofibrosis	27 (30.06) [0.31]	25 (21.94) [0.43]

There was no difference in age of presentation between those that did and did not transform to myelofibrosis (57 yrs versus 56.7 yrs). 11/37 patients (30%) had a pre-anagrelide trephine biopsy. Of 4 of these who later progressed to myelofibrosis, 50% had fibrosis grade 1 prior to anagrelide exposure. 28% (2/7) of patients receiving anagrelide who did not transform to myelofibrosis had evidence of fibrosis (grade 1) prior to treatment.

Conclusion: These findings highlight the higher incidence of fibrosis development in patients with ET treated with anagrelide. Screening for baseline fibrosis/evidence for pre-fibrotic myelofibrosis with a bone marrow biopsy prior to the commencement of anagrelide is important, with careful monitoring for signs of progression in patients on treatment.

References:

1. Harrison CN, Campbell PJ, Buck G, et al (2005). Hydroxyurea compared with anagrelide in high-risk essential thrombocythemia. *New England Journal of Medicine*, 353(1):33–45
2. Harrison CN,Butt D, Campbell P et al (2010). Guideline for investigation and management of adults and children presenting with a thrombocytosis. *British Journal of Haematology*, 149, 352---375.