CLEAR III INFORMED CONSENT GUIDE

The consent process may be one of the most important jobs a clinical research team has to tackle. Good consent practices will inform patients and allow them to make the best decision based on their personal situation. Poor consent practices may cause an otherwise eligible patient to decline enrollment or alternatively, encourage the participation of patients who may not be well suited for involvement in the trial. Best consent practices have been extensively researched. This guide describes some best consent practices which may improve the CLEAR III consenting process and aid the patient in making a well-informed choice.

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Tips to Improve the Informed Consent Process

1. **Recognize that the informed consent discussion has two distinct elements: informing and consenting.** Your presentation should first inform the patient about IVH and the CLEAR trial. The patient and family should then be given time to consider their options and to have any questions answered. When all questions have been adequately addressed, the consent process can begin. The consent form should be explained in plain language for the patient/family before they are asked to make their final decision.
2. **"Impressions are everything!"** Discuss the study as a team with both the PI and the coordinator, and be prepared with the appropriate forms. Hold the meeting in a private location to avoid interruptions. A bad first impression could influence the patient or family's final decision.
3. **Have a plan and stick to it.** It might be beneficial to practice your consent presentation a few times before attempting the first screening. A sample consent discussion outline can be found in this guide.
4. **Make time and sit down.** A study showed that families perceive physicians as more compassionate when they sit down. Discuss the trial as well as the natural history of IVH. Consider reviewing the patient's CT scan with the family and explain to them why participation in the CLEAR trial might be a good option.
5. **Know the protocol inside and out.** Be able to explain it in simple, easy to understand terms and be prepared for questions.
6. **Explain the potential benefits of rtPA for IVH treatment, but also highlight the advantages of participating in the trial even if the patient receives placebo.** Irrigation of the EVD with saline may improve clot resolution better than EVD drainage alone. Additional benefits include receiving cutting-edge care, increased follow-up during recovery, and benefit to future IVH patients.
7. **Inform the patients of risks while emphasizing the trial's safety profile.** Studies have shown that patients have a more favorable reaction when risks are presented verbally rather than numerically. For instance, telling the patient that there is a very low risk of rebleeding associated with rtPA is a better approach than saying there is a 5% risk of re-bleeding associated with the study drug.
8. **Answer any questions the family or patient has and ask open ended questions to gauge their understanding.** The family should not be approached for consent until all their questions about the protocol, risks, and follow-up responsibilities are answered.
9. **Give the family time to think about their decision.** Gently tell the patient/family about the possibility of treatment window closure.
10. **Be empathetic.** The patient and family are likely experiencing extreme emotional stress which may compromise their ability to make informed decisions.

Top 10 Reasons for Consent Failure

10. Family is not interested in being videotaped.

A proxy video can be taken by the care team based on information gathered from an interview. This allows the family and patient to never appear on video. The clause addressing video recordings can be crossed out on the consent form if necessary.

9. rt-PA is not FDA approved for treatment of IVH.

The process of becoming FDA approved involves this type of research study. Additionally, rt-PA is approved as a treatment for blood clots in other areas of the body. For example, rt-PA is given intravenously to remove clots in heart attack, deep vein thrombosis and ischemic stroke. Previous safety studies have shown that rt-PA is safe for intraventricular use (rt-PA safety study, CLEAR A and CLEAR B).

8. 72 hours is not long enough for the family to make a decision.

This is usually the response when the family has deeper concerns. Investigate what the real concern is and see if it can be addressed. A waiver is required from the Study Chairman if the family really does need more time to make their decision.

7. There is a high level of follow-up burden placed on the family and patient.

Participation in the study offers patients added opportunities for medical evaluation throughout their recovery at no cost to the patient. This could very valuable, as the follow-up visits required for the CLEAR III study go beyond the current standard of care. If transportation is an issue, offer possible solutions such as pick up arranged by the hospital or travel reimbursement.

6. The patient or family is not interested in research.

Discuss some possible benefits of participation in clinical trials. Try to engage the patient and family in this conversation to see what may be of most interest to them and tailor your conversation accordingly. Possible benefits to the patient include:

- Patients take an active role in their own healthcare
- Patients gain access to cutting edge treatments before they are widely available
- Patients receive the highest standard of care and access to experts in intracranial hemorrhage at leading international health care facilities
- Patients get increased medical evaluation throughout their recovery
- Future patients with hemorrhagic stroke will benefit from current patients' participation in the trial

Top 10 Reasons for Consent Failure

5. The patient is already doing well and there is a good prognosis.

This may be a valid reason for not participating in the trial. However, it is important to stay in touch with the care team. Continue to monitor the situation until the enrollment window has passed.

4. Patient or family are concerned about possible mortality associated with the study

Previous CLEAR studies had a 30-day mortality rate of 19-23%. Historically, the 30-day mortality rate for IVH patients is 50-80%. Therefore, all CLEAR patients, even those receiving placebo, generally had a better outcomes than IVH patients not enrolled in the CLEAR studies. The CLEAR III trial design includes independent safety monitors who ensure the continued safety of patients in the trial. The protocol has stringent guidelines that mandate optimal catheter placement, daily CT scans to assess bleeding, and strict blood pressure and intracranial pressure management.

3. Patient or family is concerned about deficits or disabilities associated with the study

The hope is that the CLEAR therapy can minimize deficits associated with IVH and improve the quality of life for hemorrhagic stroke patients. In CLEAR IVH-B, 50% of patients reached a mRS of 0-3 at 180 days. Again, all steps are taken to ensure the safety of the patient and minimize risks.

2. rt-PA bleeding risk

There is a very low recurrent bleeding risk associated with the CLEAR III trial. Previous CLEAR studies had a re-bleeding rate of 8%. The study team and safety monitors closely monitor re-bleeding events and every step is taken to minimize this risk to patients.

1. 50% chance of not receiving the study drug

All patients, even those not receiving rt-PA, may receive some benefit from participating in the CLEAR III trial. The CLEAR III procedure requires that all patients receive daily irrigation of the EVD with saline. This may improve clot resolution better than EVD drainage alone. Saline flushes are routinely used to clear clogged EVDs as standard of care measure. Additionally, all patients enrolled in the trial receive the highest level of care as well as increased medical supervision and imaging studies throughout their recovery. All trial related labs, imaging studies, and source documentation will be reviewed by an international group lead by Johns Hopkins researchers. This additional oversight offers the patient's medical care team added expertise on the management of the patient during the critical care period and throughout their recovery. This additional level of expertise is available to all study participants. Therefore, it is better to be in the trial and receive placebo than not be in the trial at all!

Informed Consent Conversation Outline

Before the meeting

- ☐ Prepare a room with adequate seating capacity and limited distractions
- ☐ Retrieve the patient's CT scans

The consent conversation

- ☐ Introduce yourself
- ☐ Describe the natural history of IVH
    - Weakened blood vessel in the brain ruptures
    - Blood pools in the brain and fills the ventricles
    - The presence of blood increases ICP and causes inflammation and neurological damage
    - Severe disabilities may result
    - No effective treatment, only supportive care
- ☐ Go over the patient's CT scan
- ☐ Describe the CLEAR therapy
    - Rt-PA or saline (placebo) is given through the an EVD to break up the blood in the ventricles
    - Clot liquefies and drains away
    - Less fluid build-up (edema) and quicker clot resolution
    - Hope is that it can limit brain injury and improve long-term outcomes for the patient
- ☐ Describe benefits of participation, even if patient receives placebo
    - There is some benefit to receiving a saline flush, this may improve clot resolution even if the patient does not receive rt-PA
    - All patients will receive increased follow-up during the recovery period
    - Patients that participate in CLEAR tend to do better than historical IVH patients
    - Trial may result in finding an effective treatment for future IVH patients

Informed Consent Conversation Outline

- Follow-up period
    - Clinic visits for CT scan and interview at 1 month, 6 months and 12 months after the CLEAR treatment.
    - In-clinic interviews will be video taped
    - Phone interviews between visits
- Possible risks
    - rt-PA has a low risk for rebleeding
    - The CLEAR trial has a very low rebleeding rate
    - There is utmost concern for the wellbeing of the patient and steps are taken to minimize risks (surgical center, independant safety monitors)
- Why CLEAR is a good option
    - There is currently no other specific, tested treatment
    - The procedure is safe
    - The procedure may improve the patient's long-term outcomes
- Review the consent form with the family
- Inform the family of the window for enrollment
- Give the family spokesperson your card with contact information and leave the family to discuss

After the consent meeting

- Contact the family spokesperson to see if there are any additional questions
- Ask if they are ready to enroll

The last page of this guide contains a talking points worksheet which can be used to structure your consent conversation

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Special Note: By agreeing to participate in the CLEAR III trial, you are acknowledging that the potential benefits of minimally invasive surgery plus rt-PA for the treatment of IVH are yet unknown. It is therefore unethical to offer off-label use of rt-PA to patients. This practice damages the authenticity of the trial and could be potentially dangerous to the patient. Using rt-PA off-label should **NEVER** be an option.

References and Additional Resources:

***** For a video recorded example of a well executed consent conversation as well as more information on this topic, see the CLEAR III June 2012 webinar "Best Consent Practice", which can viewed through the BIOS website. http://braininjuryoutcomes.com/studies/clear/clear-webinars

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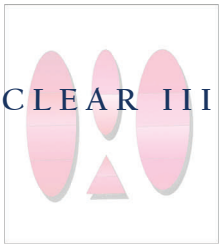
Investigative Team Informed Consent Checklist



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