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ORAL ABSTRACTS

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

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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Introduction: Rilzabrutinib is a potent oral, reversible Bruton tyrosine kinase inhibitor that can treat hematological autoimmune diseases through multiple putative mechanisms of action: (1) inhibition of B-cell activation, (2) interruption of antibody-coated cell phagocytosis by FcϒR in spleen and liver, and (3) induce sustained anti-inflammatory effects (Langrish *J Immunol* 2021). Preliminary evidence showed that rilzabrutinib treatment resulted in rapid and durable platelet responses with a favorable safety profile in previously treated patients with immune thrombocytopenia (ITP) as studied in part A of a phase 1/2 clinical study (LUNA 2; Kuter *N Engl J Med* 2022). This abstract summarizes the results of part B that focused on the durability of response with rilzabrutinib in relapsed ITP patients.
Methods: Part B of the multicenter, open-label, phase 1/2 study evaluated the efficacy and safety of rilzabrutinib 400 mg bid in patients with relapsed ITP (NCT03395210). Adult patients aged 18-80 y were eligible with ≥2 baseline platelet counts <30x10 ^{9}/L no less than 7 days apart in the 15 days before the first dose. Eligible patients were required to have a past response (achievement of platelet count ≥50x10 ^{9}/L) to intravenous immunoglobulin (IVIg)/anti-D or corticosteroid (CS) that was not sustained and failed ≥1 other ITP therapy (that was not IVIg or CS). Stable doses of concomitant CS/thrombopoietin receptor agonists (TPO-RA) were allowed with rilzabrutinib. The primary endpoints for part B were safety and durable platelet response defined as platelet counts ≥50x10 ^{9}/L on ≥8 of the last 12 weeks of rilzabrutinib without rescue medication. Patients completing 24 weeks of rilzabrutinib with platelet counts ≥50x10 ^{9}/L or ≥30x10 ^{9}/L and doubling from baseline in ≥4 of the last 8 weeks of treatment without rescue medication could continue rilzabrutinib in the long-term extension (LTE) period.
Results: At baseline, 26 enrolled patients had a median age of 57 y (range, 20-75), 62% were female, and median baseline platelet count was 13x10 ^{9}/L (range, 2-24x10 ^{9}/L). Patients had a median duration of ITP of 10.3 y (range, 0.7-48.2) and had received a median of 6 prior unique ITP therapies (range, 3-19; 46% splenectomy). Seventeen patients (65%) received concomitant non-rescue CS and/or TPO-RA. Nine patients (35%; 95% CI, 17%-56%) achieved the primary endpoint of durable

platelet response. Approximately 25% of patients achieved platelet counts ≥50x10 ^{9}/L by day 15 of rilzabrutinib treatment (Figure 1A). In 16 patients who achieved platelet counts ≥50x10 ^{9}/L, median time to first platelet count ≥50x10 ^{9}/L was 15 days (range, 7-134). Median platelet counts for all patients (responders and non-responders) increased over time, exceeding the platelet count thresholds of 30x10 ^{9}/L at day 57 and 50x10 ^{9}/L at day 120 (Figure 1B). The mean number of weeks with platelet counts ≥50x10 ^{9}/L and/or ≥30x10 ^{9}/L and doubling from baseline was both 9.3 weeks (SD, 10.1). Three patients (12%) received rescue medication in the main treatment period. Fifteen patients (58%) completed 24 weeks of rilzabrutinib and 11 (42%) entered the LTE.

Over the main treatment period, the median duration of treatment was 167 days (range, 7-169). Sixteen patients (62%) had ≥1 related treatment-emergent adverse event (AE), including 35% diarrhea, 23% headache, and 15% nausea. Most AEs were grade 1 or 2; there was 1 treatment-related AE of grade 3 blood creatinine phosphokinase increase. There was no treatment-related grade ≥2 bleeding/thrombotic events or infections, serious AEs, or deaths.

Conclusion: Part B study results were consistent with part A. Rilzabrutinib demonstrated rapid, stable, and durable platelet responses in patients with relapsed ITP, with a favorable safety profile in part B.

Disclosures Cooper: *Sobi:* Honoraria; *Sanofi:* Honoraria; *Novartis:* Honoraria, Research Funding; *Rigel:* Research Funding. **Jansen:** *Erasmus MC:* Current Employment; *Principia, Argenx, Sobi, Sanofi, CSL Behring:* Research Funding; *European Patent Office:* Patents & Royalties: P133951EP00; *Novartis, 3SBIO, Amgen, Sobi:* Speakers Bureau; *Novartis, Sanofi:* Membership on an entity's Board of Directors or advisory committees; *3SBIO, Novartis, Amgen:* Other: Travel, accommodations, expenses. **Bird:** *Amgen:* Speakers Bureau; *Rigel:* Research Funding; *Principia (Sanofi):* Research Funding. **Mayer:** *MSD:* Research Funding; *Novartis:* Research Funding. **Sholzberg:** *CSL Behring:* Research Funding; *Pfizer:* Honoraria, Research Funding; *Octapharma:* Honoraria, Research Funding. **Tarantino:** *Genentech:* Consultancy; *Biomarin:* Consultancy; *Novartis:* Consultancy; *Octapharma:* Consultancy, Other: Clinical trial investigator; *Principia:* Consultancy; *Spark:* Other: Clinical trial investigator; *Takeda:* Other: Clinical trial investigator, Research Funding; *Amgen:* Consultancy. **Garg:** *Janssen:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel, Accommodations, Expenses, Research Funding, Speakers Bureau; *Amgen:* Membership on an entity's Board of Directors or advisory committees, Other: Travel, Accommodations, Expenses, Research Funding, Speakers Bureau; *Alnylam:* Honoraria, Speakers Bureau; *Celgene:* Membership on an entity's Board of Directors or advisory committees; *Stemline Therapeutics:* Membership on an entity's Board of Directors or advisory committees, Other: Travel, Accommodations, Expenses; *Janssen:* Membership on an entity's Board of Directors or advisory committees. **Ypma:** *Janssen:* Honoraria; *Janssen:* Other: support for attending meetings and/or travel. **McDonald:** *Sobi:* Consultancy; *Novartis:* Consultancy; *Amgen:* Consultancy; *Grifols:* Research Funding; *Rigel:* Research Funding. **Percy:** *Roche-Chugai:* Consultancy, Honoraria, Speakers Bureau; *Novo Nordisk:* Consultancy, Honoraria, Speakers Bureau; *Takeda:* Consultancy, Honoraria, Speakers Bureau; *Sobi:* Consultancy, Honoraria, Speakers Bureau; *LFB:* Consultancy, Honoraria, Speakers Bureau; *University Hospitals Birmingham NHS Foundation Trust:* Current Employment. **Košťál:** *Principia Biopharma Inc, a Sanofi Company:* Consultancy. **Gernsheimer:** *Alpine Immune Science:* Consultancy. **Diab:** *Sanofi:* Current Employment. **Yao:** *Sanofi:* Current Employment. **Daak:** *Sanofi:* Current Employment. **Kuter:** *Rubius:* Current equity holder in publicly-traded company; *AIRx, Alexion (Syntimmune), Alnylam, Alpine, Amgen, argenx, BioCryst, Bristol Myers Squibb (BMS), Caremark, Cellularity, Cellphire, Chugai, CRICO, Daiichi Sankyo, Dianthus, Electra Therapeutics, Fuji, Hemopure, Hengrui. Immunovant, Incyte, Inmagenebio:* Consultancy; *AIRx, Alexion (Syntimmune), Alnylam, Alpine, Amgen, Argenx, BioCryst, Bristol Myers Squibb (BMS), Caremark, Cellularity, Cellphire, Chugai, CRICO, Daiichi Sankyo, Dianthus, Electra Therapeutics, Fuji, Hemopure, Hengrui, Immunovant, Incyte, Inmagenebio, Ke:* Honoraria; *UpToDate:* Patents & Royalties: UpToDate Chapters; *Platelet Disorder Support Association:* Membership on an entity's Board of Directors or advisory committees; *Kezar, Kyowa-Kirin, Merck Sharp & Dohme:* Honoraria; *Kezar, Kyowa-Kirin, Merck Sharp Dohme, Momenta, Novartis, Nuvig, Pfizer, Platelet Biogenesis, Platelet Disorder Support Association, Protagonist, Rigel, Sanofi (Bioveratif), Sanofi (Principia), Sanofi (Genzyme), Sobi (Dova), Takeda, UCB, Up-To-Date, Zafge:* Consultancy; *Alnylam, BioCryst, Novartis, Rigel, Sanofi (Principia), Takeda (Bioverativ), and UCB:* Research Funding.

OffLabel 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.

Figure 1. For all ITP patients receiving rilzabrutinib treatment: (A) Time to first platelet response ≥50×10^9/L and (B) Median platelet count by visit. Note: In 16 patients who achieved platelet counts ≥50×10^9/L, median time to first platelet count ≥50×10^9/L was 15 days (range, 7-134).

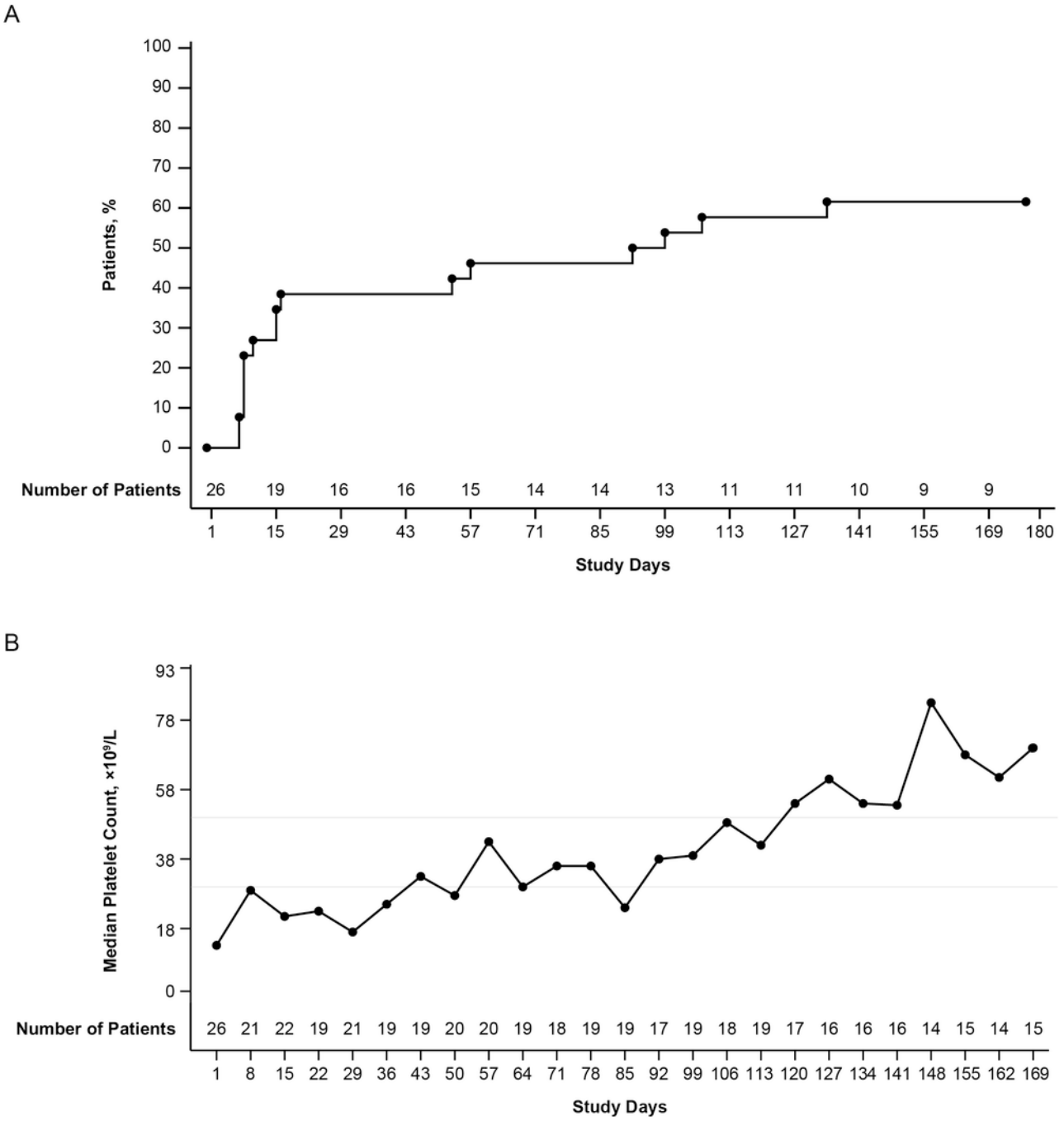

Figure 1

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