Safety and Efficacy of Intravenous Eptifibatide as Standalone Therapy for select Acute Ischemic Stroke Patients (SIESTA-I trial)

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What is Eptifibatide?
Trade name: Integrillin

- Glycoprotein IIb/IIIa inhibitor
- *Reversible* anti-platelet
- *Short* half-life (2.5 hours)
- *Intravenous* administration
- Other drugs in same class
  - Abciximab (ReoPro)
  - Tirofiban (Aggrastat)
Inhibition of platelet glycoprotein IIb/IIIa with eptifibatide in patients with acute coronary syndromes. The PURSUIT Trial Investigators. Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrillin Therapy.

**Conclusion:** Inhibition of platelet aggregation with eptifibatide reduced the incidence of the composite end point of death or nonfatal myocardial infarction in patients with acute coronary syndromes who did not have persistent ST-segment elevation.
Therapeutic potential of platelet glycoprotein IIb/IIIa receptor antagonists in acute ischemic stroke: scientific rationale and available evidence.

**Conclusion:** GP IIb/IIIa receptor antagonists are a proven component of care in ischemic coronary syndromes and have similar potential for benefit in ischemic stroke. Ongoing research offers hope.
CLEAR Stroke Trial

Stroke. 2008; 39:3268-3276
Pancioli A et al.

The Combined Approach to Lysis Utilizing Eptifibatide and rt-PA in Acute Ischemic Stroke

**Conclusion:** The safety of combination of reduced-dose rt-PA plus eptifibatide justifies further dose-ranging trials in acute ischemic stroke.
CLEAR-ER Stroke Trial

Stroke. 2013; 44:2381-2387
Pancioli A et al.

Combined Approach to Lysis Utilizing Eptifibatide and rt-PA in Acute Ischemic Stroke-Enhanced Regimen

**Conclusion:** The combined regimen of intravenous rt-PA and eptifibatide studied in this trial was safe and provides evidence that a phase III trial is warranted to determine efficacy of the regimen.
How about patients not candidates for IV r-tPa....
Safety and Efficacy of Intravenous Eptifibatide as Standalone Therapy for select Acute Ischemic Stroke Patients (SIESTA-I trial)

• Result of an open labeled retrospective registry to evaluate the safety (in regards to hemorrhagic complications) and efficacy (regarding discharge NIHSS) of administering high dose IV Eptifibatide as a standalone therapy for acute stroke in patients ineligible for IV r-tPa or neurointervention.
Methods

- All patients with acute ischemic events between 2010-13 were included that presented to our university affiliated comprehensive stroke center.

- Patients that received Eptifibatide as standalone therapy were reviewed. Eptifibatide was administered intravenously as a 135-μg/kg single-dose bolus, then a 0.5-μg/kg/min infusion.

- Charts were reviewed for all patients to assess for primary safety and efficacy endpoint.
Methods

• The primary safety endpoint was bleeding. Bleeding complications were classified as major (symptomatic intracranial hemorrhage and hemoglobin decrease by >5mg/dl), minor (hemoglobin decrease 3-5 mg/dl) and insignificant as proposed by the TIMI score (Thrombolysis in Myocardial Infarction).

• The primary efficacy end point was neurological improvement/deterioration as defined by a change in discharge NIHSS by > 4 points compared to initial NIHSS respectively.
Case Report

- 51 year old female presented with an 18 hour history of left facial droop, left upper and lower extremity hemiparesis (NIHSS 6).

- CT head showed right basal ganglia hypodensity.

- CT angiogram showed near occlusive clot at distal right Middle Cerebral Artery (MCA).
Case Report-cont’d

- Patient was out of time window for intravenous rt-PA or intra-arterial intervention. IV eptifibatide bolus followed by continuous drip was administered for 20 hours with improvement of NIHSS from 6 to 1 (left upper extremity drift). MRA at 72 hours revealed subtotal recanalization of Right MCA.
Results

• Of a total patient population of 2,329, 20 patients (mean age of 73, 50% male (n=10)) received Eptifibatide administered intravenously for a mean duration of 32.5 hours (range 17-67 hours).

• No major or minor bleeding was observed except for a patient who exhibited minor complication of knee hemarthroses.

• 9 patients demonstrated early neurological improvement with only 2 exhibiting neurological deterioration related to extension of ischemic core.
Conclusion

• Application of IV Eptifibatide in achieving recanalization and preventing extension may be a safe standalone therapy in acute ischemic stroke patients ineligible for other neurological interventions.

• Larger randomized trials are required to corroborate our findings.
Thank You!
Abciximab in Emergency Stroke Treatment Trial-II

Stroke, 2008; 39:3277-3282
Adams H. et. Al


Conclusion: Halted early because of increase rate of ICH