Comparison of Anti-coagulation and anti-Platelet Therapies for Intracranial Vascular Atherostenosis (CAPTIVA) Trial

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Financial Disclosures

Janssen is providing rivaroxaban and funding for placebo.
AstraZeneca is providing ticagrelor.
BH: Progressive Neuro, Galaxy Therapeutics, PropioVision
TT: Up-to-Date
SY: CR Bard
JB: Genentech, Roche, Brainsgate, Basking Bioscience
MC: Medtronic, Boerhinger Ingelheim
RM, JS, RB, LC, SJ, AS, JF: none

Background

Symptomatic intracranial atherosclerotic stenosis (sICAS) is one of the most common causes of stroke worldwide. Current treatment consists of risk factor management and dual antiplatelet therapy with clopidogrel and aspirin for 90 days then aspirin alone. However, the 1-year rate of symptomatic infarct, intracranial hemorrhage (ICH) or vascular death was 27% in the medical arm participants in SAMMPRIS who qualified with symptomatic infarct.

Recent data suggests ticagrelor and aspirin may be more effective than clopidogrel and aspirin for sICAS. In PRINCE, the 90-day stroke rate in participants with large artery atherosclerosis was significantly lower with ticagrelor and aspirin (6.0%) vs clopidogrel and aspirin (13.1%) (P=0.04) with no increase in major hemorrhage, but with a higher rate of any bleeding (22.3% vs 14.2%, P=0.007) and dyspnea (4.2% vs 0%, P<0.001).

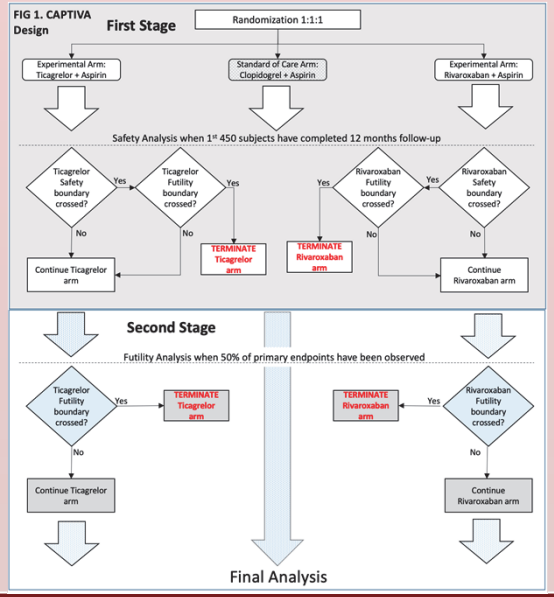
Mechanistic and clinical trial data also support studying low dose rivaroxaban and aspirin for sICAS. Combining an anticoagulant with aspirin addresses both increased platelet and procoagulant activity in sICAS. In COMPASS, participants randomized to low dose rivaroxaban and aspirin had significantly fewer strokes (ischemic or hemorrhagic) than aspirin alone: 0.9% vs. 1.6% (P<0.0001).

Objective

To determine if rivaroxaban and aspirin or ticagrelor and aspirin are superior to clopidogrel and aspirin for lowering the 1-year rate of the primary endpoint (ischemic stroke, ICH, or vascular death).

Methods and Material

Design/Population Studied/Intervention: CAPTIVA is a two-stage Phase III 3-arm, double-blind trial in which patients with symptomatic infarct in the territory of 70-99% sICAS (n=1683) will be randomized 1:1:1 to 1-year treatment of ticagrelor and aspirin, low dose rivaroxaban and aspirin, or clopidogrel and aspirin. All participants will receive intensive risk factor management.
Outcome Measures/Analysis: The first stage will assess whether there is an excess of ICH or non-ICH major hemorrhage in the rivaroxaban or ticagrelor arms of the trial that could lead to an early termination of one or both of those arms.
The second stage will determine if the experimental arm(s) (rivaroxaban or ticagrelor) that progress to the second stage are superior to the clopidogrel arm for lowering the 1-year rate of the primary endpoint (ischemic stroke, ICH, or vascular death).



American Stroke Association
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Summary

1683 subjects with symptomatic infarct due to 70-99% sICAS
1 year treatment & follow-up
First Stage: Safety Analysis
1.Parenchymal brain hemorrhage (ICH)
2.Major non-ICH hemorrhage (ISTH criteria)
Second Stage: Primary Endpoint
1.Ischemic stroke (AHA definition Sacco et al, Stroke 2013)
2.ICH
3.Vascular death
Secondary Endpoints
1.Composite of the primary endpoint and MI
2.All stroke (ischemic and ICH)
3.Ischemic Stroke
4.Ischemic stroke in the territory of the qualifying stenotic artery
5.All death
Exploratory Aim: To estimate the impact of CYP2C19 LOF carrier status on any benefit that the ticagrelor or low dose rivaroxaban arms may have in lowering the primary endpoint compared with the clopidogrel arm.

Discussion

Site investigators meeting planned for March 2022.

Subject enrollment planned to begin April 2022.

Any questions, please email: CAPTIVA-study@ufl.edu

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CAPTIVA (Comparison Of Anti-coagulation And Anti-platelet Therapies For Intracranial Vascular Atherostenosis) Trial

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Multicenter Trial

CT P1 | *Ongoing Clinical Trials Posters II*

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Background: Symptomatic intracranial atherosclerotic stenosis (sICAS) is one of the most common causes of stroke worldwide. Current treatment consists of risk factor management and dual antiplatelet therapy with clopidogrel and aspirin for 90 days then aspirin alone. However, the 1-year rate of symptomatic infarct, intracranial hemorrhage (ICH) or vascular death was 27% in the medical arm participants in SAMMPRIS who qualified with symptomatic infarct. Recent data suggests ticagrelor and aspirin may be more effective than clopidogrel and aspirin for sICAS. In PRINCE, the 90-day stroke rate in participants with large artery atherosclerosis was significantly lower with ticagrelor and aspirin (6.0%) vs clopidogrel and aspirin (13.1%) (P=0.04). Mechanistic and clinical trial data also support low dose rivaroxaban and aspirin for sICAS. Combining an anticoagulant with aspirin addresses both increased platelet and procoagulant activity in sICAS. In COMPASS, participants randomized to low dose rivaroxaban and aspirin had significantly fewer strokes (ischemic or hemorrhagic) than aspirin alone: 0.9% vs. 1.6% (P<0.0001). Objective: To determine if rivaroxaban and aspirin or ticagrelor and aspirin are superior to clopidogrel and aspirin for lowering the 1-year rate of the primary endpoint (ischemic stroke, ICH, or vascular death). Design/Population Studied/Intervention: CAPTIVA is a two-stage Phase III 3-arm, double-blind trial in which patients with symptomatic infarct in the territory of 70-99% sICAS (n=1683) will be randomized 1:1:1 to 1-year treatment of ticagrelor and aspirin, low dose rivaroxaban and aspirin, or clopidogrel and aspirin. All participants will receive intensive risk factor management. Outcome Measures/Analysis: The first stage will assess whether there is an excess of ICH or non-ICH major hemorrhage in the rivaroxaban or ticagrelor arms of the trial that could lead to an early termination of one or both of those arms. The second stage will determine if the experimental arm(s) (rivaroxaban or ticagrelor) that progress to the second stage are superior to the clopidogrel arm for lowering the 1-year rate of the primary endpoint (ischemic stroke, ICH, or vascular death). Trial Status: Anticipate enrollment beginning January 2022.

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