Response to second- and third-line therapies in children with chronic immune thrombocytopenia.

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Conclusions

1. **Alternate therapy for children with chronic ITP remains challenging with no clear direction on the best next treatment after conventional therapy fails.**
2. **Despite consensus guidelines for use of eltrombopag as second-line therapy, 73% of our cohort were only able to access eltrombopag following failure of second-line or multiple alternate therapies**
3. **Complete response is attainable but takes time and often requires multiple therapies.**
4. **Ongoing advocacy and discussion with the government PharmaCare program is needed**
   - Delay in eltrombopag coverage increases the need for further treatment with IVIG, steroids or use of other therapies often without success
   - It is hoped that these findings will improve the approval process for eltrombopag for future pediatric patients in British Columbia with chronic ITP

Introduction

- Pediatric Chronic Immune Thrombocytopenia (ITP) presents a challenge if first-line therapy fails to produce improvement in platelet count.
- The most recent American Society of Hematology (ASH) Immune Thrombocytopenia guidelines for management of pediatric patients recommend thrombopoietin agonists as second line therapy for chronic ITP[1]
- In contradiction to the ASH guidelines, our provincial government PharmaCare program continues to recommend treatment with rituximab, mycophenolate mofetil (MMF) or splenectomy before considering coverage for eltrombopag, despite adequate evidence of good response

Aim

- To evaluate the clinical outcomes of pediatric patients with chronic ITP who received second or third-line ITP therapy at our hospital
- To evaluate the challenges associated with access to eltrombopag

Methods

- Records of pediatric patients followed at British Columbia Children's Hospital between 2013-2023 with chronic ITP were reviewed
- Demographic, treatment, payer, and outcome data were collected and analyzed on all patients

Results

- Out of 147 pediatric patients seen with ITP at BCCH between 2013-2023, 44 (30%) required alternate therapy
- Median age: 9.5 years (range 0-16 years); age ranges are shown in **Table 1**
- 68% of patients had response to alternate therapy (Figure 1) but 24/44 (55%) required 2-6 alternate therapies to manage their ITP **(Figure 2)**
- 14 patients had no response to therapy, or remain on therapy and are waiting for response **(Figure 1)**
- Table 2 shows time to complete or partial response with a median time to response of just over 5 years
- The most frequent therapies used were TPO-RA (28), Mycophenolate (22) and Rituximab (20) **(Table 3).**
- Four patients had splenectomy **(Table 3).**
- 7 patients received eltrombopag as second line therapy due to having 100 % 3rd Party coverage (6) or chose to self-pay (1)
- 9 other patients required other coverage strategies in order to receive eltrombopag (**Figure 3**)
- 1 patient was able to receive full Pharmacare coverage up front
- 3 patients were able to move to full Pharmacare coverage after 3rd party coverage ended (**Figure 3, red**)

Table 1. Age distribution if ITP patients needing alternate therapy (n=44)

Age	Number of Patients
0 - 5	14
6 - 12	19
13 - 18	11

Table 2. Time to Complete or Partial Response

	CR (n=26)	PR (n=30)
Mean time (months)	73.14	87.90
Median time (months)	61.13	52.42
Range (months)	1.91 to 293	1.91 to 329
SD	69.26	91.11

Figure 1. Number of alternate therapies used (n=44)

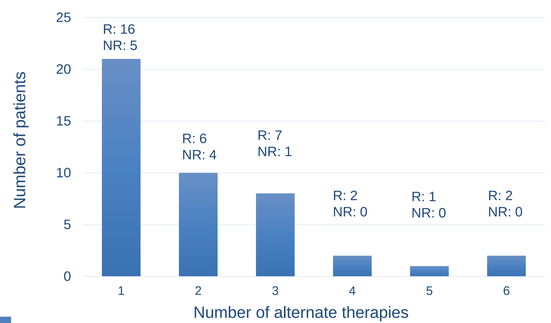

Figure 2. Response to ITP therapy (n=44)

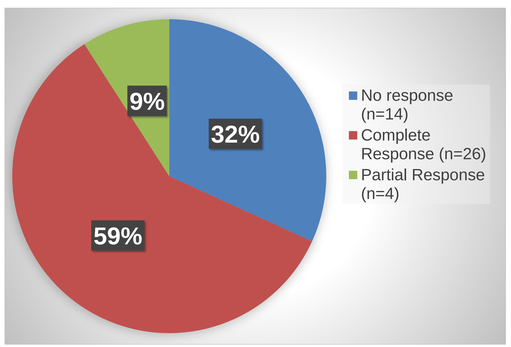

Figure 3. Eltrombopag coverage breakdown

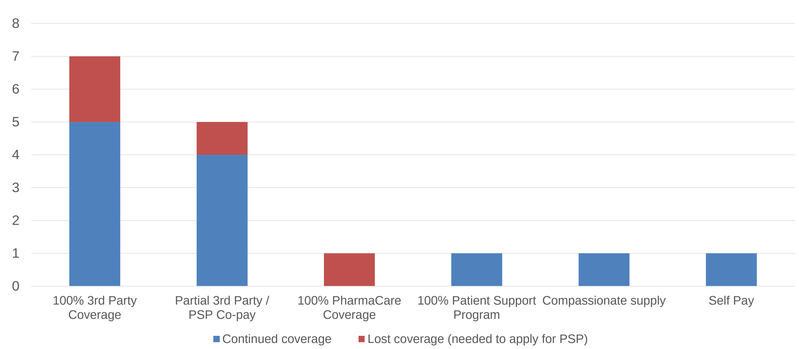

Table 3. Types and Response to Alternate Therapies

Therapy	n	CR (n)	PR (n)	CR+PR(%)
TPO-RA*	28	13	3	57
Mycophenolate	22	10	1	50
Rituximab	20	5	1	30
Plaquenil	7	3	0	42.9
Splenectomy	4	2	0	50
Other^	11	4	0	36

*Eltrombopag (21), Romiplostim (6), Avatrombopag (1)
^Vincristine (5), Sirolimus (2), Azathioprine (2), Cyclosporine (1), Danazol (1)

References

1. Neunert et. al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Advances* 2019; 3: 3829-3866.

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