FAQ for S1415CD (TrACER)
[Updated April 13, 2017]

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PRE-ACTIVATION

Pre-Activation questions should be directed to: TrACER@fredhutch.org

Q: Where can I find a general description of this study?

A: A general description of this study is in the protocol, Section 7.1.

Q: What are the objectives and measured outcomes of this study?

A. The objectives are listed in Section 1.0 of the Protocol; a description of the measured outcomes is in Section 10.0.

Q: Will this study use the Central IRB?

A: No. The CIRB is only covering CCD studies that were approved after March of 2016. S1415CD will rely on local institution IRBs for the participating components. A **Cover Letter** with language tailored for local IRBs explaining the unique aspects of this study is available to download from the Other Study Materials section of the www.swog.org S1415CD Protocol Abstract page or can be requested by emailing TrACER@fredhutch.org.

Q: Can we use CCD funds towards costs accrued for preparation prior to study activation?

A: Yes, as long as the costs are for activities necessary to get your component ready to participate in the trial. The NCI has announced that CCDR components can and should use their CCDR funds for study startup activities. This includes time spent communicating about the trial with study staff and preparing for implementation at the site. Note that participating intervention arm sites will receive $6500 in addition to funds available through CCDR to facilitate the protocol required order system modifications. See the S1415CD Funding Memo available on the S1415CD Protocol Abstract page for more information.

Q: What is the difference between the Cohort group and Usual Care group?

A: Both Cohort and Usual Care groups are not making any changes to their standing orders. Whereas components in the Cohort group already have guideline-informed CSF ordering in their existing EHR/EMR, the components in the Usual Care group (and the Intervention arms) do not. Data collection is the same for all study arms (Cohort, Usual Care, Intervention). See Protocol Section 2.0 - Cohort Study.

Q: How is the risk of febrile neutropenia determined?

A: The standing orders in the intervention arm are informed by the NCCN Guidelines, which are based on the chemotherapy regimen. A complete list of approved regimens and their risk levels can be found in Protocol Appendix 18.1. The study process for assessing febrile neutropenia risk is described in the Protocol, Section 7.3.

Q: What if insurance does not cover the recommended intermediate risk chemotherapy treatments or protocol directed CSF recommendations are denied for payment?

A: Data from two surveys of CCDR SWOG practices conducted in 2015 indicates this will not be a significant issue. However, we have heard from some components that they have recently experienced insurance denials in this population prior to starting the trial. Physicians should be aware that it is an outcome of the trial to look at barriers like this that patients may experience that impact whether they receive CSF. As this is a pragmatic trial, we want to study delivery issues as they unfold naturally, in the different practice settings (Cohort, Usual Care, and Intervention). The Study Chairs would like to monitor this issue closely so if you have specific concerns or have experienced denials at your clinic, we encourage you to share them with TrACER@fredhutch.org.

INTERVENTION IMPLEMENTATION

See Protocol Section 7.2 for an overview of the intervention process. Intervention Arm components should also read the Order Entry Change Protocol document, available on the www.swog.org S1415CD Protocol Abstract webpage or by contacting TrACER@fredhutch.org.

Q: Can physicians override the standing orders/default settings?

A: Yes. The study intervention involves adding these standing orders or default settings to the component's existing order entry system. Physicians are still able to manage their patient's clinical care and can choose to override the standing orders for individual patients. Each addition or removal of CSF to the order set by a physician is not a protocol violation, but a data point that will be used to determine the appropriateness of the CSF default setting.

Q: Is this study advocating for increased use of Primary Prophylactic CSF?

A: No. S1415CD does not endorse the inclusion or exclusion of CSF in a chemotherapy order for any particular patient. It remains the duty of the provider to consider the necessity of CSF for each patient and act in a way that is consistent with both guidelines and the patient's needs.

S1415CD is designed to investigate the operational and clinical effects of including or excluding CSF standing orders in prescriptions of certain types of chemotherapy in a pragmatic setting where providers still maintain the ability to provide individualized patient care.

Q: Do I need to add standing orders for just intermediate risk regimens?

A. For this study, you will be asked to modify or touch ALL regimens included in Protocol Section 18.1 that your site uses. This includes adding standing orders and system notes that alert the ordering physician that a regimen is designated high, intermediate, or low risk per guidelines and notes the clinic's randomization assignment. Please refer to the Protocol Section 7.2, and Table 3 of the **Order Entry Change Protocol** document, available for download from the Other Study Materials section of the S1415CD Protocol Abstract webpage on www.swog.org.

Q: What is the time frame to get the order change process implemented?

A. We would like components to complete the order change process and be ready to register patients in a six month time frame from randomization.

Q: How will this study impact patients in our clinic that have not consented to the study?

A. As this study is a clinic level intervention, all patients at your site that are on one of the study recognized regimens listed in Protocol Section 18.1 will have the default CSF orders appear in the chemotherapy order for at least the first cycle of treatment. The patients who consent to be on the study are consenting to data collection via questionnaires and medical records.

Q: Currently we do not use all regimens on the list in Protocol Section 18.1. If we start to use one of the regimens after we begin accrual, will we then have to build a protocol that includes standing orders for that regimen?

A. This is preferable but not required. Either way, please notify TrACER@fredhutch.org with any regimen additions or removals during the course of the trial so that this information may be documented for each component.

Q: If guidelines change, will we need to update our system to reflect these changes?

A. S1415CD Study Chairs will review the regimen list in Protocol Section 18.1 annually to determine if changes should be made based on Guideline revisions or other new information in the literature. Once the updated protocol is posted, it is expected that components submit the revision in a timely matter to their local IRB and that components update their order entry system to reflect any changes for patient accrual moving forward.

Q: When the study concludes, is it expected that all sites in the Intervention Group will remove the default standing orders? If so, will there be funding to support that work?
A. It is up to the individual site if they would like to keep the changes in place after the study is completed. There will not be specific funding to support removing the changes. Sites may use a portion of their PCORI funding for this.

Q: We are unsure what type of CSF and what dosage to include in our standing order. Do you provide recommendations?
A. No, this is beyond the scope of the study. Prescribing practices should be determined by the physician at your site. If you have questions on a specific regimen, we may be able to send you published references but the ultimate dosing decisions should be made by your practice.

PATIENT REGISTRATION/ BASELINE
Registration questions should be directed to: cancercontrolquestion@crab.org

Q: What are suggested best practices for approaching and registering patients within the timelines of this study?
A. It is difficult to issue a one-size-fits-all process for approaching patients due to variations in clinic and patient flow across different institutions. Patients must be registered prior to starting their first cycle of an approved chemotherapy regimen (Protocol, Section 5.2). This requires study staff to approach patients during the window after their treatment has been ordered but before it has begun. If your site has a chemo teaching visit, it is recommended patients are approached to discuss the study at this time. If this appointment occurs more than 5 days from chemo start date, you may consent patients and have them complete registration paperwork but hold off on registration until they are within 5 days of their first cycle. If there is no appointment between prescribing of chemotherapy and chemotherapy start date, it is recommended someone call the patient to discuss the study rather than introducing it for the first time on the day they start treatment. These are some suggestions based on what has worked at some of the participating sites but components are encouraged to work with their own teams to devise a strategy that will work best with their patient population and clinic flow.

Q: When is the last possible time we can register a patient?
A. Patients may be registered to the study as late as their first day of chemotherapy, as long as registration happens prior to initiation of chemotherapy. See Sections 5.2a and 13.1 of the protocol.

Q: Is there a SWOG standard regarding the amount of time between the date a patient signs the informed consent and the date the site registers the patient?
A: Always follow your institutional policies regarding patient consent. Per the SWOG Regulatory Guidance, September 2016 document (found on the QA/Audits page of www.SWOG.org), if there is a substantial delay from the time the patient signs consent and is enrolled in a study (> 30 days), it is **recommended** that the information contained in the consent form be reviewed with the subject prior to initiating any research procedures with the subject and the discussion documented in the research record. The patient must be re-

consented if there have been any significant updates to the consent (new study design, added risk, etc.). Re-consent is not required if there are no changes or only minor changes to the consent.

Q: When should patient baseline questionnaires be completed?
A. Baseline patient questionnaires should be completed after consent has been obtained and prior to the initiation of chemotherapy, and thus may be completed before or after registration. See Section 15.2 of the protocol.

PATIENT ELIGIBILITY
Eligibility questions should be directed to: cancercontrolquestion@crab.org
See protocol Section 5.0 for full patient eligibility criteria

Q: Is a patient who will be having radiation therapy as well as one of the chemotherapies listed in Section 18.1 eligible?
A. No, patients who are receiving or planning to receive concurrent radiation during their systemic therapy are not eligible. See protocol Section 5.2b.

Q: Are aromatase inhibitors, such as Anastrozole, considered "systemic therapy" and therefore not allowed under Section 5.2a?
A. Aromatase inhibitors are not considered systemic therapy for the purposes of this study because they are not chemotherapy, immunotherapy, biological therapy, or a combination thereof (Protocol Section 5.2).

Q: Is Brachytherapy considered a "systemic therapy" and therefore not allowed under Section 5.2a?
A. Brachytherapy is not considered a systemic therapy.

Q: Is TACE considered a "systemic therapy" and therefore not allowed under Section 5.2a?
A. TACE (transarterial chemoembolization) is not considered systemic therapy for the purposes of this study.

Q: Are patients who had surgery or radiation only for early stage disease and then progressed or have a recurrence of same disease site who have not been treated with prior chemotherapy eligible?
A. Yes, these patients are potentially eligible under Sections 5.1a, 5.2a and 5.2b.

Q: We have a patient starting on a combination regimen. Both of the drugs are listed individually in Section 18.1 but not as a combined regimen. Would this patient be able to participate?
A. No. This would not be considered an approved regimen because the study only recognizes and has determined FN risk of the single agent regimens listed in Section 18.1, not the combination. Please refer to Protocol Section 18.1 for guidance on determining regimen related eligibility.

Regimen specific eligibility questions- presented in alphabetical order by regimen:

DOSE DENSE AC
Q: Is dose-dense AC followed by Paclitaxel every 21 days an approved regimen for this study?
A. Yes. In sequential regimens, eligibility is determined by only the first regimen in the sequence (e.g. by AC only in the sequence AC->T). In this particular case, dose-dense AC is listed in Section 18.1 as an approved study regimen, so a patient on dose dense AC followed by paclitaxel every 21 days is eligible. See Protocol Section 18.1 for the full list of approved regimens and examples.

mFOLFOX6

Q: What are the specs of mFOLFOX6 for this study?

A. Oxaliplatin 85mg/m2 IV over 2 hours on day 1
Leucovorin 400mg/m2 IV over 2 hours on day 1
Fluorouracil 400mg/m2 IV push on day 1 followed by Flourouracil 1200 mg/m2 IV continuous infusion daily on days 1 and 2 (2400mg/m2 IV over 46-48 hours)

Q: Are levoleucovorin and leucovorin equally acceptable for the mFOLFOX6 regimen?

A. Yes.

Q: I have a patient that has been prescribed mFOLFOX6 28 day cycle, receiving treatment on day 1 and day 15. mFOLFOX6 is on the regimen list with cycle length of 14 days. Is this patient eligible since their treatment is essentially (2) 14 day cycles?

A. Yes. mFOLFOX6 is generally considered an every 2 week regimen although sometimes it is thought of as every 4 weeks with repeated dosing at 2 weeks. As long as the regimen used by a site is equivalent to the regimen listed in Section 18.1 as far as drugs, doses, and schedule, the regimen is considered an allowable regimen.

PACLITAXEL (Abraxane)

Q: What is the difference between Intermediate-risk paclitaxel q21 days and Low-risk Paclitaxel (Abraxane] weekly?

A. Intermediate-risk paclitaxel q21 days is given at 175 mg/m2 on just day 1 of the cycle. Low-risk paclitaxel weekly is given at 80mg/m2 every 7 days, which could be defined in orders as “weekly” or “every 21 days on days 1, 8, 15.”

Q: Is Paclitaxel (Abraxane) weekly and Carboplatin q 3 weeks an approved treatment for consideration for this study?

A. No. Carboplatin every 21 days with Abraxane weekly is not included in this study. Please refer to Protocol Section 18.1. for the list of approved regimens and examples.

Q: A patient is receiving Paclitaxel day 1, 8, 15 + Trastuzumab day 1, 8, 15 every 21 days while also receiving Pertuzumab day 1 every 21 days. Is it okay to use “Paclitaxel weekly + Trastuzumab + Pertuzumab Cycle Length 7 days FN Risk low” for this patient? If we do report this regimen, is it okay to see her at her true cycle 2 day 1 after 21 days for her research visit?

A. Yes, that is the correct regimen to use for this patient. Per the protocol section 14.4, this patient would be evaluated at Day 14 since the Cycle Length for Paclitaxel weekly + Trastuzumab + Pertuzumab is only 7 days per Section 18.1.

TC

Q: Which agents make up TC (Section 18.1, under Breast regimens)?

A. TC is docetaxel and cyclophosphamide.

PATIENT SCHEDULING/PROCECURES

Scheduling and procedure questions should be directed to: cancercontrolquestion@crab.org
See protocol Sections 9.0 and 14.4

Q: I am confused by the study calendar.

A. In SWOG trials, the study calendar (Section 9.0) is intended as an aid to schedule only and is not intended to replace or supersede relevant sections of the protocol. Using the calendar as the sole resource for participating in the SWOG trial will lead to misunderstandings and result in incomplete or incorrect data submission. This generates data queries, unresolved expectations, and the time needed to correct data errors. We strongly urge review of the relevant sections of the Protocol as often as necessary prior to enrolling patients or completing study forms. If you have any questions and cannot find the answer in the Protocol, please email cancercontrolquestion@crab.org.

Q: Does it matter what type of CSF a patient is prescribed?

A: Per Protocol Section 3.0, the choice of CSF is at the discretion of the practice and treating physician, provided the CSF administered is FDA-approved. All FDA approved and commercially available forms of CSF are allowed. These include original agents (filgrastim, pegfilgrastim), new agents (tbo-filgrastim, filgrastim-Sandoz) and the on-body injector for pegfilgrastim.

Q: Are the patient surveys going to be completed on paper or electronically?

A: The patient surveys will be administered to the patient on paper and submitted electronically through iMedidata Rave. See protocol Sections 14.3 and 15.2.

DATA SUBMISSION

Data submission questions should be directed to: cancercontrolquestion@crab.org

Q: My patient is on a cycle with fewer than 14 days in the cycle. When should I submit "end of first cycle" data?

A. Regimens that normally have a cycle length of fewer than 14 days will be reported as a 14-day cycle for purposes of study data collection. Specifically, regimens with a cycle length of 1 day or 7 days will have data collection at Day 14 for "end of first cycle" data, including patient completed questionnaires, using Day 14 as the Cycle End Date. See Section 14.4 for data submission requirements and Section 18.1 for study-allowed regimens and regimen-specific cycle lengths.