WAYRILZ™
(rilzabrutinib) 400 mg tablets

Modified Durable Response

Overview of LUNA-3 clinical data and post hoc analysis results

INDICATION
WAYRILZ is indicated for the treatment of adult patients with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.

IMPORTANT SAFETY INFORMATION
WARNINGS AND PRECAUTIONS
Serious Infections: An increased risk of serious infections (including bacterial, viral, or fungal) can occur in patients treated with Bruton's tyrosine kinase (BTK) inhibitors, including WAYRILZ. Fatal pneumonia occurred in one participant treated with WAYRILZ in the LUNA-3 trial. Other serious infections [one each (0.8%)] included COVID-19 infection, wound infection, urinary tract infection and kidney abscess. Monitor patients for signs and symptoms of infection and treat appropriately.

Please see additional Important Safety Information throughout and full Prescribing Information.

ITP Overview

ITP is a disease of complex immune dysregulation. Patients with ITP have isolated platelet counts <100x10^9/L and often <20x10^9/L[1-3]

Bleeding occurs in **~60% of patients; severe bleeding** occurs in **~7% of patients**[4,5,a]

In patients >60 years of age, **intracerebral hemorrhage** is the most common ITP-related cause of death, with a **50% to 80% mortality rate**[6]

Patients with ITP may face nearly **double the rate of risk of thromboembolic events (TEs)** compared with the general population[7,b]

CNS, central nervous system; ITP, immune thrombocytopenia.

[a]As seen in a cross-sectional study of 302 French patients enrolled in clinical registries.

[b]Data from a retrospective cohort study of 1140 patients with ITP and 5657 patients without ITP. Adjusted risk ratio of 1.7 in venous thrombosis, 1.2 in CNS arterial TEs, and 1.5 in non-CNS arterial TEs. Adjusted for smoking, arterial events, hyperlipidemia, hypertension, diabetes, cardiac arrhythmia, cerebral infarction due to occlusion/stenosis/embolism/thrombosis, cerebrovascular stenosis or occlusion, and related syndromes without infarction.

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WAYRILZ Durable Platelet Response in LUNA-3[8,9]

LUNA-3 Study Design[8,9]

LUNA-3: A phase 3, randomized, double-blind, placebo-controlled, parallel-group, multicenter study to evaluate the efficacy and safety of oral WAYRILZ (400 mg BID) for 24 weeks, followed by a 28-week open-label extension, in adults with persistent or chronic ITP who had an insufficient response to either intravenous immunoglobulin or corticosteroids, or had a documented intolerance or insufficient response to any appropriate course of standard-of-care ITP therapy.

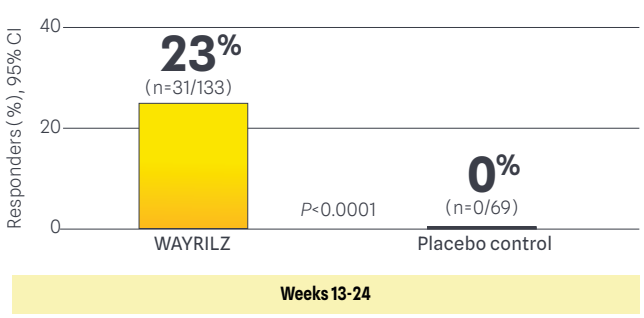
The primary endpoint in the LUNA-3 study was durable platelet response, which was defined as at least 5 platelet counts of at least $50x10^9$/L out of a minimum of 8 weekly measurements in the last 12 weeks of the 24-week DB period, and including a minimum of 2 such responses during the last 6 weeks of the DB period without rescue therapy.[a]

At the end of 12 weeks of treatment, patients were assessed for platelet response (≥$50x10^9$/L or between ≥$30x10^9$/L and <$50x10^9$/L and at least doubled from baseline) at any time. Nonresponders or those who used rescue medication after Week 8 either discontinued the study or entered the 28-week, open-label period to receive WAYRILZ.

Demonstrated Durable and Rapid Platelet Response vs Placebo[8,9]

PRIMARY ENDPOINT:
Significant durable platelet response by Week 25

A platelet count of ≥$50x10^9$/L for ≥5 of at least 8 nonmissing weekly measurements during the last 12 weeks of the DB period, including ≥2 such responses in the last 6 weeks without rescue therapy.



BID, twice daily.

IMPORTANT SAFETY INFORMATION (cont'd)
WARNINGS AND PRECAUTIONS (cont'd)
Hepatotoxicity, Including Drug-Induced Liver Injury (DILI): Hepatotoxicity, including severe, life-threatening, and potentially fatal cases of DILI, can occur in patients treated with BTK inhibitors. Elevations of liver transaminases occurred with WAYRILZ in the ITP clinical trials and were generally mild to moderate in severity. Evaluate bilirubin and transaminases at baseline and as clinically indicated during treatment with WAYRILZ. For patients who develop abnormal liver tests after WAYRILZ, monitor more frequently. If DILI is suspected, withhold WAYRILZ. Upon confirmation of DILI, discontinue WAYRILZ.

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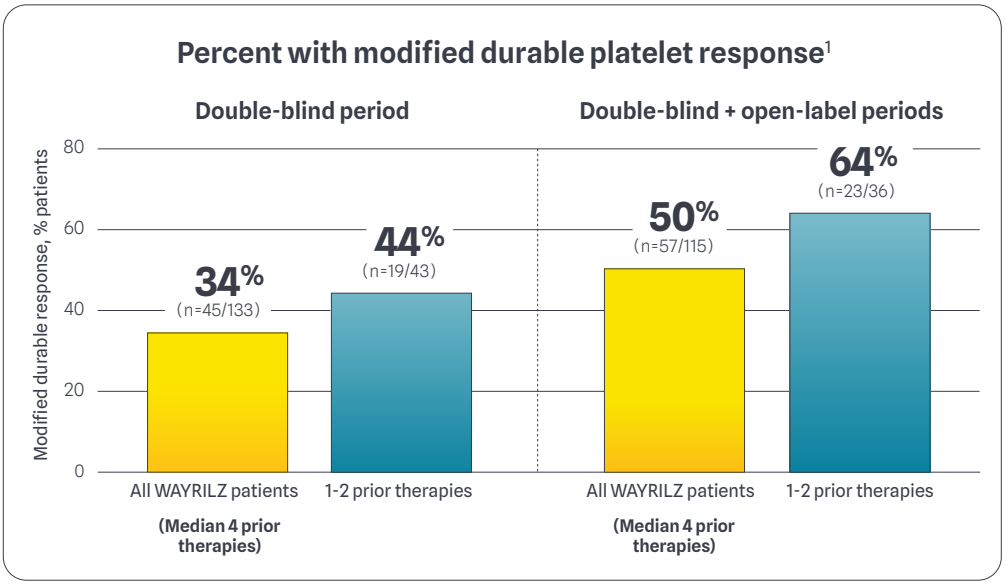
WAYRILZ Modified Durable Platelet Response in a Post Hoc Analysis of the LUNA-3 Study[10,11]

Modified durable platelet response: Defined using the IWG[a] standard for platelet response as part of the criteria:

- **Platelet count:** ≥30x10^9/L and at least doubled from baseline
- **No bleeding:** Must be in the absence of bleeding
- **Duration:** For ≥50% of assessments during:
  - Last 12 weeks of the DB period, OR
  - Last 16 weeks of the OL period
- **Data availability:** Provided that ≥6 or ≥8 nonmissing platelet counts were available in the DB and OL periods, respectively

Study design: Data are from a post hoc analysis of patients with persistent or chronic ITP who were enrolled in the LUNA-3 clinical study. Analyses were conducted by applying a modified durable platelet response criteria while preserving the randomization from the LUNA-3 study. Modified durable response was defined using the IWG standard for platelet response as part of the criteria.[11]

Study limitations: This post hoc analysis was not designed or powered to establish statistical significance. Results are descriptive only and definitive conclusions cannot be made.



BTK, Bruton's tyrosine kinase; DB, double blind; IWG, International Working Group; OL, open-label.

[a]To address the need for standardization of response criteria with the introduction of novel targeted therapies, the IWG has established standardized terminology, definitions, and outcome criteria for ITP. The IWG criteria define platelet response thresholds that are clinically meaningful and safe, aiming to guide treatment decisions and bleeding risk.[10]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Embryo-Fetal Toxicity: Based on findings from preliminary animal reproduction studies, WAYRILZ may cause fetal harm when administered to a pregnant woman. Verify pregnancy status of females of reproductive potential prior to initiating WAYRILZ treatment. Advise females of reproductive potential to use effective contraception while taking WAYRILZ and for 1 week after the final dose.

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Established Safety Profile in LUNA-3 With WAYRILZ[8]

Common adverse reactions in patients with ITP during the double-blind period of the LUNA 3 study[a]

Most common ARs (≥5%)	**WAYRILZ** (N=133)		Placebo control (N=69)	
	All Grades,%	Grade 3 or Higher,%	All Grades,%	Grade 3 or Higher,%
Diarrhea	32	0	10	0
Nausea	20	0	6	0
Headache	18	0	7	0
Abdominal pain[b]	14	0	1	0
COVID-19	14	(0.8)	4	0
Arthralgia	9	0	4	0
Dizziness	8	0	1	0
Nasopharyngitis[b]	7	0	3	0
Vomiting	7	0	1	0
Dyspepsia	5	0	0	0
Cough	5	0	0	0

In patients who experience gastrointestinal symptoms, taking WAYRILZ with food may improve tolerability.

Consider WAYRILZ, a multi-immune modulator that targets complex immune regulation via BTK inhibition for your members with chronic or persistent ITP who have had an insufficient response to a previous treatment.

Learn more

AR, adverse reactions.
[a]ARs that occurred in at least 5% of WAYRILZ-treated patients and at least 3% higher than placebo-treated patients.
[b]Grouped term.

IMPORTANT SAFETY INFORMATION (cont'd)
ADVERSE REACTIONS
Most common adverse reactions reported (incidence ≥10%) were diarrhea, nausea, headache, abdominal pain, and COVID-19.

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IMPORTANT SAFETY INFORMATION (cont'd)

DRUG INTERACTIONS

- Avoid concomitant use of WAYRILZ with strong or moderate CYP3A inhibitors, which increases the risk of WAYRILZ adverse reactions. If short term use of these inhibitors cannot be avoided, interrupt treatment with WAYRILZ. Avoid concomitant use of grapefruit, starfruit and products containing these fruits, and Seville oranges with WAYRILZ.
- Avoid concomitant use with a strong or moderate CYP3A inducer, which may reduce WAYRILZ efficacy.
- Administer the dose of WAYRILZ at least 2 hours before administration of an antacid or histamine H2 receptor antagonist. Avoid concomitant use of proton pump inhibitors with WAYRILZ. Concomitant use of acid reducing agents may reduce WAYRILZ efficacy.
- Rilzabrutinib is a moderate inhibitor of CYP3A and increases exposure of these substrates. Monitor for adverse reactions and consider dosage adjustment of the CYP3A substrate.
- Rilzabrutinib is an inhibitor of P-gp, BCRP and OATP1B *in vitro*. The effect of concomitant use of WAYRILZ with OATP1B and BCRP substrates has not been established in clinical studies. Monitor for adverse reactions of the concurrently administered P-gp, BCRP, or OATP1B substrate more frequently where minimal substrate concentration changes may lead to serious adverse reactions.

USE IN SPECIFIC POPULATIONS

- **Lactation:** Due to the potential for adverse reactions in a breastfed child, advise lactating women not to breastfeed while taking WAYRILZ and for at least 1 week after the final dose
- **Hepatic Impairment:** Avoid administration of WAYRILZ in patients with moderate or severe hepatic impairment (Child-Pugh class B-C)
- **Renal Impairment:** Avoid use in patients with severe renal impairment

Please see full Prescribing Information.

References: 1. Cooper N, Ghanima W. Immune thrombocytopenia. *N Engl J Med.* 2019;381(10):945-955. **2.** Hill QA, Newland AC. Fatigue in immune thrombocytopenia. *Br J Haematol.* 2015;170:141–149. doi:10.1111/bjh.13385 **3.** Schoonen WM, Kucera G, Coalson J, et al. Epidemiology of immune thrombocytopenic purpura in the General Practice Research Database. *Br J Haematol.* 2009;145(2):235-244. **4.** Piel-Julian ML, Mahévas M, Germain J, et al. Risk factors for bleeding, including platelet count threshold, in newly diagnosed immune thrombocytopenia adults. *J Thromb Haemost.* 2018;16(9):1830-1842. **5.** Audia S, Bonnotte B. Emerging therapies in immune thrombocytopenia. *J Clin Med.* 2021;10(5):1004. **6.** Al-Samkari H, Kuter DJ. Immune thrombocytopenia in adults: Modern approaches to diagnosis and treatment. *Semin Thromb Hemost.* 2020;46(3):275-288. **7.** Langeberg WJ, Schoonen WM, Eisen M, Gamelin L. Thromboembolism in patients with immune thrombocytopenia (ITP): a meta-analysis of observational studies. *Int J Hematol.* 2016;103(6):655-664. **8.** Wayrilz. Prescribing information. Sanofi; 2025. **9.** Kuter DJ, Ghanima W, Cooper N, et al. Safety and efficacy of rilzabrutinib vs placebo in adults with immune thrombocytopenia: the phase 3 LUNA 3 study. *Blood.* 2025;145(24):2914-2926. **10.** Data on File. Sanofi; 2025. **11.** Ghanima W, Miyakawa Y, Cooper N, et al. Presented at International Society on Thrombosis and Haemostasis; June 21–25, 2025; Washington DC OC75.5.

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