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POSTER ABSTRACTS

311.DISORDERS OF PLATELET NUMBER OR FUNCTION: CLINICAL AND EPIDEMIOLOGICAL

Improved Health-Related quality of Life (HRQoL) with Oral Bruton Tyrosine Kinase Inhibitor (BTKi) Rilzabrutinib Vs Placebo in Adults with Previously Treated Immune Thrombocytopenia (ITP): Phase 3 Luna 3 Multicenter Study

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Introduction: ITP is characterized by low platelet count with consequent increased bleeding risk, fatigue, and diminished overall HRQoL. Mechanisms for the covalent, reversible BTKi rilzabrutinib may include inhibiting B cell activation and inflammatory pathways, and interrupting platelet phagocytosis (via FcγR). The phase 2 LUNA 2 study showed rapid and durable platelet responses, favorable safety, and improved fatigue and HRQoL in previously treated ITP patients. Presented here are HRQoL results from the multicenter phase 3 LUNA 3 study in adults (NCT04562766; 2020-002063-60).
Methods: Adults ≥18 y and pediatric patients 10-<18 y with previously treated primary persistent/chronic ITP for >3 mo and platelet counts $<30\times10^9$/L within 2 weeks of treatment were enrolled. Patients were randomized 2:1 to oral rilzabrutinib 400 mg bid or placebo for up to 24 weeks (double-blind), with subsequent open-label/long-term extension periods. The primary endpoint was durable platelet response: platelet counts $\geq50\times10^9$/L for ≥8 of the last 12 weeks of the 24-week blinded period without rescue therapy. HRQoL was measured using the ITP-PAQ (scores 0 worst to 100 best). Change from baseline in ITP-PAQ item 10 (physical fatigue) at week 13, a key secondary endpoint, was measured in all patients and among responders/non-responders. Anchor-based psychometric analyses from LUNA 3 blinded data determined between-group meaningful score difference (MSD) thresholds for ITP-PAQ item 10 (physical fatigue) using change from baseline data to weeks 13 and 25. Between-group mean change scores and mixed-models for repeated measures (MMRMs) were used to estimate between-group MSD threshold range of 8-18. HRQoL was assessed with exploratory endpoint EQ-5D-5L + EQ-VAS.
Results: As of March 14, 2024, 202 adults were randomized to either rilzabrutinib (n=133) or placebo (n=69). Durable response was met in 31 (23%) rilzabrutinib vs 0 placebo patients ($P<0.0001$). Mean (SD) baseline ITP-PAQ scores for physical fatigue were 52.5 (31.3) for rilzabrutinib and 54.7 (29.5) for placebo. Physical fatigue showed statistically significant and clinically meaningful improvement from baseline at week 13 with a least squares (LS) mean change (SE) of 8.0 (2.1) with rilzabrutinib vs -0.1 (2.9) for placebo (LS mean difference 8.1, $P=0.01$), and at week 25 with a LS mean change (SE) of 4.7 (2.3) for rilzabrutinib vs -7.3 (3.0) for placebo (LS mean difference 12.0, $P=0.0003$). Among 30 evaluable rilzabrutinib patients achieving durable response, physical fatigue score improved with mean changes (SD) from baseline at weeks 13 and 25 of 17.5 (24.7) and 15.8 (27.5), respectively. Interestingly, non-durable responders to rilzabrutinib also showed improvement in physical fatigue, with mean changes (SD) from baseline at weeks 13 and 25 of 7.2 (23.8; n=87) and 7.5 (21.9; n=30), respectively.

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ITP-PAQ domains showing improvements in rilzabrutinib vs placebo, respectively, in mean changes from baseline at week 25 included psychological health (11.9 vs -1.0), overall HRQoL (10.6 vs 2.3), symptoms (10.3 vs 2.1), bother-physical health (10.0 vs -4.7), social activity (9.4 vs 1.3), fatigue/sleep (9.3 vs -5.0) and activity (10.0 vs -1.3). Numerical increases were also observed for rilzabrutinib vs placebo in mean changes from baseline to week 25 in all other ITP-PAQ domains: fear (7.8 vs -5.0), women's reproductive health (5.8 vs -16.7), and work (4.9 vs 3.8).
Improvements in fatigue with rilzabrutinib were associated with improvements in health status (per EQ-VAS) at weeks 13 and 25. Mean (SD) baseline EQ-VAS scores were similar for rilzabrutinib (71.7 [18.9]) and placebo (70.2 [21.9]). At week 13, mean (SD) change from baseline in the rilzabrutinib group was 3.4 (12.6) and with placebo was -2.0 (14.5). Similarly, week 25 mean (SD) change from baseline was 5.2 (13.2) with rilzabrutinib (indicating continued improvement) vs -3.2 (10.0) with placebo.
Conclusion: Statistically significant andclinically meaningfulimprovement in physical fatigue was observed at weeks 13 and 25 with rilzabrutinib vs placebo, with improvements also seen in both durable and non-durable responders and other disease-specific HRQoL endpoints, indicative of potential multiple modalities of action. These HRQoL results provide additional evidence of rilzabrutinib's effects beyond increased platelet counts and reduced bleeding in previously treated adults with ITP.

Disclosures Ghanima: *SOBI:* Consultancy, Honoraria, Research Funding, Speakers Bureau; *Sanofi:* Consultancy, Honoraria, Research Funding; *Novartis:* Consultancy, Honoraria; *Grifols:* Consultancy, Honoraria; *Amgen:* Consultancy, Honoraria; *Hutchmed:* Consultancy, Honoraria; *Argenx:* Consultancy, Honoraria; *Alpine:* Consultancy; *Kedrion:* Consultancy; *Pfizer:* Consultancy; *Principia Biopharma Inc- a Sanofi Company:* Consultancy; *UCB:* Consultancy; *Argenx:* Consultancy; *Cellphire:* Consultancy; *Alpine:* Consultancy; *Kedrion:* Consultancy; *HiBio:* Consultancy; *HUTCHMED:* Consultancy; *Takeda:* Consultancy; *Bristol Myers Squibb:* Honoraria; *Bayer:* Honoraria. **Liebman:** *University Southern California- Keck School of Medicine:* Current Employment; *Novartis:* Consultancy; *Sanofi:* Consultancy, Research Funding; *Alpine:* Consultancy; *Momenta:* Research Funding. **Miyakawa:** *Zenyaku:* Consultancy; *BioMarin:* Research Funding; *CSL Behring:* Research Funding; *Alexion:* Research Funding; *Chugai:* Research Funding; *Asahi Kasei:* Honoraria; *Janssen:* Research Funding; *Novartis:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Sanofi:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Pfizer:* Research Funding; *Novo Nordisc:* Research Funding; *UCB:* Consultancy, Research Funding; *argenx:* Consultancy, Honoraria. **Cooper:** *Argenx:* Consultancy, Honoraria; *Rigel:* Honoraria, Research Funding; *Griffols:* Consultancy, Honoraria; *Amgen:* Consultancy, Honoraria; *Sobi:* Consultancy, Honoraria; *Novartis:* Consultancy, Honoraria, Research Funding; *Sanofi:* Consultancy, Honoraria. **Saydam:** *MSD:* Research Funding. **Hütter-Krönke:** *University Hospital Charité- Universitätsmedizin Berlin:* Current Employment; *Amgen:* Honoraria; *Sanofi:* Honoraria; *Jazz Pharmaceuticals:* Honoraria; *SOBI:* Honoraria. **Audia:** *Sanofi:* Honoraria; *Argenx:* Honoraria; *Novartis:* Honoraria; *Amgen:* Honoraria. **Daak:** *Sanofi:* Current Employment, Current equity holder in publicly-traded company. **Gouia:** *Sanofi:* Current Employment, Current holder of *stock options* in a privately-held company. **Cordoba:** *Sanofi:* Current Employment, Current holder of *stock options* in a privately-held company. **Kuter:** *Biocryst:* Consultancy, Research Funding; *Hutchmed:* Consultancy, Research Funding; *Novartis:* Consultancy, Research Funding; *Principia:* Consultancy, Research Funding; *Rigel:* Consultancy, Research Funding; *Sanofi:* Consultancy, Research Funding; *Alexion:* Consultancy; *Alnylam:* Consultancy, Research Funding; *Alpine:* Consultancy; *Amgen:* Consultancy; *Apellis:* Consultancy; *Argenx:* Consultancy; *Bristol Myers Squibb:* Consultancy; *Caremark:* Consultancy; *Cellularity:* Consultancy; *Cellphire:* Consultancy; *Chugai:* Consultancy; *Hengrui:* Consultancy; *Immunovant:* Consultancy; *Inmagenebio:* Consultancy; *Ligand:* Consultancy; *Medscape:* Consultancy; *Merck Sharp Dohme:* Consultancy; *New York Blood Center:* Consultancy; *Peerview:* Consultancy; *PER:* Consultancy; *Pfizer:* Consultancy; *Platelet Disorder Support Association:* Consultancy; *Regeneron:* Consultancy; *Seismic:* Consultancy; *Sobi:* Consultancy; *Takeda:* Consultancy, Research Funding; *UCB:* Consultancy, Research Funding; *Up-To-Date:* Consultancy; *Verve:* Consultancy; *AIRx:* Consultancy; *CRICO:* Consultancy; *Daiichi Sankyo:* Consultancy; *Dianthus:* Consultancy; *Electra Therapeutics:* Consultancy; *Fuji:* Consultancy; *Hemopure:* Consultancy; *Incyte:* Consultancy; *Kezar:* Consultancy; *Kyowa-Kirin:* Consultancy; *Momenta:* Consultancy; *Nuvig:* Consultancy; *Platelet Biogenesis:* Consultancy; *Protagonist:* Consultancy; *Zafgen:* Consultancy.

Off Label Disclosure: Yes, it is off label. Rilzabrutinib is an investigational therapy being evaluated in a clinical study for the treatment of patients with immune thrombocytopenia.

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