Research participation & clinical trials - without you, there can be no cure!

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Chief Scientific Officer, Angioma Alliance
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Pre-Clinical | Phase One | Phase Two | Phase Three
---|---|---|---
**RHO KINASE INHIBITORS**
- LIPITOR (Atorvastatin) – Enrolling September 2018
- BA-1049
- Lescol & Reclast

**SUPEROXIDE DISMUTASE**
- REC-994 (Tempol) – Enrolling Late 2018

**INFLAMMATORY INHIBITORS**
- Sulindac
- B-cell Depletion

**NUTRITIONAL SUPPLEMENT**
- Vitamin D3

**BETA BLOCKER**
- Propranolol - Italian study now enrolling

**MICROBIOME**
- Gut Bacteria

**ANGIOGENESIS INHIBITOR**
- Thrombospondin1
Considerations for Trial Design

• Rare Disease Population

Knowledge Gaps

• Variable Clinical Symptoms

• What to measure?
  • Clinical Endpoints
    • Hemorrhage
    • Quality of Life
  • Surrogate Endpoints
    • Imaging Biomarkers
Would you like to participate in Research?

Stop

Yes

No

Clinical Drug Trials

Learn more about Research Studies

Have you experienced hemorrhage within the last 12 months?

No

Yes

Learn more about Research Studies

Have you been treated with a statin drug within the last 12 months?

No

Yes

Learn more about Research Studies

Are you willing to travel to the University of Chicago 3 times over the next 2 years?

No

Yes

Learn more about Research Studies

AT CASH EPOC

Research Studies

Have you had a recent or upcoming surgical resection?

No

Yes

DNA/Tissue Bank

Do you have a brain stem lesion (or had one removed surgically)?

No

Yes

Quality of life in patients with brainstem malformations

Have you experienced hemorrhage within the last 12 months?

No

Yes

CASH Trial Readiness (Multiple sites)

Does cavernous angioma run in your family?

Don’t Know

No

Yes

BVMC and/or Microbiome Study (Multiple sites)

Learn more about sporadic cavernous angioma

Microbiome Study (University of Chicago Site, only)
DNA & Tissue Bank

• Providing Resources to Researchers
• Why?
  • Clinical Records provide data for natural history & disease progression
  • Tissues samples help us understand better the biology of the lesion
• How can you help?
  • Currently enrolling those scheduled for upcoming surgery
• What is involved?
Quality of Life - Brainstem Lesions

• Why
  • To provide data on clinical management of brainstem lesions

• How can you help?
  • Enrolling study participants through the end of 2018

• What is involved?
  • Up to 1 hour of answering several health-related questionnaires
Brain Vascular Malformation Consortium

• Why?
  • Natural History & Endpoint Definition

• How?
  • Develop a clinical registry, investigate natural history & Biomarkers
  • Modifiers of lesion burden/disease severity

• How can you help?
  • Enroll at your local site, or remotely
BVMC Key Findings & Continuing Work

• Genetic Risk Factors - Polymorphisms in inflammatory and immune response pathways contribute to variability.
• BVMC data supports microbiome research in humans

Drug Hypothesis: Change bacteria in gut, or block TRL4 to prevent lesion development
Endpoints

• Clinical endpoints related to patient health
  • Hemorrhage
  • Seizures
  • Focal neurological deficits without hem
  • Headaches (common but non-specific)
  • Neurological function
  • Lesion growth & number
  • Functional outcome (mRS, NeuroQoL)
CCM Health Index

• Why?
  • To develop a tool to measure the quality of life of our community

• How you can help?
  • Phase I: to enroll 20 participants for focus groups
  • Phase II: to enroll 40 participants to test question reliability
  • Phase III: to enroll several hundred to assess validity of Index (year 2)
Developing the CCM Health Index

1. Qualitative Research
   - CCM Patient Interviews
   - Survey Second Group of CCM Patients

2. Developing the Tool
   - Follow FDA & Psychometric Research Protocols

3. Validation Testing
   - Beta-Test CCM-HI
   - New CCM Patients & Semi-Structured Interviews
   - Re-test with Patients Categories into like-symptom Groups

   Determine most important Symptoms for CCM Patients
   Validate Items of Importance & Remove Unimportant Items
   Develop First Draft of CCM-Health Index
   Optimize & Remove Unimportant or Confusing Questions
   Finalize Paper Version of CCM-HI

Year 1 - Development
Year 2 - Validation
Endpoints

• Clinical endpoints related to patient health
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Prepare for large multi-center trials by assessing the knowledge gaps:
1. Analyze potential participation numbers & recruitment rate
2. Validate imaging biomarkers across sites
3. Annual follow-up (subset of participants)
CASH Trial Readiness Participation

• At local site, baseline & clinical history
• Research MRI & labs
• Follow-up for 2 years

• Research Goals
  • Identify/confirm participant cohort
  • Validate imaging biomarkers for multi-center trials
Biomarkers – Dynamic Contrast-Enhanced Quantitative Perfusion Assess Permeability

Biomarkers – Quantitative Susceptibility Maps Assess Iron Concentration

Tan et al. *Investigative Radiology*, 2014
Clinical Trials

a drug development journey

**Phase I**
- **Duration**: < 1 year
- **Volunteers**: 20-100 Healthy volunteers for new drugs
- **Purpose**: Safety

**Phase II**
- **Duration**: 1-2 years
- **Volunteers**: 100-200 Cavernous Angioma Patients
- **Purpose**: Safety, efficacy & dosing

**Phase III**
- **Duration**: 2-3 years
- **Volunteers**: 200+ Patients
- **Purpose**: Comparative effectiveness & Risk-Benefit Analysis

**Market**
- RX
- Post-marketing Surveillance

**FDA Approval Process (6-12 months)**
- Long-term Safety & Comparative effectiveness

*The duration of a trial and required number of participants is dependent upon the outcome that is measured. Trials that measure hemorrhage, for example, an infrequent event, are likely to be longer in duration than a trial that measures a more frequent outcome, like headache or seizure.*
Atorvastatin CASH Clinical Trial

• Phase I/II
• To block hemorrhage
• As measured by QSM
Rho Kinase Inhibitors Target Cell Junctions

From Fischer et al, 2013. Trends in Molecular Medicine
Why study atorvastatin and CASH?

- Treated mice show fewer lesions and less bleeding
- Expect statin therapy to restore junctions and to see a decrease in QSM signal (iron on the brain)

(Awad, U Chicago)
Now Enrolling Study Participants

• 80 participants
• No prior surgery
• Symptomatic hemorrhage within last 12 months
• No statin therapy within last 12 months
• Travel stipends available
AT-CASH-EPOC Trial Timeline

• Enrollment (Visit #1 to Chicago)
  • Physical/Neuro exam
  • mRS & QoL evaluations
  • MRI & Labs

• Follow up phone call (6 & 9 months)
  • Current medications, other events & mRS

• Visit #2 (12 months)

• Follow up phone call (15, 18 & 21 months)

• Visit #3 (24 months)
How to enroll?

• Contact the study team at the University of Chicago
  • Kristina Piedad, RH, BSN Trial Nurse
  • ATCASH@uchospitals.edu
  • 773-326-9839

• Join the Patient Registry
Upgraded Patient Registry, coming soon
…without you, there can be no cure!

“Behind most every treatment, medicine, therapy & medical device...are millions of people who have volunteered to take part in clinical trials.”

The Impact Clinical Trials Have on All of Us - CISCRP