Abstract: P827

Title: PREDICTIVE FACTORS FOR THE RESPONSE TO ROMIPLOSTIM IN PATIENTS WITH IST-REFRACTORY APLASTIC ANEMIA: DATA FROM TWO CLINICAL TRIALS

Abstract Type: Poster Presentation

Topic: Bone marrow failure syndromes incl. PNH - Clinical

Background:

Romiplostim, a thrombopoietin receptor agonist, has been reported to be effective and safe for treating immune suppressive therapy (IST)- or eltrombopag-refractory aplastic anemia (AA) and for IST-naïve AA patients. Predictive factors for the use of romiplostim in eltrombopag-refractory AA patients include baseline absolute reticulocyte count, neutrophil count, and hemoglobin level. However, there are few reports on factors that predict the efficacy of romiplostim in IST-refractory AA patients.

Aims:

To explore factors that predict the response to romiplostim in patients with IST-refractory AA, and to explore the threshold of baseline reticulocyte count that predicts efficacy.

Methods:

Patient background and baseline laboratory data from two clinical trials in IST-refractory (eltrombopag-naïve) AA patients, 531-KR001 (NCT02094417) and 531-002 (NCT02773290), were combined and analyzed. The definition of response was based on modified version of the international criteria for response (BJH 2009; 147:43–70) (Table 1). Logistic regression analysis was used to evaluate patient background factors and baseline laboratory data that predict response to romiplostim. Additionally, receiver operating characteristic (ROC) curve analysis was used to explore the response-predictive threshold of baseline reticulocyte count.

Results:

Data from 66 patients (35 from 531-KR001 and 31 from 531-002), 40 (60.6%) female, median (range) age 47.0 (20–78) years, were analyzed. Of these, 34/66 (51.5%) patients had non-severe AA, 57/66 (86.4%) had received anti-thymocyte globulin + cyclosporine A as pre-treatment, and 53/66 (80.3%) were transfusion-dependent. At 27 weeks, no patient achieved a complete response, while 35/61 (57.4%) patients achieved a partial response, and 24/49 (49.0%) patients were red blood cell transfusion independent. Univariate logistic regression analysis identified duration from diagnosis (p=0.040), baseline reticulocyte count (p<0.001) and platelet count (p<0.001) as factors predicting response to romiplostim at 27 weeks. Additionally, ROC curve analysis identified a cut-off value of 30.77 x 109/L (sensitivity: 82.9%, specificity: 73.1%) as the threshold reticulocyte count for predicting response to romiplostim.

Summary/Conclusion:

A threshold baseline reticulocyte count of 30.77 x 109/L was predictive of response to romiplostim treatment for IST-refractory AA patients at 27 weeks. However, it should be noted that the initial dose included in this analysis was lower than that used in real-world clinical practice because the analysis includes the results of the 531-KR001 study, which had a dose-finding phase.

Table 1 Definition of hematological response

	Severity at Baseline	
	Patients with SAA/VSAA	Patients with NSAA
CR (Complete response)	All of the following criteria are met: • Hemoglobin (Hb) concentration $\geq$ 10 g/dL • Neutrophil count $\geq$ 1.0 x 10^9/L • Platelet count $\geq$ 100 x 10^9/L	
PR (Partial response)	Platelet and erythrocyte transfusion independence, and two or more of the following criteria are met: • Neutrophil count $\geq$ 0.5 x 10^9/L • Platelet count $\geq$ 20 x 10^9/L • Reticulocyte count $\geq$ 20 x 10^9/L	Transfusion independence (if previously dependent) or doubling or normalization of at least one cell line or increase of baseline : • Hb of >3.0g/dL (if initially <6.0g/dL) • Neutrophil count of > 0.5 x 10^9/L (if initially <0.5 x 10^9/L) • Platelet count of >20 x 10^9/L (if initially <20 x 10^9/L)
NR (No response)	No longer meeting the above criteria	