



COVID-19
Coronavirus

Highlights and Summary of Part 11 Webinar:

The Impact of COVID-19 on Oncology
Research: Immediate and Long-term Effects

More clinical trials are conducted for cancer than for any other therapeutic area. These trials often include participants who have exhausted the available treatment options, so when COVID-19 forced a re-assessment of ongoing and upcoming cancer studies, patients and care providers were placed in a difficult situation: continue or halt the study?

During this webinar, we heard two perspectives: a leading cancer researcher's, and that of a patient who was in screening for a new clinical trial when everything closed down.

Featured speakers:

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George Demetri, MD

Senior Vice President for Experimental Therapeutics, Dana-Farber Cancer Center; and Professor of Medicine, Harvard Medical School



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Rene Roach

Stage IV Colorectal Cancer Survivor, Patient Advocate Working with Colontown and Tom's Trial Guides



Lindsay McNair, MD, MPH, MSB, *Chief Medical Officer, WCG*, moderated.

This is the 11th in [a series of WCG webinars](#) that address the coronavirus-related challenges facing the clinical trial industry. You can find links to this webinar and an array of COVID-19 resources on our [WCG Insights Program](#) page.

The View from a Major Cancer Center

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George Demetri, MD

*Senior Vice President for Experimental Therapeutics, Dana-Farber Cancer Center;
and Professor of Medicine, Harvard Medical School*



The COVID-19 pandemic has had dramatic impacts on cancer clinical care and research on every level, including immediate and long-term impacts, as well as positive and negative impacts.

Immediate Negative Impacts

The immediate impact on the United States and Western Europe, and elsewhere, was incredibly negative.

Fear and concerns for safety among patients, family members, healthcare professionals at all levels: We were facing something we had little data on. And we all knew that our cancer patients were an especially vulnerable population.

One patient was featured in a [New York Times](#) article. He's lived with a rare type of cancer for 21 years. When he needed a procedure during the pandemic, he feared being hospitalized and contracting the coronavirus. The fear of COVID has led many patients, including cancer patients (but not only cancer patients) to either delay or forego treatment.

Confusion: In the United States, there was a tremendous amount of confusion and no clear message about how we should deal with oncology treatment at the national level, and states and regions were left on their own to figure it out.

Shutdowns resulted in staffing concerns, problems with accruals and compliance. Cancer clinical trials were open in some places, closed in others. And we were seeing a great deal of heterogeneity in terms of dealing with the issue of how to continue clinical research and clinical trials, or whether to just simply stop them cold turkey.

Some of the decisions to close research were very justifiable. If you don't have a lot of staff to conduct a clinical trial, you just can't conduct a clinical trial. Many centers said, "We can't put our staff there. We can't put the patients at risk to participate with too few staff." So they simply shut down the trials. Another concern: Would patients be willing to come in to a site or hospital for protocol-related assessments? Naturally, sites were worried about accruals and compliance before the FDA was giving clear guidance.

Immediate Positives

There were a few immediate positives.

Public attention to the positive impact and absolute necessity of clinical research: Everybody knew this was a virus the world had never seen before. It was shutting down economies and livelihoods and killing people around the world. And everybody said, we need researchers. We need an answer to this, and it's only going to come from research.

Concerns for the welfare of people with cancer as an especially vulnerable population.

The immediate impact, positive and negative, led to near-term advancements.

Near-term Advances for Cancer Research

FDA communications: The FDA made it as clear as they possibly could that they would use common sense and put patient protections at the forefront of good trial practice.

- March 2020, the FDA communicated guidelines for clinical research trials in a time of pandemic, offering reassurance to investigators, to sponsors, to companies, CROs, that trial deviations such as delayed or missed dosing or minor changes and visit dates, due to patients or participants not wanting to come in on a certain day, would be acceptable.

- The FDA took to Twitter to get the word out about those changes.
- The FDA Oncology Center of Excellence posted a message to patients and providers, reassuring them that modifications could be made and updating them on Expanded Access/Compassionate Use and Emergency Use requests.
- Outside of oncology, the FDA continued to push guidance for industry and other stakeholders.

Release from (unnecessary) regulatory burdens: The FDA was saying, we're going to use common sense. We understand there's a pandemic going on. "And I thought that was extraordinary."

Sponsor acceptance of virtual visit data on patient status; use of local labs; and shipping study drugs to patients' homes: Novartis and some others immediately sent out a message saying, for all of our patients on all of our trials that use oral study drugs, you can ship drugs to the patient's home. Eventually, virtually every sponsor with an oral study drug was able to say, "Okay, ship it."

- **Reimbursement for services rendered via telemedicine:** (CMS and states ultimately forced payors to cover services.) Some states, including New York, waived some licensing regulations, saying in effect, "If you're in Massachusetts, if you're not licensed in New York but you want to do a telemedicine consult in New York, feel free, go right ahead. Our patients need your help."

▪ **Rapid reviews and approvals of clinical trials:**

We were seeing a lot of COVID-19 clinical trials being fast-tracked in their development, and their review and implementation. And these rapid reviews and approvals showed the system really can approve things quickly. It doesn't have to take three to six months to get a trial off the ground and get patients treated. (On the other hand, not all of those trials are of high quality.)

BUT, immediate Impacts also resulted in near-term challenges

Complete and utter confusion about conclusions which could be drawn from poorly designed and woefully uncontrolled "studies" of agents literally "thrown at" COVID-19; this led to lack of public trust in clinical research.

Non-transparent Emergency Use Authorizations for testing led to lack of trust in FDA reviews and politicization of research and review processes for tests and drugs.

Clunky initial application of FDA rules for lab-developed tests at academic centers without providing sufficient alternatives; this led to delays in adequate access to viral testing and no clue as to what should be done for antibody testing.

All of these challenges, related to COVID-19 research issues, bled over into cancer and other scientific research.

Near-term diversity in cancer research solutions:

There was no single approach. Many clinical trial sites

and studies simply stopped. (Rene Roach will address that next.)

Some, including Dana-Farber, chose which studies to continue based on internal rules. That included continuing trials of therapies already proven to benefit patients. Those yet to show benefit were put on hold for a month or two, until there was more certainty and clarity.

And a few centers tried to continue as if nothing had changed, but that didn't last long.

The Most Important Changes in Cancer Research

Telemedicine tops the list: "What a breakthrough for our patients to have that level of convenience. I hope we don't go back too far." Telemedicine can reduce disparities--or intensify them in areas with limited bandwidth.

Discerning which trials are critical for patients near-term: Centers focused on keeping open trials that really make a near-term difference for patients: e.g. Expanded Access Program trials of drugs that were close to FDA approval based on already-documented patient benefit.

Longer-term Implications and Impact of the COVID-19 Pandemic on Cancer Research and Clinical Trials

We're seeing **positive impacts** from:

- **Telemedicine**
- **Recommitment to the "Urgency of Now"** for cancer research



- **Respect for high-quality, reliable and interpretable clinical research** that leads to substantive benefits and real answers for patients and doctors
- **Respect for patient preferences and values:** What trials do PATIENTS want? Focusing on what patients want and how to keep patients and participants safe
- **The potential for legislation that could set a level playing field** for reimbursement that would decrease “geographic disparities” in cancer research and support diversity in accruals
- **Speed of review and approval** of trials, while preserving appropriate protection of participants
- **Identification of mechanistic linkages** between cancer trials, infectious disease trials, pulmonary and inflammation trials, etc. (e.g. vaccines against cancer may benefit from anti-COVID-19 vaccine investments)

Negative impacts include the following:

- **Public funding may decrease in cancer research** as the world shifts to fund COVID.
- **Reliance on industry funding may become nearly pathologic** (since there are many questions which need to be asked but will not be funded by industry).
- **Hospitals will be more financially challenged than ever, and cancer care/research may suffer.**

- Cancer--and other--research may be more limited if the pandemic is not controlled quickly.
- For some, science has been perceived as an economic competitive force rather than a force for global good and rule-of-law-based cooperation. We need to feel like we’re part of a world and not withdraw into our own part of this globe.

To sum up:

- Cancer clinical trials are drafting after the push for high-quality COVID-19 clinical research, and the science of cancer is informing the most innovative aspects of COVID-19 research.
- Science is perceived as the “way out of this mess” by the general public and most governments.
- Globally, we really are all in this together, and solutions will come only from scientific advances and wise public policy.
- We will get through this, and we have tools that never existed before this time to help us.
- We will get out of our own way in research and development to find the best solutions (while protecting our most vulnerable compatriots).

A Patient Perspective

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Rene Roach

Stage IV Colorectal Cancer Survivor,
Patient Advocate Working with Colontown and Tom's Trial Guides



Rene Roach, a mechanical engineer, was diagnosed with stage IV colorectal cancer in June 2016. With her scientific background, she became very interested in learning about the evolving treatment and cancer screening landscape. She's a member of Colontown, a support group for colorectal cancer patients, their caregivers and the healthcare providers who treat them, and of Tom's Trial Guide, an organization to help educate colorectal cancer patients and their caregivers about clinical trial participation and options.

A Timeline of Diagnosis and Treatment

2016

June: Diagnosed with stage IV colorectal cancer--a primary tumor and a 1 cm liver metastasis (met)

Treatment: Microwave liver ablation, Folfox chemotherapy regimen and surgery

December: No evidence of disease

2017

Follow-up chemo plus temporary ileostomy reversal. "And then I was good. I went back to work and I thought life was good."

2018

May: CEA increases but scans clear. "I remember my doctor at the time just said, 'We have to let the story play out.' Well, that's not good enough for me."

Screened for an NIH trial using rising CEA as a measure. They found a 9 mm brain lesion; assumed it was a brain met.

August: One dose SBRT--stereotactic radio therapy--and stable since.

"I'm not convinced it was a met, though, only because my CEA never dropped; it continued to rise. And I know you can have benign lesions in the brain, but given what we knew at the time I just decided to opt for the treatment. Looking back, I probably would have waited three months just to confirm, to see if maybe it was benign, because it has now haunted me when I look for clinical trials."



December: CT scan shows recurrence in left iliac chain and retroperitoneal lymph nodes.

2019

January: Eight rounds of Folfiri and Avastin; CEAs started rising again.

June: Began NCT02671435--Study of Durvalumab and Monalizumab.

- Assigned to arm that receives Monalizumab and Erbitux ("I really wish we could get better names for these drugs.")
- Great quality of life, initial results show 25% reduction, next scan shows stable tumors

December: Leaves trial due to lymph nodes increasing in size and a suspicious site next to original brain met.

2020

January: Johns Hopkins confirms the brain site is just scar tissue due to SBRT.

- Screened for trial at Duke--NCT03822117--Efficacy and Safety of Pemigatinib.
- Foundation One report from Jan. 2019 showed an FGFR1 rearrangement in variants of unknown significance, but a biopsy done Dec. 24, 2019 did not show the rearrangement, so she did not qualify.

Physicians (at Duke and Hopkins) encouraged her to consider another trial at Duke: NCT03866239--Cibisatamab in Combination With Atezolizumab After

Pretreatment With Obinutuzumab in Participants With Previously Treated Metastatic Colorectal Adenocarcinoma. Told she was a great candidate because she was healthy, despite her cancer.

Prescreened, then everything shut down because of COVID-19.

May 2020: Back on CAPOX chemo regimen.

No word from Roche or Duke about when the study will reopen. One complication: Tocilizumab, used in the trial to prevent cytokine storm, is being used to treat COVID-19 patients.

"So the fear that myself and other people who were screening for this trial is that this may never reopen because of drug shortage. If they're using this drug to treat COVID patients, will they still be able to open the trial up? I guess we'll have to see."

Making it Better: How Could Clinical Trials Be Improved?

1) Flexibility

Take some of the things that were used to respond to COVID-19 and apply them to all trials, especially oncology trials:

- **Telemedicine visits** during the trial and especially during pre-screening.
 - Cost savings for patient: "During prescreening,

there's such... a time cost to the patient. There's usually travel and possibly a hotel visit that you're not reimbursed for."

- Broadening access for potential patients

- **Move trial activities closer to home**

- Coordination of study drug administration closer to home: For example, collaborate with other hospitals. "Maybe you go to Anderson for your initial visit, for your biopsies, your blood work, but then maybe they could coordinate with a hospital like Hopkins where you could get your infusion. That would really help."

- Oral medicine shipped to home

- Scans done closer to home

- Build in more flexibility to avoid putting studies on hold--this will be important if we see a resurgence of COVID-19 this Fall

- When trials of targeted therapies start seeing promising results, have ability to add additional arms to combine with other known targeted therapies or chemo

2) Expanding eligibility criteria

When study population is strictly defined, fewer studies are available as options; if one goes on hold there may not be any others.

"For instance, that's something that I'm finding. I'm fortunate that CAPOX seems to be working, but as most stage IV cancer patients will tell you, there's going

to come a point where it's not, and I don't have a lot of options in front of me."

- Many trials exclude potential participants based on presence of brain metastases. If brain metastases are stable for a year or more this should not exclude you. The FDA and sponsors can be more flexible on this.
- Prior immunotherapy is often excluded. Perhaps add another arm to studies to allow this.
- Have more trials available for people with minimal residual disease: Typically these patients are healthier and may respond better than when disease is advanced. "You think about that snowball, turn it into an avalanche. It's lot easier to stop that snowball."

For instance, when I was declared "no evidence of disease" but we had the rise in CEA, there really weren't many trials out there that I could look at. One at NIH popped up and that looked promising, but of course I was excluded."

3) Improving communication

We need more collaboration among sponsors, sites and patients in deciding what studies are going on hold, if possible. For example, for patients with stage IV cancer the risk of progression may outweigh the risks of COVID-19.

- Communicate with patients about study status.
 - Clinicaltrials.gov shows studies as recruiting now when they are actually on hold.
 - Sponsors and sites don't return calls or emails about whether studies are open. "I don't

know if they're overloaded or if it's just maybe understaffed, but just a simple email back saying we're on hold or something. Just so patients aren't left wondering what's going on; I think that would be important."

- Share study information when possible.
 - Important for patients to feel more informed.
 - Participants in trials typically have biopsies and additional procedures and blood tests. Data learned from these would be appreciated and helpful.

"I know for myself, the trial I did at Hopkins, I had several biopsies, so much blood work. I used to joke around if they were leaving me any. And I have yet to hear anything. I probably will never hear anything about what my contribution was to this study. And that's a shame, because you would like to feel like you had a positive impact."

Final Thoughts

We need to get trials open ASAP. Cancer isn't stopping due to COVID-19. It will take time to get people back in the study.

"I always say nothing moves fast in the cancer world, at least from my perspective. Every time I reached out for a trial, it's usually taken weeks, if not a month, to find out if you're even going to be on the trial. And then usually once you get admitted to the trial, it's another week or two before you start treatment, at least from my experience."

When you're a stage IV cancer patient and you're not on any treatment because you're waiting for this trial, you kind of feel like you're rolling the dice. Patients are feeling frustrated and helpless and forgotten.

"I just hope that we're not forgotten. And that things start moving."



Questions from Audience

Questions for George

&

Questions for Rene

George Demetri, MD

*Senior Vice President for Experimental Therapeutics,
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Harvard Medical School*



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Q

George, how did you make decisions about what visits could be done remotely and what you still needed to have people come into the clinic for?

A

Dr. Demetri: This was all completely personalized. We really assessed what the risk of the intervention was, the treatment was, how the patient had been tolerating it, whether there were any symptoms. The doctors, the nurses, the nurse practitioners, the research nurses were all calling the patients, trying to get a sense of how they were doing. And frankly, we have a low threshold to say, "Look, it's safer to come in and let us see you than to try to do this from afar." But we also use common sense.

We have a number of people on oral drugs for, let's say, two years for these targeted therapies. Somebody is on an investigational oral drug for two years, they don't have to really come in every month even if the protocol says they do. So those were easy shots. Those were easy telemedicine visits. I don't think that's unique to cancer clinical trials, I think that's an issue with telemedicine in general.

How does the primary care doc assess a patient with chest pain in telemedicine when you can't really do a physical exam? I think the future of telemedicine is going to be better tools that are going to be at the patient's bedside so that we can really do more. And in the meantime, we do the best we can. And I think the patients recognize that, and they responded wonderfully, as did the sponsors. I think the sponsors have been very pleased with the quality of data we've been able to collect despite the telemedicine format.

Q

In terms of being able to have IV drugs available closer to home, scans done closer to home: George, I think you may have some experience with actually being able to do those things. Could you tell us a little bit about that?

A

Dr. Demetri: I will say, I try to take the patient's perspective as much as I can. And we had a patient who was coming up from Florida for a study written by one of my colleagues here at Dana-Farber. We were technically the sponsor, even though the drugs... there are two drugs, one given by a pharmaceutical company called Eisai, one given by a pharmaceutical company called Merck. So two drugs, both FDA approved for other indications. So it's research, and it's under our control, and it's IRB approved. This patient was flying up from Florida once a month to get the treatments. And then COVID hit. And he calls me, and he says, "I don't feel comfortable getting on a plane." I said, "Well, what do you want to do? We could give you these drugs outside of the protocol."

He said, "Yeah, but..." Oh, by the way, they were helping him, his tumors had already shrunk about 40%. He's doing great, not having a lot of side effects. So he said, "No, I want to continue on the study." I said, "But the study doesn't allow us to ship the drugs down there, because we have a supply of drugs that's given to us but let me see what I can do." So I called a friend at the University of Miami Cancer Center... and explained the situation to him. And he said, "I bet if he's got good insurance, I can get the insurance company to pay for it, because it's already helped him."

So he was able to get that. And we actually changed the patient over to get the same protocol with the drug, now commercial, but we're going to try to use his data in the protocol, because frankly he's getting the same stuff. We shipped the rules and the protocol down to Dr. Trent. He's conducting the protocol, just like we would do, only with a commercial supply of drugs. And our research nurses are checking in with the patient by phone at the same periodicity, the same frequency. So to me, that was a novel, somewhat disruptive solution to a problem of not wanting to travel. If he were my brother, I wouldn't want to be on an airplane six weeks ago. Frankly, I don't want to be on an airplane now, for that matter.

And again, I hear sometimes from the industry, "Well, but study procedures might have to be done at the site, because the investigators are trained."

Well, I get that. But I also think we have to show both common sense, and recognize that not all study procedures are the same. A standard CAT scan is a standard CAT scan. It's going to be the same in Boston, at Dana-Farber, in New Hampshire, frankly, and Canada and France. And if you get it at Dana-Farber, I don't really tell the radiologists how to do it. As the principal investigator, yes, I'm responsible, but there's no special rule. So I think that's a commodity. Now what about a more complicated thing,

like genetically engineering your T-cells with a special gene to go in and fight the cancer, then freezing them, and thawing them, and giving them back to the patient? I wouldn't want to have that done at a random community hospital that doesn't have training in that. But I think study procedures run from the commodities is highly bespoke, personalized, sophisticated stuff that you have to be highly trained to do.

So again, I think this is where we, as an investigative community, as patients, and as patient advocates, and frankly, eventually legislators, we just need to have some common sense and make the rules feasible, protect patients, protect the integrity of science, but also emphasize that you can be flexible and still conduct a high quality study. After all, if everything has to be done at Dana-Farber, and you get a certain answer, and you don't get that answer somewhere else, how reliable is that data? If you have to take hydroxychloroquine only at one place in the south of France to get benefit, it's not reliable. And I just read that France has now taken away hydroxychloroquine as something they would treat COVID-19 with, based on the bulk of data. Again, I think we all have to be recognizing that science is self-correcting, and that if we do our jobs, well, it should be reproducible regardless of the type of service. Unless it's a highly sophisticated intervention like engineered T-cells, or CAR-T's or something. But that would be my comment.

Q

Rene, can you tell us a little bit about the impact and considerations for the patients' and participants' social network? What is the experience like for caregivers, spouses, parents, children who may be involved in the participants' care as part of the trial? What has COVID-19 done to their experience with regard to studies?

A

Roach: I live about an hour from Hopkins. And so when I go in for my infusions, I typically need someone to take me on this current chemo, just because I tend to get side effect, where it locks up my muscles a little bit in my legs and I just don't feel comfortable driving. Luckily for me, my daughter is now done with college, so she can drive me. I even had a friend's daughter, that lives next door, take me, so that my husband could keep working, since he has his own business and is our primary source of income, to the treatments. But what that means is, they're sitting in a car for about four hours at least. And then, of course, they drive back and forth. So you're talking about six hours-plus of someone's time.

And at first, when we were going to Hopkins, I wasn't even sure my daughter could come in to use the restroom, but they have the first floor open now. So for people waiting, they can use the restroom.

But of course, nothing in Baltimore is really open at this point because of the virus. So, you're basically stuck sitting in a garage. The other thing that I see is, that I am doing icing, which is to help with the Oxaliplatin side effects. And it's been wonderful. But it has been challenging, because I had to do it by myself. Whereas my first treatment, I was able to have a friend come with me. And things like that make it tougher. Also, just having your loved one there, I think sometimes they feel isolated and left out.

At least with the telemed visits now, they can be in on that, when you're talking to the doctor, or if you're getting results. But it's something that I hope will change. I know I was talking to the nurse at Hopkins yesterday, and they really want to be able to have visitors come, but they just need to find out a way to do it safely.

Q

George, I think you had some examples of Dana-Farber kind of having this same challenge, because people come in from such a long distances to get treated there in Boston, and how they have tried to make some accommodations to the needs of caregivers and companions. Could you tell us a little about those?

A

Dr. Demetri: I have infinite respect for our facility's leadership; they met with us--physicians and nurses. And we recognize that since patients had to be dropped off at the door, and then the driver would be going away somewhere, we opened up a whole floor of our parking garage, installed special high speed Wi-Fi, so that they could be there. Made sure they had adequate bathroom access, so they could be there. But I've had consultations with people, with the spouse in the car downstairs, on the phone, so that they're virtually participating. It made it possible. We have some trustees who knew the Red Sox leadership. As you may know, Dana-Farber is a charity of the Boston Red Sox. So when we really got busy, they let us send the spouses over to parking areas over at Fenway Park, which had easy access to places to use the bathrooms, to walk around, to have Wi-Fi.

So, I think we always try to put the patient experience at the top of our mind. And with the patient experience, which we know is terrible when the patient is alone, we also put the caregiver and a friend or whoever's bringing the patient in, their experience as well. They're part of the care team too.