



Quick MISTIE Overview

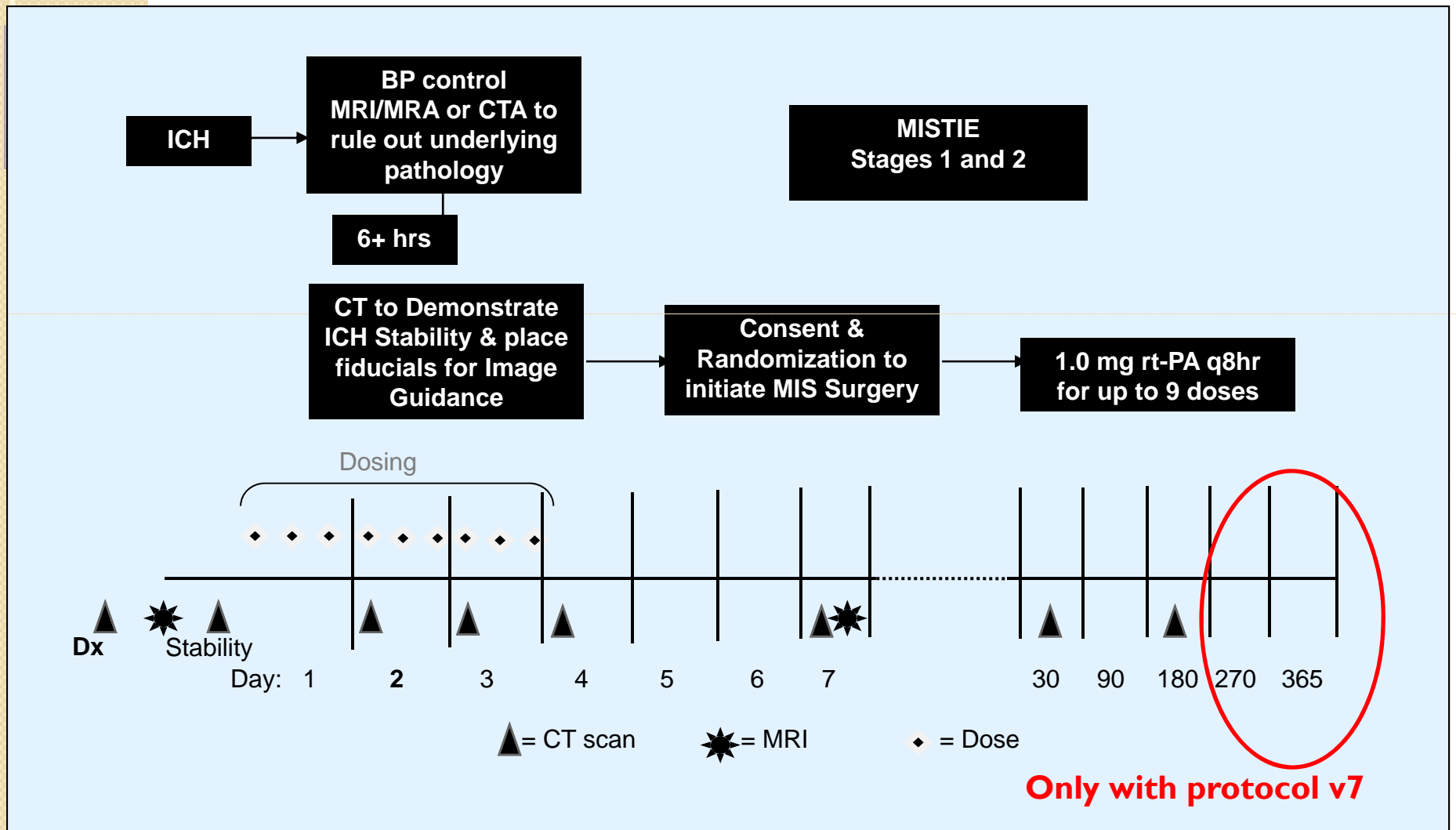
Checklist at enrollment

Run-In Subject



- First subject automatically surgery
 - No PK collections necessary for run-in subjects
-

MIS+rt-PA Surgical Protocol



We are in Stage 2: Safety Study



- 50-subject safety tier
- 1:1 randomization
- 25 MIS+rtPA vs. 25 medical management

Randomized to Surgery



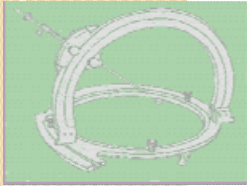
- Performed by certified neurosurgeon
- Performed in OR preferred
- Use protocol-specified introducer and catheter
- Single aspiration with 10 ml syringe
- Antibiotic coverage

Imaging Goals During Tx



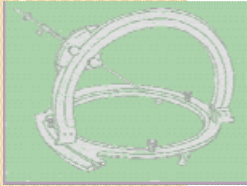
- Imperative all subjects scanned Q24^o
- Want 4 days of CTs
- CT through day 4 or 5 (depending on whether surgery on day of randomization (Day 1) or day 2 post randomization
- Then 24 hrs post catheter removal
- CT any time catheter manipulation or revision or neuroworsening
- Day 7 MRI

Aseptic Technique



- Administered with sterile field and gown
- Administer port closest to head
- Most sites needle-less
- Use flush to clear the tubing and deliver drug into the clot

Administration



1.0 ml CathFlo[®] (1.0mg/1 ml) syringe

3.0 ml NS flush syringe

= 4 ml total instilled

Schedule



- Q 8 hrs x 72 hours
- Total daily dose = 3.0 mg
- Catheter closed to drainage 1 hour

Stopping Drug: Surgical endpoints



Compare to stability CT scan

The ICH volume approaches 10 cc

or

80% reduction

or

9 doses of rt-PA

Stopping Study Drug



- Treatment failure
 - Clinically significant rebleeding
 - Withdrawal from the trial would be in the patient's best interest
- The patient withdraws consent.

Catheter Management



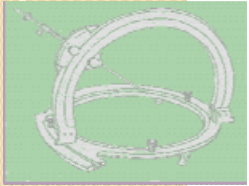
- Avoid aspiration and irrigation
 - Exceptions:
 - PK sampling
 - Culture for suspected infection
 - Irrigation for catheter blockage
- Remove 24-36 hrs post last dose
- Get CT scan 24 hr after removal

Permitted Medications



- For reversal of anticoagulation.
 - NovoSeven
 - DDAVP
 - FFP
 - Plasma concentrate
 - Vitamin K

Prohibited Medications During Tx



- Coumadin (warfarin)
- Antithrombotics/antiplatelets
- Low molecular-weight heparins
(whenever possible)

Acute Period is Six Days (v7)



- Vital Signs & Neurochecks
 - Q 1 HR (Days 1-4)
 - Q 4 hr (Days 5-6)
- Specific concomitant medications
- AE/SAE
- Safety labs