

Rheumatologists and Pulmonologists at Temple University Weather the COVID-19 Storm Together

Roberto Caricchio and Gerard J. Criner

The Journal of Rheumatology June 2020, jrheum.200740; DOI: <https://doi.org/10.3899/jrheum.200740>

Dr. Earl Silverman (ES): Hi, I'm Earl Silverman, editor-in-chief of *The Journal of Rheumatology*. I hope you're all doing well and healthy during the coronavirus pandemic. Today, I'm pleased to be speaking to Dr. Roberto Caricchio, who is the Chief of the Division of Rheumatology at the Lewis Katz School of Medicine at Temple University, who with Dr. Gerald Criner, who is the Chair of Thoracic Medicine and Surgery at the same institution, are the authors of a research letter entitled, "Rheumatologists and Pulmonologists at Temple University Weather the COVID-19 Storm Together".

This research letter is available via open access at *The Journal's* website at www.jrheum.org.

Dr. Caricchio, I want to thank you and Dr. Criner for writing this research letter, and for joining me and agreeing to discuss how Temple University Hospital has been dealing with the COVID-19 pandemic.

So, let's start with the questions! To my knowledge and correct me, the combined input of thoracic medicine and rheumatology to treat patients with COVID-19 is unique, at least, certainly formalized. Please explain to me why Temple had decided on this approach.

Dr. Roberto Caricchio (RC): Yes, first of all, thank you for having me here. It's always nice to talk across the border.

We are in a way rare, I would say, unique, but we're not completely unique.

In fact, in the recent survey by the American College of Rheumatology on this very topic found that, yes, a minority of rheumatology sections and divisions in the United States have actually collaborated fully with the lung institutes or centers to actually approach COVID-19 infection, which is obviously primarily a lung disease. Nevertheless, it is a systemic at some point, with the major organ involvement, as well.

And so, why were we, in the rheumatology section, the lucky ones? Well, I'd say, there are several factors that play in these events.

First of all, Temple University prepared itself to the pandemic. We were watching from Europe what was going on, the news that were coming in, and then watching New York state about the pandemic going there.

In that period, which was the end of February, Temple prepared itself to the pandemic in a way by redeploying, basically, the entire structure of the complex. So one building at Temple University was transformed into an ICU structure, eight floors of ICU, to make up for the numbers that we were anticipating, which were roughly 300-350 a day worth of patients needing of ICU care.

And so, this was happening at the end of February and the first 2 weeks of March.

Meanwhile, I was actually recovering from a surgery at the end of February and was on medical leave the first two weeks. I was a person learning about this condition and of course quickly noticed that the medications that were at some point used in China and then later on anybody in Italy were biologics that rheumatologists usually employ in a variety of conditions, including cytokine storms, which I have an interest in.

And so, in mid-February, I reached out to Dr. Criner, mentioning to him the fact that those medications were rheumatological and we had a great expertise, and of course experience, and if we could be of help. He emailed me back the very evening, on the 15th, saying, "Well, why don't you participate to our call."

So, meanwhile, they were having daily updates on our restructuring of the Temple University for the pandemic. And so, at 4:30 I went onboard. I prepared a presentation for them, and there were roughly at that point, up to 200 individuals on that daily meeting at 4:30.

I prepared a presentation on the cytokine storms, that occur under certain circumstances, such as HLA, HLH, MAS, and the CAR-T cell cytokine storms as well, and made the case to say, hey, this is what is used in Italy and Europe in general, but also some data from China. I think we should, altogether, approach this disease, not always, of course, but under certain circumstances, with those medications.

And so it began.

ES: That's great. Very good foresight. You really have to be prepared if you're going to do something well.

RC: Yes, we had really one week after the 15th of March because the week after, by the 21st, we were having 10 to 15 patients admitted a day.

ES: Wow, that's impressive.

RC: Unfortunately, because it was very taxing for everybody.

ES: Sure. In the research letter you mentioned that you've treated several hundred patients in the combined approach, and that 92% — I was impressed — the hospitalized patients went home.

RC: Yes, it was. We had these 4:30 phone calls with, roughly again, 200 individuals. By the way, those 200 individuals were not by any stretch of imagination only part of the thoracic medicine or surgery department. There were multiple teams. We were involved in the cytokine storm treatment, by which

we helped in recognizing it by having daily laboratory markers, to be drawn on day zero, actually from the emergency room.

So, we have seen them in that regard too, but also the cardiology team was on board, the infectious disease was on board, the nephrology team was on board, being these patients, there is a higher percentage incidence of patients in it with the chronic kidney disease or end-stage renal disease. There were a variety of teams. Neurology because of the neurological manifestations and gastroenterology.

It was not just from rheumatology. It was a very inclusive approach to the COVID-19.

So every day, we were receiving 20 to 30, at some point, 40 patients a day actually admitted for a couple of weeks. And what happened is that, based on the way we set up, and there was, yes, the lab work, but also a high-resolution CT besides the nasal swabs for the active PCR.

The patient was diagnosed at various stages — severity stages. So, if the patient was just having some oxygen need and the ground glass opacity now classic, they would have stayed in the hospital for a few days, most likely with the now classic combination, which is azithromycin.

In our case, we did give some low-dose steroids, as now everybody else is doing, and many of those patients, after a few days with really extensive respiratory support would have gone home.

But there was this fraction, which was roughly 20–25%, who went off in developing much more systemic inflammatory response. And so, the pulmonologists were aware of that because we, with the presentations that we gave them, we basically trained them in recognizing that. And if that were the case, they would have consulted rheumatology, and we would have gone through the type of therapy that the patient would have been more suited for. That amounted to roughly 250–300 patients.

ES: Right. So, you said that now you have your protocol, and I know certainly worldwide and I'm sure throughout the US, Canada, and these big collaborations, are you now part of trials with the drugs? You mentioned some of the drugs, and I'm sure the anticytokines.

RC: Yes. Quite a few, actually.

So, the patients that rheumatology was consulted on were those that, yes, certainly had these features of systemic inflammation, hyperimmune response, but also, either did not feed the clinical trials that we were or are participating in, or they just didn't want to have the placebo risk, which is understandable.

So, yes, now we participate in quite a few. For the pulmonary team, they set up trials with remdesivir for the first wave in investigative trials, but also sarilumab, which is another anti-IL-6 receptor.

We are part of the tocilizumab trial — two of them. The gimsilumab, the anti-GMCF trial. Canakinumab, the anti-IL- β trial, which just finished the recruiting, as well as also for sarilumab has finished the recruitment, and we are most likely getting on board with anakinra which are trying to reproduce the phase I that they did in Italy.

And also, we've already been selected for the baricitinib biosimilar trial.

Of course, you know, we have a tremendous success in the recruiting. It's like almost half of the population that was offered. I think we're looking into that, and that there would be publications on that, because our population is, by far, minority.

We have roughly 80% of the population is minority, of which of these 80%, 65–70% are African American and the rest is Hispanic.

So, I think the pandemic and really the lack of medications that we know, for sure, they work have pushed individuals to actually be more open to clinical trials, because it's either that, although we did offer the alternative, which was the same thing, but outside of clinical trial. But, nevertheless, I think that the success was also that part, that the pandemic might change minds because of the availability of medications.

We did use hydroxychloroquine, but only for two weeks. It took some time before starting the use. We couldn't really agree, yes or no, and I was partially skeptical, but we only use in very few patients.

ES: So, you know, with the cytokine storm, the analogy as you said, is in MAS, HLH — hyperactive immune system and I think what you were saying, I think, the key to what is what you're doing. It always struck me with these diseases is that, it seems like the people who do worse are always a day behind, so that to test everybody to look for ferritin and the other markers that we know are associated with cytokine storm when they enter, I agree, is the way, and maybe that's why your patients are doing well.

You don't have to answer this question if you don't want to, what's your gut feeling about IL-1 versus IL-6 blockade in a patient not entering a trial.

RC: Well actually, we are preparing our experience. We are writing as we speak. As preliminary, because we have patients that we treated with tocilizumab and patients treated with IL-6 and patients treated with IL-1 outside of clinical trials, and we are not seeing much of a difference.

Now, it is prospective work, obviously, and outside of clinical trial, so we may have been biased with one over the other, and we are analyzing the data as such.

By that, I mean, if you look back a month or two months ago, which seems in the 1950s at this point. But if you had looked at the clinical trials in March in the world, the tocilizumab trial, so the anti-IL-6 trials were really targeting the lung. So the criteria were mostly lung severity.

While the few emerging from Italy, with the anti-IL-1 blockade, we're not just looking at the lung, but also at the inflammatory markers. And that's what we replicated at Temple.

So despite that we were looking at inflammatory markers, there might be a bias toward, not just toward the lung, rather than the inflammatory markers, one versus the other. What I can tell you is that the preliminary data that we have, we did not see much of a difference in terms of relative success because, fortunately and unfortunately, we do not have a control group.

We treated everybody that we needed to treat.

ES: Of course.

RC: We have a control group for what has been published, and I think if we look pretty good in those terms, certainly.

ES: Yeah. I'm not surprised. It does remind me a lot of what I'm used to in systemic JIA. They both work well. They don't work in everybody. But it's going to work in two-thirds of the patients and probably to flip one, you never know.

It's interesting that canakinumab was used because, you know, the nice beauty of IL-1 blockade with anakinra, is the half-life and you can just ramp it up because the safety is so good of increasing it, but we'll see what we mean.

RC: I specifically mentioned the anakinra and the tocilizumab because I cannot comment on canakinumab because all the 30 patients that we had were all in clinical trials, so that is not something that we publish before we decide to do so. So, that I cannot comment, but for the anakinra, there is no particular difference.

And the other thing that I would add, is that we're being very careful in how to present this cohort because, as I mentioned, we have a very large part of minorities and also a much higher compared to other cohorts, a much higher incidence of diabetes, renal disease, COPD, coronary artery disease, obesity is much higher in our population, which in a way, makes us feel good about what we were able to do, because they tend to have worst disease.

ES: Absolutely. Well, that was great. Is there anything you'd like to add that we might have missed?

RC: Yes, I would like to add something. Two things, actually.

The first thing is the fact that I didn't mention enough how inclusive Dr. Criner, the Chair of the Thoracic Medicine and Surgery was. I understand, from talking to my colleagues in rheumatology around the country, that that doesn't happen very often.

Somehow, there isn't much of a communication or an established line of communication that might help both. I cannot emphasize enough how inclusive he has been and continues to be and that is very key to our collaborations. A great experience and professional satisfaction of feeling that we belong to this effort — we as rheumatologists; I cannot say enough good things about that frankly.

And the other thing though is that, what I did find very important is that to explain myself why we could have been of help.

Certainly, I was given a chance. But if that chance is given, or in a way pushed to be given, I think it's also important to be humble, and be part of this disease as helpers because ultimately it is a disease of the lung and it is an infectious disease.

In several meetings in which we invited speakers to let us know of new approaches that we might have used, I asked questions and they wondered what a rheumatologist is doing here, but it makes a lot of sense. We as rheumatologists, nowadays, we also need to be good immunologist. Otherwise, we become less knowledgeable, for sure. With all these biologics, they pinpoint the immune mechanisms and it's wonderful, but we also need to demonstrate that that's where we are.

We are not just rheumatologists. We're also immunologists and given the chance, I think many more could collaborate with the pulmonology and infectious diseases.

But I must say that my treat was to have such an inclusive personality and be ready to help. I mean, I didn't get a day off since March 15.

ES: I know, it's what happens, when you're wanted. It's good to be wanted, and then the downside. But I think it's fantastic, and I agree with you said. I was just so impressed when you said that there were 200 people.

RC: Yeah, yeah.

ES: That's a very big division — I'm just teasing. 150 people, you know!

I knew you had to have everybody; that's great that the leaders — you need leadership. I agree 100%, you need a good leader, and everybody has to know their role.

What are you good at? What do you know? What don't know about lung disease? That's not what we do, but we do understand, I agree completely, what these molecules are capable of doing.

RC: Yes.

ES: And I think your contribution to getting on the hyperimmune system, the HLH-like cytokine storm is really our expertise. And I agree, so I think that's fantastic at Temple. I really wish it happened everywhere.

I want to thank you very much. This has been very enlightening for me, and it's nice to see that people talk to each other and get up and collaborate because we can't have disease like this. We can't live in our islands, we can't do that for anything.

RC: Absolutely. Thank you for having me.

ES: I want to thank you and I want to encourage everybody who's been listening, please read the research letter entitled, "Rheumatologists and Pulmonologists at Temple University Weather the COVID-19 Storm Together," as well as our other editorials, articles, and research letters about the SARS-CoV-2 infection and COVID-19 disease, and its effects and its implications for rheumatologists and rheumatology practices. We can certainly see how this affected the rheumatologists at Temple, who don't get any time off anymore.

You can read the article at www.jrheum.org/covid19.

If you have any questions or comments, please send them to us via Twitter @jrheum or email us at manuscripts@jrheum.com.

Thank you for joining us and continue follow all the regional national guidelines from your health authorities, and be sure to maintain social distancing to stay safe. And you can see how far, myself and Roberto are, so we have some good social distancing.

And thanks, Roberto.

RC: Thank you, Earl.

