Introduction

- Immune thrombocytopenia (ITP) is a rare autoimmune disorder characterized by a low platelet count, which leads to increased risk of bleeding.
- Although it is well recognized that rituximab, a monoclonal anti-CD20 antibody, can be used off-label as a second-line therapy for ITP, data on its use in large real-world ITP patient populations are lacking.
- We described incidence, patient characteristics, and treatment patterns of rituximab use in a population-based cohort of elderly patients with newly diagnosed ITP.

Methods

- **Data source**: 100% Medicare hematologic disease files (2007-2015).
- **Inclusion criteria**: Patients newly diagnosed with primary ITP at age ≥67 years in 2010-2014 who were continuously enrolled in Medicare Parts A and B (FFS) for 24 months before diagnosis.
- **ITP diagnosis**: ≥21 inpatient or ≥2 outpatient claims ≥30 days apart but within 365 days carrying an ICD-9-CM code for ITP (287.31).
- **Date of ITP onset**: date of the first ITP claim or, when applicable, the first general thrombocytopenia claim (287.3x, 287.4x, 287.5) within the 12 months before the first ITP claim.
- **Exclusion criteria**: Patients with secondary causes of thrombocytopenia or prior exposure to rituximab in the 12 months before the date of ITP onset.
- **Baseline period**: 12 months before ITP onset.
- **Follow-up period**: from the date of ITP onset until the first of rituximab initiation, death, disenrollment from FFS coverage, or 09/30/15.

Rituximab identification and treatment patterns:

- **Initiation**: first appearance of a claim for rituximab infusion with a diagnosis code for ITP and without codes for chronic lymphocytic leukemia, non-Hodgkin lymphoma, or rheumatoid arthritis (all conditions approved for rituximab use).
- **Treatment course**: consecutive rituximab claims ≥17 days apart ending at the last administration plus 7 days.
- **Number of administrations**: number of claims for rituximab on different service dates.
- **Dose**: 100 mg multiplied by service count reported on the claim.

Statistical Analyses:

- **Baseline characteristics at ITP onset were reported using descriptive statistics.**
- **Cumulative probability of rituximab initiation was estimated using the Kaplan-Meier method with log-rank test to assess differences by baseline characteristics.**
- **History of bleeding and receipt of other ITP therapies before rituximab initiation and patterns of rituximab use in the first course of treatment were characterized.**

Results

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall (%)</th>
<th>Yes (%)</th>
<th>No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>51% (51%)</td>
<td>48% (48%)</td>
<td>52% (52%)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>86% (86%)</td>
<td>83% (83%)</td>
<td>89% (89%)</td>
</tr>
<tr>
<td>Race</td>
<td>86% (86%)</td>
<td>83% (83%)</td>
<td>89% (89%)</td>
</tr>
<tr>
<td>Age at ITP onset (years)</td>
<td>79.6±7.6</td>
<td>79.4±7.7</td>
<td>80.0±7.5</td>
</tr>
<tr>
<td>Sex</td>
<td>51% (51%)</td>
<td>48% (48%)</td>
<td>52% (52%)</td>
</tr>
</tbody>
</table>

Table 2. Cumulative probability of rituximab initiation after ITP onset (%)

<table>
<thead>
<tr>
<th>Time from ITP onset</th>
<th>Overall</th>
<th>6 months</th>
<th>1 year</th>
<th>3 years</th>
<th>5 years</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at ITP onset, years</td>
<td>6.7</td>
<td>8.7</td>
<td>10.2</td>
<td>11.2</td>
<td>0.022</td>
<td></td>
</tr>
<tr>
<td>66-74</td>
<td>6.7</td>
<td>8.7</td>
<td>10.2</td>
<td>11.2</td>
<td>0.022</td>
<td></td>
</tr>
<tr>
<td>75-84</td>
<td>6.6</td>
<td>8.6</td>
<td>10.1</td>
<td>11.0</td>
<td>0.108</td>
<td></td>
</tr>
<tr>
<td>85+</td>
<td>6.4</td>
<td>8.3</td>
<td>10.2</td>
<td>11.0</td>
<td>0.105</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>5.6</td>
<td>8.3</td>
<td>10.2</td>
<td>11.0</td>
<td>0.105</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>7.0</td>
<td>9.1</td>
<td>11.0</td>
<td>11.7</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td>7.7</td>
<td>9.5</td>
<td>11.5</td>
<td>12.1</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>7.0</td>
<td>9.1</td>
<td>11.0</td>
<td>11.7</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>5.1</td>
<td>4.4</td>
<td>5.8</td>
<td>6.7</td>
<td>0.647</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>4.7</td>
<td>6.1</td>
<td>8.1</td>
<td>8.5</td>
<td>0.034</td>
<td></td>
</tr>
</tbody>
</table>

Table 3. History of bleeding and use of specific ITP therapies among rituximab users (%)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Overall (%)</th>
<th>6 months</th>
<th>1 year</th>
<th>3 years</th>
<th>5 years</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of any bleeding</td>
<td>25.2</td>
<td>46.3</td>
<td>59.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of specific bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervertnal hemorrhage</td>
<td>2.4</td>
<td>3.4</td>
<td>4.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal hemorrhage</td>
<td>7.6</td>
<td>13.8</td>
<td>19.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematuria</td>
<td>3.3</td>
<td>7.6</td>
<td>13.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esophagitis</td>
<td>7.8</td>
<td>13.6</td>
<td>17.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epistaxis</td>
<td>6.6</td>
<td>11.2</td>
<td>13.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of specific therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV Anti-D</td>
<td>1.5</td>
<td>2.6</td>
<td>3.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV Ig (excluding Anti-D)</td>
<td>28.0</td>
<td>38.3</td>
<td>49.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV steroids</td>
<td>9.6</td>
<td>22.0</td>
<td>32.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelet transfusion</td>
<td>23.8</td>
<td>36.7</td>
<td>41.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Splenectomy</td>
<td>1.3</td>
<td>2.9</td>
<td>3.0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Rituximab use in the first course of treatment

<table>
<thead>
<tr>
<th>Mean(SD)</th>
<th>5th PCTL</th>
<th>Median(IQR)</th>
<th>95th PCTL</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of administration</td>
<td>3.6 (1)</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Course duration, weeks</td>
<td>3.7 (1)</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Avg. days b/w administrations</td>
<td>7.2 (1)</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Avg. weekly dose, mg</td>
<td>735 (136)</td>
<td>500</td>
<td>700-750</td>
</tr>
<tr>
<td>Avg. dose per administration, mg</td>
<td>752 (136)</td>
<td>600</td>
<td>700-750</td>
</tr>
</tbody>
</table>

Summary

- We identified 17,117 elderly patients with newly diagnosed ITP in 2010-2014; of these, 1,562 (9%) received rituximab with a median (IQR) time to rituximab of 3 (1-8) months.
- Overall, cumulative probability (95% CI) of initiating rituximab at 3 years was 10.6% (10.1%-11.1%). While patients and those without select comorbidity conditions were more likely to receive rituximab than their counterparts (Table 2).
- Among rituximab-treated patients, at initiation, 59% had a history of any bleeding, 4% were splenectomized, and 36% received IV immunoglobulins, IV steroids, or platelet transfusions (Table 3).
- The median number of infusions during the 1st course of rituximab was 4 (IQR, 3-4) over a median duration of 4 weeks (IQR, 3-4); 9% of patients received only 1 dose, while 60% received 24 doses (Table 4).

Conclusions

- About one in ten elderly patients with newly diagnosed ITP received rituximab.
- White patients and those without select comorbidity conditions were more likely to receive rituximab, while older patients (age ≥75 years) had similar incidence of rituximab use as their counterparts.
- Data suggest that weekly rituximab infusion for 4 weeks is the standard schedule for the first course of treatment in this setting.
- Further studies assessing the potential factors associated with rituximab initiation and its benefits and risks are warranted.