

MISTIE
Minimally Invasive Surgery plus rt-PA
for Intracerebral Hemorrhage Evacuation
Pharmacist Training

OVERVIEW

- Multicenter, international, open label, randomized study
- Approximately 110 patients will be enrolled across 40 study centers


Stage II RANDOMIZATION
1:1
(maximum of 9 doses)

MIS + rt-PA 1mg/ml every 8 hours (N=25)	medical management (N=25)
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DRUG SUPPLY

- Recombinant tissue plasminogen activator (Cathflo® Activase®) 2mg vials for reconstitution
 - Active drug
 - Packaged in boxes containing 6 vials/box
 - Manufactured by Genentech
 - Storage – refrigerated 2-8° C
 - Provided for the study
- 0.9% Sodium Chloride for Injection, USP
 - Placebo and Flushes
 - Use pharmacy supply- not provided

Cathflo® Activase®



Drug Shipments

- Distributed to sites by the Investigational Drug Service (IDS), Johns Hopkins Hospital (JHH)
- FedEx utilized as the courier
- Shipped in multi-purpose insulated shippers with refrigerant packs
- Upon arrival, drug should be unpacked immediately, examined, verified and placed in a refrigerator

Drug Shipments (cont.)

- Temperature monitoring devices used for international site
- A signed copy of the invoice must be faxed to the shipper
- Initial shipments will be sent when all regulatory documentation has been received from the site
- To re-order drug
 - Domestic -contact JHH IDS
 - International- contact DPGL

DRUG PREPARATION (Active)

- Obtain study supply of Cathflo® Activase®
- Utilizing aseptic technique, reconstitute* the vial with 2.2ml Sterile Water for Inj., USP
- Slight foaming is not unusual. Let the vial stand undisturbed for several minutes to allow dissipation of any large bubbles.
- DO NOT shake the vial.

*Based on product package insert for Cathflo® Activase®. Each vial contains 2.2mg of Alteplase, which includes a 10% overfill

DRUG PREPARATION

- Final concentration is 1mg/ml
- Draw up syringe(s) of 1mg/ml Cathflo® Activase® into 3ml sterile syringes
- Cap the syringe with a sterile tip cap
- Label the syringe in a blinded fashion
- Expiration date for the syringe is 8 hours after reconstitution if stored at 2-30°C

DRUG PREPARATION
(Placebo)

- Obtain a vial of 0.9% Sodium Chloride for Injection, USP
- Utilizing aseptic technique, draw up 1ml into a 3ml sterile syringe
- Cap the syringe with a sterile rubber tip cap
- Label the syringe in a blinded fashion
- Expiration date for the syringe is 8 hours after preparation (to match active drug syringe)

DRUG PREPARATION (cont.)

- Complete the drug accountability log
- Used Cathflo® Activase® vials can be discarded
- Expiration date for the syringe is 8 hours after reconstitution/preparation if stored at 2-30°C

PREPARATION of FLUSHES

- Obtain a 10ml vial of 0.9% Sodium Chloride Injection, preservative-free.
- Utilizing aseptic technique draw 3 ml of 0.9% Sodium Chloride into a sterile 5ml syringe
- Cap the syringe with a sterile tip cap
- Label the syringe
- Expiration of syringe is 24 hours

Can I Freeze TPA?

- At time of preparation of subject's dose, draw up the appropriate dose into a syringe
- Cap syringe with a sterile tip cap
- Label syringe
- Store at -25° to -10°C
- Discard frozen syringe(s) after 45 days*
- Thaw syringe prior to dispensing
- Re-label the drug for enrolled subject in a blinded fashion

*Based on USP 797 Beyond Use Dating

DRUG ACCOUNTABILITY & DOCUMENTATION

- Drug Accountability log
 - Document receipt and disposition of drug
 - Complete a log for Cathflo® and placebo
 - Running balance must be maintained
- Subject Specific log
 - Document preparation for an individual subject

DRUG ACCOUNTABILITY

- Receipt and disposition of study drug is documented on the drug accountability log
- Unused vials/expired vials must be returned to Johns Hopkins Hospital
- Document return of drug on drug accountability log

PHARMACIST RESPONSIBILITIES

- Training requirement
- Adherence to study protocol
- Staff preparing compounded sterile products are trained and competent (USP 797 Guidelines)
- Appropriate documentation is maintained
- Storage and security of investigational drug
- Temperature monitoring

PHARMACY MANUAL

- Located on the MISTIE website
- www.mistietrial.com
- Study Documents
- Current protocol version
- Login & Password

REFERENCES

- MISTIE website - www.mistietrial.com
- Genentech- www.gene.com
- Cathflo® Activase® product information - www.gene.com/gene/products/information/cardiovascular/cathflo-activase/index
- USP* 797 Guidelines - www.usp.org
- Coordinating Center (phone) 410.614.6996
- JHH- Investigational Drug Service (phone) 410.955.6337 (fax) 410.614.8074

*USP - United States Pharmacopeia



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