STRIVE-ON: Safety and TolerRability of GTX-104 (IntraVenous NimodipinE) Versus Oral Nimodipine in Aneurysmal Subarachnoid Hemorrhage: a Prospective, Randomized Trial

Choi A, Chou SH-Y, Ducruet A, Kimberly WT, **Macdonald RL**, Rabinstein AA

Acasti Pharma USA, Princeton NJ

International Stroke Conference

Study Highlights

- Aneurysmal subarachnoid hemorrhage (aSAH) patients
- Phase 3
- Prospective, open-label, randomized (1:1 ratio)
- Subjects randomized to
  - GTX-104 (intravenous [IV] formulation of nimodipine)
  - Standard of care oral nimodipine capsules
- Study consists of 3 phases:
  - Pre-randomization (screening)
  - Treatment phase (21 days)
  - Follow-up
- 100 subjects, approximately 25 sites in the USA

Investigational Products

- GTX-104
  - Nimodipine dispersed in micelles in aqueous solution for IV infusion
    - Dose is continuous IV infusion of 0.15 mg/hour AND IV bolus of 4 mg every 4 hours
    - This dose provides same pharmacokinetics as standard oral dose of nimodipine
    - Duration up to 21 days or until the subject is transferred to a location that cannot administer IP
- Oral nimodipine (provided by Acasti)
  - 60 mg (two 30 mg capsules) every 4 hours for up to 21 days, preferably in a fasting state (more than 1 hour before or 2 hours after meals)

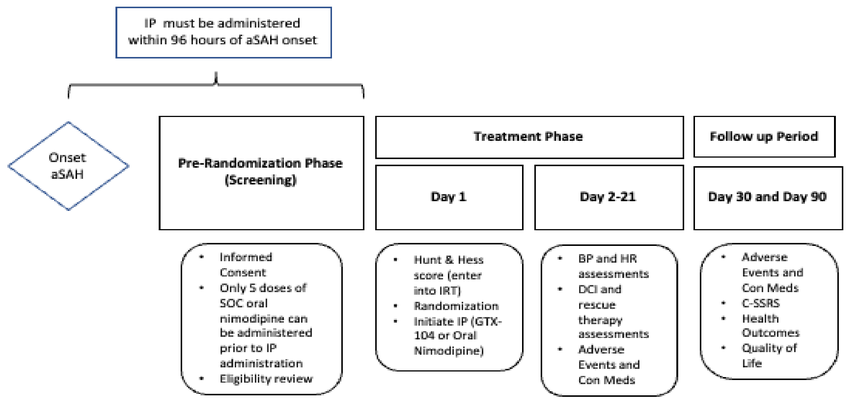
Safety Assessments

- This is primarily a safety study (100 subjects, 50 IV and 50 oral nimodipine)
- There is no sample size estimation or statistical analysis planned
- Safety assessments include
  - Close monitoring of blood pressure while subjects are taking IP
  - 12-lead ECGs
  - Clinical laboratory values
  - All adverse events
  - Delayed cerebral ischemia and use of rescue therapy

Study Objectives and Endpoints

Objectives	Safety Endpoints
To evaluate the safety and tolerability of GTX-104 compared to oral nimodipine	**Primary** Incidence (% or proportion) of subjects with at least 1 episode of clinically significant hypotension with a reasonable possibility that GTX-104/oral nimodipine caused the event
	Secondary • Duration and total number of episodes of clinically significant hypotension • Incidence and severity of Adverse Events (AEs) • Incidence of delayed cerebral ischemia (DCI) and rescue therapy • Suicidal ideation using the Columbia-Suicide Severity Rating Scale (C-SSRS) score of ≥ 4
To evaluate the clinical and health economic outcomes of GTX-104 and oral nimodipine	**Clinical and Health Economic Outcomes (to day 90)** • Durations and number of hospital and intensive care unit (ICU) stays • Duration of mechanical ventilation • Therapeutic Intensity Scale • Hospital discharge disposition (e.g., home, rehabilitation, long-term care) • Quality of Life as measured by EQ-5D-3L • Modified Rankin Scale (mRS)

Study Design



Note: Aneurysm repair can be performed after screening.

aSAH: aneurysmal subarachnoid hemorrhage; BP: blood pressure; C-SSRS: Columbia-Suicide Severity Rating Scale; DCI: delayed cerebral ischemia; HR: heart rate; IP: Investigational Product ; IRT: interactive response technology; SOC: standard of care,

Key Inclusion and Exclusion Criteria

- **Inclusion**
  - Male or female ≥ 18 years of age
  - aSAH based on CT scan and angiography (CTA, DSA, MRA)
  - **Hunt and Hess assessment scores from I to V just prior to randomization**
  - Informed consent before any study-specific procedures are performed
  - **Able to start IP within 96 hours from the onset of aSAH**
- **Exclusion**
  - Received less than 12 doses of oral nimodipine before randomization
  - Cardiovascular events (CPR at time of aSAH, hypotension, heart block, etc.)
  - Liver failure, elevated liver enzymes
  - Contraindications to nimodipine capsules (allergy to nimodipine, taking strong CYP3A4 inhibitors)

Definition of Primary Endpoint - Hypotension

- Hypotension is defined as:
  - Decrease in systolic BP > 20 mm Hg or diastolic BP > 10 mm Hg, or systolic BP ≤ 100 mm Hg, confirmed by 2 consecutive readings within 5 minutes
- Categorized as:
  - **Not clinically significant (NCS):** not requiring any medical treatment (pharmacotherapy or other intervention)
  - **Clinically significant (CS):** requiring medical treatment, including but not limited to intravenous fluids, postural changes, dose reduction of IP, interruption of antihypertensive medications, prescription of vasopressors, increasing dose of a vasopressor, or addition of a new vasopressor

Follow-up Period

- Day 30 (± 7 days) and Day 90 (± 10 days)
- Assessments include:
  - Adverse events, concomitant medications and procedures
  - Columbia-suicide severity rating scale, if capable
  - Quality of life (EQ-5D-3L)
  - Modified Rankin scale

CONTACT FOR QUESTIONS

R. Loch Macdonald, Chief Medical Officer, Acasti Pharma
l.macdonald@acasti.com

RESEARCH POSTER PRESENTATION DESIGN © 2015
www.PosterPresentations.com