Research Review
EDUCATIONAL SERIES

Chronic Immune Thrombocytopenia

About the Reviewer

Dr Kenneth Romeril
MBChB, FRACP, FRCPA

Clinical Haematologist at Capital and Coast Health. Lead Haematologist Aotea Laboratory.

Dr Romeril has a special interest in myeloma and is the NZ Representative on the International Myeloma Working Group. He is also involved in several clinical trials and has organised investigator-initiated trials in ITP as well as being on the SAC for the ALLG.

This review is intended as an educational resource for health professionals. It presents a concise background on chronic immune thrombocytopenia, including its prevalence, disease burden, and clinical management. In terms of treatment, the review highlights the newer pharmacological agents available, in particular, eltrombopag, which currently is the only thrombopoietin receptor agonist both approved by Medsafe and funded for the treatment of chronic immune thrombocytopenia.

Immune Thrombocytopenia

Immune thrombocytopenia (ITP), formerly known as idiopathic thrombocytopenic purpura, is an acquired autoimmune disorder that is characterised primarily by a low platelet count and an attendant increased risk of bleeding. For most children, ITP is a self-limiting disease. However, for some children and most adults the condition can become chronic. Chronic ITP is defined as ITP having a duration of >1 year since diagnosis.[1-3]

A specific activating cause for ITP has not yet been identified. Antibody-mediated platelet destruction, mainly involving immunoglobulin G autoantibodies, has been the generally accepted hypothesis to explain ITP pathogenesis. More recently, however, impaired platelet production has been implicated. Platelet destruction occurs via the rapid clearance of antibody-coated platelets by the reticuloendothelial system in the spleen and liver. Impairment of platelet production may occur via autoantibody-induced apoptosis and inhibition of megakaryocyte maturation.[1-3]

Disease Epidemiology and Burden

Epidemiological studies from the US, UK, and Japan suggest that the incidence of chronic ITP is 1.6-3.9 per 100,000 person-years, with a slight predominance in women observed until the age of 65 years.[1-2] Although ITP is a relatively uncommon condition, it nonetheless carries with it personal and societal burdens of consequence.

Reduced platelet counts, associated disease symptoms, and treatment side effects adversely affect the quality of life of patients with ITP.[4,5] In a health-related quality of life (HRQoL) study conducted in the US, the HRQoL of adult patients with ITP was shown to be significantly worse than that of the general US population.[4] It was also worse than that of patients with hypertension, arthritis, or cancer; similar to that of patients with diabetes; but better than that of patients with congestive heart failure or a missing or paralyzed limb.[4] In terms of specific HRQoL domains, emotional and functional health, work life, social and leisure activities, and reproductive health are the primary facets of life affected by ITP and its treatments.[5]

ITP and its sequelae also place a burden on the healthcare system. Both US and European healthcare resource utilisation studies, mainly in patients with chronic ITP, have demonstrated the costs of managing ITP to be substantial.[6-9] In the US, hospitalisation with ITP was associated with higher costs, longer duration of stay, and more in-hospital deaths on average than all other hospitalised patients combined.[7] Although pharmacological therapy (mainly immunoglobulins and corticosteroids) and whole blood transfusions were the most frequently used treatments, hospital and emergency room use accounted for the majority of ITP-attributable costs.[6,8,9] The considerable personal and healthcare system burden of chronic ITP emphasises the need for more effective and better tolerated treatments for ITP.[6,9]

Diagnosis and Prognosis

In 2009, an international working group established a platelet count threshold of <100 x 10^9/L for diagnosis of ITP, which is less than the previous threshold of 150 x 10^9/L.[10] The working group also recommended using the term 'immune' rather than 'idiopathic' thrombocytopenia, to emphasise the role of underlying immune mechanisms in its pathogenesis. It also recommended avoiding the term purpura, to reflect the fact that many patients have no or minimal signs of bleeding at the time of diagnosis.[10]

Initially, a low platelet count may be the only clinical feature of ITP. If signs and symptoms are present they are typically those associated with an abnormally low platelet count. These include petechiae, purpura, epistaxis, menorrhagia, gum bleeding, and other types of mucocutaneous bleeding.[2]

ITP is considered primary if it occurs in isolation of clinically-apparent associated conditions or other causes. Specific diagnostic criteria do not currently exist to confirm ITP, and the diagnosis is established only after excluding other causes of thrombocytopenia. Prominent causes of secondary ITP requiring exclusion include:

- drug therapy side effect (especially with sulphonamides, anti-epileptics, and quinine)
- *Helicobacter pylori (H. pylori)* infection
- human immunodeficiency virus (HIV) infection
- hepatitis C virus (HCV) infection
- lymphoproliferative disorders
- systemic lupus erythematosus and other autoimmune disorders.[2,11]

In the absence of specific criteria, diagnosis of ITP is based principally on patient history, physical examination, complete blood count, and review of the peripheral blood smear (see Diagnostic checklist).[2,11] A positive response to initial treatment with corticosteroids, intravenous immunoglobulin, or anti-D immunoglobulin supports the diagnosis.[12]

The prognosis for adults with ITP is generally favourable, with much of the morbidity being due to complications of treatment rather than the disease itself.[13] The longer term outcome is less favourable in those whose ITP is unresponsive to standard treatment options – these patients have an increased risk of death, disease, and treatment-related complications.[2]

Treatment Options

The aim of treatment for chronic ITP is to achieve a platelet count that is associated with adequate haemostasis, rather than a platelet count that is in the normal range, while minimising treatment-related toxicity. Treatment should always be individualised. In consultation with the patient, the decision to treat should be based on consideration of the frequency and severity of bleeding, anticipated surgical procedures, medication side effects, and HRQoL (see Treatment Considerations checklist).[2]

Advances in the treatment of ITP provide three main approaches for achieving an increase in platelet count:

- suppression of platelet clearance, e.g. splenectomy
- suppression or modification of abnormal immune responses, e.g. corticosteroids or rituximab
- stimulation of platelet production, e.g. thrombopoietin receptor agonists.[1]

A proposed treatment algorithm for treatment of chronic ITP is depicted in **figure 1**.

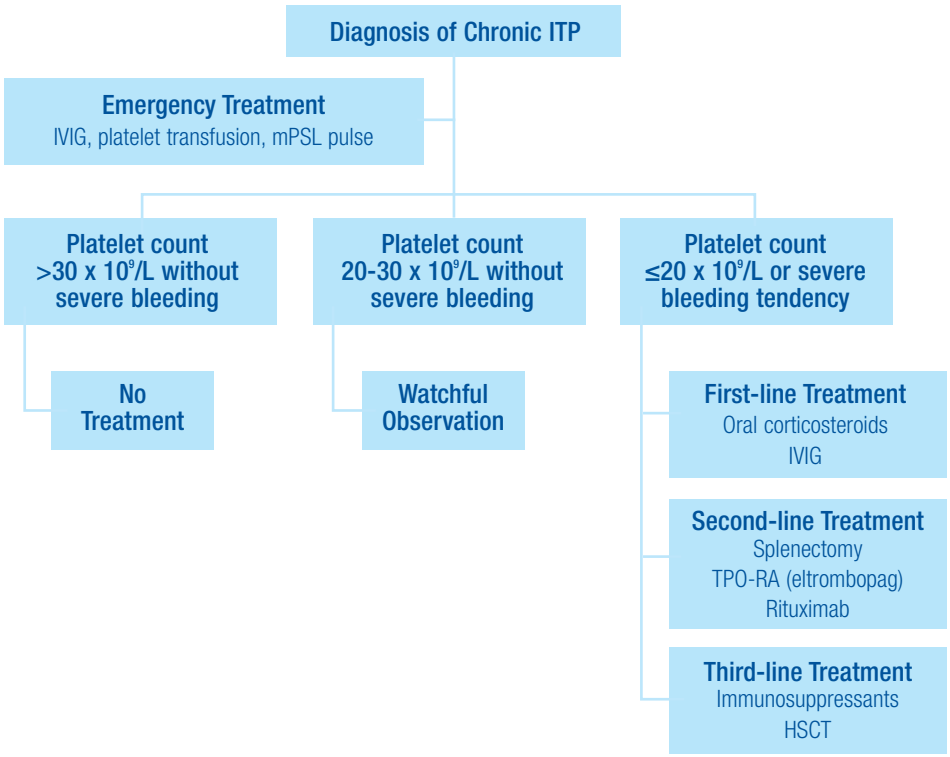

Figure 1. Suggested treatment algorithm for chronic ITP.[1,2,11]
Abbreviations: IVIG = intravenous immunoglobulin; HSCT = haematopoietic stem cell transplantation; mPSL=methylprednisolone; TPO-RA = thrombopoietin receptor agonists.

First-line Therapy

ITP does not necessarily require treatment; hence, the initial decision is to decide whether treatment or observation is indicated.[2,12] According to Japanese guidelines, patients with platelet counts in the range 20-30 x 10^9/L without severe bleeding are candidates for observation while those with counts ≤20 x 10^9/L or severe bleeding are candidates for treatment.[1]

Oral corticosteroids, usually prednisone or high-dose dexamethasone, are first-line treatment for chronic ITP, primarily due to their effectiveness, low cost, and ease of use. However, remission is sustained in only 10-30% of patients and continuation of corticosteroids is limited by their long-term complications, which include infection and osteoporosis. Intravenous immunoglobulin is recommended for patients unresponsive to corticosteroids and is used in pregnancy. It achieves an increased platelet count in 65-80% of patients and is generally well tolerated, but the platelet response is not durable and frequent administration is required. Intravenous anti-D immunoglobulin is an alternative to IVIG in Rh-positive non-splenectomised individuals, although caution is required due to risk of severe haemolysis.[1,2,12]

In emergency situations, i.e. patients with active bleeding or who are at high risk of bleeding, combination treatment with prednisone and intravenous immunoglobulin is recommended. High-dose methylprednisolone and platelet transfusions, alone or in combination with intravenous immunoglobulin, are alternative options.[1,2,12]

Second-line Therapy

In terms of second-line treatments, splenectomy has historically been the 'gold standard' for treatment of chronic ITP. The procedure is recommended in patients with a platelet count of ≤20 x 10^9/L. Approximately two-thirds of patients respond to this procedure with no further requirement for treatment; however, surgical complications including sepsis and thrombosis are important considerations.[2] Although splenectomy remains the most effective and durable treatment in cases that are refractory to first-line therapy, its use has declined because of the availability of alternate pharmacological agents, the associated risk of infection, and concern for surgery-related complications.[2]

The newest agents being used as second-line therapy include the rituximab and the thrombopoietin receptor agonists, including eltrombopag. There is some evidence that rituximab may avoid the need for splenectomy in certain types of patient, or at least delay it. However, its use as a splenectomy-sparing agent in ITP has not been evaluated in randomised controlled trials. The thrombopoietin receptor agonists are mainly used in cases of insufficient response to corticosteroids, immunoglobulins or splenectomy.[2]

Third-line Therapy

Many pharmacological agents have been tried for treatment of patients who have failed corticosteroids, intravenous immune globulin, and splenectomy.

Immunosuppressants, such as azathioprine, cyclosporine, cyclophosphamide, and mycophenolate, either alone or in combination, have traditionally been the most widely used agents in third-line therapy for ITP. However, drug-related toxicity and other safety concerns may limit their use.

Because of the potential for severe toxicities, graft-versus-host disease and septicaemia, haematopoietic stem cell transplantation is reserved for severe refractory ITP with bleeding complications unresponsive to other therapies.[2]

Therapy for Secondary ITP

The approach to treatment of secondary ITP should be determined by the cause of the thrombocytopenia.[2]

Drug-induced ITP requires prompt identification and withdrawal of the causative pharmacological agent.[2]

Management of ITP due to another condition involves treatment of the underlying condition, e.g. treating ITP secondary to HCV infection involves the administration of antiviral agents to suppress viral replication. If treatment of the ITP is required, consideration must be given to the possible clinical effects of the specific ITP drugs on the underlying condition, e.g. intravenous immunoglobulin should be used in preference to corticosteroids to treat ITP secondary to HCV infection to minimise a possible corticosteroid-induced increase in viral load.[2] Eltrombopag is used to treat thrombocytopenia secondary to HCV infections, when the severity of thrombocytopenia prevents antiviral therapy.[14]

Eradication therapy is recommended in ITP patients with confirmed *H. pylori* infection.[2] In Japan, a country that has a high background prevalence of *H. Pylori* infection, eradication of *H. pylori* is associated with a high platelet-response rate.[1]

Newer Pharmacological Agents

Rituximab

Initially approved for treatment of B-cell non-Hodgkin's lymphomas in the late 1990s, rituximab, a chimeric anti-CD20 monoclonal antibody, is increasingly being used in the treatment of ITP. It was first employed in the treatment of ITP some 10 years ago. It produced platelet count increases that lasted many months and exhibited a generally favourable safety profile. Rituximab prevents the destruction of platelets by destroying CD20+ B cells that are responsible for the production of antiplatelet antibodies.[2,3]

Rituximab is not yet approved in New Zealand for the treatment of chronic ITP, but is eligible for PHARMAC funding for this indication, subject to special authority criteria.

Eltrombopag

The latest class of drugs to become available for the treatment of chronic ITP is the thrombopoietin receptor agonists. Rather than inhibit platelet destruction, these agents increase platelet production.[2,12]

First-generation thrombopoietin receptor agonists had considerable amino acid homology with endogenous thrombopoietin, leading to the development of antibodies against natural thrombopoietin in some patients and risk of severe refractory thrombocytopenia. Newer thrombopoietin receptor agonists, however, have no sequence homology to endogenous thrombopoietin, and antibody production is not a significant problem.[12]

In 2008, two of later generation thrombopoietin receptor agonists, romiplostim and eltrombopag, were approved for clinical use in the USA. This was followed by approvals in 2009 in Europe and increasingly elsewhere.

Approved by Medsafe in New Zealand in 2011 for the treatment of adult patients with chronic ITP who have had an inadequate response or are intolerant to corticosteroids and immunoglobulins, and funded under special authority for use pre- and post-splenectomy, eltrombopag is the only thrombopoietin receptor agonist currently marketed in New Zealand.

PHARMAC's requirements for funding of eltrombopag by special authority application are depicted in **figure 2**. Essentially, PHARMAC's funding for eltrombopag targets patients who have already tried other available treatments, including splenectomy, and require further treatment.[15]

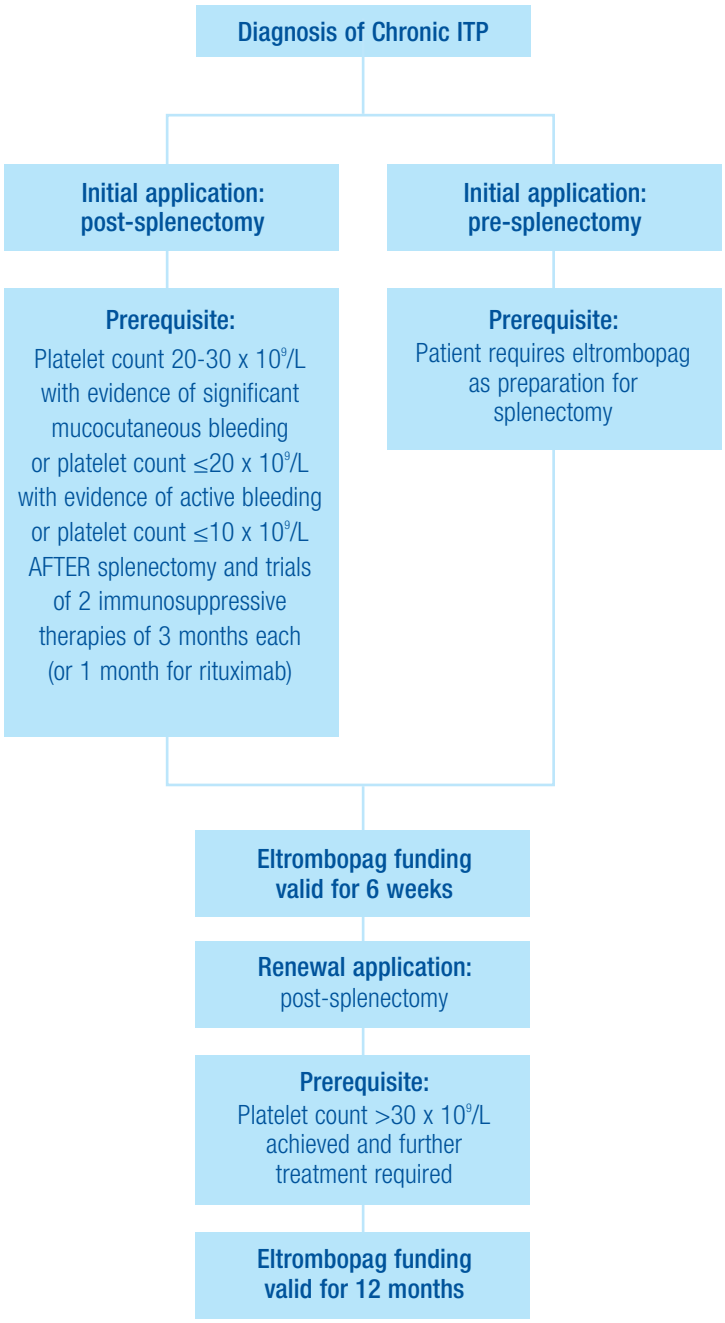

Figure 2. PHARMAC application process for funding of eltrombopag by special authority (to be completed by a haematologist).[18,19]

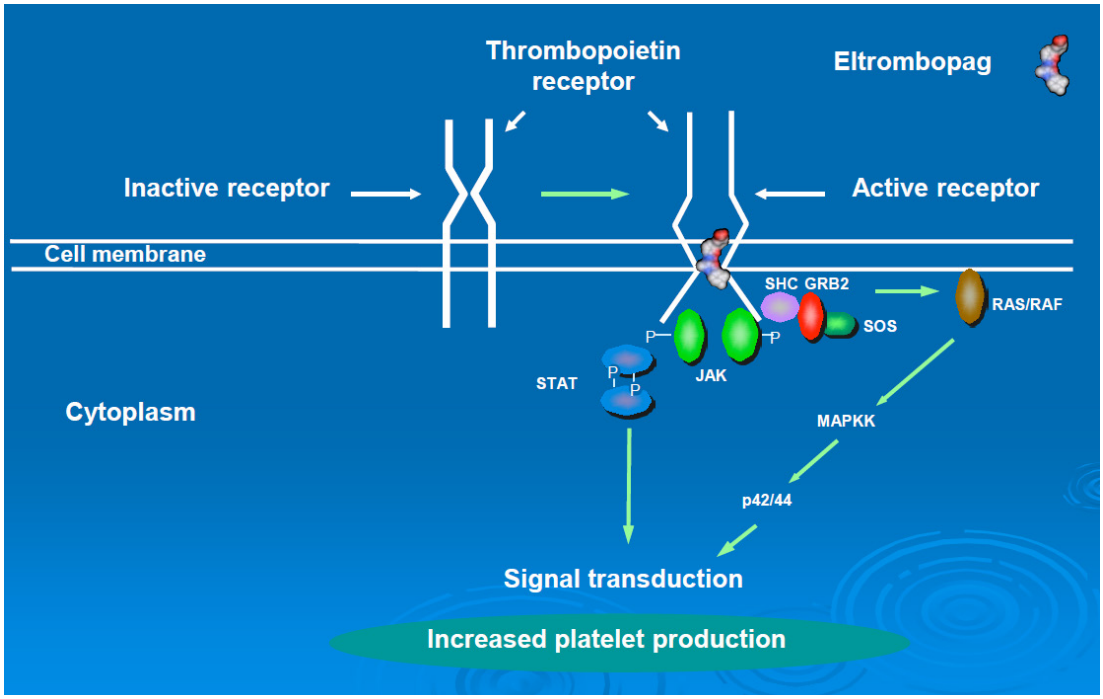

Figure 3. Mechanism of action of eltrombopag

Two pivotal studies were central to the approval of eltrombopag. RAISE, a well-designed, double-blind 6-month trial, demonstrated that eltrombopag was more effective than placebo at increasing platelet count and decreasing the incidence of bleeding in patients with chronic ITP refractory to previous treatments, including splenectomy, and was generally well tolerated.[16] These initial results were supported by the long-term non-comparative EXTEND trial in patients with chronic ITP treated with eltrombopag for up to three years (median duration 100 weeks).[17]

Thrombopoietin is the endogenous cytokine primarily responsible for regulation of megakaryopoiesis and platelet production. Eltrombopag mimics the effect of thrombopoietin, stimulating the production of platelets by binding to the transmembrane region of the thrombopoietin receptor and activating the JAK/STAT and RAS/RAF/MAPK pathways (**Figure 3**).[1]

Therapeutic use of Rituximab and Eltrombopag

Eltrombopag and rituximab are used mainly in patients who have had an insufficient response to corticosteroids, immunoglobulins or splenectomy. The comparative features of these agents are summarised in **table 1**. Eltrombopag and rituximab are effective in increasing platelet counts in chronic ITP and are generally well tolerated.[2,12]

	Eltrombopag	Rituximab
Drug class	Small molecule thrombopoietin receptor agonist	Anti-CD20 monoclonal antibody
Route	Oral	Intravenous
Dosage	25-75mg daily	375 mg/m^2 weekly x 4*
Approximate platelet count response rate (platelet count > 50 x 10^9/L)	70% (50mg dose) 80% (75mg dose)	60%
Approximate time to response	2 weeks	1-8 weeks
Duration of response	Platelet count returns to baseline 2 weeks after discontinuing treatment	Up to 2 years (median 10.5 months)
Safety concerns	Elevated liver enzymes, bone marrow recticulin formation, thrombosis	Mild infusion reaction Rare: infection, serum sickness, bronchospasm

*A low dose of 100mg weekly for 4 weeks is an acceptable initial option.

Table 1. Comparative features of rituximab and eltrombopag for the treatment of chronic ITP.[2]

They do, however, have some disadvantages. Neither rituximab nor eltrombopag are options for emergency treatment because it typically takes at least one week of administration to achieve an adequate platelet count.[2] Eltrombopag does not appear to modify the course of the condition, requiring ongoing administration to sustain an elevated platelet count.[2] A recent case-series study of patients presenting with sustained responses after discontinuing eltrombopag does, however, suggest the need for research into specific characteristics that could identify patients in whom a durable response is likely after stopping eltrombopag without additional therapy.[20] Importantly, the platelet response to long-term treatment with eltrombopag has been shown to be durable in a 3-year study.[17] Although platelet responses to rituximab can be enduring, the rates of durable response appear to be low.[21] Additionally, rituximab requires monitoring for progressive multifocal leukoencephalopathy and eltrombopag requires monitoring for hepatotoxicity.[2,12]

Special Considerations in the Use of Eltrombopag

Sub-populations

The recommended starting dose for eltrombopag is 50mg once daily in adults with ITP, except in those of East Asian descent (e.g. Japanese, Chinese, Taiwanese or Korean) in whom it should be 25mg once daily. After commencement, the dose should be individualised with the aim of maintaining the level of platelets high enough to prevent bleeding (>50 x 10^9/L). The daily dose should not exceed 75mg.[14,22]

In adults with thrombocytopenia secondary to HCV infection, the recommended starting dose is 25mg once daily in patients of all ethnicities. After commencement of treatment, the platelet level should be monitored and the dose of eltrombopag adjusted as necessary every two weeks to achieve platelet levels that permit antiviral therapy for HCV infection to be started. Monitoring should continue during treatment for HCV infection. The dose of eltrombopag should be adjusted to keep the platelet level high enough (approximately 50 x 10^9/L to 75 x 10^9/L) to prevent bleeding or the need to reduce the antiviral dose. The daily dose of eltrombopag should not exceed 100mg.[14,22] In Europe, eltrombopag is indicated in adult patients with HCV infection for treatment of thrombocytopenia, where thrombocytopenia is the main factor preventing the commencement or limiting the ability to maintain optimal antiviral therapy.[14]

Summary of Special Prescribing Considerations for Eltrombopag

- Starting dose for eltrombopag is 50mg once daily in Caucasians and 25mg once daily in East Asian patients.
- Due to chelation with polyvalent cations impairing absorption, eltrombopag should be taken at least four hours before or after taking antacids, calcium-containing foods, and mineral supplements.
- A food planner can be used to help minimise the risk of reduced exposure to eltrombopag.

Meal Planning

Eltrombopag chelates with polyvalent cations, such as aluminium, calcium, iron, magnesium, selenium, and zinc, which impairs absorption of eltrombopag. To avoid significant reduction in the absorption of eltrombopag, patients should not take any antacids, dairy foods, calcium-rich (>50mg) or calcium-fortified foods and drinks, or mineral supplements for at least four hours before or four hours after taking eltrombopag. Food low in calcium (<50mg calcium), including fruit, lean ham, beef and unfortified (no added calcium, magnesium, iron) fruit juice, unfortified soy milk, and unfortified grain, does not significantly lower plasma eltrombopag exposure, regardless of calorie and fat content.[14,22]

Maintaining optimal exposure to eltrombopag is important to ensure ongoing funding. The funding criteria for eltrombopag require a platelet response of >30 x 10^9/L during initial approval or subsequent renewal periods.[18,19] Use of a patient meal planner may help to reduce the risk of sub-optimal eltrombopag exposure.

Checklist for Diagnosis of ITP*		
Essential Evaluations		
History	• Isolated bleeding symptoms consistent with thrombocytopenia without constitutional symptoms?	
Physical Examination	• Bleeding symptoms in the absence of hepatosplenomegaly, lymphadenopathy, or visible evidence of congenital conditions?	
Complete Blood Count	• Platelet count is <100 x 10^9/L?	
	• Anaemia due to significant bleeding?	
	• Red cell indices, white blood cell count and differential are normal?	
Peripheral Blood Smear	• Platelets normal to large in size?	
	• Red and white blood cell morphology is normal?	
Additional Evaluations		
	• Bone marrow examination or other appropriate investigations done (if abnormalities present in the history, physical examination, or the complete blood count and peripheral blood smear)	
	• HIV and HCV testing done in adult patients with newly diagnosed ITP	

*Adapted from The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia.[11]

Checklist of Treatment Considerations for ITP*		
Initial Management of ITP		
Disease Status Assessment	• What bleeding is the patient experiencing? (timing, location, severity)	
	• Does the patient have any additional risk factors?	
	• Is a surgical procedure anticipated?	
	• Is the patient likely to comply with recommended treatments?	
	• Is the bleeding interfering with the patient's quality of life?	
Subsequent Management of ITP		
Disease Status Assessment	• What bleeding is the patient experiencing? (timing, location, severity)	
	• Does the patient have a change in history or physical examination requiring evaluation for another diagnosis that could be causing thrombocytopenia?	
	• Does the patient have any contraindications to splenectomy?	
	• How is the diagnosis of ITP affecting the patient's QOL?	
	• Does the patient respond intermittently to their current drug therapy?	
	• Is the patient experiencing side effects from chronic medication use?	
	• How is the patient coping psychologically with having a low platelet count?	

*Adapted from The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia.[11]

Expert's Concluding Remarks

The approach to managing primary ITP in adults has changed with the advent of rituximab and the thrombopoietin receptor agonists (TPO-RAs) as potential options for second-line therapy. It is well established that splenectomy will provide the best cure rate at around 65% at 5 years. Splenectomy is invasive, has associated post-operative complications and there are possible vascular sequelae. There has been a trend in physician and patient preference for alternative second-line approaches, using either rituximab or one of the two established TPO-RAs.

Rituximab has now been given to a vast number of patients and the 5-year data in ITP indicates that 21% will be durable responders.[1] Newer approaches using rituximab such as lower dosing and maintenance doses have also been trialed.[2]

The TPO-RAs are able to induce platelet counts at safe levels in up to 80% of patients with ITP and are well tolerated with little toxicity. The major disadvantage is the relatively long duration of treatment although some patients have been able to stop treatment and maintain a safe platelet count.

If patients are not responding on the standard 50 mg dose of eltrombopag then rapid consideration needs to be given to escalate to 75 mg dose to achieve a response.

The specific approach to patients tends to be individualised. Splenectomy might be a preferred option in younger patients who do not want to embark on daily treatment. Splenectomy is best avoided in patients over 65 to 70 years of age because of the higher complication rates. There has been difficulty in performing robust comparative studies in the area because of many reasons and probably it is unlikely that there will be much enthusiasm to do so. Treatment will continue to be a personalised approach based around patient characteristics and preference.

References:

1. Patel VL, et al. Outcomes 5 years after response to rituximab therapy in children and adults with immune thrombocytopenia. Blood. 2012;119(25):5989-95.
2. Romeril KR, et al. A prospective multi-centre, single arm, phase II study to evaluate the efficacy of a weekly 100 mg dose of Rituximab over 4 weeks in patients with refractory or relapsing immune thrombocytopenia (the R-100ITP study). Oral presentation. HAA 2013, 20-23 October, Gold Coast.

Take-Home Messages

- Diagnosis should be aimed at identifying evidence of bleeding and excluding other causes of thrombocytopenia or secondary ITP.
- Treatment should be considered in patients with platelet counts $<30 \times 10^9$/L.
- Treatment should always be tailored to individual patients, with the ultimate treatment goal being to improve patents' health and well-being.
- Treatment usually begins with corticosteroids, but their duration of use is limited by adverse effects.
- Patients who fail treatment with corticosteroids or intravenous immunoglobulin generally require splenectomy, eltrombopag, or rituximab.
- Patients who relapse and have a platelet count $<20 \times 10^9$/L should be considered for splenectomy.

References

1. Kashiwagi H, Tomiyama Y. Pathophysiology and management of primary immune thrombocytopenia. Int J Hematol. 2013 Jul;98(1):24-33.
2. Thota S, et al. Immune thrombocytopenia in adults: an update. Cleve Clin J Med. 2012 Sep;79(9):641-50.
3. Toltl LJ, Arnold DM. Pathophysiology and management of chronic immune thrombocytopenia: focusing on what matters. Br J Haematol. 2011;152(1):52-60.
4. McMillan R, et al. Self-reported health-related quality of life in adults with chronic immune thrombocytopenic purpura. Am J Hematol. 2008;83(2):150-4.
5. Mathias SD, et al. Impact of chronic Immune Thrombocytopenic Purpura (ITP) on health-related quality of life: a conceptual model starting with the patient perspective. Health Qual Life Outcomes. 2008 8;6:13.
6. Bauer M, et al. A retrospective observational single-centre study on the burden of immune thrombocytopenia (ITP). Onkologie. 2012;35(6):342-8.
7. Danese MD, et al. Cost and mortality associated with hospitalizations in patients with immune thrombocytopenic purpura. Am J Hematol. 2009;84(10):631-5.
8. Khellaf M, et al. Costs of managing severe immune thrombocytopenia in adults: a retrospective analysis. Ann Hematol. 2011;90(4):441-6.
9. Saleh MN, et al. Analysis of the impact and burden of illness of adult chronic ITP in the US. Curr Med Res Opin. 2009;25(12):2961-9.
10. Rodeghiero F, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. Blood. 2009;113(11):2386-93.
11. Neunert C, et al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood. 2011;117(16):4190-207.
12. McCrae K. Immune thrombocytopenia: no longer 'idiopathic'. Cleve Clin J Med. 2011;78(6):358-73.
13. Portielje JE, et al. Morbidity and mortality in adults with idiopathic thrombocytopenic purpura. Blood. 2001 1;97(9):2549-54.
14. European Medicines Agency. Revolade (eltrombopag) EPAR summary for the public (PDF). EMA/563687/2013. London: European Medicines Agency.
15. PHARMAC (2013). Funding for new drug to treat rare bleeding condition (Web Page) Media release (9 December 2013). Wellington: Ministry of Health. Accessed: 10/01/14.
16. Cheng G, et al. Eltrombopag for management of chronic immune thrombocytopenia (RAISE): a 6-month, randomised, phase 3 study. Lancet. 2011;377(9763):393-402.
17. Saleh MN, et al. Safety and efficacy of eltrombopag for treatment of chronic immune thrombocytopenia: results of the long-term, open-label EXTEND study. Blood. 2013;121(3):537-45.
18. Pharmac (2014a). Application for subsidy by special authority (PDF). Form SA1412 (February 2014). Wellington: Ministry of Health.
19. PHARMAC (2014b). Widening of funding restrictions for rituximab and eltrombopag (PDF). Notification A669763 (20 February 2014). Wellington: Ministry of Health.
20. Gonzalez-Lopez, et al. Sustained response after discontinuation of short- and medium-term treatment with eltrombopag in patients with immune thrombocytopenia. Platelets 2014 Feb 5. [Epub ahead of print].
21. Patel VL, et al. Outcomes 5 years after response to rituximab therapy in children and adults with immune thrombocytopenia. Blood. 2012;119(25):5989-95.
22. GlaxoSmithKline (2013). Revolade® tablets data sheet (PDF). Version 3.0 (04/04/2013). Auckland: GlaxoSmithKline NZ Ltd.

This publication has been created with an educational grant from GlaxoSmithKline.
The content is entirely independent and based on published studies and the writer and commentators' opinions.
Please consult the full Data Sheets for any medications mentioned in this article at www.medsafe.govt.nz before prescribing.
Treatment decisions based on these data are the full responsibility of the prescribing physician.