Dr. Cesar Boggiano

Behind the Mask Interview

October 15, 2020

Barr: Good morning. I'm Gabrielle Barr from the Office of NIH History and Stetten Museum. Today is October 15, 2020, and I have the pleasure of speaking to Dr. Cesar Boggiano. He is the Chief of Preclinical Research in the Development Branch at the National Institute of Allergy and Infectious Diseases (NIAID). Thank you very much for talking to us today. Can you describe the work that you have been doing in leading a team of experts in assessing, prioritizing, and advancing therapeutic and prophylactic interventions against COVID-19?

Boggiano: Good morning, Gabrielle. Around mid-April 2020 it became clear that monoclonal antibodies targeting SARS-CoV-2, the virus that cause COVID-19, were going to be an important part of the effort to treat and prevent the disease. With that in mind, Dr. Mary Maravich, the Director of the Vaccine Program at the Division of AIDS, encouraged and organized a team that was to look into the design and development of monoclonal antibodies. That team was formed to facilitate the path to the clinic of those products.

The team—that I was assigned to lead—what we were doing pretty much was the review of all the different applications and individuals, academic or companies, that had developed those types of antibodies. This is pretty much what we were doing. There were a lot of applications getting into NIH. We were funneling those to the specific areas so, if they were ready for the clinic, they already had a manufactured product that they wanted, we would send them to the network and, if they were needing more data on their products, for example, experiments with animals or in vitro data, we were funneling to different services and opportunities. They should be able to improve the data they have and to be able to get those products to the clinic. The final goal was to try to get those products to the clinic, especially the ones that were more ready to get into the network to be tested and to send the ones that were not so ready to the services that could help them get there.

Barr: Okay. That's interesting. So, when did you start assembling your team and what kind of experts are those who are on your team?

Boggiano: First, I'm in the Division of AIDS. However, we in the team we included expertise with other sister divisions. Our sister divisions are the Division of Microbiology and Infectious Diseases (DMID) and the Division of Allergy, Immunology and Transplantation (DAIT). So, the team included members from the three divisions. Regarding expertise, we have Ph.Ds., we have M.D.s, we have people with experience in manufacturing, we have experience with regulatory, and we needed a very comprehensive group from really basic science to translational science to be able to define and to evaluate properly those applications.

Barr: How many therapeutics have your team assessed so far and what is the process like in vetting? You've talked a little bit of how you go about your process, but what is it like to vet these therapeutics and how many are sort of abandoned before they ever get to trial?

Boggiano: So far, we have evaluated about thirty of these products. They cover pretty much from a polyclonal, monoclonal, or even nanobodies (that are one very small version of antibodies). The way we set up the assessment depends on the criteria that we use. First, the potency was important, and the potency can be evaluated in vitro. We can see how potent those products are in inhibiting the replication in vitro of SARS-CoV-2. The other way to evaluate potency is with animal models, so there you can use hamster, mouse, or other non-human primates. The more potent they are, the better they are because, when we need to manufacture it, if they are very potent, if you have 100 kilos, you can vaccinate way more people. It's very important that, if they are not so potent, it was a key factor.

The other thing that we take into consideration is how they were ready regarding the manufacturing process, that they have a final plan for their product. They have a manufacturing partner because we need to be able to translate from the research that is in the lab to get it into the clinic. We need a product that is manufactured under GMP, that is Good Manufacturing Practice. The product has to meet certain standards. One of the things that we look into is how far they were in the process, if some of them already have the part of GMP product. That was very important for us.

The other thing that was important is they were already in discussion with FDA. At that point we were not pursuing with our group any Phase I trial—that is first in humans—so it was very important for us to hear what was the FDA take on that. And of course, we sign for every single one of these, we have a specific confidentiality agreement. So always the first step of this process was to sign a CDA [Confidential Disclosure Agreement], between the company or the academic institution and NIH. After that we could continue the conversations.

Barr: Wow! That's a larger process than I think a lot of people realize when we read about it in the newspaper or see it on tv. Much longer! Do you think there has been equal attention to therapeutics and prophylactic treatments or do you approach them similarly or differently or is one area getting more concentration than another?

Boggiano: Actually, in this group that I'm working with we have representatives from both: from the people with interest in therapeutic and prophylactic use of the antibodies. In general, I think that's the clinical approach from the company that is in discussion with the FDA. In general, what has happened usually—this is not set in stone—what we have been seeing is usually first these products are tested in infected people, in people who are hospitalized to see and how they work. Then later they get into people who are not infected, that is the prophylactic use.

You have to think the same with vaccines, that you need to think about the risk, but also the balance, the risk:benefit ratio. The risk:benefit ratio in someone who is hospitalized has a benefit much higher than when you think about putting it in a healthy person. That usually goes up, so in general the path of this project was first to using it as a therapeutic and then later as a prophylactic.

Also, for a prophylactic usually you don't want something that is an IV, that is put in your veins. That is easier when somebody is hospitalized. It depends if the formulation of the product is easier to formulate as [an] IV and then later you move into subcutaneous or intramuscular application. Those are some of the multiple pieces to take into consideration. Clearly, there it is case by case; it depends, but that is the general path that the products that we have seen have gone through.

Barr: Interesting. So, you have worked with the vaccine research program at the Division of AIDS for many years. You know about leading a team doing design development and evaluation of potential AIDS vaccines to stop the spread of HIV. How has that knowledge and your experience that you've gained in that role equipped you to tackle COVID-19?

Boggiano: I think we wouldn't be where we are without the last 30 years of HIV research. I think we have learned so much, as I always say, I think COVID vaccine rests on the shoulders of HIV research in general. I think, so far, the understanding from the biology and the immunology of the structure of the spike of the SARS-CoV-2 virus and all we learned from HIV over the years has been extremely helpful. The mistakes that we have made in HIV over the years, now we can let the COVID-19 investigators look out for these.

Also, we have better tools right now than we had 20 years ago with HIV.

The other thing that is very important is, as you know, the COVID-19 Prevention Trials Network was created/establish and to evaluate vaccines and antibodies to prevent SARS-CoV-2 infection. Many of the HIV networks are part of that, including the HVTN [HIV Vaccine Trials Network]. The HPTN is the HIV Prevention Trials Network and also other non-HIV ones like the Infectious Disease Clinical Research Consortium and the ACTG, the AIDS Clinical Trials Group, is also part of that.

So, these networks provided a structure and organization that you need. We are running clinical trials with 30,000 people and, without the structure that we had from this pre-existing network, we would never have been able—and that includes developing the protocol for the trials, the regulatory and the clinical sites to test the vaccines—to do the recruiting. We have people that are experts looking for people and making a case on why it's important for them to sign up for this trial. All that has been extremely important to be able to move forward with the vaccine.

You look at the list. If you go to the World Health Organization, they have a list of all the different approaches that are being used for COVID vaccines. Pretty much every single one of those approaches has been one way or another associated with HIV, with HIV vaccine research. So, regarding antibodies for prevention of infectious disease that is very widespread right now, we are… HIV-spearheaded as the only efficacy trial testing a monoclonal antibody to prevent HIV infection and it is about to be wrapped up very soon. We have years of experience using monoclonal antibodies to prevent and treat HIV

infection. I think that's the reason why our group in the vaccine program, where we are very involved with monoclonal antibodies, were tasked to do this participation and sieving of the applications that were coming in.

Barr: That's interesting. Do you think it'll be easier since you know the viruses although they seem very different, HIV and COVID-19? Do you think it will be easier to have effective treatments for COVID-19 than it has been for HIV?

Boggiano: I'm very hopeful for now and one of the reasons I am hopeful is: in HIV infection, after a person gets infected, it takes about two to three years for the infected individual to develop these super powerful antibodies that are able to neutralize the virus, in about 20 to 30 percent of the people. In COVID-19 it takes weeks to develop those antibodies. Looking into that is one reason why I'm hopeful that it is a more achievable target. The other reason is, although both are RNA viruses, RNA viruses mutate a lot. Just looking at the diversity of, for example, the diversity of HIV in one individual is equivalent to the diversity of flu in the whole world.

SARS-CoV-2 doesn't mutate as much as HIV, so that also gives me hope that the virus itself doesn't have the tools that HIV has to be able to mutate and escape from whatever thing that we throw at it. So, taking just those two things into consideration, I'm more hopeful that a vaccine will be more successful and the treatment that we are doing with antibodies will also be more effective.

Barr: Okay. Hopefully so. At this time or during the pandemic are you on campus or at your home or a combination, and what has it been like to work in a very different environment?

Boggiano: I've been back to the office only once since February 18. I was on vacation before the pandemic, so I never came back after February 18 except I went one day to pick up a flash drive. It was very eerie to see the empty building; it was very weird. To continue to work remotely, we have to learn. In general, we were very prepared for telework, however, usually, people were teleworking one or two times a week, so pretty much we were set up to work remotely. However, it's very different to really not see anybody ever than to telework only one time a week. But I think we managed to get this job done. There are a lot of limitations that happen with this medium of communication, but we don't have many other choices and I think we have proved that we can be very effective to continue working remotely until the conditions are better, I think we may need to continue working remotely. I think this is challenging because you need to adjust your living space; you need to share the space, your working space, with your family and that is very challenging for everybody. But everybody's being patient and considerate and we keep moving forward.

Barr: Definitely. So, what has kept you grounded during this very exhilarating, but I imagine very stressful, time for you?

Boggiano: Well, I think we always, everybody, rely a lot on our friends and the way that we, without the physical contact, relied a lot on Zooming with our friends and family. I think that's the main support that we've all been getting.

And the most important is the privilege of the mission that you get the opportunity to contribute to something affecting the whole world. I think I understand a little bit more the feeling of some of my colleagues who they were working very early in the HIV pandemic and you get this feeling of how wildly impactful is the job that you are doing. And from one side I think it's pretty much, as immunologists and virologist, is what you were called for; something that you trained for your whole life. I think it's like this is my playground. This is what I know. It's the privilege to be able to contribute to that.

Also doing the work from home and that lack of separation between work and home life. Also, I think something that happened to us is to have a Zoom call in the afternoon. You finish working, you turn the TV on, and the same guy who was in your Zoom call is in NBC News giving an interview. It's funny to see that he's wearing the same shirt he was wearing, so it's weird to see that mix between work, home, life, news.

Barr: I'm an archivist and it's weird that what you're watching in the morning, you're preserving for history that afternoon. It's very weird. Usually we have more time. What have been some other personal challenges and opportunities for you during the pandemic?

Boggiano: I think every time of crisis is an opportunity to grow and to think about innovation and how you get out of this. I think that's evolution. I think go keep your mind open as to what are the different choices that you have to choose and be open, don't be close minded, I think that is Darwinian evolution. If you don't have many choices, you won't survive. Keep an open mind of all the different paths ahead. It's key to find the right path forward.

Barr: Yes. Has there been an experience during the pandemic that you feel has made you grow as a scientist and as a person?

Boggiano: Absolutely. It's like a textbook of virology and immunology. From the first day you can follow the knowledge and how there are a lot of gaps in the knowledge and what we don't know. And here we start from—everything was a gap. So, I think that process—and so literal—that is, you start from zero. In general, in every other project as a scientist that you approach there is always a lot of background that you need to do to get to see where the field is, and then to move forward. In this case, pretty much is almost starting from zero has been fascinating as a scientist to be part of that process and to be participating in what has been an incredible growth absolutely as a scientist.

And as a person—I think all of us have known people who have lost loved ones during this period. We've seen people without jobs, so I think it is a privilege for us to have a roof, have food, have a job, have the security that so many people don't have. I think all those things are extremely important to have at present and also to drive you as to why we need to solve this puzzle and to provide tools, so we come back to normal life as fast as possible.

Barr: Definitely. So, this is our last question. What has been a moment during the pandemic that has made you smile among all these guys? There must have been some happy times, too.

Boggiano: Most of the happy times had come with memes—all the memes about working at home were hilarious, the self-haircut memes were amazing, and the 2020 memes, also I love them. What you have planned for your January versus June? I always love those. These have been my happy times. Memes have delivered most of my happy times over the last eight months.

Barr: Thank you very much for being with us and I wish you the best, you and your team, in all your work. It's very important.

Boggiano: Thank you very much, Gabrielle. Take care.