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ORIGINAL ARTICLE

Antibody-Based Ticagrelor Reversal Agent in Healthy Volunteers

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RobotReviewer report

Here are the results from 1 PDFs. Risk of bias table

trial	design	n	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment
antagonista del Ticagrelor (Brilique, Astra Zeneca).pdf	RCT	64	?	?	+	?

Characteristics of studies

antagonista del Ticagrelor (Brilique, Astra Zeneca).pdf

Population	1. Trial Design and Oversight We conducted a single-center, randomized, doubleblind , placebo-controlled, single-ascending-dose, phase 1 trial to evaluate the safety, efficacy, and pharmacokinetic profiles of PB2452 in healthy volunteers 18 to 50 years of age who were pretreated with ticagrelor. 2. In particular, dual antiplatelet therapy ‚Äî the combination of aspirin with an oral P2Y 12 receptor antagonist ‚Äî is the predominant approach in patients with acute coronary syndromes, coronary-artery stenting, or previous myocardial infarction.
Intervention	1. Cohorts 7 through 10 consisted of volunteers who were assigned to receive an 18.0-g fixed dose of PB2452 according to one of four infusion regimens or placebo after ticagrelor pretreatment . 2. Volunteers in cohorts 4 through 10 were pretreated with a 180-mg loading dose of oral ticagrelor at 7 a.m. on day ‚à2, and then with a 90-mg dose every 12 hours starting at 7 p.m. on day ‚à2, for a total of five doses and 48 hours of pretreatment before the evaluation of PB2452. 3. Cohorts 1, 2, and 3 each consisted of four volunteers who were randomly assigned to receive a 30-minute infusion of PB2452 at a dose of 0.1 g, 0.3 g, and 1.0 g, respectively, or placebo, in the absence of ticagrelor pretreatment, to assess the initial safety of PB2452.

Outcomes	1. The primary efficacy outcome was reversal of the antiplatelet effects of ticagrelor as assessed by analysis of platelet aggregation with the use of light transmission aggregometry at multiple time points before and after the administration of PB2452 or placebo in volunteers who were pretreated with ticagrelor. 2. The primary safety outcome was the frequency and severity of adverse events that occurred after the initiation of PB2452 or placebo. 3. Other secondary outcomes included the pharmacokinetic profiles of PB2452 and ticagrelor.

Bias	Judgement	Support for judgement
Random sequence generation	high/ unclear	1. Trial Design and Oversight We conducted a single-center, randomized, doubleblind , placebo-controlled, single-ascending-dose, phase 1 trial to evaluate the safety, efficacy, and pharmacokinetic profiles of PB2452 in healthy volunteers 18 to 50 years of age who were pretreated with ticagrelor. 2. Shown are the onset and duration of ticagrelor reversal among volunteers in cohorts 4, 5, and 6, who were randomly assigned to receive either a 30-minute infusion of PB2452 at a dose of 1 g, 3 g, and 9 g, respectively, or placebo (Panel A), as well as among volunteers in cohorts 7, 8, 9, and 10, who were randomly assigned to receive an 18-g fixed dose of PB2452 with an infusion duration of 8 hours, 12 hours, 16 hours, and 16 hours, respectively, or placebo (Panel B). 3. Cohorts 1, 2, and 3 each consisted of four volunteers who were randomly assigned to receive a 30-minute infusion of PB2452 at a dose of 0.1 g, 0.3 g, and 1.0 g, respectively, or placebo, in the absence of ticagrelor pretreatment, to assess the initial safety of PB2452.
Allocation concealment	high/ unclear	1. Trial Design and Oversight We conducted a single-center, randomized, doubleblind , placebo-controlled, single-ascending-dose, phase 1 trial to evaluate the safety, efficacy, and pharmacokinetic profiles of PB2452 in healthy volunteers 18 to 50 years of age who were pretreated with ticagrelor. 2. Shown are the onset and duration of ticagrelor reversal among volunteers in cohorts 4, 5, and 6, who were randomly assigned to receive either a 30-minute infusion of PB2452 at a dose of 1 g, 3 g, and 9 g, respectively, or placebo (Panel A), as well as among volunteers in cohorts 7, 8, 9, and 10, who were randomly assigned to receive an 18-g fixed dose of PB2452 with an infusion duration of 8 hours, 12 hours, 16 hours, and 16 hours, respectively, or placebo (Panel B). 3. Details regarding the final trial design and regarding enrollment , randomization, and follow-up are shown in Table S1and Figure S1, respectively, in the Supplementary Appendix.
Blinding of participants and personnel	low	1. Shown are the onset and duration of ticagrelor reversal among volunteers in cohorts 4, 5, and 6, who were randomly assigned to receive either a 30-minute infusion of PB2452 at a dose of 1 g, 3 g, and 9 g, respectively, or placebo (Panel A), as well as among volunteers in cohorts 7, 8, 9, and 10, who were randomly assigned to receive an 18-g fixed dose of PB2452 with an infusion duration of 8 hours, 12 hours, 16 hours, and 16 hours, respectively, or placebo (Panel B). 2. Pharmaceutical Product Development was responsible for the collection and handling of the data. 3. RESULTS Of the 64 volunteers who underwent randomization, 48

		were assigned to receive PB2452 and 16 to receive placebo.
Blinding of outcome assessment	high/ unclear	1. The primary efficacy outcome was reversal of the antiplatelet effects of ticagrelor as assessed by analysis of platelet aggregation with the use of light transmission aggregometry at multiple time points before and after the administration of PB2452 or placebo in volunteers who were pretreated with ticagrelor. 2. Trial Design and Oversight We conducted a single-center, randomized, doubleblind , placebo-controlled, single-ascending-dose, phase 1 trial to evaluate the safety, efficacy, and pharmacokinetic profiles of PB2452 in healthy volunteers 18 to 50 years of age who were pretreated with ticagrelor. 3. Shown are the onset and duration of ticagrelor reversal among volunteers in cohorts 4, 5, and 6, who were randomly assigned to receive either a 30-minute infusion of PB2452 at a dose of 1 g, 3 g, and 9 g, respectively, or placebo (Panel A), as well as among volunteers in cohorts 7, 8, 9, and 10, who were randomly assigned to receive an 18-g fixed dose of PB2452 with an infusion duration of 8 hours, 12 hours, 16 hours, and 16 hours, respectively, or placebo (Panel B).