Challenges of Conducting Clinical Trials during the SARS-CoV-2 Pandemic: The ASCEND Global Program Experience


Key Points
- The coronavirus disease 2019 pandemic has had an unprecedented effect on health and health care and posed challenges to the conduct of clinical trials.
- Targeted mitigating strategies, on the basis of early and continued data collection from site surveys, limited disruption to the ASCEND trials.
- Flexibly allowing hemoglobin assessment at local laboratories to inform randomized treatment dosing was key to limiting the discontinuation of treatment.

Introduction
The coronavirus disease 2019 (COVID-19) pandemic has had an unprecedented effect on health and health care. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has strained health care systems and caused disruption to non-COVID-19-related health care. Although the premature interruption or disruption of clinical trials is less well recognized, it has the potential to threaten the development of new non-COVID-19-related therapies (1–3).

Study disruptions need to be rapidly identified and addressed to preserve the integrity of ongoing studies and the design of new ones. Here, we describe the challenges that arose in three global phase 3 trials and the strategies undertaken to maintain and adapt the conduct of the studies safely during the COVID-19 pandemic.

Materials and Methods
The Anemia Studies in Chronic Kidney Disease: Erythropoiesis via a Novel Prolyl Hydroxylase Inhibitor Daprodustat (ASCEND) program encompassed five phase 3 trials, of which three were sponsored by GlaxoSmithKline (CSK) and conducted by Pharmaceutical Product Development (PPD). Study details for the nondialysis (ASCEND-ND; NCT028768355), dialysis (ASCEND-D; NCT02879305), and incident dialysis (ASCEND-ID; NCT03029208) trials are provided in the Supplemental Material.

Survey of Study Sites about Operations during the SARS-CoV-2 Pandemic
The sponsor developed and administered a questionnaire in collaboration with PPD to assess the effect of the COVID-19 pandemic on ASCEND research activities at clinical sites (the complete survey is provided in the Supplemental Material). Questions covered whether sites were open or temporarily closed and whether study visits and monitoring activities could be completed as usual or with adaptations such as remote visits and/or use of local laboratories. Furthermore, dialysis-specific questions were used to determine if participants were treated in their usual or different dialysis facilities, and the challenges of the latter in conducting the trials.

Survey Distribution and Analysis
Surveys were disseminated to active study sites beginning April 13, 2020. Survey data were updated...
every 2 weeks, then monthly, and thereafter on a targeted basis, depending on COVID-19 rates in the region. For sites with more than one participant in a study, multiple responses could be provided to describe study activities for participants. For these reasons, denominators for survey questions vary slightly. Survey results were not part of the trial clinical database, and data were not reconciled to the electronic case report forms.

Other Study Adaptations

Beginning February 24, 2020, processes were implemented to ensure continuity of randomized treatment. Where HemoCue hemoglobin (Hb) could not be assessed, study sites were able to transmit locally obtained Hb values to PPD through a query platform. When local Hb values could not be obtained, participants were temporarily placed on standard of care or received no anemia treatment.

Results

Key survey questions and results are presented in Tables 1 and 2.

Site Capabilities on the Basis of Initial Survey (April 13–May 6, 2020)

Across ASCEND-D, ASCEND-ID, and ASCEND-ND, 830 unique study sites in 41 countries received a survey between April 13 and May 6, 2020 (Figure 1). Responses to the initial survey were obtained from 792 sites (95% response rate) and reached 100% by July 13, 2020. Because many sites participated in more than one ASCEND study, they contributed responses to each study; 75% reported that they were able to complete study visits per protocol, with 64% completing all procedures and 7% limited to a subset of procedures (Table 1). Twenty-one percent of study sites reported that study visits could not be completed in clinic. Sixteen percent were able to

<table>
<thead>
<tr>
<th>Table 1. Results of the initial ASCEND site survey (April 13–May 6, 2020): Effect on conducting study visits by study site staff who responded to initial surveya</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survey Responses</td>
</tr>
<tr>
<td>Are site staff able to complete patient visits as per protocol?</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>Full study visits</td>
</tr>
<tr>
<td>Limited to a subset of procedures</td>
</tr>
<tr>
<td>Combination of full/limited study visits</td>
</tr>
<tr>
<td>No response given</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Only by telephone or telehealth</td>
</tr>
<tr>
<td>Only at participants’ homes</td>
</tr>
<tr>
<td>No remote visits completed</td>
</tr>
<tr>
<td>Combinations of above</td>
</tr>
<tr>
<td>No response given</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Is hemoglobin being checked?</td>
</tr>
<tr>
<td>Yes, at the study site/participants’ homes</td>
</tr>
<tr>
<td>Yes, at a local laboratory</td>
</tr>
<tr>
<td>Combinations of “yes” responsesb</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>No response given</td>
</tr>
<tr>
<td>Is the research office able to accept randomized treatment supply samples as normal?</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Is the site able to ship lab samples to central lab?</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>No response given</td>
</tr>
<tr>
<td>If site cannot ship lab samples to central lab, can the site store frozen samples?</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
</tbody>
</table>

Response tallies may be >100% due to rounding. N, the number of site staff contacted. ASCEND, Anemia Studies in Chronic Kidney Disease: Erythropoiesis via a Novel Prolyl Hydroxylase Inhibitor Daprodustat.

aOnly Research sites that had patients on dialysis were included.

bFor “Combination of ‘yes’ and ‘no’ responses,” sites had participants that aligned with each of these responses.
complete study visits by telephone or telehealth, and <1% were able to travel to participants’ homes. In 3% of sites, study visits could not be completed during temporary site closures. Hb testing was largely performed via HemoCue at the study site or at participants’ homes (66%) or at a local laboratory (6%) or some combination of these approaches (10%); 10% reported they were unable to monitor Hb at the time of the initial survey.

Ninety-four percent of sites reported that all patients receiving dialysis continued to dialyze in their usual facilities, 2% reported some patients dialyzing elsewhere, and 4% a combination of the two (Table 2). Overall, for the sites with participants at new dialysis units, 20% indicated that some patients could not continue randomized treatments.

Use of Local Hb Values between March 1 and May 6, 2020 and Overall

At the participant level, 4224 participants (across all three studies) were receiving randomized treatment and monitoring between March 1 and May 6, 2020. Although the majority received study treatment guided by Hb according to the protocol, approximately 3% received randomized treatment on the basis of Hb results obtained at local laboratories, with randomized treatment delivered to their homes; this rose to 5% when looking cumulatively from March 1 to August 24, 2020 (Table 3). Few participants (<2%) were temporarily converted to standard of care anemia treatment, and this outcome was more likely among nondialysis and incident dialysis participants (around 3% each) than for the D study (1%). A temporary switch to no anemia treatment was a rare occurrence (<1%).

Site Status over Time

Figure 2 shows the percentage of study sites experiencing closures through September of 2020 overall and by region. Most regions were able to reopen sites between May and mid-June, despite varying levels of community spread of COVID-19. This pattern was particularly evident for Latin America, which had more site closures than other regions initially but similar percentages by mid-June.

Table 2. Results of the initial ASCEND site survey (April 13–May 6, 2020): Effect on dialysis participants by study site staff who responded to initial survey

<table>
<thead>
<tr>
<th>Are study participants being dialyzed at their regular dialysis facilities?</th>
<th>N=718</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>94%</td>
</tr>
<tr>
<td>No</td>
<td>2%</td>
</tr>
<tr>
<td>Combination of “yes” and “no” responses&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4%</td>
</tr>
</tbody>
</table>

For sites where study participants have changed sites, are the study staff still able to have oversight of participants’ dialysis?

| N=41 |
|---|---|
| Yes | 51% |
| No | 12% |
| Yes, for some participants but not all | 22% |
| No response given | 15% |

For sites where “oversight” is in question, are the staff at the new units aware that the patients are participating in ASCEND?

| N=20 |
|---|---|
| Yes | 30% |
| No | 30% |
| Combination of “yes” and “no” responses<sup>b</sup> | 10% |
| No response given | 30% |

For sites where study participants at new dialysis units, are the staff having difficulty obtaining information about participants, including AE/SAE?

| N=41 |
|---|---|
| Yes | 15% |
| No | 59% |
| Combination of “yes” and “no” responses<sup>b</sup> | 20% |
| No response given | 7% |

For sites with study participants at new dialysis units: Are participants able to continue randomized treatment?

| N=41 |
|---|---|
| Yes | 59% |
| No | 20% |
| Combination of “yes” and “no” responses<sup>b</sup> | 15% |
| No response given | 7% |

For sites with study participants at new dialysis units where randomized treatment could not be continued, is there a possibility that they will resume randomized treatment when they return to regular dialysis units?

| N=14 |
|---|---|
| Yes | 57% |
| No | 21% |
| No response given | 21% |

Response tallies may be >100% due to rounding. ASCEND, Anemia Studies in Chronic Kidney Disease: Erythropoiesis via a Novel Prolyl Hydroxylase Inhibitor Daprodustat; N, the number of site staff contacted. AE, adverse event; SAE, serious adverse event.

<sup>a</sup>Only research sites that had patients on dialysis were included.

<sup>b</sup>For “Combination of ‘yes’ and ‘no’ responses,” sites had participants that aligned with each of these responses.
Discussion

Despite widespread disruption during the COVID-19 pandemic, the effect on the ASCEND trials was limited. Extensive surveying of sites within weeks of the onset of the pandemic and rapid analysis of survey data allowed study leadership to provide guidance to sites to adjust and adapt study procedures. This limited the effect of the pandemic on study centers, research personnel, and participants.

Survey data were also important in driving modifications of study procedures. Mitigation strategies included conducting study visits remotely in participants’ homes, collecting and processing blood samples in a local laboratory or at a participant’s home to inform randomized treatment dosing, and using couriers to deliver randomized treatment to participants’ homes. In some hard-hit areas, sites were temporarily closed because hospital or research facilities were instructed to lockdown and/or study personnel were restricted to working remotely or were deployed elsewhere. In addition, some participants were transferred temporarily to facilities where study personnel could not ensure they would receive treatment according to study protocols. In these cases, the risk of continuing randomized treatment outweighed the potential benefit, and a small number of participants were temporarily switched to standard of care anemia treatment or to no anemia treatment.

Nevertheless, most participants were able to continue to receive randomized treatment according to study protocols. More participants not receiving dialysis had their randomized treatment temporarily interrupted than participants who were on dialysis. Temporary site closures in nondialysis settings were more disruptive to providing randomized

Table 3. Patient-level randomized treatment outcomes

<table>
<thead>
<tr>
<th>Study</th>
<th>Expected Number of Dispensings of Randomized Treatment per Protocol</th>
<th>Continue Randomized Treatment, Dispensed on the Basis of Hb from Local Lab</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial</td>
<td>Cumulative</td>
</tr>
<tr>
<td>ASCEND-ND</td>
<td>2861</td>
<td>7890</td>
</tr>
<tr>
<td>ASCEND-ID</td>
<td>111</td>
<td>162</td>
</tr>
<tr>
<td>ASCEND-D</td>
<td>2640</td>
<td>6785</td>
</tr>
<tr>
<td>Total</td>
<td>5612</td>
<td>14,837</td>
</tr>
</tbody>
</table>

Initial, March 1, 2020, through May 6, 2020; Cumulative, March 1, 2020, through August 24, 2020. ASCEND, Anemia Studies in Chronic Kidney Disease: Erythropoiesis via a Novel Prolyl Hydroxylase Inhibitor Daprodustat; D, dialysis study; Hb, hemoglobin; ID, incident dialysis study; ND, nondialysis study.

a Data reported by Interactive Response Technology system.

b Data reported via queries to Medical Monitors.
treatment because monitoring of Hb was not possible, compared with dialysis settings where routine Hb measurement occurs even outside of study activities.

The approach used by the ASCEND trials during the COVID-19 pandemic had several strengths and some limitations. An important strength was that survey data were disseminated to operational and scientific leaders in real time during the first and subsequent waves of the pandemic to enable mitigation strategies to be developed and used. Second, the high survey response rates of 95%–100% meant that the surveys were highly representative of what was happening globally. Potential limitations included a lack of information about what was happening in the minority of nonresponding sites, especially with respect to whether these sites were closed. Despite site closures in the early stages of the pandemic, study sites became more resilient as the pandemic evolved. Indeed, from May to September 2020, the number of temporarily closed sites decreased substantially. The reasons for fewer closures were likely a combination of lower rates of COVID-19 over time and better adaptation to COVID-19, even when rates were high.

A key lesson learned early during the COVID-19 pandemic for the ASCEND trials was that because COVID-19 occurred in waves that varied across regions and countries, adaptations to study conduct were required. Finding safe ways to continue the trial were creative and diverse and included conducting study visits by telephone or telehealth.

A second important lesson was that Hb assessment needed to be flexible. When the HemoCue Hb assessment could not be done at study sites, allowing Hb assessment at local laboratories to inform dosing of randomized treatment was key to success as evidenced by the small percentage of participants whose randomized treatments were discontinued.

Our lessons on mitigating study disruption during a pandemic may assist the wider clinical research community to consider modifying their approach in designing or conducting clinical trials. The overarching guiding principles were the importance of early and continued assessment of site capabilities and the necessity to act nimbly with site-specific responses, given different patterns and surges of disruptions in different countries. The ultimate goal was to provide optimal care for participants while protecting the integrity of study performance and data collection. Implementation of mitigating strategies that were flexible and targeted limited the extent of disruption to the conduct of the ASCEND trials due to COVID-19.

Disclosures

A. Acharya reports consultancy fees from GlaxoSmithKline. B. Cizman, A.R. Cobitz, and A.M. Meadowcroft are employees of and stockholders in GlaxoSmithKline. R. Correa-Rotter reports scientific consulting and financial support for participation in clinical trials: AstraZeneca DAPA-CKD trial steering committee, GlaxoSmithKline for ASCEND Investigator and National Leader, Novo-Nordisk FLOW national leader and investigator; is an advisory board member for Amgen, AbbVie, Boehringer Ingelheim, and Medtronic; and is a speaker for Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Janssen, and Sanofi. I. Dasgupta reports research grants from Medtronic and Sanofi-Genezyme and is an advisory board member for AstraZeneca and GlaxoSmithKline. K.L. Johannsen reports consultancy fees from GlaxoSmithKline and Akebia. V. Kher reports local INDA consultancy agreements with AstraZeneca, Biocon Pharmaceuticals, GlaxoSmithKline, Intas Pharmaceuticals, Novartis, Panacea, Roche, RPG Life Sciences, Sanofi Aventis, and Torrent Pharmaceuticals; research funding from Astellas India, Novartis India, and Sanofi Aventis India; honoraria from Astellas India, Intas India, JB Pharmaceuticals India, Novartis India, Reddy’s India, Roche India, and Torrent India; is a scientific advisor for Biocon India, Medtronics, Novartis India, Reddy’s India, Roche India, Sanofi Aventis, Torrent, and Wockhardt India;
participates in a speakers’ bureau for AstraZeneca India, Biocon India, Intas India, JB Pharmaceuticals, Johnson and Johnson, Novartis India, Panacea India, Pfizer, Roche India, and Sanoﬁ Aventis India. R.D. Lopes reports grants and personal fees from Bristol-Myers Squibb and Pfizer, personal fees from Bayer AG and Boehringer Ingelheim, and research grants from Amgen, Inc., GlaxoSmithKline, Medtronic plc, and Sanoﬁ Aventis. B. Rayner reports honoraria for CME talks from AstraZeneca, Boehringer Ingelheim, Merck, Novartis, Sandoz, and Servier, and has served on a Servier Advisory Board. A.L. Silver reports research funding from Akebia, Ardelyx, Boehringer Ingelheim, Bayer AG, DiaMedica, Fibrogen/AstraZeneca, GlaxoSmithKline, Goldﬁnch Bio, Novartis, ProKidney, Reata, and Retrophin; consultancy fees from Ardelyx, Boehringer Ingelheim, Novartis, ProKidney, and Reata; and participates in a speakers’ bureau for Amgen, AstraZeneca, and Aurinia. A.K. Singh reports consultancy fees from GlaxoSmithKline. All remaining authors have nothing to disclose.

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Author Contributions
B. Cizman, A.R. Cobitz, K.L. Johansen, R.D. Lopes, L. Matsu moto, A.M. Meadows, O. Merege, A.K. Singh, H. Thomas contributed to conception or design. R. Correa-Rotter, I. Dasgupta, V. Kher, B. Rayner, A.L. Silva contributed to acquisition of data. All authors contributed to the data analysis or interpretation, critically reviewed the manuscript and approved the final version for submission.

Data Sharing Statement
Partial restrictions to the data and/or materials apply. Anonymized individual patient data and study documents can be requested for further research from https://www.clinicalstudydatarequest.com/.

Supplemental Material
This article contains supplemental material online at http://kidney360.asnjournals.org/lookup/suppl/doi:10.34067/KID.0006212021/-/DCSupplemental.

Brief description of ASCEND studies. Complete survey administered to sites.

References

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Supplemental Materials

Challenges of conducting clinical trials during the SARS-CoV-2 pandemic: The ASCEND global program experience


Brief description of ASCEND studies

ASCEND-ND (NCT02876835) is an ongoing cardiovascular outcome trial (CVOT) enrolling patients with chronic kidney disease (CKD) not requiring dialysis treatment, ASCEND-D (NCT02879305) was a CVOT that enrolled patients receiving maintenance hemodialysis (HD) or peritoneal dialysis (PD), and ASCEND-ID (NCT03029208) was a 52-week study that enrolled incident HD or PD patients. All three are open-label (sponsor-blind), randomized controlled trials of daprodustat versus recombinant human erythropoietin (rhEPO).

Participants in ASCEND-ND were adults with CKD stage 3 to 5 who had anemia (hemoglobin [Hb] 8-10 g/dL for those not using erythropoietin-stimulating agents [ESAs] and 8–11 g/dL for prior ESA users). ASCEND-ID participants were patients who were initiating dialysis with anemia (Hb 8–11 g/dL) but had not been receiving ESAs, aside from limited use as part of dialysis initiation. ASCEND-D enrolled prevalent dialysis patients with anemia treated with ESAs (Hb 8–11.5 g/dL); design and baseline characteristics have been previously published (1). Across all
studies, participants were not iron deficient (based on serum ferritin >100 ng/mL and transferrin saturation >20%).

Participants were randomly assigned to receive daily oral daprodustat or rhEPO (ASCEND-D: intravenous [IV] epoetin alfa for those on HD or subcutaneous [SC] darbepoetin alfa for those on PD; and ASCEND-ID and ND: SC/IV darbepoetin alfa). Randomized (study) treatments were titrated to achieve and maintain Hb between 10 and 11 g/dL during a 28-week titration period and a maintenance period from Week 28 through the end of the study. All three trials had a primary endpoint of mean change in Hb between the baseline and efficacy period (mean over Weeks 28–52), while the CVOTs had an additional (co-primary) endpoint of time to first occurrence of an adjudicated major cardiovascular event, a composite of all-cause mortality, non-fatal myocardial infarction and non-fatal stroke.

ASCEND-D recruited 2964 participants from September 28, 2016 to June 15, 2018, had participants receiving randomized treatment after the onset of the COVID-19 pandemic, and completed the last study visit in November 2020; ASCEND-ID enrolled 312 participants between May 11, 2018 and July 22, 2019, with the last study visit on September 24, 2020. ASCEND-ND enrolled 3872 participants from September 27, 2016 through September 25, 2020 which included enrollment during the pandemic, with follow-up concluded in April 2021.

Routine study operations involved participant visits at least every 4 weeks during the titration and efficacy phases of the study (4–52 weeks), and for the CVOTs, at least every 12 weeks after Week 52 until the end of study. During these visits, blood was drawn for Hb determination by a central laboratory for efficacy assessments, and point-of-care Hb testing (HemoCue, Angelholm, Sweden) was performed in order to titrate study medications to maintain Hb in the target
range. Additional blood samples were sent to a central laboratory for routine safety
evaluations, as well as for future analysis of biomarkers.

References

1. Singh AK, Blackorby A, Cizman B, Carroll K, Cobitz AR, Davies R, et al. Study design and
baseline characteristics of patients on dialysis in the ASCEND-D trial. *Nephrol Dial Transplant*.
Complete Survey Administered to Sites

QUESTIONS:

1. Questionnaire completion date: ______

2. Region: ______

3. Site Country: ______

4. Site #s (only complete multiple numbers if the sites have the same PI AND the answers are the same across all studies, otherwise complete 1 survey per site #):
   ASCEND-D: ________
   ASCEND-ND: ________
   ASCEND-ID: ________

5. Name of PPD/LDO person completing questionnaire: __________

6. Role of person completing questionnaire:
   a. RSM-L
   b. CRA
   c. LDO staff
   d. Other: __________

7. Check this box if site personnel was not available to complete questionnaire □
   Reason:
   a. No answer after 3 attempts [please ensure at least 2 attempts with SC + 1 with PI are documented in CTMS. If only PI was reached, no need to go through the entire survey, just check status of the site and who should be contacted for additional information. If no successful attempt, try again in 2 weeks.]
   b. No time to provide answers to the Survey, but subject care is being maintained.
   c. Other - Describe: _______

Site level activities
8. Is research site opened/ temporarily closed/opened part time? (note: only select “temporarily closed” if ALL activities have stopped at the site – even remote activities)
   a. Opened normal hours
   b. Fully closed
   c. Opened part time
      a. If part time what days/hours? ______

9. Who (PI/SI/SC) from ASCEND research site staff is available to oversee the study(ies)?
For the first survey completed for each site, please complete the fields for the PI/SC/Sub-I/Other as applicable. For the subsequent surveys, only complete if there were changes from previously completed Surveys:

i. No changes from previously completed surveys (no need to re-enter name/role/email/phone)
ii. Changes from previously completed surveys (please update name/role/email/phone below)
   i. No (if no, no need to re-enter name/role/email/phone)
   ii. Yes (if yes, please update name/role/email/phone below)

PI

a. Name: ____
b. Email: ____
c. Phone: ____
d. Are the staff listed above available full time/part time?
   i. Full time
   ii. Part time
      If part time, what days/hours? ______
e. Check this box if this person is the primary contact for PPD □

SC

a. Name: ____
b. Email: ____
c. Phone: ____
d. Are the staff listed above available full time/part time?
   i. Full time
   ii. Part time
      If part time, what days/hours? ______
e. Check this box if this person is the primary contact for PPD □

Sub-I

a. Name: ____
b. Email: ____
c. Phone: ____
d. Are the staff listed above available full time/part time?
   i. Full time
   ii. Part time
      If part time, what days/hours? ______
e. Check this box if this person is the primary contact for PPD □

Other

a. Name: ____
b. Role: ____
c. Email: ____
d. Phone: ____
e. Are the staff listed above available full time/part time?
   i. Full time
   ii. Part time
If part time, what days/hours? ______
f. Check this box if this person is the primary contact for PPD □

As per COVID-19 Letter Pack that was distributed 31 March, PPD will be aiming to contact each site every 2 weeks during the pandemic.

10. Confirm with site staff what is a good day/time to set up the first call in 2 weeks? ______________________

Subject study visits and potential safety (tick all applicable options)

11. Are site staff able to complete patient visits in clinic as per protocol at research site?
   a. Yes - If yes, are these full study visits or limited to a subset of procedures (e.g., checking HemoCue Hgb)
      i. Full study visits
      ii. Limited to a subset of procedures (e.g., checking HemoCue Hgb)
   b. No - If no, is a remote visit being completed:
      i. By phone or by telehealth (telemedicine)
      ii. At subject home
      iii. No remote visit is being completed (please add details to the Comments free text field below)

C. Is hemoglobin being checked:
   i. HemoCue (site/subject’s home)
   ii. Local lab
   iii. Not at all

12. Answer ONLY if site has subjects in ASCEND-D study (807), or ASCEND-ID study (410), or subjects in ASCEND-ND study (808) who transitioned to dialysis:
   Are study subjects being dialyzed at their regular units? [reminder: ask site to provide information on a subject basis. In CTMS, Subject Screen, under the “Comments” free text field, enter #COVIDDIFFDIALYSIS to track subjects who have NOT been dialyzed at their regular dialysis units]
   a. N/A site does not have any subjects in dialysis
   b. Yes
   c. No [reminder: ask site to provide information on a subject basis. In CTMS, Subject Screen, under the “Comments” free text field, enter #DIFFDIALYSIS to track subjects who have NOT been dialyzed at their regular dialysis units]
   d. A combination of above

   ONLY answer next 4 questions if you answered ‘NO’ or ‘A COMBINATION OF ABOVE’ to last question and subjects ARE at new dialysis units
   i. Are the study staff (PI/SC) still able to have oversight of subjects dialysis? [reminder: ask site to provide information on a subject basis. If study staff will NOT have oversight of subject at the different dialysis facility to ensure no repeated double ESA dosing, subjects should temporarily stop RT and initiate SOC. In CTMS, Subject Screen, under the “Comments” free text field,
enter #COVIDSOC to track subjects switched to temporary SoC OR #COVIDNOTRT to track subjects with NO anemia treatment (ie. switched off RT and SoC not an option)
   a. Yes
   b. No [reminder: ask site to provide information on a subject basis. If study staff will NOT have oversight of subject at the different dialysis facility to ensure no repeated double ESA dosing, subjects should temporarily stop RT and initiate SOC. In CTMS, Subject Screen, under the “Comments” free text field, enter #COVIDSOC to track subjects switched to temporary SoC OR #COVIDNOTRT to track subjects with NO anemia treatment (ie. switched off RT and SoC not an option)]
   c. A combination of above

ii. Are the staff at the new units aware that the patients are participating in the ASCEND study?
   a. Yes
   b. No
   c. A combination of above

iii. Are the staff having difficulty obtaining information about the subjects including AE/SAE?
   a. Yes
   b. No
   c. A combination of above

iv. Are subjects able to continue randomized treatment? (Select all options that apply) Jagadeeswari, can we allow them to select all options for this question?
   a. No - If subjects cannot continue randomized treatment is there a possibility that subjects will resume randomized treatment when the subjects return to their regular dialysis units?
      i. Yes
      ii. No
   b. Yes - If subjects can continue randomized treatment at the new unit, what process has been implemented to prevent double dosing - Add Comments: ________________________________

Monitoring Activities / Data Queries

13. Are the site staff able to complete onsite AND remote monitoring visits as planned?
   a. Yes
   b. No - If no, can monitoring visit be done remotely?
      i. Yes
      ii. No
14. Are the site staff able to process data queries during COVID-19 pandemic?
   a. Yes
   b. No
   c. Limited

Shipments
15. Is the research office/dialysis centre able to accept randomized treatment supply shipments as normal?
   a. Yes
   b. No - If no, is there an alternative address to send shipments?
      i. No
      ii. Yes, list: _______________

16. How often is the site monitoring randomized treatment storage temperature?
   a. Normal RT temperature monitoring on business days
   b. Partial RT temperature monitoring – describe: _______________
   c. No RT temperature monitoring is possible

17. Is the site able to ship lab samples to Q2 central labs?
   a. Yes - If yes, are there any restrictions on days/couriers?
      a. No, no shipment restrictions
      b. Yes, specify_____________
   b. No - If no, does the site have capacity to store frozen samples?
      a. Yes
      b. No

18. Does the site have sufficient lab kit supplies?
   a. Yes
   b. No - If no, has this issue already been flagged to PPD?
      i. Yes
      ii. No

Comments (please feel free to add any additional information about the site status or clarify any responses provided): _______________