Quantum Leap Healthcare Collaborative

MEMO

To: I-SPY 2 Site Investigators
From: I-SPY 2 Leadership and Quantum Leap Healthcare Collaborative
Subject: COVID-19 Mitigation and Response
Date: March 17th, 2020

Dear Investigators,

Thank you all for your ongoing collaboration on the I-SPY2 TRIAL. As a PI-led consortium, we have always stressed flexibility and joint-decision making in tackling the challenges of breast cancer. It is now more important than ever that we work together to maintain operations of the I-SPY TRIAL safely through the COVID-19 pandemic. The I-SPY TRIAL will remain open during this difficult time and we will continue to execute at the highest possible standard of quality, but we will adapt to the circumstances as necessary. That means patients on study will continue on study. Patients who you feel are appropriate and strong candidates for the trial will continue to be screened as we believe that the care that they would receive is likely to give them better options than standard of care.

In consideration of the unprecedented levels of local, regional and national response to COVID-19, please be advised that the I-SPY Study Leadership endorses the following actions to be taken by participating sites to retain patients and collect the most data possible during interruptions to normal clinical practice.

Adherence to National, Regional and Institutional Policies on Patient Care
Sites participating on the I-SPY2 Trial are expected to follow all applicable regulations, policies and interim guidance on patient treatment provided by your institutions, IRB/IECs, health authorities or other relevant state agencies. We anticipate a rapid evolution of policies at each institution. Please provide as much documentation as possible to your Study Monitor or Site Management group as these policies change, as this will allow guidance on trial activity to appropriately respond to real world considerations for patients on trial. We will be sending a survey to ease the burden of documentation and to make sure we understand how sites are responding and learn what works best- but we will not get to that until later in the week.

Your local IRB and any other oversight bodies regulating clinical trial activity at your site must be informed of the following additional guidance regarding study conduct, <u>applicable immediately</u>:

I-SPY Trial Protocol Procedures
The following study procedures should be continued for patients screening for eligibility or starting treatment:

- Diagnostic biopsy can be submitted to Agendia for MammaPrint assessment. They will remain open and support us during this period
- **MammaPrint** orders:
  To avoid delays and reduce reliance on multistep processing at the I-SPY lab we recommend that MammaPrint orders request use of the diagnostic specimen, if these are available.
  We will continue to process formalin samples but our ability to turn them around in one day may be impacted. If baseline biopsy is needed for MammaPrint, the research biopsy should be performed.
- Baseline breast MRI must be performed
- Eligibility laboratory tests will need to be performed

The following study procedures should be continued for patients currently on therapy:

- Laboratory tests for AE assessment and treatment suitability
- Breast MRI – this is a study endpoint and essential to the adaptive randomization
- Please ship any samples that you currently have that include:
  - ALL formalin preserved research (pre-treatment or inter regimen) core needle biopsies and surgical specimens.
  - ALL CPT blood tube collections
  - These samples must be processed immediately and should still be shipped on the day of collection
- 30-day follow up visit (via telephone) and safety laboratory tests

The following study procedures may be deferred at this time:

- We are postponing research blood draws for the next month with the intention that we will draw them at a later date (tentatively 1 month) pending resolution of the COVID crisis
- Temporary suspension of shipments of frozen blood samples, frozen inter-regimen and surgical tissue samples. Continue to collect these specimens if staffing resources allow but we request that sites hold all frozen material (except pre-treatment frozen cores, which may be needed for MammaPrint) at their site, in -80°C freezers. If -80°C storage is not available, please contact the I-SPY lab ispylab@ucsf.edu for guidance. If there is not lab personnel to process the blood to a point that it can be frozen, suspend collections.

In-Person Study Visits and Treatment

For study timepoints that require an on-site visit, all efforts should be made to conduct these visits per the protocol schedule of assessments. It is our intention to keep patients on assigned therapy to the extent possible.

To minimize risk to study participants and staff, we encourage you to have your research staff contact patients the day before scheduled treatment to assess any possible AEs and provide instructions. Patients should be screened for symptoms of COVID-19 as well. Patients should be instructed to have laboratory tests locally if desired, and those outside laboratory tests should be reviewed prior to the patient reporting for treatment. This will enable patients who have laboratory results that are "out of range" and who are otherwise medically stable to avoid coming to treatment visit and being turned away. Patients who pass this initial screen should report to regularly scheduled visit and be assessed by the provider directly prior to treatment.

Sites will be provided an "I-SPY COVID-19 Communication to Patients" to distribute directly to patients or use in their communication with patients. **Please submit to your IRB for expedited review**. All patients currently in the study (screening or treatment) should be contacted and the communication should be documented in your clinical notes. For all patients in follow up post-surgery, who were expecting to come in for a clinical care visit, we are recommending a delay of 2 months given the coronavirus situation unless the patient has a specific complaint in which case they should call their provider's office and be evaluated.

Use of Local Laboratories and Medical Centers for Standard Assessments
Noting that many hospitals and clinics are implementing restrictions on routine patient visits, we will allow patients on the I-SPY2 TRIAL to have all required hematology and chemistry tests conducted at local laboratories, including medical facilities and commercial laboratories. Records of these tests must be sent to the enrolling treatment site for PI review in a timely manner.

Guidance for Patient Management
It is essential that all efforts be made to maintain and assure patient safety during this time. We advise sites to refrain from enrolling patients who may be at high risk of poor outcomes from COVID-19 infection, including those age ≥ 65 or those with comorbidities (e.g. pulmonary conditions, heart disease, and diabetes).

The I-SPY TRIAL leadership recommends the following:

- Hold therapy for any patient with documented fever and perform testing for COVID-19 if available.
- Report immediately any patient testing positive for COVID-19 as an AE of special interest (AESI) to the ISPY trial leadership via the safety CRO ispy2safety@ccsainc.com
- Use growth factors as needed to minimize neutropenia

Remote Patient Visits
Any patient visits described in the I-SPY2 Trial Protocol that do not require patients to be in clinic for study assessments may be carried out remotely via telephone or telemedicine app. Visits defined in the protocol solely for the collection of patient health information such as safety assessments, concomitant medications and disease recurrence/progression can be immediately transitioned to telephone contact. Remember to document that a remote patient visit was conducted in the clinic notes.

Interruptions to I-SPY2 TRIAL Sponsor Activity
We anticipate that during the course of global COVID-19 response, some I-SPY PMO-managed processes or services may encounter delays or suspensions. Study biorepositories, systems access portals and monitor availability may be temporarily out of service as staff and other resources transition to remote work areas. Any suspension of key trial service will be announced by the I-SPY leadership to all impacted sites, along with timelines for anticipated resumption of activity.

Flexibility and Maximizing Data Collection
This situation remains fluid and we anticipate further adjustments to local clinical practice will evolve in response to COVID-19. When managing these changes at the site level, please work with your monitors, study sponsors and I-SPY2 TRIAL Leadership to continue to collect the most study data possible given current restrictions at your sites. Fortunately, much of this work can be performed off site.

As COVID-19 response stretches into the coming weeks and months, please keep the study team informed about impact on patient treatment, patient retention and overall trial activity at your site. The entire I-SPY2 TRIAL organization will remain an available resource to all sites when addressing emerging concerns as we manage COVID-19 response.

Documentation of Site's Revised Approach for Patient Visits due to COVID-19 Restrictions
I-SPY will send a survey to document the approaches you are taking for patient care during the response to COVID-19. As this is a fluid situation, we will likely update the survey as things change and resend it over the coming weeks so that we can have an accurate understanding of activities at your site.

Communication Plan
There will be a I-SPY 2 standing meeting every Monday at 1 PM PT/4 PM ET to discuss this fluid situation; if the situation changes dramatically, we will set up an interim call immediately.

Additional Resources
ASCO Coronavirus Resources and FAQs https://www.asco.org/asco-coronavirus-information

For patients, a good resource is: https://www.cdc.gov/coronavirus/2019-ncov/index.html

If you have any questions, please do not hesitate to contact your site's I-SPY 2 CRA or the I-SPY PMO office, ispyadmin@ucsf.edu.

Sincerely,

I-SPY Leadership Team

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