POINT: Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke Trial

Objective: To determine whether clopidogrel 75 mg/day by mouth after a loading dose of 600 mg of clopidogrel is effective in preventing major ischemic vascular events (ischemic stroke, myocardial infarction, and ischemic vascular death) at 90 days when initiated within 12 hours of TIA or minor ischemic stroke onset in patients receiving aspirin 50-325 mg/day (with a dose of 162 mg daily for 5 days followed by 81 mg daily strongly recommended).

Study Design: A prospective, randomized, double-blind, multicenter trial with the primary null hypothesis that, in patients with TIA or minor ischemic stroke treated with aspirin 50-325 mg/day, there is no difference in the event-free survival at 90 days in those treated with Clopidogrel (600 mg loading dose then 75 mg/day) compared to placebo when therapy is initiated within 12 hours of onset.

Number of Subjects: Total sample size for the study is 4,150 subjects.

Inclusion/Exclusion Criteria
Inclusion Criteria
1. Neurologic deficit (based on history or exam) attributed to focal brain ischemia and
   EITHER:
   High risk TIA: Complete resolution of the deficit at the time of randomization
   AND ABCD2 score ≥ 4
   OR
   Minor ischemic stroke: residual deficit with NIHSS ≤ 3 at the time of randomization
2. Ability to randomize within 12 hours of time last known free of new ischemic symptoms.
3. Head CT or MRI ruling out hemorrhage or other pathology, such as vascular malformation, tumor, or abscess, that could explain symptoms or contraindicate therapy.
4. Ability to tolerate aspirin at a dose of 50-325 mg/day.

Exclusion Criteria
1. Age < 18 years.
2. TIA symptoms limited to isolated numbness, isolated visual changes, or isolated dizziness/vertigo.
3. In the judgment of the treating physician, a candidate for thrombolysis, endarterectomy or endovascular intervention, unless the subject declines both
endarterectomy and endovascular intervention at the time of evaluation for eligibility.

4. Receipt of any intravenous or intra-arterial thrombolysis within 1 week prior to index event.

5. Gastrointestinal bleed or major surgery within 3 months prior to index event.


7. Clear indication for anticoagulation (e.g., warfarin, heparin) anticipated during the study period (atrial fibrillation, mechanical heart valve, deep venous thrombosis, pulmonary embolism, antiphospholipid antibody syndrome, hypercoagulable state).

8. Qualifying ischemic event induced by angiography or surgery.

9. Severe non-cardiovascular comorbidity with life expectancy <3 months.

10. Contraindication to clopidogrel or aspirin:
    a. Known allergy
    b. Severe renal (serum creatinine >2 mg/dL) or hepatic insufficiency (prior or concurrent diagnosis, with INR>1.5, or any resultant complication, such as variceal bleeding, encephalopathy, or icterus)
    c. Hemostatic disorder or systemic bleeding in the past 3 months
    d. Current thrombocytopenia (platelet count <100 x10^9/l) or neutropenia/granulocytopenia (<1 x10^9/l)
    e. History of drug-induced hematologic or hepatic abnormalities

11. Anticipated requirement for long-term (>7 day) non-study antiplatelet drugs (e.g., dipyridamole, clopidogrel, ticlopidine), or NSAIDs affecting platelet function (such as prior vascular stent or arthritis).

12. Not willing or able to discontinue prohibited concomitant medications.

13. Inability to swallow medications.

14. At risk for pregnancy: premenopausal or post-menopausal woman within 12 months of last menses without a negative pregnancy test or not committing to adequate birth control (e.g., oral contraceptive, two methods of barrier birth control, or abstinence).

15. Unavailability for follow-up.

16. Signed and dated informed consent not obtained from patient.

17. Other neurological conditions that would complicate assessment of outcomes during follow-up.

18. Ongoing treatment in another study of an investigational therapy or treatment in such a study within the last 7 days.

19. Previously enrolled in the POINT study.