RESEARCH ARTICLE

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Management of Adult Primary Immune Thrombocytopenia: Delphi-Based Consensus Recommendations

Erişkin Primer İmmün Trombositopeni Yönetimi: Delphi-Temelli Uzlaşı Önerileri

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Abstract

Objective: Primary immune thrombocytopenia (pITP) is an acquired autoimmune disorder related to the increased destruction and/or impaired production of platelets. Its diagnosis and management are challenging and require expertise and the interpretation of international consensus reports and guidelines with national variations in availability. We aimed to assess the agreement of hematologists in Türkiye on certain aspects of both first-line and second-line management of patients with pITP.

Materials and Methods: Applying a modified Delphi method, the Turkish National ITP Working Group (14 steering committee members), founded under the auspices of the Turkish Society of Hematology, developed a 21-item questionnaire consisting of statements regarding the first-line and second-line treatment of pITP. A total of 107 adult hematologists working in either university or state hospitals voted for their agreement or disagreement with the statements in two consecutive rounds.

Results: The participants reached consensus on the use of corticosteroids as first-line treatment and with limited duration.

Öz

Amaç: Primer immün trombositopeni (pITP), trombositlerin artan yıkımı ve/veya bozulmuş üretimi ile ilişkili edinsel bir oto-immün hastalıktır. pITP'nin tanı ve yönetimi zorludur; ayrıca hem uzmanlık hem de uluslararası fikir birliği raporları ile kılavuzlarının, ulusal farklılıkları da göz önünde bulundurarak, yorumlanmasını gerektirir. Bu çalışmada Türkiye'deki hematologların pITP hastalarının birinci ve ikinci basamak tedavisinin belirli alanlarındaki fikir birliği düzeylerini değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Türk Hematoloji Derneği bünyesinde kurulan Türkiye Ulusal ITP Çalışma Grubu (14 yürütme kurulu üyesi), modifiye Delphi yöntemi ile pITP'nin birinci basamak ve sonraki tedavilerine ilişkin ifadelerden oluşan 21 maddelik bir anket geliştirdi. Üniversite veya devlet hastanelerinde çalışan 107 yetişkin hematolog, ardışık iki tur boyunca ifadelere katılıp katılmama yönünde oy kullandı.

Bulgular: Katılımcılar kortikosteroidlerin birinci basamak tedavi olarak ve sınırlı süreyle kullanılması konusunda fikir birliğine vardı. Metilprednizolonun, dekzametazondan ziyade tercih edilen kortikosteroid olduğu gözlendi. İntravenöz immünoglobulin tedavisinin

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Abstract

Methylprednisolone was the corticosteroid of choice rather than dexamethasone. Use of intravenous immunoglobulin was not preferred for patients without bleeding. It was also agreed that thrombopoietin receptor antagonists (TPO-RAs) or rituximab should be recommended as second-line treatment and that splenectomy could be considered 12-24 months after diagnosis in patients with chronic pITP.

Conclusion: The optimization of the dose and duration of TPO-RAs in addition to corticosteroids is necessary to improve the management of patients with pITP.

Keywords: Adult primary immune thrombocytopenia, Management, Delphi method

Öz

kanama dışında kullanımı tercih edilmez iken, trombopoietin reseptör antagonistleri (TPO-RA) veya rituksimab ikinci basamak tedavi olarak önerilebileceği, kronik pITP hastalarında tanıdan 12-24 ay sonra splenektomi düşünülebileceği konusunda da görüş birliğine varıldı.

Sonuç: pITP'li hastaların yönetimini iyileştirmek için kortikosteroidlerin yanı sıra TPO-RA'ların doz ve süresinin optimizasyonu gerekli olduğu konusunda fikir birliği sağlanmıştır.

Anahtar Sözcükler: Erişkin primer immün trombositopeni, Hastalık yönetimi, Delphi metodu

Introduction

Primary immune thrombocytopenia (pITP) is an acquired autoimmune disorder characterized by reduced platelet counts related to increased destruction due to immune dysregulation and impaired production of platelets [1]. Diagnosis is based on the exclusion of conditions leading to platelet consumption or impaired thrombopoiesis related to stem cell disorders, and the disease is classified as newly diagnosed (within 3 months), persistent (3-12 months), or chronic (≥12 months) [2].

With the classification being mainly based on disease duration, the goals of treatment have been established accordingly. Rather than normalizing the platelet count (reaching beyond $100x10^9$/L), the long-term goal has been described as any platelet count above $30x10^9$/L without bleeding [2,3].

Data regarding the effectiveness of pITP treatments have been accumulating and practical recommendations for the management of pITP are needed. To provide such recommendations, as the National ITP Working Group of Türkiye, we aim to determine the actual needs as well as the views of practicing hematologists in Türkiye and we used a modified Delphi technique to assess all aspects of the management of pITP, from diagnosis to treatment.

Materials and Methods

The Delphi method is a survey-based process wherein certain statements are reviewed and scored for a few rounds by a predefined group of experts until consensus is achieved. The group members freely and anonymously vote for their agreement/disagreement of statements in a graded manner. After the results are collected and reviewed by the committee, the statements are evaluated in terms of agreement rates as well as the supporting evidence from published guidelines or the lack of agreement and the possible contributing factors [4,5].

The Turkish National ITP Working Group (consisting of 14 steering committee members) was founded under the auspices of the Turkish Society of Hematology and the Hemostasis and Thrombosis Scientific Subcommittee by hematologists with significant expertise in pITP. A questionnaire consisting of 21 items regarding the first-line (9 items) and second-line (12 items) treatment of pITP were developed and 107 adult hematologists of varying ages and institutions agreed to participate in the study. Seventy-seven (71.9%) participated in the first round of voting and 72 (93.5%) participated in the second round. Sixty-eight (88.3%) of the participants were under 50 years of age. Thirty-one were working at university hospitals (40.2%) while 43 were working at state hospitals (55.8%) and the remaining participants were working at private practices.

As voters, the hematologists were asked to consider each statement and select their level of agreement using a 5-point Likert-type scale (1: disagree/never, 2: somewhat disagree/rarely, 3: neither disagree nor agree/sometimes, 4: somewhat agree/often, 5: agree/always). Consensus of agreement was defined in this study as the sum of the percentage of votes for "somewhat agree/often" and "agree/always."

This study was approved by the relevant local ethics committee (Trakya University Faculty of Medicine Scientific Ethics Committee, Protocol No: TUTF-GOBAEK 2023/322, Decision No: 13/31, Date: 11.09.2023). Informed consent was obtained from all participants.

Results

First-line Treatment of pITP

Statement 1: In newly diagnosed pITP patients who are asymptomatic or with minor bleeding and platelet counts of $<30x10^9$/L, treatment shall be commenced.

Agreement: 90% in favor of commencing treatment.

Though the risk of bleeding is not correlated with any platelet count, it is accepted that risk of bleeding is higher in patients with platelet counts of $<20x10^9$/L [2]. The panel recommends commencing treatment for patients who are asymptomatic or have minor bleeding and platelet counts of $<30x10^9$/L.

Statement 2: In young patients with newly diagnosed pITP and platelet counts of $<30x10^9$/L, dexamethasone should be commenced at 40 mg/day for 4 consecutive days within 28-day cycles.

Agreement: 30%.

Statement 3: In young patients with newly diagnosed pITP and platelet counts of $<30x10^9$/L, methylprednisolone should be commenced at 0.5-2.0 mg/kg/day.

Agreement: 71%.

In patients diagnosed with pITP and who are in need of treatment, corticosteroids are recommended [2,3]. In a randomized controlled trial comparing dexamethasone with prednisone, both type of corticosteroids were well tolerated, with dexamethasone resulting in better short-term but poorer long-term responses [6].

Statement 4: In patients with newly diagnosed pITP and platelet counts of $<30x10^9$/L, how long shall corticosteroids be used?

Agreement: 72% for less than 6 weeks and not more than 12 weeks.

The duration of corticosteroids is recommended to be limited to 6 weeks (maximum: 8 weeks) including the tapering period even if the platelet count decreases [2,3]. The prolonged use of corticosteroids is not recommended as there is no evidence in favor of the use of corticosteroids for more than 6 weeks [3]. We have observed a tendency to limit the use of corticosteroids in Türkiye.

Statement 5: The treatment of patients with pITP who are asymptomatic or have minor bleeding and platelet counts of $<30x10^9$/L can be managed in an outpatient setting.

Agreement: 75%.

For patients with pITP, treatment and follow-up can be managed in an outpatient setting if there is no active bleeding or other conditions such as the need for anticoagulant treatment, and with platelet counts of $>20x10^9$/L [3]. The panel also concluded that there are factors other than clinical condition and platelet counts, such as distance to an appropriate healthcare facility or availability of beds, that may be taken into account in decisions for hospitalization.

Statement 6: In patients with newly diagnosed pITP, corticosteroids shall be combined with rituximab as first-line treatment.

Agreement: 73% disagreed regarding the use corticosteroids and rituximab in combination.

Rituximab is not recommended beyond cases of patients who have relapsed or are refractory to corticosteroids, intravenous immunoglobulin (IVIG), or splenectomy, and the practice in Türkiye has been consistent with international guidelines [2,3,7].

Statement 7: In patients with pITP without bleeding, IVIG shall be used as treatment.

Agreement: 88% in agreement against the use of IVIG in patients without bleeding.

The panel recommends the use of IVIG in patients with pITP who have bleeding and are in need of an intervention at doses of 1 g/kg/day for two consecutive days. IVIG may also be considered for newly diagnosed pITP patients in the event that corticosteroids are contraindicated [2,3,8,9].

Statement 8: During the tapering of corticosteroids, if the platelet count decreases, the corticosteroid dose shall be increased.

Agreement: 48%.

If a platelet response to corticosteroids is observed (increasing to $>50x10^9$/L), the use of corticosteroids is not recommended to be prolonged for more than 6 weeks (maximum: 8 weeks), including the tapering period, even with a decrease in platelet count [2,3]. The lack of consensus on this statement demonstrates a need to increase the awareness and education regarding the definitions of corticosteroid dependency and refractoriness and the need to limit the prolonged use of corticosteroids.

Statement 9: For patients who have responded to corticosteroids, second-line treatment is indicated for a relapse within the first year.

Agreement: 63%.

In adult patients, the natural course of pITP is still unclear. It is reported that 20%-45% of patients reach remission within 6 months; however, spontaneous remission beyond 6 months is regarded as relevant. In patients with persistent or chronic pITP who are refractory to or dependent on corticosteroids or who have relapsed after corticosteroids, the panel recommends the use of thrombopoietin receptor antagonists (TPO-RAs) or rituximab. Re-using corticosteroids in patients who responded to them as first-line treatment but then relapsed is not recommended [2,7].

Treatment of Relapsed pITP

Statement 1: Bone marrow biopsy shall be performed for all patients requiring second-line treatment.

Agreement: 35%.

Bone marrow evaluation should be performed for patients who have additional abnormal blood counts or who are non-responsive to first-line treatment or for whom splenectomy is considered [2,3,7].

Statement 2: For relapsed pITP patients with bleeding, TPO-RAs shall be preferred as treatment.

Agreement: 62%.

For patients with persistent pITP who are refractory to or dependent on corticosteroids, either eltrombopag or romiplostim as a second-line treatment is recommended [2,3].

Statement 3: The decision to use TPO-RAs (eltrombopag or romiplostim) shall be individualized with respect to the patient's preference.

Agreement: 88%.

Since the availability of different TPO-RAs varies among countries, international guidelines have suggested the decision be based on both resources and patients' preference [2,3]. The panel recommends patients' preferences to be taken into account in making this decision as once weekly subcutaneous administration of romiplostim or daily usage by oral route while fasting may be burdensome for patients.

Statement 4: TPO-RAs shall be used as second-line treatment before splenectomy.

Agreement: 71%.

Statement 5: Rituximab shall be used as second-line treatment before splenectomy.

Agreement: 49%.

Rituximab has been recommended for patients who prefer a limited duration of treatment. However, it may have adverse effects such as secondary immune deficiency or hepatitis B reactivation. The recent severe acute respiratory syndrome-coronavirus-2 pandemic has also limited the use of rituximab. The panel took these perspectives into account and regarded both rituximab and TPO-RAs as alternatives before splenectomy.

Statement 6: For patients with chronic pITP (>12 months) who are refractory to available treatments and have relapsed, splenectomy shall be performed.

Agreement: 71%.

Statement 7: For patients with persistent pITP (3-12 months) who are refractory to available treatments and have relapsed, splenectomy shall be performed.

Agreement: 34%.

With the short-term and long-term complications of splenectomy having been recognized, the use of splenectomy has been observed to be decreasing worldwide. Spontaneous remission rates within the first year and fifth year of pITP diagnosis are reported as 30% and 80%, respectively. International guidelines have recommended splenectomy to be postponed by at least 12-24 months for possible spontaneous remission. For patients with persistent pITP who are refractory to or dependent on corticosteroids, rituximab or TPO-RAs are recommended rather than splenectomy [2,3,7]. Regarding this statement, study participants younger than 40 years tended to vote against the use of splenectomy, while those older than 40 voted in favor of the use of splenectomy in this setting (p=0.013).

Statement 8: For patients with pITP who have reached platelet counts of >30x10^9/L after splenectomy, prophylactic anticoagulation shall be considered.

Agreement: 65%.

Postoperative prophylaxis against thromboembolism is recommended for all patients with platelet counts of >30-50x10^9/L.

Statement 9: If a TPO-RA is not effective, switching to another TPO-RA shall be considered.

Agreement: 30%.

Switching to another TPO-RA or sequential treatment with TPO-RAs was demonstrated to improve the rates of efficacy while decreasing the rates of adverse events [2,3]. The panel observed a lack of consensus primarily due to romiplostim being approved but only conditionally reimbursed in Türkiye.

Statement 10: In patients who have sustained platelet counts of >100x10^9/L, TPO-RAs shall be tapered and discontinued.

Agreement: 46%.

Statement 11: In patients who have sustained platelet counts of >50x10^9/L, TPO-RAs shall be used at the minimum possible effective doses.

Agreement: 88%.

The optimal duration of treatment with TPO-RAs once they have become effective has not been established. For patients who have reached sustained platelet counts of >50x10^9/L, tapering and discontinuation of TPO-RAs may be considered after 6-12

months [2,3,7]. The panel tended to regard treatment with TPO-RAs as long-term treatment, even at tapered doses.

Statement 12: Rituximab may be used in patients with pITP who have not been responding to TPO-RAs.

Agreement: 75%.

For patients who have failed to respond to multiple treatment alternatives, the use of other available treatments such as mycophenolate, fostamatinib, rituximab, azathioprine, dapsone, or danazol is recommended [2,3].

Statements with consensus rates and the recommendations of international guidelines are summarized in Supplementary Table 1.

Discussion

Before TPO-RAs became available, the management of pITP was mainly based on expert opinions. With the development of TPO-RAs, there has been a huge leap in the understanding of the pathophysiology of megakaryopoiesis as well as future possibilities of further treatment options. Nevertheless, the diagnosis and management of pITP are still largely based on expert opinions and consensus statements. One major factor in this course of development was the perception of pITP as a non-malignant disease of platelet counts alone without any implications for life expectancy. However, we are now aware of how quality of life is affected in patients with pITP, with fatigue, lack of concentration and productivity, and a dependency on healthcare facilities at all times [9,10].

Another factor that has contributed to the lack of solid evidence is the discrepancy of treatment alternatives among countries. Beyond corticosteroids being the first-line and fully available treatment method in every country, specific TPO-RAs, rituximab, fostamatinib, and other acknowledged treatment methods may not be approved by national health authorities. This has been the main factor that this working group has aimed to address.

The goal of pITP treatment is to prevent or decrease the risk of significant bleeding rather than to normalize the platelet count. However, the risk of bleeding for each individual patient might not be easy to estimate. Patients who have a history of bleeding, who have platelet counts of $<10x10^9$/L, and who are older than 60 years are generally accepted to have higher risk [2,3]. The management of pITP should start with the decision as to whether treatment is indicated and then proceed with the individualization of the goal of treatment according to the platelet threshold the patient would require. We observed that our expert panel was congruent with the international guidelines on commencing treatment for patients with newly diagnosed pITP who have platelet counts of $<30x10^9$/L.

The choice of initial treatment has been corticosteroids for patients who are asymptomatic or have minor cutaneous bleeding with either oral methylprednisolone at 1 mg/kg or dexamethasone at 40 mg/day for four consecutive days [2,3,7]. For patients who have received methylprednisolone, the total duration of treatment, including the tapering period, should not exceed 6-8 weeks (maximum: 12 weeks) [2,3]. Although there is no single corticosteroid recommended worldwide, methylprednisolone is the preferred type of corticosteroid rather than dexamethasone in Türkiye. Furthermore, other forms of corticosteroids such as prednisone and prednisolone have not entered regular practice in Türkiye, probably due to issues of availability.

While limiting the use of corticosteroids is intended, we have observed significant hesitation when platelet counts decrease during tapering. Practices involving the prolonged use of corticosteroids in cases of other hematological or rheumatological conditions may also contribute to this hesitation and should be addressed with educational programs.

The complete long-term remission rate with first-line corticosteroids has been reported as 20%, and the majority of patients will probably relapse [2,3]. However, spontaneous remissions may occur in up to 10%-20% of cases, most frequently within 6 months after diagnosis. TPO-RAs, rituximab, and splenectomy are options for second-line treatment and the decision should be individualized. We have observed that hematologists younger than 40 years of age tend to delay splenectomy as long as possible, and this inconsistency needs to be addressed with educational programs. Considering the possibility of spontaneous remission within the first 12 months after diagnosis, our expert panel reached a consensus on delaying splenectomy for relapsed and refractory patients.

Conclusion

As the Turkish National ITP Working Group, we have observed a need to improve the national management of pITP in the first-line setting so as to limit the prolonged use of corticosteroids and in the second-line setting so as to optimize the dose and duration of TPO-RAs. This survey may serve as a guide for educational programs to improve the management of pITP.

Ethics

Ethics Committee Approval: This study was approved by the relevant local ethics committee (Trakya University Faculty of Medicine Scientific Ethics Committee, Protocol No: TUTF-GOBAEK 2023/322, Decision No: 13/31, Date: 11.09.2023).

Informed Consent: All of the participating physicians provided their written informed consent.

Authorship Contributions

Concept: A.M.D.; Design: A.M.D., E.G.Ü., M.Ayr., M.C.A., M.Ayl., V.K., E.K., F.Ö., N.S., M.S., F.Ş., S.K.T., T.T., İ.Y.; Data Collection or Processing: A.M.D., E.G.Ü., M.Ayr., M.C.A., M.Ayl., V.K., E.K., F.Ö., N.S., M.S., F.Ş., S.K.T., T.T., İ.Y., Ü.Ç.; Analysis or Interpretation: A.M.D., E.G.Ü., M.Ayr., M.C.A., M.Ayl., V.K., E.K., F.Ö., N.S., M.S., F.Ş., S.K.T., T.T., İ.Y.; Literature Search: A.M.D., E.G.Ü., M.Ayr., M.C.A., M.Ayl., V.K., E.K., F.Ö., N.S., M.S., F.Ş., S.K.T., T.T., İ.Y., Ü.Ç.; Writing: A.M.D., E.G.Ü., M.Ayr., M.C.A., M.Ayl., V.K., E.K., F.Ö., N.S., M.S., F.Ş., S.K.T., T.T., İ.Y.

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Supplementary Table 1. Consensus statements from the administered questionnaire and corresponding international recommendations.

Statement		Agreement*	International recommendations**
1. First-line treatment of pITP			
1.1	In newly diagnosed pITP patients who are asymptomatic or with minor bleeding and platelet counts of <30x10^9/L, treatment shall be commenced	90% in favor of commencing treatment	The risk of bleeding is higher in patients with platelet counts of <20x10^9/L, and commencing treatment shall be considered for patients with platelet counts of <30x10^9/L
1.2	In young patients with newly diagnosed pITP and platelet counts of <30x10^9/L, dexamethasone at 40 mg/day for four consecutive days within 28-day cycles should be commenced	30%	In newly diagnosed pITP patients with platelet counts of <30x10^9/L, both types of corticosteroids may be used
1.3	In young patients with newly diagnosed pITP and platelet counts of <30x10^9/L, methylprednisolone at 0.5-2.0 mg/kg/day should be commenced	71%	
1.4	In patients with newly diagnosed pITP and platelet counts of <30x10^9/L, how long shall corticosteroids be used?	72%: less than 6 weeks, not more than 12 weeks	Duration of corticosteroids is recommended to be limited to 6 weeks (maximum: 8 weeks), including the tapering period, even if the platelet count decreases
1.5	The treatment of patients with pITP who are asymptomatic or have minor bleeding and platelet counts of <30x10^9/L can be managed in an outpatient setting	75%	In patients with pITP, treatment and follow-up can be managed in an outpatient setting if there is no active bleeding or other conditions
1.6	In patients with newly diagnosed pITP, corticosteroids shall be combined with rituximab as first-line treatment	73% in disagreement about the use of corticosteroids and rituximab in combination	Rituximab is not recommended beyond cases of patients who have relapsed or are refractory to corticosteroids, IVIG, or splenectomy
1.7	In patients with pITP without bleeding, IVIG shall be used as treatment	88% against the use of IVIG in patients without bleeding	IVIG may be used in patients with pITP who have bleeding, who are in need of an intervention, or who have a contraindication for the use of corticosteroids
1.8	During the tapering of corticosteroids, if the platelet count decreases, the corticosteroid dose shall be increased	48%	If a response to corticosteroids is observed (platelets increasing to >50x10^9/L), the use of corticosteroids is not recommended to be prolonged for more than 6 weeks (maximum: 8 weeks), including the tapering period, even with a decrease in platelet count
1.9	In patients who have responded to corticosteroids, second-line treatment is indicated for a relapse within the first year	63%	Re-using corticosteroids in patients who responded to them as first-line treatment but then relapsed is not recommended
2. Treatment of relapsed pITP			
2.1	Bone marrow biopsy shall be performed for all patients requiring second-line treatment	35%	Bone marrow evaluation should be performed for patients who have additional abnormal blood counts or who are non-responsive to first-line treatment or for whom splenectomy is considered
2.2	For relapsed pITP patients with bleeding, TPO-RAs shall be preferred as treatment	62%	For patients with persistent pITP who are refractory to or dependent on corticosteroids, either eltrombopag or romiplostim as a second-line treatment is recommended
2.3	TPO-RAs are better tolerated than corticosteroids or other available treatments for pITP	97%	
2.4	The decision to use TPO-RAs (eltrombopag or romiplostim) shall be individualized with respect to the patient's preference	88%	Since the availability of different TPO-RAs varies among countries, international guidelines suggest that the decision be based on both resources and patients' preferences
2.5	TPO-RAs shall be used as second-line treatment before splenectomy	71%	
2.6	Rituximab shall be used as second-line treatment before splenectomy	49%	Rituximab has been recommended for patients who prefer a limited duration of treatment.

Supplementary Table 1. Continued.

Statement		Agreement*	International recommendations**
2. Treatment of relapsed pITP			
2.7	For patients with chronic pITP (>12 months) who are refractory to available treatments and have relapsed, splenectomy shall be performed	71%	Splenectomy should be postponed by at least 12-24 months for possible spontaneous remission. For patients with persistent pITP who are refractory to or dependent on corticosteroids, rituximab or TPO-RAs are recommended rather than splenectomy
2.8	For patients with persistent pITP (3-12 months) who are refractory to available treatments and have relapsed, splenectomy shall be performed	34%	
2.9	For patients with pITP who have reached platelet counts of >30x10^9/L after splenectomy, prophylactic anticoagulation shall be considered	65%	Postoperative prophylaxis against thromboembolism is recommended for all patients with platelet counts of >30-50x10^9/L
2.10	If a TPO-RA is not effective, switching to another TPO-RA shall be considered	30%	Switching to another TPO-RA or sequential treatment with TPO-RAs has been demonstrated to improve the rates of efficacy while decreasing the rates of adverse events
2.11	In patients who have sustained platelet counts of >100x10^9/L, TPO-RAs shall be tapered and discontinued	46%	For patients who have reached sustained platelet counts of >50x10^9/L, tapering and discontinuation of TPO-RAs may be considered after 6-12 months
2.12	In patients who have sustained platelet counts of >50x10^9/L, TPO-RAs shall be used at the minimum possible effective doses	88%	
2.13	Rituximab may be used in patients with pITP who have not responded to TPO-RAs	75%	For patients who have failed to respond to multiple treatment alternatives, the use of other available treatments such as mycophenolate, fostamatinib, rituximab, azathioprine, dapsone, or danazol is recommended

*: Consensus of agreement was defined in this study as the sum of the percentage of votes for "somewhat agree/often" and "agree/alwayss".
**: For the relevant international recommendations, please see references 2 and 3 in the main text.
pITP: Primary immune thrombocytopenia; IVIG: intravenous immunoglobulin; TPO-RA: thrombopoietin receptor agonist.