Clinicians in Conversation podcast series

CLARITY IBD: Pragmatic pointers from a trial delivered in a pandemic.

Intro 00:02

Welcome to our clinicians in conversation podcast series, part of the NIHR, National Institute for Health Research, podcast programme. In this episode you will hear from Professor Tariq Iqbal, National Specialty Lead for gastroenterology at the NIHR Clinical Research Network, and Dr. Tariq Ahmad Consultant Gastroenterologist, and a member of the NIHR gastroenterology national specialty group. Dr. Ahmad is also chief investigator for CLARITY IBD. They will be discussing highlights from the CLARITY IBD study, the results and delivery highlights, plus key learning points.

Professor Tariq Iqbal 00:46

Hi, so I'm Tariq Iqbal. I'm a gastroenterologist in Birmingham and National Specialty Lead for the NIHR gastroenterology group. And it's a great pleasure today to be talking to my colleague, Dr. Ahmed, who's going to introduce himself now.

Dr Tariq Ahmad 01:04

Hello, Tariq Ahmad. I'm a consultant gastroenterologist in Exeter in Devon.

Professor Tariq Iqbal: 01:09
Great. Well, it's a real pleasure to talk to you today Tarik about your wonderful CLARITY IBD study, which is probably the most important gastroenterology study, well it is the most important gastroenterology study, undertaken during the recent COVID pandemic. It was a huge logistical exercise and it's great to hear from you about how you went about delivering it and some of the highlights. So over to you, really thank you.

Dr Tariq Ahmad: 01:40
Thank you Tariq. So, as many of you will know, CLARITY IBD is a UK NIHR COVID-19 Urgent Public Health study investigating the impact of biologic and immunomodulator drugs which we use commonly in IBD, on SARS-CoV-2 infection risk and immunity, whether that follows infection or vaccination. And it is now a prospective 64 week observational study, it was initially set out as a 40 week study, which is following 7000 People with IBD treated with either infliximab, an anti TNF, drug, or vedolizumab. And vedolizumab is a gut selective, anti integrin monoclonal antibody which, in contrast to anti TNF, is not associated with increased susceptibility to systemic infection or attenuated responses to vaccine. So the vedolizumab treated patients were the control group. And we recruited 7000 patients from 92 UK hospitals in just 12 weeks, a remarkable feat and this wouldn't have been possible without the infrastructure of the NIHR.

Professor Tariq Iqbal: 02:56
So it's a really important question, isn't it, asked to address whether these very common and powerful immunosuppressants we use have a detrimental impact on the vaccine in terms of the immunity development? When did you come up with it? When did you think about it?

Dr Tariq Ahmad: 03:16
Well, as you will remember, March 2020, was a frightening time for us, it was an even more worrying time for our patients. And for our patients lock down really meant locked down and, and based on government guidance, many of our patients were told to shield. But of course, this was based on very little data in terms of risk. And so we felt that it was important to try and work out the risk to patients from the therapies they were receiving. And essentially, this plan was put together in the space of a few evenings with a group of six or seven UK gastroenterologists. We came together to write a pragmatic protocol that allowed us to follow patients when they attended for routine clinical visits in infusion units in UK hospitals.

Professor Tariq Iqbal: 04:16
And of course, this is building on the wonderful platform you've developed already, isn't it? In terms of monitoring biologics.

Dr Tariq Ahmad: 04:26
Absolutely so I think the reason that we were able to get this study up and running quickly, is because we'd already established a network of sites across the UK. So we had the contacts in terms of principal investigators and research nurses and we were able to call on them to get up and running. But I think the support of the NIHR through the urgent public health badge meant that we were able to establish this project and roll it out quicker than we've done any previous multi-site work.

Professor Tariq Iqbal: 05:02
Yeah that was very impressive. So it really, how long did it take from, you know, thinking about it in the bath or whatever, to actually getting it on the road? It was very fast, wasn't it to actually set it up?

Dr Tariq Ahmad: 05:14
Yeah. So from completion of the first draft of the protocol, which was the middle of May, to first patient recruited in the beginning of September. And, I guess we could have done it quicker. But there were some funding issues that we obviously needed to address, first of all.

Professor Tariq Iqbal: 05:36
So would you like to give us some sort of key highlights and some pragmatic pointers from this study, please?

Dr Tariq Ahmad: 05:43
Well, in terms of results, first of all, a brief word about those. Our first data came a while back before the vaccine, and we first demonstrated that infliximab is associated with attenuated responses to the SARS-COV-2 infection despite similar rates of symptomatic and proven infections, compared to as vedolizumab treated patients. And then we then followed the patients after vaccination and we reported after both one and two doses of vaccine, antibody concentrations were lower, but also less durable in infliximab compared to their vedolizumab treated patients, irrespective of whether they received the Pfizer for the AstraZeneca vaccine. Importantly, what we've shown very

recently is that patients treated with infliximab also experienced a 50% increase in breakthrough infections after vaccination. But fortunately, only 1% of these breakthrough infections have resulted in hospitalisation. So patients on these medicines, or anti TNF drugs shouldn't be too concerned. But, you know, based on our data, we've recommended that patients on anti TNF should be prioritised for the third dose, so of course, they are now anyway.

So in terms of the delivery highlights, I've already mentioned that the speed of site setup and patient recruitment, I think, was unprecedented, certainly, in terms of inflammatory bowel disease studies. And that was down to the Urgent Public Health badge.

The second point I wanted to highlight was this has been a dynamic study where we've added new objectives to the study as the pandemic has evolved, and vaccines have been rolled out. And I think we're very grateful that the HRA approval process was also accelerated so that major amendments came through in two or three days. And previously, we're waiting for weeks, if not months for these approvals to be granted.

Also important to highlight the fact that we have used a REDCap database and been granted permission to hold personal data for individual subjects. And this has allowed us to reach out to patients directly with our questionnaires and also to link data to nationally held PCR testing and vaccine information. So that's been really key. It's also allowed us to push out results to patients. So we've been rolling out antibody test results to patients in real time and we did some work at the beginning and identified that patients really want to know their results, even if the significance of the results is not completely understood. So, that was certainly new.

In terms of support, we use nurse PI's in lots of the centres and also SPR PI's, which proved, I think popular at sites and also allowed us to reach sites that previously were not engaged with our work. So that was key. Another important aspect, Tariq was that, you'll remember, that during the pandemic, subcutaneous vedolizumab and infliximab became available. Previously, it was all intravenous. And this meant that some of our patients were not coming into the hospital. It was good for them, because they weren't coming near COVID affected hospitals but it was bad for the study. Because in terms of allowing us to sample them. And so we developed a home capillary blood testing kit that meant that people could stay in the study and conduct their own blood tests and send them in the post to us in Exeter.

Professor Tariq Iqbal: 09:47
So I think that's fantastic. Despite the sort of tragedy that we had in this pandemic, there have been some bright spots haven't there? I mean, you've been able to be very agile obviously, you've got a track record of pretty rapid delivery anyway. But the system seems to have made things very streamlined in this case, and you've been able to develop your ideas almost as quickly as they're conceived, which has been a very useful learning exercise I think from COVID. for the way we carry out these sort of multicenter research trials. So I mean, what have you learned? I mean, what have you learned from where we were two years ago, what has this experience told us about delivering these sorts of studies? What do you think, going forward, what should we keep?

Dr Tariq Ahmad: 10:42
Well, I think there's a number of elements that we would definitely want to keep. I think, first of all, Microsoft Teams has been an essential way to communicate with patients and with the study management group, and also with individual sites. And I think one of the key things that we've done is to engage the sites by holding regular site update calls, where we've, we've discussed problems, we share data as soon as it's available, and sought

feedback from sites. And I think one of the problems, particularly when you're running an investigator led study, is that often, focus is taken off your study on to commercial type research. So you have to keep sites interested, we have to remind them, we're still here still looking for patients, we still need to keep them in the study. And so Teams has been invaluable,and I think we should definitely keep that. So we've had Teams meetings every two, three weeks, on lunchtime, half an hour to an hour slot, and it's worked well.

The other thing that I think that we've done is we have also maintained contact with our patients and this has been through Twitter, through email, we've released a video and, and various newsletters have been produced. I think these have been reasonably well received. And certainly we've had lots and lots of emails such that we've had to employ somebody to respond to all the participant emails, but having that engagement has been helpful. Also, I think incentivizing the patient. So we're giving them something back in terms of their data has been important. What else would we do? Let the patients collect the data, they do a good job of it, we found.

Professor Tariq Iqbal: 12:44
So Tarik, did you say that you were able to get associate PIs going in this programme? Is that something that or did you not?

Dr Tariq Ahmad: 12:55
The study was actually set up, I think, a month or two too early for the associate P.I. scheme. But, despite that, we did manage, some of the principal investigators at sites decided that they would allow their registrar's to run the project on their behalf as sort of sub P.I's And that happened. I mean, whether they were, I don't think they were officially designated as associate PI's because we weren't eligible, because we'd already opened when the scheme started.

Professor Tariq Iqbal: 13:25
That's obviously going to be something which we would like to develop in the future,certainly. Great. So, where to, I mean, are you ambitious to continue this through the sort of six monthly booster programmes that we're going to engage in in the near future? Are you going to extend this data collection?

PDr Tariq Ahmad: 13:47
Yes, we have funding and permission to extend the study for further 24 weeks. And the aim of this is to look at antibody and T cell responses to a third dose. We are particularly interested in those patients who don't appear to have mounted an antibody response to two doses. And there's a small proportion of patients who either haven't mounted any response or have very rapidly lost response. So we're interested in following these patients for a longer period of time. We also have some other spin off projects that we plan to do in the next 24 weeks. One of which is looking at long COVID in the IBD population and the second project, looking at chronic nasopharyngeal carriage in patients on these medicines.

Professor Tariq Iqbal 14:44
Well, thank you very much. That's very exciting. And as ever, congratulations. And if I speak for the national gastroenterology group, we're excited to continue to work and be led by you in these large data projects. Thank you very much.

Outro: 15:01

To find out more about how the NIHR supports gastroenterology research, visit the NIHR website. This was an episode of the NIHR Clinicians in Conversation podcast series. Thank you for listening.