**RHAPSODY-2 FREQUENTLY ASKED QUESTIONS**

**The CTA says the startup payment is $2500, but the Payment Schedule says it is $3500, which is correct?**

The start-up payment is $3500.

**Can you send the imaging manual, lab manual, pharmacy manual, and MOP?**

The RHAPSODY-2 manuals are undergoing revisions at this time and will be sent/posted as soon as they are completed/approved. If there is something specific that you need, please reach out to Harriet Howlett-Smith, RHAPSODY-2 project manager (howletha@ucmail.uc.edu).

Since the WebDCU Toolbox for RHAPSODY-2 has not yet been activated we are posting some things on the StrokeNet website under the RHAPSODY-2 trial resource tab [RHAPSODY TRIAL - StrokeNet (nihstrokenet.org)](https://nihstrokenet.org/rhapsody/resources).

**Are the baseline scans billed as Standard of Care?**

Yes, these would be done as standard of care for a stroke work-up and should not be billed to the research grant.

**Do we need a local read on the MRI?**

The MRIs at Day 30 and Day 90 do not need to be read by your local radiologist.

**Will there be a central read on the MRI?**

There will not be any central reads of the MRIs at Day 30 or Day 90.

**Can we invoice for the MRIs? What is the CPT code?**

No, this is built in to the per patient payment. This is a research MRI that follows a specific algorithm, not a standard of care MRI (it most closely aligns with an MRI brain without contrast). Remember, you will get an additional payment of $1000 if the dicom images for the Day 30 and Day 90 MRIs are uploaded to LONI.

**Are the Day 30 and 90 MRI scans billed to the research grant?**

Yes, the MRI scans at Day 30 and Day 90 are done specifically for research. The MRI scans at Day 30 and Day 90 follow a specific algorithm for RHAPSODY-2, they are not the standard of care MRIs. The cost of the Day 30 and Day 90 MRI scans is built in as part of the per-patient payment. Remember that you do not need a local read on the MRI scans so that should decrease the cost.

**Can we invoice for lab specimens? What is the CPT code?**

No, this is built in to the per patient payment. There are no CPT codes because these are study specific lab draws that are processed at a central lab. Remember you will get an additional payment of $1000 if all lab specimens (PK/ADA) are received at USC.

Some institutions are required to include a venipuncture fee. That would come from the per patient payment.

**Will we have to pay for shipping labs out of our per patient payment?**

No, the Univ. of Southern California will provide shipping labels and containers for you to ship the blood specimens at specified timepoints.

You will have to pay for dry ice from your per patient payment.

**Can the PK sample be drawn from the line in which the study drug is infusing?**

NO! The PK sample should ideally be drawn from the opposite arm from where study drug is infusing. If it is not possible to draw in the opposite arm it should be drawn from below the IV site where the drug is infusing.

**How long does the study drug vial have to be out of the refrigerator before it can be reconstituted?**

The RHAPSODY-2 study drug vial should be removed from the refrigerator at the time of preparation of the dose.

**How long is the study drug stable once it is prepared?**

Once the lyophilized powder has been reconstituted and injected into the 100 ml (0.9% sodium chloride in water) bag it should be infused within 8 hours.

**Who can administer the study drug? Does it have to be a member of the research team?**

The drug can be administered by the hospital nurses/pharmacists, it does not have to be the research team.  The hospital nurses/pharmacists do not have to be listed on the DOA. It will be your institutional policy that applies regarding training of the hospital staff about the administration of the drug.  We will be providing the pharmacy manual which will give not only specifics about preparation, but also administration.

**Can we use the NIHSS upon arrival or will study team need to repeat the NIHSS after the consent process/randomization?**

It may need to be repeated after consent if it was not performed by a member of the study team, or if it has been longer than 30 minutes.  The NIHSS must be performed by a member of the study team listed on the DOAwithin 30 minutes of randomization.  We know that there will be some cases where they improve after tPA and they are no longer eligible.  Doing the NIHSS just prior to randomization will catch the patients that are rapidly improving.

**At baseline, if the patients NIHSS improves to less than 5 after randomization BUT before study drug is started do we start study drug?**

NO! If the patients NIHSS improves and the patient no longer has an NIHSS of >5 before the study drug infusion has started, the patient is no longer eligible for the trial. You should not start study drug!

**What if the patient has waxing/waning symptoms and the NIHSS is changing frequently?**

Exclude the patient or wait to see if the deficit stabilizes at an includable level.

**In Section 8.5.3 it says “Adverse events will not be reported for subjects who do not receive study drug. How will we know who to record AEs on if we do not know who received the study drug?”**

In this trial “study drug” refers to both placebo and 3K3A-APC.  We refer to 3K3A-APC as the investigational product. If a patient is randomized but never starts placebo/3K3A-APC we will not follow those patients at all.  They will be considered never “enrolled” since they did not get any study drug (placebo/3K3A-APC).

For subjects who received study drug, reportable AEs include all AEs from study drug initiation through Day 7 and all SAEs through Day 30. The exception is an AE of positive COVID-19 test result (regardless of whether the subject was symptomatic), which will be reported from study drug initiation through Day 90. Reportable AEs will be followed to resolution or Day 90 (whichever comes first).

**In Section 6.1.2.2-6.1.2.4 it says that “clinically significant abnormal labs/vital signs” must be reported as Adverse Events on days 1-7. What is considered “clinically significant” for this study?**

“Clinically significant” is based on the local PI determination.  For instance, if the normal potassium level for your institution is 3.5-5.0 and the patient has a potassium of 3.4 it would be out of range, but not necessarily treated.  If the abnormality is treated (i.e., transfusion for a low hgb/hct; pressors for a low blood pressure, etc.) you would need to complete an adverse event CRF.

**Can we pay our patients for participation or for travel reimbursement even though the template consent says there will be no compensation for this study?**

Absolutely yes! That is why we made that section of the consent editable. Those patient payments or travel reimbursements will come from your per-patient payments. There will not be additional funds from NIH/RHAPSODY-2/StrokeNet for patient payments or travel reimbursement.

**Should I mark that we require a partial HIPAA waiver on the Advarra application?**

Yes, unless your local IRB requires that the partial HIPAA waiver approval comes through your local institutions IRB instead of Advarra.

**Are prisoners excluded from participating in the trial?**

Yes, even though this is not a specific exclusion criterion you would not be able to ensure that they could return for the Day 30/90 visit and MRI.

**Other Advarra submission comments:**

Please make sure you are checking the box for cognitively impaired under the “Investigational/Research Location and Subject Recruitment” section of the submission. This will actually open another set of questions about the use of an LAR which is permitted in this study.

Under the number of patients your site expects to enroll this is referring to the entire duration of the study. We estimate 4 patients per year per site.

Is this study part of a network? The answer should be “yes”, StrokeNet.

Please mark that you will use eConsent even if you will not be using it initially. It will prevent having to submit a modification at a later date.

**Do you have any patient facing materials that we need to submit with our Advarra application.**

At this time there are no patient facing documents.