Initial Report of Part B Phase 1/2 Efficacy and Safety Results for Bruton Tyrosine Kinase Inhibitor Rilzabrutinib in Patients With Relapsed Immune Thrombocytopenia

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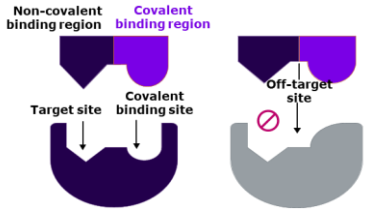
Disclosures

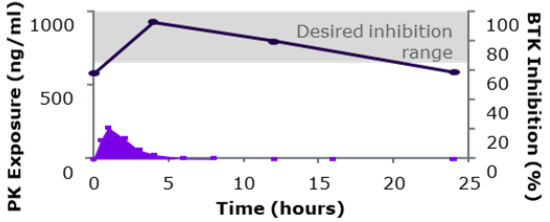
Brad Ward: An employee and public stock shareholder of Sanofi

Rilzabrutinib is an Oral, Reversible, Potent BTK Inhibitor and Does not Impact Platelet Aggregation[1]



Selective/Reversible

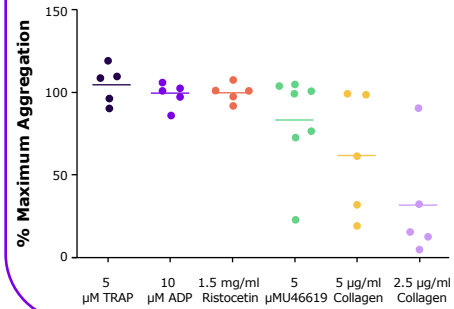
Precise Inhibition; No Permanent Modification of Proteins and Peptides



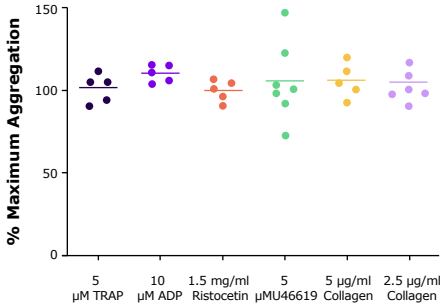
Durable BTK Inhibition With Low Exposure

Potential Optimized Clinical Benefit

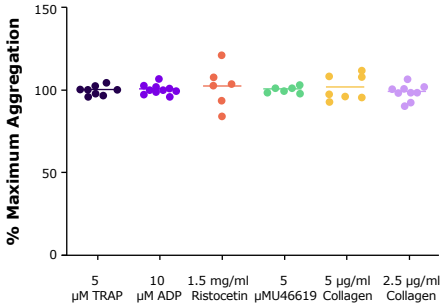
1 µM Ibrutinib in Healthy Volunteers



1 µM Rilzabrutinib in Healthy Volunteers



1 µM Rilzabrutinib in Patients With ITP



No Inhibition of Platelet Aggregation

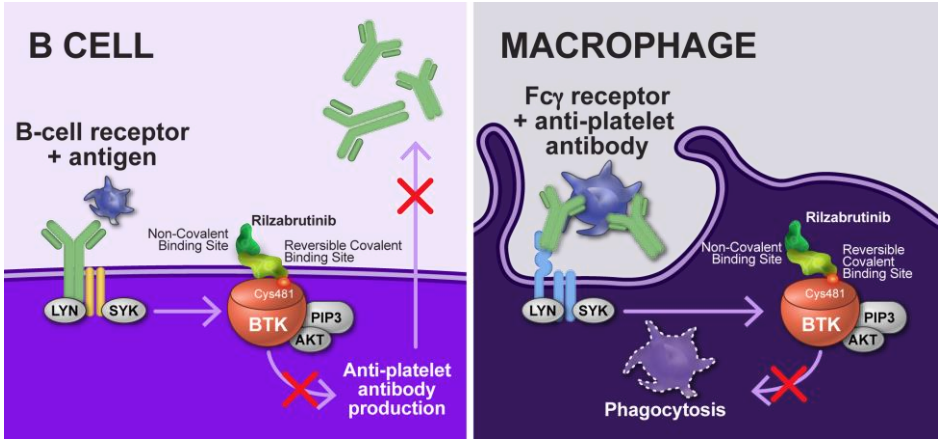
Potential Reduced Risk of Bleeding

ADP, adenosine diphosphate; TRAP, thrombin receptor activating peptide; BTK, bruton's tyrosine kinase; ITP, immune thrombocytopenia purpura; PK, pharmacokinetics.

1. Langrish C, et al. *J Immunol*. 2021;206:1454–1468.

Bruton Tyrosine Kinase Inhibitor Rilzabrutinib is Specifically Designed for Immune-Mediated Diseases

- Rilzabrutinib mediates ITP therapeutic effects through dual mechanisms of action[1,2]
  - Inhibition of B cell activation
  - Interruption of platelet phagocytosis by FcγR in spleen and liver



AKT, protein kinase B; BTK, bruton's tyrosine kinase; Cys, cysteine; Fcγ, crystalline fragment gamma; ITP, immune thrombocytopenia purpura; PIP3, phosphatidylinositol-3,4,5-trisphosphate; SYK, spleen tyrosine kinase.

1. Bradshaw JM, et al. *Nat Chem Biol*. 2015;11:525–531. 2. Kuter DJ, et al. *Ther Adv Hematol*. 2023;14:1–14. DOI:10.1177/20406207231205431.

Rilzabrutinib Clinical Studies in Immune Thrombocytopenia

LUNA 2 Part A: Phase 1/2 adaptive study (N = 60)[1]
NCT03395210, EudraCT 2017-004012-19
Completed

- **Adult primary ITP with platelet counts <30×10^9/L**, ≥1 prior therapy, no response to prior/concomitant therapy
- **Efficacy: 40% met primary endpoint (platelet response)**, median time to first platelet count ≥50×10^9/L was 11.5 days
- **Safety:** All related adverse events were grade 1/2; no related grade ≥2 bleeding/thrombotic events, SAEs, deaths
- **Identified rilzabrutinib 400 mg bid for future studies**

↓

LUNA 2 Part B: Phase 1/2 study in adults with relapsed/refractory primary ITP (N = 26) — **Presented here**

↓

LUNA 3 Phase 3 placebo-controlled study in adults and adolescents with persistent/chronic primary ITP[2] — **Ongoing**

bid, twice daily; ITP, immune thrombocytopenia purpura; N, total number of patients; SAE, serious adverse event.

1. Kuter DJ, et al. *N Engl J Med*. 2022;386:1421–1431; 2. Kuter DJ, et al. *Ther Adv Hematol*. 2023;14:1–14. DOI: 10.1177/20406207231205431.

LUNA 2 Part B – Study Design

- Adaptive, open-label, phase 1/2 study of oral rilzabrutinib in relapsed/refractory ITP

Key Inclusion Criteria
- Age 18–80 years
- Persistent/chronic primary or secondary ITP
- Prior response to IVIg/anti-D or CS that was not sustained **AND failed ≥1 other ITP therapy (not IVIg or CS)**
- ≥2 platelet counts <30×10^9/L at study entry
- Stable concomitant CS and/or TPO-RA allowed

Main treatment period
(24 weeks)
Oral rilzabrutinib 400 mg bid

Primary endpoints
- Durable platelet response: platelet counts ≥50×10^9/L on ≥8 of the last 12 weeks without rescue medication
- Safety and grade ≥2 bleeding events

LTE inclusion

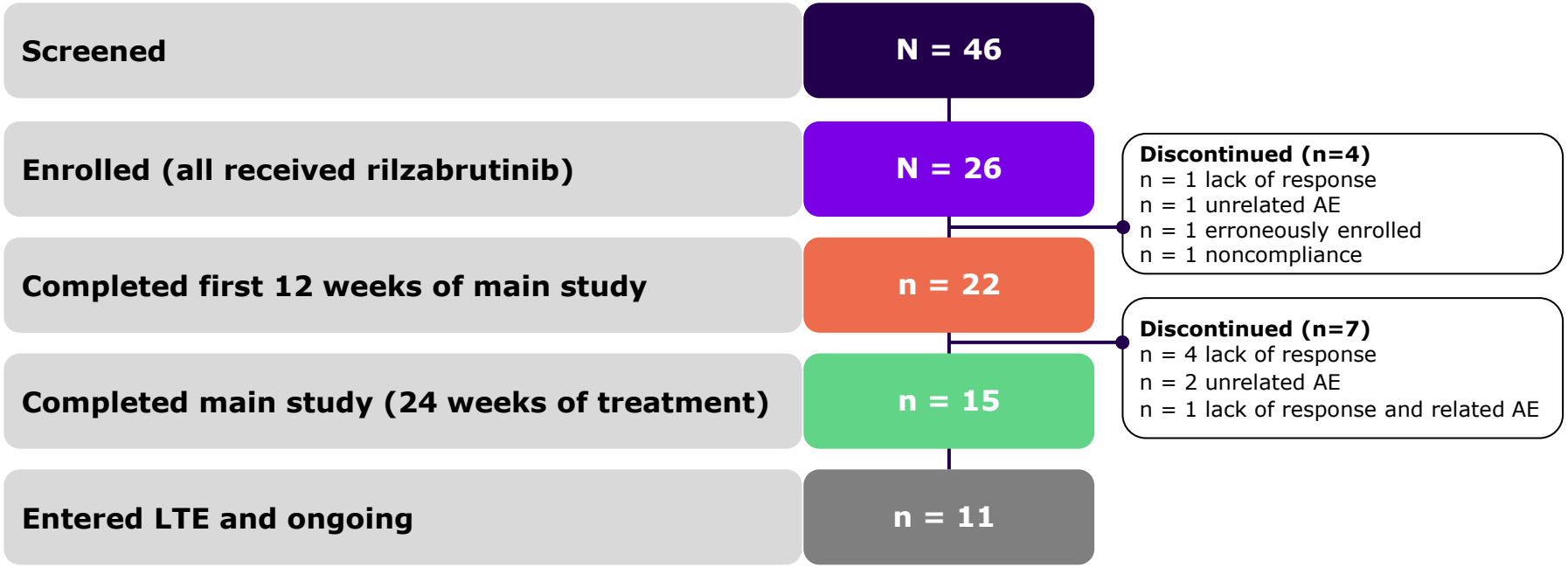
Platelet counts ≥50×10^9/L or ≥30×10^9/L and doubling of baseline for ≥4 of last 8 weeks of treatment without rescue medication

Long-term extension (LTE)
Oral rilzabrutinib 400 mg bid

LTE endpoints
- Safety
- Platelet count assessment

bid, twice daily; CS, corticosteroids; ITP, immune thrombocytopenia purpura; IVIg, intravenous immunoglobulin; LTE, long term extension; TPO-RA, thrombopoietin receptor agonist.

LUNA 2 Part B – Disposition



Study period: 22 Mar 2018–31 Jan 2023.
AE, adverse event; LTE, long term extension; n, number of patients in particular group; N, total number of patients.

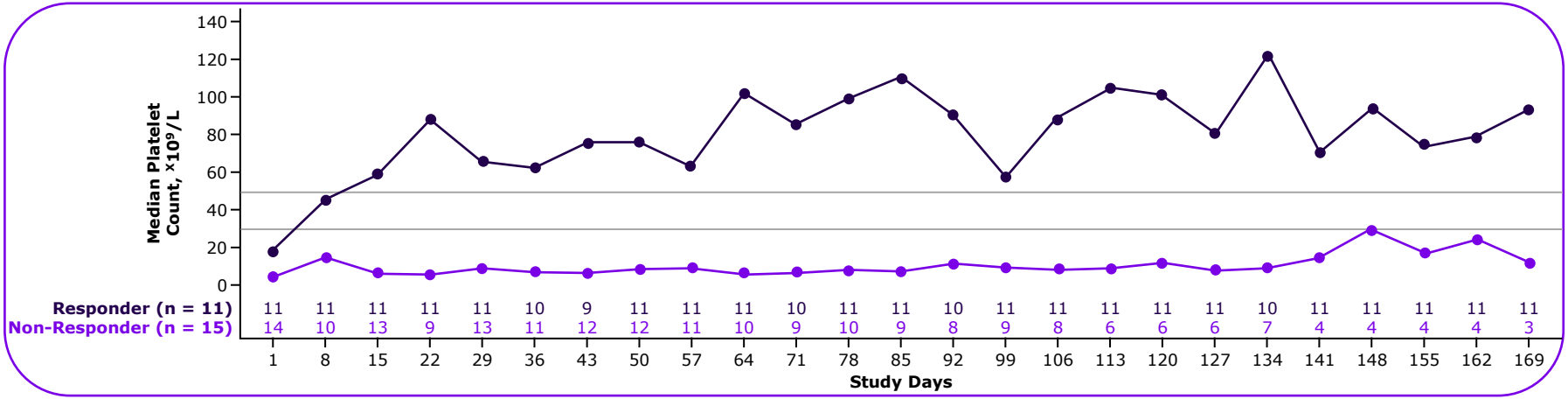
Baseline Demographics and Characteristics

	Patients (N = 26)
Median age, y (range)	57 (20–75)
Gender, n (%)	
Female	**16 (62)**
Male	10 (38)
Median platelet count at baseline, $\times 10^9$/L (range)	13 (2–24)
Median duration of ITP, y (range)*	**10.3 (0.7–48.2)**
Median number of unique prior ITP therapies (range)†	**6 (3–19)**
Most common prior ITP therapies, n (%)	
CS	26 (100)
TPO-RA	22 (85)
Immunosuppressants (including cyclophosphamide)	21 (81)
IVIg	21 (81)
Rituximab	21 (81)
Splenectomy	**12 (46)**
Fostamatinib	4 (15)

Data cut-off: 31 Jan 2023.
*From the date of initial diagnosis to initial rilzabrutinib dose. †Splenectomy may be included.
CS, corticosteroids; ITP, immune thrombocytopenia purpura; IVIg, intravenous immunoglobulin; n, number of patients in particular group; N, total number of patients; TPO-RA, thrombopoietin receptor agonist.

Efficacy Results

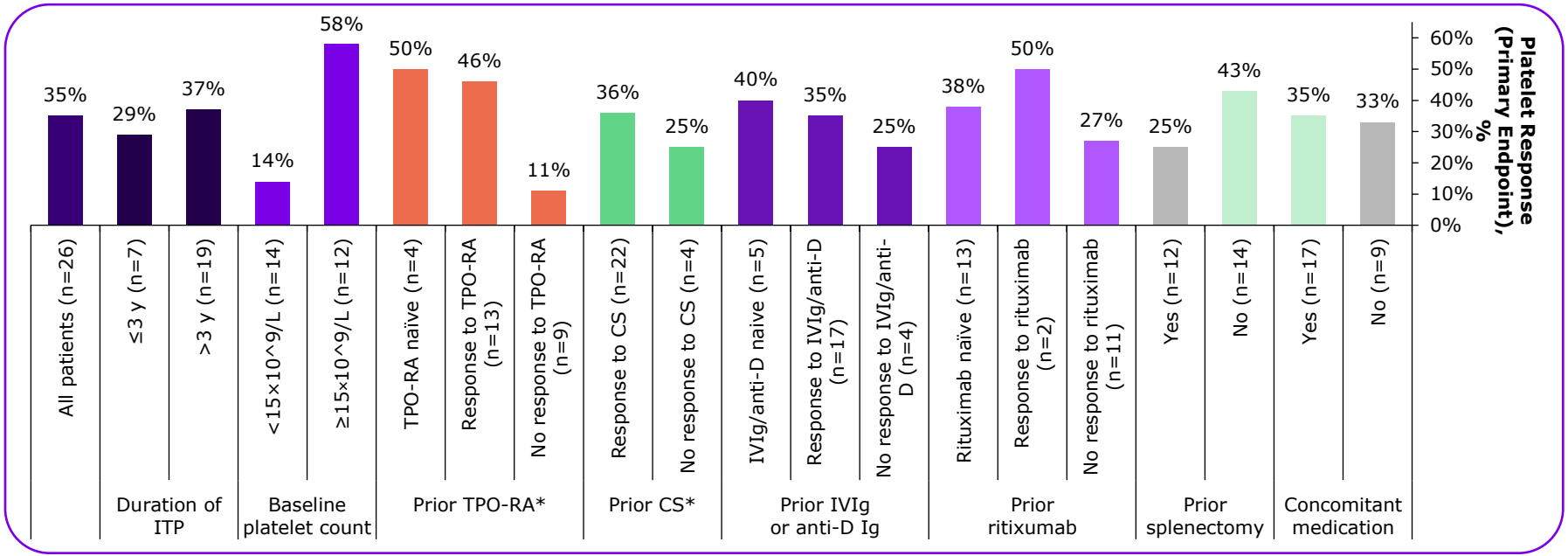
- **9 (35%) patients (95% CI, 17%–56%) achieved primary endpoint of durable response**
  - Durable response: Platelet counts ≥50×10^9/L on ≥8 of the last 12 weeks without rescue medication
- **11 (42%) Responder patients continued in the LTE period (n = 9 met primary endpoint + n = 2 LTE eligible)**
  - LTE eligibility: Platelet counts ≥50×10^9/L or ≥30×10^9/L and doubling of baseline for ≥4 of last 8 weeks without rescue medication



Data cut-off: 31 Jan 2023.
CI, confidence interval; LTE, long term extension; n, number of patients in LTE period.

Subgroup Analysis: Platelet Response by Baseline Factors and Concomitant Therapy

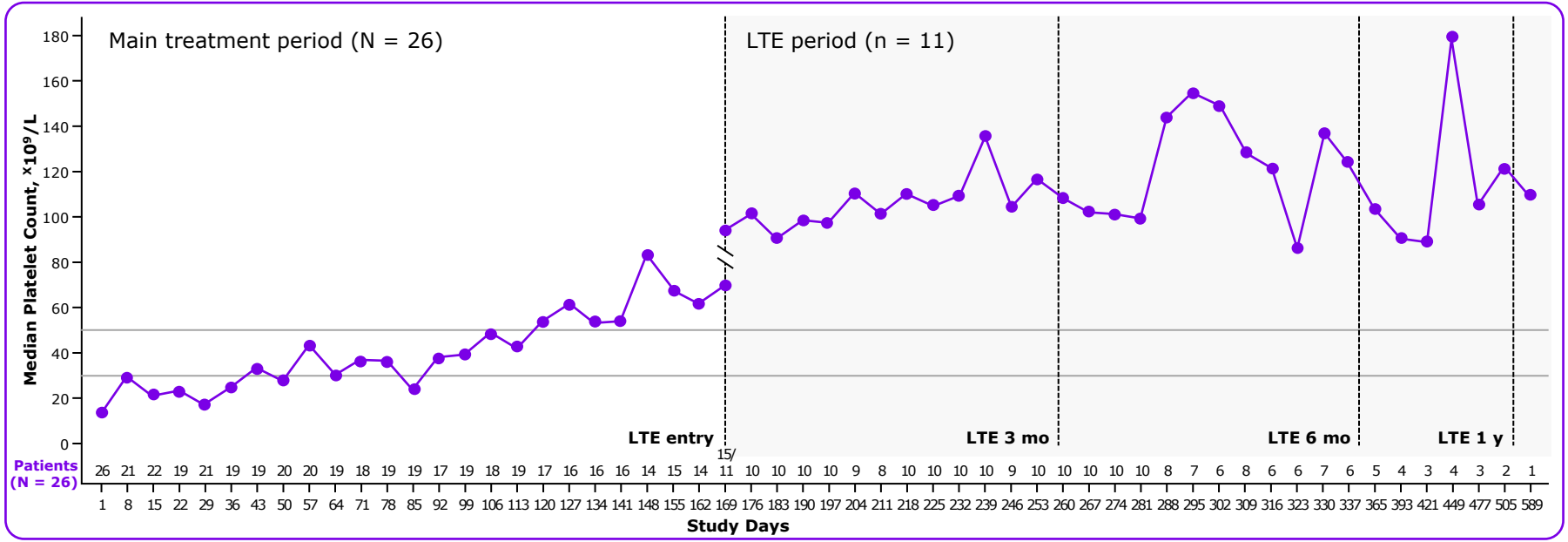
Subgroup analysis of platelet response by baseline factors, prior treatment, and concomitant therapy showed consistent results with that of the primary endpoint for all patients and subgroups with >10 participants



Responses to prior therapy were defined as achieving platelet counts ≥50×10⁹/L on the prior therapy.
*Note: Prior therapy consisted of TPO-RA only (n=0), CS only (n=4), and received both CS and TPO-RA (n=22); all patients were exposed to prior CS.
CS, corticosteroids; ITP, immune thrombocytopenia purpura; IVIg, intravenous immunoglobulin; n, number of patients; TPO-RA, thrombopoietin receptor agonist.

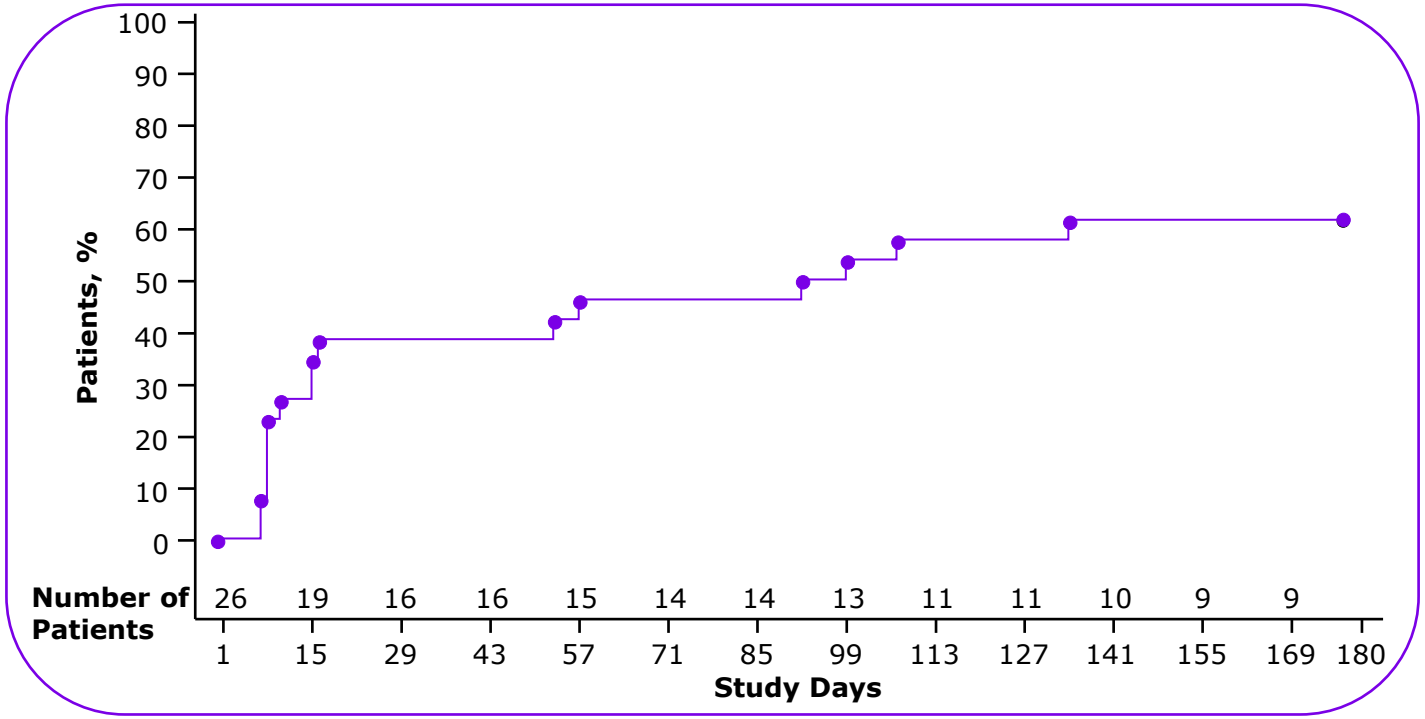
Efficacy Results: Main and LTE Periods

- 11 LTE patients maintained >80×10^9/L median platelet counts through the LTE period



Data cut-off: 31 Jan 2023.
LTE, long term extension; N, total number of patients, n, number of patients in LTE period.

Time to First Platelet Count ≥50×10^9/L



For all patients (KM estimate; N = 26)

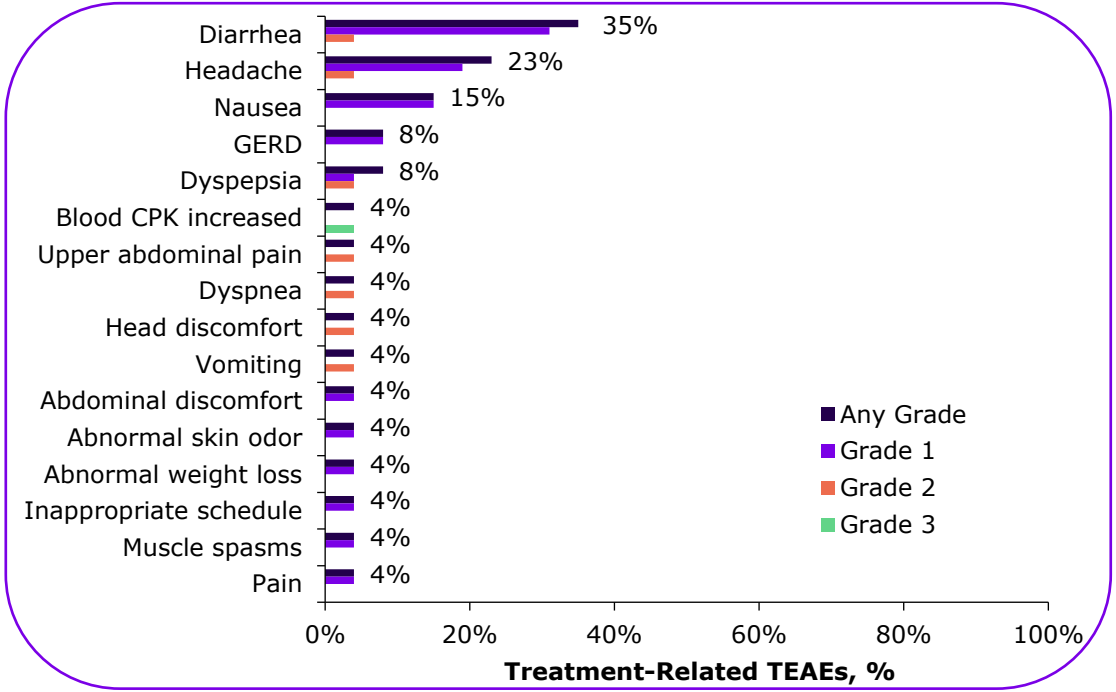
Median = 95.5 days
(95% CI, 15–NA)

For LTE eligible patients (n = 11)

Median = 15 days
(95% CI, 8–57)

Data cut-off: 31 Jan 2023.
CI, confidence interval; KM, Kaplan Meier; LTE, long term extension; NA, not applicable.

Safety in Main Treatment Period (24 Weeks)

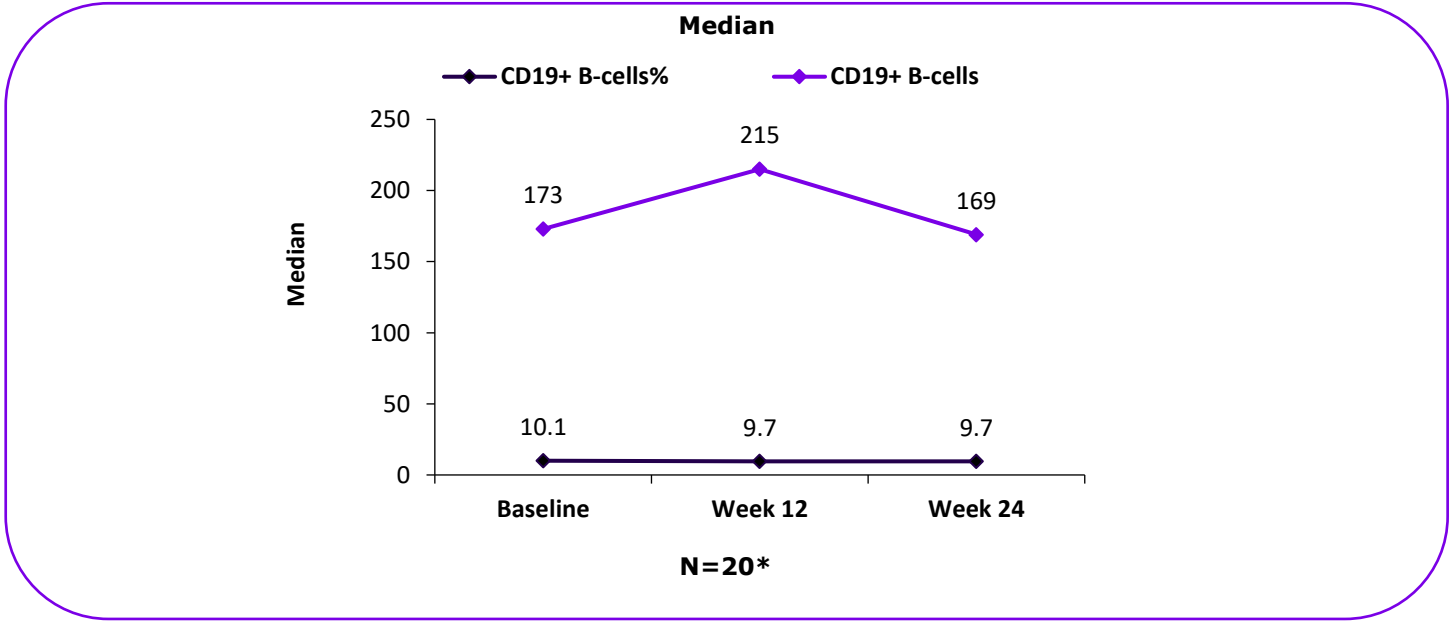


- Median treatment duration was 167 days (range, 7–169); 99% median compliance
- 85% any-cause TEAEs
  - 12% SAEs: none were treatment related per investigators and all resolved
- 62% treatment-related TEAEs, mainly grade 1 or 2
- No related grade ≥2 bleeding/thrombotic events or infections, SAEs, or deaths in main or LTE periods

Data cut-off: 31 Jan 2023.
CPK, creatinine phosphokinase; GERD, gastroesophageal reflux disease; LTE, long term extension; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Safety: B Cell Subtype Levels

- Rilzabrutinib treatment was associated with stable B cell levels



*patients with available data at both timepoints.
CD, cluster of differentiation; N, total number of patients.

LUNA 2 Part B Efficacy and Safety Conclusions

- Rilzabrutinib 400 mg bid demonstrated rapid and durable platelet responses in heavily treated primary ITP, with a well-tolerated safety profile during the main treatment and LTE periods

Efficacy

- **Durable response:** 35% of patients achieved primary platelet response
- **Rapid response**: median time to first platelet count ≥50×10^9/L among patients achieving platelet counts ≥50×10^9/L was 15 days
- 11 patients are ongoing in LTE

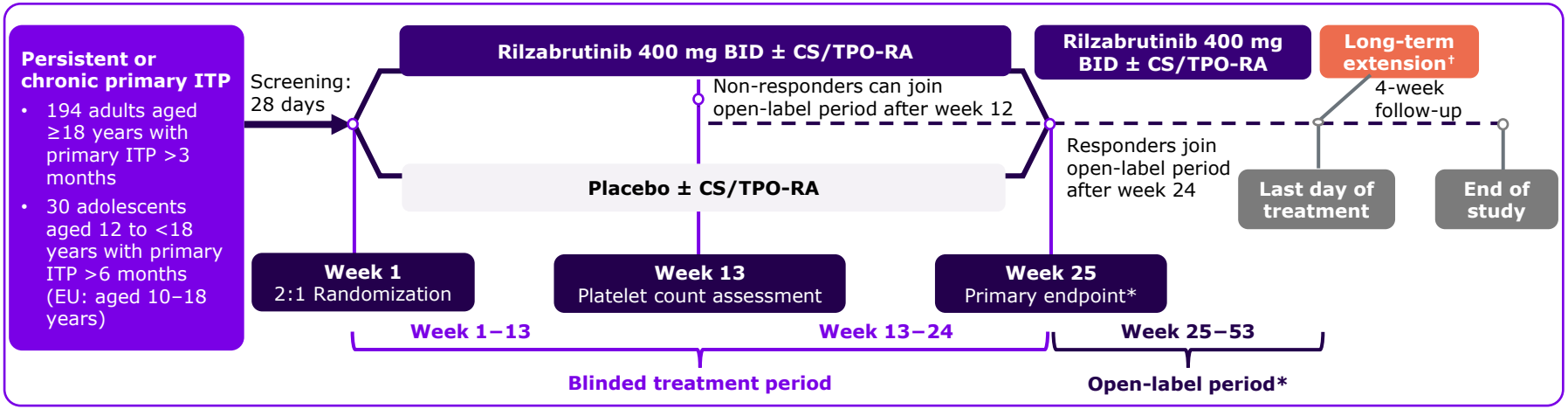
Safety

- No related grade 3/4 TEAEs, grade ≥2 SAEs, or deaths
- No related TEAEs led to treatment discontinuation
- No related grade ≥2 bleeding/thrombotic events or infections, or other safety concerns associated with BTK inhibitor drug class (ie, neutropenia, atrial fibrillation)
- No new safety observation were observed in the LTE
- B cell levels were stable

bid, twice daily; BTK, Bruton's tyrosine kinase; ITP, immune thrombocytopenia purpura; LTE, long term extension; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

LUNA 3 Ongoing Phase 3 Study

- Multicenter, double-blind, placebo-controlled study assessing the efficacy and safety of oral rilzabrutinib 400 mg bid in adults and adolescents with relapsed/refractory ITP
  - 202 adult patients randomized and enrolled; target 30 adolescents - enrollment is ongoing
  - Primary endpoint: durable platelet response in first 24 weeks



*Week 25 is the last visit of the blinded treatment period and the start of the open-label period; †Following long-term extension completion, patients will undergo the last day of study drug and end of study assessments.
bid, twice daily; CS, corticosteroid; EU, European Union; ITP, immune thrombocytopenia purpura; TPO-RA, thrombopoietin receptor agonist.
Kuter DJ, et al. *Ther Adv Hematol*. 2023;14:1–14. DOI: 10.1177/20406207231205431.

Thank you

Acknowledgement:

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Funding:

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