Comparison of Adherence, Persistence, and Bleed-related Event Rates in Patients Diagnosed With Immune Thrombocytopenia and Treated With Thrombopoietin Receptor Agonists

PSY101

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Background

- Immune thrombocytopenia (ITP) is an immune-mediated acquired disease of adults and children characterized by transient or persistent decrease of the platelet count and increased risk of bleeding[1]
- In August of 2008, romiplostim, a subcutaneously administered thrombopoietin receptor agonist (TPO-RA) and in November 2008, eltrombopag, an oral TPO-RA received approval by the Food and Drug Administration for the treatment of thrombocytopenia in individuals with chronic ITP who had an insufficient response to corticosteroids, immunoglobulins, or splenectomy
- However, there is limited real-world information on the utilization of TPO-RAs, including eltrombopag and romiplostim, for the treatment of ITP and their associated outcomes.

Study Objectives

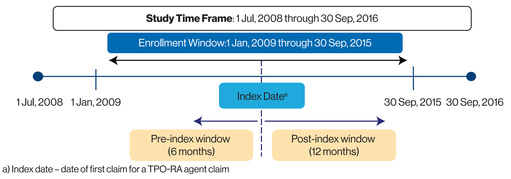
- Compare adherence, persistence, and bleed-related event (BRE) rates among patients diagnosed with ITP and treated with eltrombopag, to those treated with romiplostim.

Methods

Data Source and Study Design

- Retrospective claims database analysis using MarketScan® Commercial plus Medicare Supplemental databases, and IMS' PharMetrics Plus™ database
- Target population: Patients with a diagnosis of ITP initiating TPO-RA therapy

Figure 1. Study Design



a) Index date – date of first claim for a TPO-RA agent claim

Sample/Population Selection Inclusion criteria

- Inclusion
  - ≥2 prescription claims for a TPO-RA (eltrombopag or romiplostim) within the enrollment window and ≤30 days apart, of which the date of the first was deemed the index date
  - ≥2 non-diagnostic outpatient claims separated by ≥30 days (but ≤365 days) or ≥1 inpatient claim carrying an ICD-9-CM diagnosis code for ITP (ICD-9-CM: 287.31) with ≥1 claim in the pre- or post-index window
  - Age ≥18 years on index date
  - Continuous enrollment in medical and pharmacy benefits for 6 months prior to and 12 months after the index date
- Exclusion
  - Prescription claim for a TPO-RA during the pre-index window

Study Outcomes

- All outcomes were assessed during the 12-month post-index window
- Adherence: Medication possession ratio (MPR) was used to measure adherence as both a continuous and binary measure

$$\text{Eltrombopag MPR} = \frac{\text{Sum of total days' supply for all fills}}{\text{\# of days between the first and last fill plus days}^{\wedge *}\text{ supply of the last fill}}$$

$$\text{Romiplostim MPR} = \frac{\text{Sum of covered days}^{*}\text{ for each injection}}{\text{\# of days between the first and last injection plus 7 days}}$$

*Covered days was defined for each injection as the lesser of 7 days or the time between injections.

- Patients were considered to be adherent if the MPR was ≥0.8
  - Persistence: Patients were considered persistent if they did not have any gap of ≥30 days in the TPO-RA therapy regimen during the fixed 12-month post-index window
  - Percent of patients who discontinue treatment with TPO-RA: Percent of patients who had a gap of ≥30 days in the therapy regimen during the fixed 12-month post-index window
  - Time to treatment discontinuation: Number of days from initiation of TPO-RA to first gap in therapy of ≥30 days
  - BRE: was defined as a claim for a bleeding event and/or use of rescue therapy (IVIg administration, IV steroid administration, or platelet transfusion) using a combination of diagnosis and procedure codes.[2] The evidence of (binary variable) and number of such events (continuous variable) was captured over the fixed 12-month post-index period.

Statistical Analysis

- Descriptive statistics (percentages, means, medians, standard deviations [SDs]) were used to characterize the study sample.
- Inferential statistics were used to describe and quantify inter-cohort differences in demographic and baseline characteristics, and endpoints between eltrombopag and romiplostim users.
  - For categorical variables, $\chi 2$ tests or Fisher's exact tests were used.
  - For interval variables, Student's t- tests or Wilcoxon-Mann-Whitney tests were used as appropriate for the distribution.
  - All statistical tests performed tested a 2-sided hypothesis of no difference between patient cohorts at a significance level of 0.05
- All analyses were conducted using SAS® version 9.4 (SAS Institute; Cary, NC, USA).

Results

Sample Characteristics

- Eligible Population:
  - MarketScan: 1,325 patients
    - 365 (27.5%) eltrombopag users
    - 959 (72.4%) romiplostim users
    - 1 (0.1%) patient who received both eltrombopag and romiplostim on index date (excluded).
  - In PharMetrics, 1,010 patients
    - 297 (29.4%) eltrombopag users
    - 713 (70.6%) romiplostim users
    - Demographic characteristics
  - Demographic characteristics were similar between patients receiving eltrombopag and romiplostim (**Table 1**)
- Clinical characteristics
  - The average comorbidity score, although only slightly higher among romiplostim users, was statistically significantly different (**Table 1**)
  - A larger proportion of eltrombopag users received a corticosteroid and other ITP-related treatments (including azathioprine, danazol, vincristine/vinblastine, cyclophosphamide, mycophenolate, cyclosporine, and hydroxychloroquine) during the pre-index period compared to romiplostim users (**Table 1**)

Table 1. Demographic and Clinical Characteristics

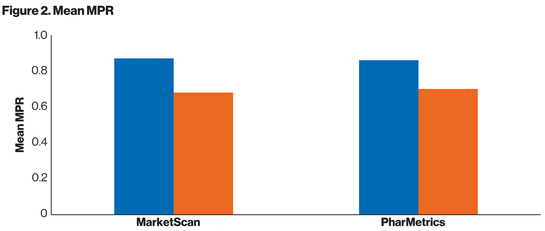
Characteristic	MarketScan					PharMetrics				
	Eltrombopag (n= 365)		Romiplostim (n=959)		P-value	Eltrombopag (n=297)		Romiplostim (n=713)		P-value
Age in years, Mean (SD)	58.6	17.0	59.3	16.7	0.4739	52.2	15.0	54.5	14.6	0.0250
Males, n (%)	173	47.4%	440	45.9%	0.6210	132	44.4%	360	50.5%	0.0798
Charlson Comorbidity Index, Mean (SD)	1.6	(1.9)	1.9	(2.3)	**0.0117**	1.2	(1.8)	1.8	(2.3)	**<0.0001**
ITP-treatment Naive, n (%)	73	20.0%	277	28.9%	**0.0011**	60	20.2%	183	25.7%	0.0642
ITP-treatment Related Prescription Classes, n (%)										
Corticosteroids	260	71.2%	612	63.8%	**0.0110**	220	74.1%	479	67.2%	**0.0306**
Intravenous immunoglobulin (IVIg)	71	19.5%	211	22.0%	0.3112	67	22.6%	173	24.3%	0.5619
Anti-D immunoglobulin (Anti-D)	16	4.4%	34	3.5%	0.4746	10	3.4%	33	4.6%	0.3657
Rituximab	61	16.7%	168	17.5%	0.7290	77	25.9%	143	20.1%	**0.0395**
Other[a]	43	11.8%	77	8.0%	**0.0336**	39	13.1%	59	8.3%	**0.0175**
Splenectomy	20	5.5%	41	4.3%	0.3503	12	4.0%	28	3.9%	0.9329

[a]Azathioprine, danazol, vincristine/vinblastine, cyclophosphamide, mycophenolate, cyclosporine, hydroxychloroquine, interferon-alfa

Study Outcomes

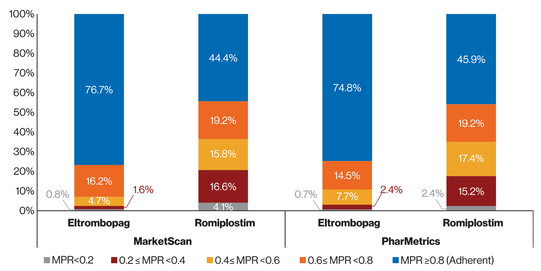
- Adherence
  - Mean MPR was higher for patients receiving eltrombopag compared to patients receiving romiplostim in both databases (P<0.0001) (**Figure 2**)

Figure 2. Mean MPR



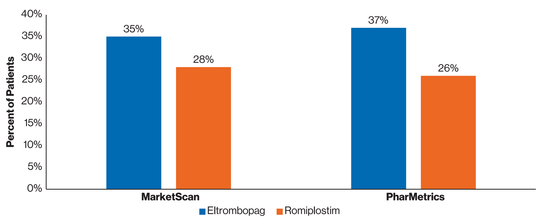
- More than three-quarters of eltrombopag users in both databases were adherent compared to <50% of romiplostim users (**Figure 3**)

Figure 3. Proportion of Patients by MPR Categories



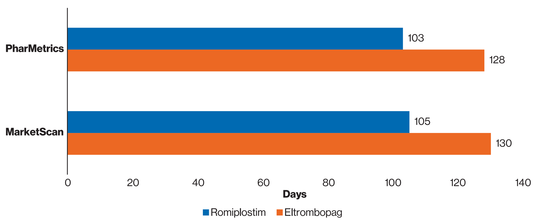
- Persistence
  - A higher proportion of eltrombopag patients compared to romiplostim patients, continued treatment (no gap of ≥30 days) for ≥1 year (P=0.011 MarketScan, P=0.0004 PharMetrics) (**Figure 4**)

Figure 4. Percent of Patients Persistent for 12 Months



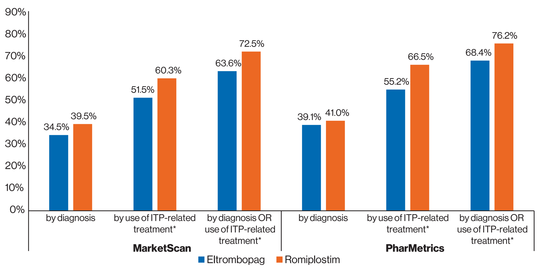
- Time to treatment discontinuation
  - Mean time to treatment discontinuation was longer for patients receiving eltrombopag compared to those receiving romiplostim (P=0.0002 MarketScan, P=0.0008 PharMetrics) (**Figure 5**)

Figure 5. Mean Time to Treatment Discontinuation



- Bleed-related Events
  - A smaller proportion of patients receiving eltrombopag had a BRE in the follow-up period compared to patients receiving romiplostim (P<0.05) (**Figure 6**)

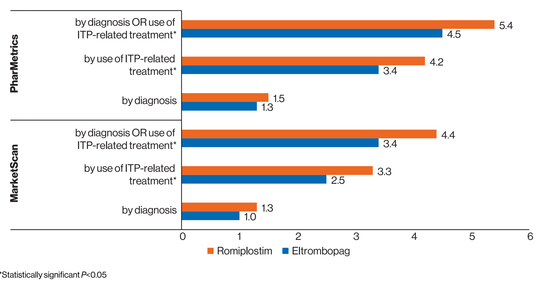
Figure 6. BRE Rates by Diagnosis and/or Use of Rescue Therapy



*Statistically significant P<0.05

- Compared to patients receiving romiplostim patients receiving eltrombopag had fewer mean number of BREs during the follow-up period (P<0.05) (**Figure 7**)

Figure 7. Mean Number of BREs by Diagnosis and/or Use of Rescue Therapy



*Statistically significant P<0.05

Limitations

- Healthcare claims lack clinical data, limiting assessment of ITP severity and duration of disease, and some clinical and patient characteristics that might influence physicians' prescribing behavior
- Patients with ITP may discontinue treatment due to sustained remission or adverse events. Data from administrative claims databases do not allow us to distinguish the reason for discontinuation
- BRE events were captured over the 12 months post-index, patients may have discontinued or switched index TPO-RA therapy during the post-index period
- Results are generalizable to commercially insured and Medicare populations, but these may not be applicable to other populations such as Medicaid

Conclusions

- ITP patients receiving eltrombopag were more adherent, had a longer duration of treatment, and had improved outcomes in terms of fewer BREs, compared to patients receiving romiplostim.
- Further research is needed to confirm the benefits of TPO-RAs among patients with ITP in real-world settings.

References

1. Cooper N, Bussel J. 2006. The pathogenesis of immune thrombocytopaenic purpura. *Br J Haematol.* 2006;133(4):364-374.
2. Altomare I, Cetin K, Wetten S, Wasser JS. Rate of bleeding-related episodes in adult patients with primary immune thrombocytopenia: a retrospective cohort study using a large administrative medical claims database in the US. *Clin Epidemiol.* 2016;8:231-239.

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