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Pharmacological Management of Immune Thrombocytopenia: Established and Emerging Therapeutic Options

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Key messages

•Immune thrombocytopenia (ITP) is a heterogeneous, antibody- and T-cell-mediated bleeding disorder driven by accelerated peripheral platelet destruction and inappropriately low, ineffective platelet production; treatment goals have shifted from a fixed platelet-count target to control of bleeding and preservation of quality of life.

•Corticosteroids remain the standard first-line therapy, but should be limited in duration; intravenous immunoglobulin (IVIg) and, where available, intravenous anti-D immunoglobulin, are reserved for rapid platelet elevation in active bleeding or before invasive procedures.

•Thrombopoietin receptor agonists (TPO-RAs: romiplostim, eltrombopag, avatrombopag, and, in Asia, hetrombopag) and rituximab are the best-established second-line options and, per the 2019 American Society of Hematology (ASH) guidelines, are now generally favoured over splenectomy as first steroid-sparing strategies, splenectomy being reserved for patients who fail or are unsuitable for medical second-line therapy.

•Fostamatinib, an oral spleen tyrosine kinase (Syk) inhibitor, and rilzabrutinib, an oral reversible Bruton tyrosine kinase (BTK) inhibitor approved by the FDA in 2025, provide non-TPO-RA, non-immunosuppressive alternatives for multirefractory disease with distinct safety profiles.

•A wave of agents targeting IgG recycling (FcRn antagonists: efgartigimod, rozanolixizumab, nipocalimab), complement activation (sutimlimab, iptacopan), long-lived autoreactive plasma cells and B cells (ianalumab, anti-CD38 and anti-BCMA strategies), and, investigationally, chimeric antigen receptor (CAR) T cells, is being developed for patients with insufficient response to current second-line agents.

•Choice among available options should be individualised, taking into account bleeding phenotype, comorbidities (thrombosis risk, infection risk, pregnancy, renal or hepatic impairment), patient preference for route and frequency of administration, and, where relevant, cost and local marketing authorisation status.

Keywords

Autoantibodies, B-cell immunity, Monoclonal antibody.

Search strategy and selection criteria

We searched MEDLINE/PubMed, Embase and ClinicalTrials.gov from January 2000 to September 2026, using combinations of the terms 'immune thrombocytopenia', 'ITP', 'thrombopoietin receptor agonist', 'romiplostim', 'eltrombopag', 'avatrombopag', 'hetrombopag', 'rituximab', 'splenectomy', 'fostamatinib', 'rilzabrutinib', 'Bruton tyrosine kinase', 'efgartigimod', 'FcRn',

'sutimlimab', 'complement inhibitor', 'ianalumab', 'CAR-T' and 'immune thrombocytopenia', and 'stem-cell transplantation' and 'immune thrombocytopenia'. Priority was given to randomised controlled trials, pivotal registration studies, large real-world cohorts, and the 2019 American Society of Hematology (ASH) and International Consensus Report (ICR) guidelines and their subsequent reviews. This Seminar is a focused, expert-guided narrative review rather than an exhaustive systematic review; evidence for the newest agents (complement inhibitors, B-cell/plasma-cell-directed biologics, cellular therapies) is limited to early-phase and, in most cases, unpublished or preliminary trial data, and is presented with that caveat.

Introduction

Immune thrombocytopenia (ITP) is an acquired autoimmune disorder defined by a peripheral platelet count below 100×10^9/L in the absence of other identifiable causes of thrombocytopenia. It may be primary or secondary to another condition (systemic lupus erythematosus, common variable immunodeficiency, lymphoproliferative disease, hepatitis C or HIV infection, Helicobacter pylori infection, or drugs, including some vaccines). Diagnosis remains one of exclusion, supported by a compatible clinical picture, blood count and film, and response to first-line therapy; bone-marrow examination and specific platelet-antibody assays play a limited, selective role.

The disease course is classified as newly diagnosed (within 3 months of diagnosis), persistent (3–12 months), and chronic (beyond 12 months). Clinical severity ranges from asymptomatic incidental thrombocytopenia to life-threatening mucocutaneous or intracranial haemorrhage. Management has moved away from a rigid platelet-count threshold towards individualised, bleeding- and quality-of-life-driven decisions, reflecting the substantial burden of fatigue, anxiety and treatment-related morbidity reported by patients in large surveys.

Epidemiology

Population-based studies estimate the incidence of adult primary ITP at roughly 2–4 per 100,000 person-years, with a prevalence in the range of 9–12 per 100,000, a bimodal age distribution with peaks in young adulthood and after age 60 years, and a female predominance in early-to-middle adulthood that attenuates in older age groups. Chronicity develops in the majority of adults with newly diagnosed disease, in contrast to children, in whom spontaneous remission is the rule.

Pathophysiology

The pathophysiology of ITP is multifactorial. Autoantibodies, typically directed against platelet glycoprotein IIb/IIIa or Ib/IX, opsonise circulating platelets, which are then cleared prematurely by Fcγ-receptor-bearing macrophages, principally in the spleen and, to a lesser extent, the liver. A second, non-Fcγ-receptor pathway involves antibody- and complement-mediated desialylation of platelet surface glycans, exposing Ashwell-Morell receptor ligands and driving hepatic clearance independently of splenic Fcγ-receptor phagocytosis — a mechanism that may explain resistance to therapies that act purely on Fcγ-receptor-mediated destruction.

Beyond antibody-mediated peripheral destruction, cytotoxic CD8+ T cells can directly lyse platelets and megakaryocytes, regulatory T-cell number and function are frequently impaired, and megakaryopoiesis is intrinsically defective, with inappropriately low or unchanged circulating thrombopoietin concentrations relative to the degree of thrombocytopenia — in contrast to the marked thrombopoietin elevation seen in bone-marrow failure states. This combination of increased peripheral destruction (by both Fcγ-receptor-dependent and desialylation-dependent routes), impaired megakaryocyte platelet production, and dysregulated T- and B-cell immunity provides the rationale for the diversity of mechanistic targets now being pursued therapeutically: thrombopoietin receptor agonism to boost production; anti-CD20 and more recently, anti-CD19/BAFF-receptor and anti-plasma-cell strategies to reduce autoantibody synthesis; Syk and BTK inhibition to interrupt Fcγ-receptor and B-cell-receptor signalling; FcRn blockade to accelerate autoantibody clearance; and complement inhibition to prevent complement-dependent platelet destruction.

Overview of therapeutic strategy

Across the 2019 ASH guideline, the 2019 International Consensus Report (ICR, updated from 2010) and their subsequent expert reviews, management follows a broadly similar sequence: short-course corticosteroids as first-line therapy for most adults with clinically significant bleeding or a platelet count low enough to warrant treatment; IVIg or, where licensed, intravenous anti-D immunoglobulin, for rapid platelet elevation; and, for patients who are corticosteroid-dependent or fail first-line therapy after 3 months, a choice between a TPO-RA, rituximab, fostamatinib, or splenectomy as second-line therapy, informed by shared decision-making. Both guideline bodies now suggest medical second-line therapy (TPO-RA or rituximab) ahead of splenectomy where possible, reflecting splenectomy's irreversibility and its own long-term risks, while acknowledging the low certainty of the underlying comparative evidence.

First-line therapy

Corticosteroids

Oral prednisone (0.5–2 mg/kg/day) or high-dose dexamethasone (40 mg/day for 4 days, repeated for up to 3–4 cycles) are the standard first-line agents, raising platelet counts in most patients within 1–2 weeks. Response is frequently transient once steroids are tapered, and only a minority achieve durable remission. Guidelines recommend limiting corticosteroid exposure to a maximum of 6–8 weeks (including taper) because of cumulative toxicity — hyperglycaemia, hypertension, osteoporosis, myopathy, mood disturbance, weight gain, cataracts, avascular necrosis and increased infection risk — which becomes clinically significant with cumulative courses. There is no absolute contraindication, but pre-existing diabetes, uncontrolled hypertension, active infection,

psychiatric illness and osteoporosis warrant particular caution and monitoring. Dexamethasone pulses appear to induce more durable responses than prolonged prednisone in some comparative series, at the cost of more pronounced short-term glucocorticoid adverse effects.

Intravenous immunoglobulin (IVIg) and anti-D immunoglobulin

IVIg (typically 1 g/kg once, or 0.4 g/kg/day for 2–5 days) produces a rapid but transient (2–4 week) rise in platelet count through FcRn saturation and reduced Fcγ-receptor-mediated platelet clearance, and is the treatment of choice when an urgent platelet rise is required — active bleeding, prior to surgery or delivery, or as a bridge while awaiting response to another agent. Intravenous anti-D immunoglobulin, where available, offers similar efficacy in Rh(D)-positive, non-splenectomised patients through competitive Fcγ-receptor blockade, at lower cost, but carries a boxed warning for intravascular haemolysis and disseminated intravascular coagulation, and is contraindicated in Rh(D)-negative patients, splenectomised patients, and those with a positive direct antiglobulin test or evidence of autoimmune haemolysis. Common IVIg adverse effects include headache (occasionally severe, aseptic-meningitis-like), fever, nausea, and, rarely, renal impairment (especially with sucrose-containing formulations), thromboembolism and anaphylaxis in IgA-deficient patients.

Established second-line and steroid-sparing therapy

Thrombopoietin receptor agonists (TPO-RAs)

TPO-RAs stimulate the thrombopoietin receptor (MPL) on megakaryocytes and their progenitors, increasing platelet production and compensating for the inappropriately low thrombopoietin response characteristic of ITP. Romiplostim, a subcutaneously administered peptibody, was validated in two pivotal phase 3 randomised, placebo-controlled trials in splenectomised and non-splenectomised adults with chronic ITP, achieving durable platelet response in the large majority of treated patients versus a small minority on placebo, with reduced bleeding and rescue-medication use; [1,2]. long-term extension data support sustained efficacy over several years. Eltrombopag, an oral small-molecule TPO-RA, was similarly validated in the RAISE phase 3 trial (6-month randomised, placebo-controlled study) and in a dedicated phase 3 study in Chinese patients, both showing sustained platelet responses and reduced bleeding and rescue therapy versus placebo [3,4]. Avatrombopag, a newer oral TPO-RA that, unlike eltrombopag, does not require food restriction or chelate polyvalent cations, was validated in a phase 3 randomised trial in both splenectomised and non-splenectomised chronic ITP, achieving durable platelet responses with a favourable hepatic safety profile [5]. Hetrombopag, an oral TPO-RA developed and approved in China, has shown comparable efficacy to eltrombopag in Chinese registration trials and is not currently authorised in Europe or North America.

Common class adverse effects include headache, fatigue, arthralgia/myalgia, and, for eltrombopag, dose-dependent hepatotoxicity requiring liver-function monitoring, and cataract formation with prolonged use (an association not confirmed for romiplostim or avatrombopag). Thromboembolic events occur in a small but consistent excess of TPO-RA-treated patients relative to placebo across the class, and bone-marrow reticulin fibrosis, generally mild and reversible on discontinuation, has been described with romiplostim; periodic blood-film review is recommended during long-term therapy. Rebound thrombocytopenia, sometimes below baseline, can occur on abrupt discontinuation and warrants a tapering strategy. TPO-RAs are contraindicated in patients with known hypersensitivity to the agent or its excipients; caution is advised in patients with a personal history of venous or arterial thromboembolism, hepatic impairment (particularly eltrombopag), and in pregnancy, where data remain limited. Romiplostim, eltrombopag and avatrombopag are approved by both the FDA and the European Medicines Agency (EMA, with a corresponding French AMM) for adults (and, for romiplostim and eltrombopag, children) with chronic ITP who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.

Rituximab

Rituximab, a chimeric anti-CD20 monoclonal antibody, depletes circulating and, to a variable degree, splenic and lymph-node B cells, reducing production of anti-platelet autoantibodies by short-lived plasmablasts (long-lived, CD20-negative plasma cells are relatively spared, which limits durability of response). The RITP trial, a multicentre, randomised, double-blind, placebo-controlled study in steroid-unresponsive adult ITP, did not show a significant difference in the primary endpoint of treatment failure at 78 weeks, but showed significantly higher complete response rates with rituximab and a trend toward fewer splenectomies [6]. Extended follow-up of the RITP cohort confirmed that roughly 20–25% of rituximab-treated patients maintain a durable, treatment-free response beyond 5 years, indicating a genuinely curative effect in a minority [7]. Rituximab is used off-label (unlicensed for ITP in most jurisdictions, including no dedicated French AMM for this indication, though used within recommended practice) at a standard dose of 375 mg/m² weekly for 4 weeks, or increasingly at fixed lower doses (e.g. 100 mg weekly × 4, 'low-dose rituximab') which appear comparably effective with reduced cost and possibly reduced infusion-related toxicity in some series.

Adverse effects include infusion reactions (usually with the first infusion), an increased risk of infection (including reactivation of hepatitis B, which must be screened for before treatment, and, rarely, progressive multifocal leukoencephalopathy), hypogammaglobulinaemia with repeated courses, and a small risk of serum sickness. Live vaccines should be avoided for several months after treatment, and vaccination status should ideally be updated before administration where feasible. Rituximab should be avoided in patients with active hepatitis B infection, severe active infection, or known hypersensitivity to murine proteins.

Splenectomy

Splenectomy removes both the principal site of antibody-coated

platelet destruction and a major source of autoantibody-producing B cells, and remains the most durable therapy for chronic ITP, with sustained complete response in roughly two-thirds of patients in long-term systematic reviews, most durably in those without prior response to medical therapy predicting failure [8]. Laparoscopic splenectomy is preferred over open surgery where feasible, and pre-operative platelet elevation (corticosteroids, IVIg, or a short TPO-RA course) is usual practice to reduce peri-operative bleeding risk. Splenectomy carries irreversible long-term risks, including overwhelming post-splenectomy infection (mandating pneumococcal, meningococcal and Haemophilus influenzae type b vaccination, ideally 2–4 weeks pre-operatively, and consideration of long-term prophylactic antibiotics in selected patients) and a significantly increased incidence of venous thromboembolism and pulmonary hypertension over long-term follow-up [9]. Because of this irreversibility and the efficacy of medical alternatives, both the ASH and ICR guidelines now suggest deferring splenectomy for at least 12–24 months after diagnosis where clinically feasible, to allow for the possibility of spontaneous or treatment-induced remission, reserving it for patients with persistent bleeding risk who fail or are unsuitable for TPO-RA, rituximab or fostamatinib therapy.

Fostamatinib (spleen tyrosine kinase inhibitor)

Fostamatinib is an oral prodrug of the active moiety tamatinib (R406), a spleen tyrosine kinase (Syk) inhibitor that blocks Fcγ-receptor-mediated, phagocytosis-dependent platelet destruction downstream of antibody opsonisation — a mechanism distinct from, and potentially complementary to, TPO-RAs. Two identically designed phase 3, randomised, double-blind, placebo-controlled trials (FIT1 and FIT2) in heavily pretreated adults with persistent/chronic ITP (median 8.5 years' disease duration, median several prior lines of therapy) showed a stable platelet response in 18% of fostamatinib-treated patients versus 2% on placebo, with responses occurring rapidly (median around 2 weeks) in responders, and with subgroup analyses suggesting greater efficacy when used earlier (second-line) rather than after multiple prior therapies [10-12]. Common adverse effects include diarrhoea, hypertension (requiring blood-pressure monitoring, particularly in the first weeks), transaminase elevation, neutropenia and, rarely, diarrhoea-related dehydration; dose reduction from 150 mg to 100 mg twice daily is used to manage toxicity. Fostamatinib is approved by the FDA and EMA (French AMM present) for adult chronic ITP with insufficient response to a previous therapy, and should be avoided or used with caution in patients with uncontrolled hypertension or significant hepatic impairment.

Other immunosuppressive and steroid-sparing agents

A group of older, non-specific immunosuppressive and steroid-sparing agents remains in use, principally as later-line or adjunctive options where access to newer therapies is limited, or in specific clinical contexts. Danazol, an attenuated androgen, can produce sustained responses in a subset of patients, particularly postmenopausal women, at the cost of virilising effects, hepatotoxicity and dyslipidaemia, and is contraindicated in pregnancy and significant hepatic disease. Azathioprine and mycophenolate mofetil act as broader immunosuppressants with steroid-sparing potential, requiring weeks to months for effect and carrying myelosuppression and infection risk, with mycophenolate contraindicated in pregnancy. Ciclosporin has shown activity in refractory ITP, particularly in combination regimens, but requires monitoring of renal function and blood pressure. Vincristine and vinblastine can produce rapid, though usually short-lived, platelet responses through effects on macrophage Fcγ-receptor function and are occasionally used for urgent bridging in multirefractory bleeding, at the cost of neurotoxicity and myelosuppression. Dapsone, used off-label at doses of 75–100 mg/day, can produce durable responses in a minority of patients and is generally well tolerated aside from haemolysis in glucose-6-phosphate dehydrogenase (G6PD) deficiency, which should be excluded before use, and methaemoglobinaemia. None of these agents carries a dedicated ITP marketing authorisation in most jurisdictions, and their use is guided by expert consensus rather than randomised trial evidence.

Emerging and investigational therapies

Bruton tyrosine kinase (BTK) inhibition: rilzabrutinib

Rilzabrutinib is an oral, reversible, covalent BTK inhibitor that interrupts both B-cell-receptor signalling (reducing autoantibody production) and Fcγ-receptor-mediated macrophage phagocytosis of opsonised platelets, and, unlike irreversible BTK inhibitors developed for B-cell malignancies, does not impair platelet function in vitro — a mechanistic feature relevant to its use in a bleeding disorder. In the phase 3 LUNA3 trial, previously treated adults and adolescents with persistent/chronic ITP (median 7.7-year disease duration, 28% prior splenectomy) were randomised to rilzabrutinib 400 mg twice daily or placebo; 64% of rilzabrutinib-treated patients achieved a platelet response within the first 12 weeks versus 32% on placebo, with rapid onset, reduced bleeding and rescue-medication use, and improvement in patient-reported fatigue, alongside a favourable safety profile dominated by mild gastrointestinal and headache events [13-15]. On the basis of LUNA3, rilzabrutinib received FDA approval for adult ITP in August 2025; European regulatory review is ongoing at the time of writing, and there is as yet no French AMM [16]. As an oral agent active through a Fcγ-receptor/B-cell-receptor pathway distinct from TPO-RAs, rilzabrutinib may be particularly suited to patients in whom thrombopoietic stimulation is undesirable (e.g. concern for reticulin fibrosis or marked thrombocytosis) or as an option after TPO-RA or rituximab failure.

Neonatal Fc receptor (FcRn) antagonists

FcRn recycles IgG (including pathogenic autoantibodies) back into the circulation, extending its half-life; blocking FcRn accelerates IgG (and autoantibody) clearance without directly suppressing antibody production, offering a rapid-onset, reversible mechanism attractive for bridging or maintenance therapy. Efgartigimod, an engineered human IgG1 Fc fragment that selectively blocks FcRn, showed efficacy and an acceptable safety profile in phase 2 and phase 3 (ADVANCE) studies in adult chronic primary

ITP and a further phase 3 study (ADVANCE NEXT) using an intravenous formulation is evaluating patients with inadequate response to prior ITP therapies; a subcutaneous formulation has also been studied [17]. Rozanolixizumab, a subcutaneously administered anti-FcRn monoclonal antibody already approved for other autoantibody-mediated diseases (generalised myasthenia gravis, chronic inflammatory demyelinating polyneuropathy), has shown activity in a phase 2 multiple-dose study in primary ITP [18]. Nipocalimab, another anti-FcRn antibody, is in earlier-stage clinical development for ITP. Class-wide adverse effects reported to date include headache, upper respiratory and urinary tract infections, and a transient reduction in serum albumin (a consequence of the shared FcRn recycling pathway for albumin), generally without clinical sequelae; because FcRn antagonists lower total IgG, including protective antibodies, infection risk and vaccine response require ongoing surveillance. None of the FcRn antagonists currently carries a marketing authorisation for ITP; efgartigimod and rozanolixizumab are approved for other indications, providing an established safety base from which ITP development proceeds.

Complement inhibition

A subset of patients with ITP show evidence of classical-pathway complement activation on the platelet surface, providing a rationale for complement-directed therapy. Sutimlimab, a humanised monoclonal antibody that selectively inhibits C1s and is already approved for cold agglutinin disease, prevented complement-enhanced destruction of autoantibody-coated platelets in preclinical and early clinical (proof-of-concept) studies in chronic ITP [19]. Iptacopan, an oral factor B inhibitor of the alternative complement pathway approved for paroxysmal nocturnal haemoglobinuria and C3 glomerulopathy, is being explored in adjacent complement-mediated cytopenias and may extend to ITP; robust phase 3 ITP-specific efficacy and safety data are not yet available for either agent, and neither is currently authorised for this indication. As with other complement inhibitors, an increased risk of encapsulated bacterial infection (particularly Neisseria meningitidis) is anticipated and would require vaccination and, in some regimens, antibiotic prophylaxis, based on experience in other complement-inhibitor-treated populations.

B-cell- and plasma-cell-directed biologics

Because long-lived, CD20-negative plasma cells that persist after rituximab can continue to secrete autoantibody, several agents targeting earlier B-cell stages or plasma cells directly are in development. Ianalumab, a monoclonal antibody that both blocks the B-cell-activating factor receptor (BAFF-R) and depletes B cells through antibody-dependent cytotoxicity, was evaluated in combination with eltrombopag in a phase 3, randomised, double-blind trial in adults with primary ITP and an insufficient response or relapse after first-line glucocorticoid therapy, with results reported in the New England Journal of Medicine in 2026 [20]. Anti-CD38 antibodies (e.g. daratumumab, used for its plasma-cell-depleting activity in multiple myeloma and antibody-mediated conditions) and anti-B-cell-maturation-antigen (BCMA) approaches, including early-phase anti-BCMA CAR-T constructs (below), are being explored on the rationale that direct plasma-cell depletion may achieve more durable autoantibody suppression than B-cell depletion alone. None of these agents is currently authorised for ITP, and evidence is limited to early-phase or single-trial data.

Cellular therapies: CAR-T cells and autologous haematopoietic stem-cell transplantation

Chimeric antigen receptor (CAR) T-cell therapy, established in B-cell malignancies, is under early clinical investigation for severe, multirefractory autoimmune cytopenias, including ITP. Anti-CD19 and anti-BCMA CAR-T constructs are being tested in single-centre, early-phase (phase 1/2) trials in patients with chronic or refractory ITP unresponsive to conventional first- and second-line therapies, with the rationale of eliminating both autoreactive B cells and, for anti-BCMA constructs, long-lived autoantibody-secreting plasma cells (ClinicalTrials. gov identifiers NCT06352281 and related anti-BCMA protocols); published experience remains limited to small case series and is not yet sufficient to define efficacy or a safety profile specific to ITP, though the class carries known risks of cytokine-release syndrome, immune-effector-cell-associated neurotoxicity syndrome, and prolonged cytopenias extrapolated from oncological use. Autologous haematopoietic stem-cell transplantation (HSCT) after myeloablative or reduced-intensity conditioning has been described, almost exclusively in isolated case reports, to induce durable remission of severe refractory ITP, generally in patients undergoing HSCT for a concurrent haematological indication; it is not a standard therapeutic option for ITP outside this context, given the substantial treatment-related morbidity and mortality of the procedure relative to available pharmacological alternatives. Both cellular approaches should currently be considered strictly investigational and restricted to clinical trials or highly selected, multirefractory cases discussed within specialist multidisciplinary settings.

Special populations

Management requires adaptation in specific populations. In pregnancy, corticosteroids and IVIg remain first-line, given the extensive safety experience; TPO-RAs, rituximab, fostamatinib and rilzabrutinib all lack robust human safety data in pregnancy and are generally avoided unless benefit clearly outweighs uncertain risk. In secondary ITP (associated with systemic lupus erythematosus, common variable immunodeficiency, lymphoproliferative disorders, or chronic viral infection), treatment of the underlying condition is integral, and immunosuppressive escalation should account for the specific infective or malignant context. Older adults carry a higher baseline bleeding and thrombotic risk, favouring careful agent selection (e.g. avoiding agents with the highest reported thromboembolic signal where alternative thrombotic risk factors are present) and closer monitoring of corticosteroid-related toxicity.

Regulatory status of established and emerging ITP therapies (adult indication)

Agent	Mechanism	Pivotal evidence	FDA	EMA / French AMM	Typical adverse effects
Corticosteroids (prednisone, dexamethasone)	Broad immunosuppression, reduced Fcγ-receptor expression	Long-standing clinical practice; guideline-endorsed	Approved (general)	Approved (general)	Hyperglycaemia, osteoporosis, mood/ psychiatric effects, infection
IVIg	FcRn saturation, Fcγ-receptor blockade	Long-standing clinical practice; guideline-endorsed	Approved	Approved	Headache, fever, renal impairment, thromboembolism
Anti-D immunoglobulin (IV)	Fcγ-receptor competitive blockade	Long-standing clinical practice	Approved (Rh(D)+, non-splenectomised)	Limited availability	Haemolysis (boxed warning), DIC
Romiplostim	TPO-receptor (MPL) agonist, subcutaneous	Phase 3 RCTs [1,2]	Approved	Approved (AMM)	Headache, arthralgia, thrombosis, reticulin fibrosis (rare)
Eltrombopag	Oral TPO-receptor agonist	Phase 3 RCTs (RAISE and others) [3,4]	Approved	Approved (AMM)	Hepatotoxicity, cataract, headache, thrombosis
Avatrombopag	Oral TPO-receptor agonist	Phase 3 RCT [5]	Approved	Approved (AMM)	Headache, fatigue, favourable hepatic profile
Hetrombopag	Oral TPO-receptor agonist	Phase 3 RCT (China)	Not approved	Not approved	Similar to eltrombopag class effects
Rituximab	Anti-CD20, B-cell depletion	RCT (RITP) [6,7]	Off-label (approved for other indications)	Off-label; no dedicated AMM for ITP	Infusion reactions, infection, hepatitis B reactivation
Splenectomy	Surgical removal of principal destruction/ antibody site	Long-term systematic reviews [8,9]	N/A (procedure)	N/A (procedure)	Post-splenectomy infection, venous thromboembolism
Fostamatinib	Oral Syk inhibitor	Phase 3 RCTs (FIT1/ FIT2) [10-12]	Approved	Approved (AMM)	Diarrhoea, hypertension, transaminitis, neutropenia
Rilzabrutinib	Oral reversible BTK inhibitor	Phase 3 RCT (LUNA3) [13,14]	Approved (Aug 2025)	Under review; no AMM yet	Headache, gastrointestinal effects, fatigue
Efgartigimod / rozanolixizumab (FcRn antagonists)	FcRn blockade, accelerated IgG clearance	Phase 2/3 in progress [17,18]	Approved for other indications; not for ITP	Approved for other indications; not for ITP	Headache, infection, transient hypoalbuminaemia
Sutimlimab / iptacopan (complement inhibitors)	C1s or factor B inhibition	Early-phase / proof-of-concept [19]	Approved for other indications; not for ITP	Approved for other indications; not for ITP	Encapsulated bacterial infection risk
Ianalumab (BAFF-R/B-cell)	BAFF-receptor blockade and B-cell depletion	Phase 3 RCT with eltrombopag [20]	Not approved for ITP	Not approved for ITP	Infusion reactions, infection (data maturing)
CAR-T (anti-CD19/ anti-BCMA)	B-cell / plasma-cell elimination	Early-phase, single-centre studies	Not approved (investigational)	Not approved (investigational)	CRS, ICANS, cytopenias (extrapolated)

Conclusions and future directions

The therapeutic landscape of ITP has expanded considerably beyond the traditional sequence of corticosteroids, IVIg, splenectomy and older immunosuppressants. TPO-RAs, rituximab and, more recently, fostamatinib and rilzabrutinib give clinicians four mechanistically distinct, non-splenectomy options for corticosteroid-dependent or refractory disease, each with a different balance of route, onset, durability and toxicity. The next wave of agents — FcRn antagonists, complement inhibitors, B-cell/plasma-cell-directed biologics, and, at the experimental frontier, CAR-T cells and autologous HSCT — target mechanisms only partially addressed by current therapy, in particular the desialylation-dependent, Fcγ-receptor-independent destruction pathway and long-lived autoantibody-secreting plasma cells, and may eventually allow more precise, mechanism-matched treatment selection. Until head-to-head comparative and long-term real-world data accumulate for these newer agents, treatment choice should remain individualised, guided by bleeding phenotype, comorbidity, patient preference, and local marketing-authorisation status, within the framework of the ASH and ICR guidelines and their periodic updates.

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