REALTIME FILE

Treatment Action Group (TAG)
IMPLEMENTING AN INJECTABLE-FREE REGIMEN
FOR DRUG-RESISTANT TB
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>> MARCUS LOW: Hello, everybody. Welcome to this webinar on "Implementing an Injectable-Free Regimen for Drug-Resistant TB." My name is Marcus Low. I'm the moderator for today. I am a co-technical lead of the Global TB Community Advisory Board and I edit a publication here in South Africa called Spotlight. This webinar is hosted by the Global TB CAP, the Treatment Action Group and DR-TB.

Some housekeeping. You will see there are captions available. I think that's particularly important and I thank you to TAG for organizing that. When I was looking at this earlier, I realized that in the MDR-TB community there must, by definition, be lots of people who have hearing problems so I think it's great that we do this. And I think for this kind of discussion we should always be doing this.

So I'll just say a few words of introduction before we get to our three excellent speakers today. We are in August 2018. We are still using injectable medicines in most of the world. And as all of you are aware, these injections cause hearing loss in quite a high percentage of cases. It varies substantially from what we've seen in trials but it can go as high as 50%.

Recently, the South African government announced change in our MDR-TB treatment guidelines so we're phasing out the injectables and replacing them with bedaquiline.

Similar recommendations we thought would have been out by now, the guidelines to the committee met in July, but unfortunately we will not have any new guidance yet. So apologize for the slight misadvertisement in how we promoted this webinar. We thought we would have that information by now.

So, that is where we are at the moment. I think that many discussions over recent years about the problems with evidence-based and especially in drug resistant TB it's difficult to come up with guidelines. We don't have all the randomized control trials we want. But there's an earnest on treatment programs to do the best with the evidence we have. And I would argue that South Africa's set the tone in how we go about doing that. How do we develop guidelines in the public interest while fully understanding that the evidence is not what it would otherwise be.

Our first speaker today is Dr. Nobert Ndejka from the South African Department of Health. I'm sure he's familiar to most people on this webinar. He's led a lot of the work regarding bedaquiline in South Africa. And then we've asked him to speak a bit about South Africa's experiences with bedaquiline and the new regimen, what's involved in introducing this new regimen.

So with that I'll hand it over to Dr. Ndejka.

>> DR. NORBERT NDEJKA: All right. Thank you so much. Can I get my slides? I sent them earlier on or do you want me to upload them?

>> MARCUS LOW: Just a second.

>> Dr. Ndejka, we just shared with you the screen so if you accept, you can present directly from your screen.

>> DR. NORBERT NDEJKA: Ok. Ok. Can you see the slides?

>> Yes, we can.

>> DR. NORBERT NDEJKA: Thank you so much.

So my presentation is really on the South African experience. As introduced by the moderator of the discussion,we made an announcement recently. People have been asking why we did it and how we're going to do it. I should start by saying that we just came to a conclusion that the randomized controlled trials alone are not enough to bring about a resolution that is a call for us to reverse the negative effect of rifampicin that we see. We started working with academia and NGOs locally. So the work here has really been, you know, the fruit of that as well as collaboration with other organizations.

My first slide is really to underscore the fact that we're a low burden country; you can see here approximately 10%. There have been a lot of efforts in terms of identifying these patients. Although we do not treat 60% -- do not treat all but at least we are about 50%. It's not good enough but it is a work in progress.

You can see our MDR success rate has shifted very slowly from the 40s to the 50s. MDR 2014 was 27%. We're going to see what has happened to that now. I think that that's very important to see such a change.

The other thing which is very important is, in this slide is to show that healthcare -- our physicians initiate treatment. We also have nurse initiated program and clinical-associated. So we don't just limit this to physicians alone. Access to laboratory, quality medicine, audiology with extended frequency is standards in all of our treatment initiation site.

So this is really where -- the question of decentralization of treatment with pretty much the help of the World Health Organization. We followed every single recommendation that was made to that effect. To understand that, 86% of sub districts have at least one

initiation site which I have described earlier on. We've established a huge network of portable audiometry, 156 sites, and also provided ECGs, to physicians.

In the meantime, we have a strong National Advisory Committee that reviewed each and every case of the 200 patients, between 2013 to 2015. And this decentralization was then key to scale up when we managed to treat successfully a large proportion of our first 200 patients that went with the bedaquiline program, between March [Inaudible] and 2015. Physicians understood what was happening, what to do.

We also introduced to individuals living with HIV because our council initially said we must use it [Inaudible] because clinical trials never used it in individuals. We felt that would defeat the purpose because 3/4 are living with HIV and we've been able to show that it works with -- if someone is HIV positive or negative, they take their tablets, just works well.

So this is an illustration of the collaboration I'm talking about. This was our first paper we published to indicate our commitment with the NGOs. From that time till now together we are working very hard to try and solve some of the challenges that we have, though still a work in progress.

After initiating a number of patients on bedaquiline, we picked up a very good conversion rate. This was very encouraging. But we are very concerned about the safety. We did really -- the ECGs, monitored very carefully.

I must say that these patients received essentially bedaquiline, linezolid, clofazimine, ofloxacin among other products. But those four were the main ones. And those living with HIV had -- they didn't stay on [Indiscernible] which is the standard of care.

Now, this is very interesting. As you can see, very good conversion, survival, regardless of HIV and XDR, pre-XDR. But I find this very interesting because as you can see, the median criteria was below 450. And the experience with bedaquiline, this is something that we've noticed whether the patient is HIV positive or negative, you know, way below 450 whether they get clofazamine or not, the increase was below 50, regardless of HIV status or drug that was given. It was a very good experience for us to get used to this molecule and slowly scale up. That's why between 2013 and 2015 only used 200 patients. But we learned a lot and we were able to move -- sometime this year, around June, 15,000 patients because once you know how these things work, then you start to move even faster.

The other thing we've done from our program is to carefully look at patients who received bedaquiline very carefully because we knew that the initial clinical trial picked up this difference where bedaquiline group had more, 10 out of 79 died, which was big. We've always had this at the back of our mind, we've been checking very carefully. We like to believe this was smaller compared to the big number we are looking at now where we screen 24,000 patients, we included more than 19,000 records overall. We found a huge decrease in terms of mortality. We see this translated in the program. This is phenomenal. Program data is not in operational research. You see the treatment success rate between 2015 to 10 to 51%. This is phenomenal. Remember, this is TB program data, as well as the clinical access program. We validate the findings. So we picked up a few individuals which we didn't have any information about but [Indiscernible].

So we picked up about 27%. But these are the ones we never verified that way. We know that the reality would have been somewhere 55% or maybe even more. So this is a huge decrease essentially using bedaquiline among these XDR-TB patients. So we felt this was a very, very good experience.

We tried to look at 2015, which is big, 800. And you see that the success rate among

those who got either only bedaquiline or was switched from bedaquiline -- I mean from injectable after maybe a week or a few weeks straight to bedaquiline, the success rate is 65%.

It is not that 51 we see there, it is more. And those on injectable continue to have like 20s. This is exactly what we've been seeing the last few years. So we realize that this is a problem, these injectables are not helping us. For many years we used capreomycin in this group. Below 20%. But when we remove the injectable, we give them bedaquiline, linezolid, clofazamine, the real addition here was bedaquiline because not everyone got linezolid but they all got bedaquiline.

You can see even the death rate among the sub groups -- this is program data, no fancy analysis. But the papers in other peer-reviewed analysis recommendations have shown that we were thinking right. We think we are right that this is coming down to an extent that we decided that all our MDR activities should get this because we have not seen the death rate decrease, as you can see among the XDR, even MDR has been like 20% or more. Before or even after the introduction of ARVs.

Conventionally everybody knows, everybody says, that ARVs are very helpful. They have helped with decrease in terms of mortality overall but when you look at our XDR records or MDR-TB, do not see a decrease before and after. But bedaquiline has helped us to see that. And this is the reason why we decided use this regimen with bedaquiline for our patients.

So briefly in terms of laboratory, we give our patient Genexpert. And then all rifampicin-resistant patients received LPA 1st and 2nd line before we start treatment. Phenotypic DST gets done for patients who do not respond to their treatment. We really try hard to exclude XDR-TB from the beginning of the treatment. And culture and microscopies are done every month to follow patients.

I think my presentation will focus essentially on the regimen. So I want to end with a few slides on the regimen. This is the conventional for short regimen. I've spoken about the long regimen. Long regimen, like I said, we give bedaquiline, levofloxacin, linezolid, clofazimine and one or two other agents we've been giving to patients from 2013 and we see very, very good results.

Our final bedaquiline clinical access program, we wanted to publish it now. We cured 70% of our XDR that were brought on that long regimen without injectables that's why I don't have slides here because I felt maybe we would share even more as soon as it gets published.

The few slides that I have, the final ones, will focus on the short regimen. This is what is recommended by WHO. Four to six months if you don't respond first. And then Moxi, Clofazimine, pyrazinamide. So what we've done really is to replace bedaquiline with, we move kanamycin and put bedaquiline.

So you will see that this is the same as your continuation phase. Your intensive phase -- we have bedaquiline instead of the injectable. And, of course, we prefer Levo because of QT but we say that if you don't have Levo you can still give Moxi in this regimen.

You have to closely monitor your ECGs we have not seen much problems anywhere with the bedaquiline in these patients. But we continue to monitor religiously because it's very, very important.

So the only difference really is the bedaquiline here, which you can see is to six months. We didn't feel ok to say this should be four months, just to be six months. Because these drugs sometimes prolong them to six months. So this should be six months. And the rest remain exactly as recommended.

Now, the other element of difference is Linezolid which we discuss -- by the way, we

want to review this when we get final guidelines whenever they come, now towards the end of the year. But definitely we doing this way. Patients get Linezolid two months because we got up to 15% of our parents -- patients, XDR and [Indiscernible]. So if we don't do this, several experts think that we will get some XDR on this regimen and that would be a problem. So to cover this and then stop it once you've excluded XDR or if they become XDR then switch them to the long treatment regimen which has Linezolid, just modify to continue.

But this is one area where a lot of people have questions and we are saying it's not final. Want to see all the evidence around the issue but definitely Linezolid is a very good drug. Although we are nervous about the anemia that it causes you but we've seen in our clinical access program.

So in conclusion, I'd like to say that management of DR-TB is very complex. It requires careful assessment. It is effective assessment get done on day one or baseline before people start. And it should be reviewed after two weeks and four weeks, and monthly subsequently because then you are able to see all of the mutation and adjust treatment once we get all of the results. Then you know what you're dealing with. It is critical because we know we have at least 15% XDR and pre-XDR. Some people say could be even 30%. So we were expecting a huge number and we have to really behave in a manner that is consistent with such and not a sacrifice bedaquiline. But also we don't want to keep a lot of patients with substandard treatment because you're keeping something good for them next time and there will not be that next occasion.

Laboratories are critical. Checked at every visit. Clinician adjust treatment because I've seen several -- once treatment starts people don't want to change because supposed to be standardized. But we have to do all of these lab results and they should be factored into the treatment. Recording and reporting is essential but more importantly there's a great need for operational research and NTPs around the world. With collaboration with the WHO, local researchers, NGOs and civil society is key to the improvement of patient's experience. We have to work together to improve this.

So I'd like to acknowledge the WHO, worked very closely with them. They helped us a lot with the technical assistance and several other things to document, in publication. Accolades from the province and facilities. More importantly, the committees, those physicians that help us design the regimen for our patients. They get e-mails day and night, every day, Sunday. They respond free of charge. We really appreciate that.

So that is the end of my slides. I thank you for your attention.

>> MARCUS LOW: Great. Thank you very much, Dr. Ndejka. I think it's very impressive how the South African government has moved faster than other governments but at the same time been very careful. So congratulations on that.

Our next speaker is Dr. Eunice Omesa. She is the Section Head for Monitoring, Evaluation and Research at the Kenyan Ministry of Health. Kenya is at a different stage in the journey with bedaquiline. I think as people could tell from Dr. Ndejka's presentation, it's not trivial to introduce to the healthcare system. And Dr. Omesa will speak to us about some other challenges.

Over to you, doctor.

>> DR. EUNICE OMESA: Good evening from this side and good morning the other side. I'm pleased to be making this presentation after an exemplary presentation from my colleague, Dr. Ndejka. He's one of the key people of the region and are so proud that South Africa is taking the lead in the fight against MDR-TB, again, based on the evidence they have in terms of their

experience in the rollout or the implementation for the use of bedaquiline which is a fairly new molecule with significant challenges when it comes to implementation, especially in resource-limited settings like Kenya and other sub-Saharan African countries. And I'm very happy that this will set the pace for the world and generally everyone to just focus in the implementation of bedaquiline with the compelling reasons that have just been shared.

So, just to set us off, I think it would be important to also highlight that based on the findings that Dr. Ndejka has just present, it is very encouraging to see the significant outcomes that patients who are on a bedaquiline-based regimen actually had far much better outcomes than those who are not. And perfect programical team data this is extremely impressive to pick and run with.

That reminds us all -- I'm sorry, my slides -- ok. So that reminds us that as we commit towards ending TB in reducing the number of deaths by 2035 by 95%, a lot needs to be done in terms of providing our patients with essential, patient-centered care. And then, again, of course reduce the TB incident rates by 90%. We need to really find these patients and ship them on the appropriate treatment. And then, of course, ensure that the patients do not incur any catastrophic effects while on care for tuberculosis.

So this is to remind us that we have a commitment towards ensuring that our patients receive the utmost care, is patient-centered at the earliest opportunity and also reminds us that we need to make bold policies and come up with supportive systems to ensure that we have participation from across all stakeholders to provide these patient-centered care to the TB patients.

And for that reason, I must say that South Africa taking the lead with this bold policy based on what they have observed in their country is very, very -- is a very good lead to the region and to the world at large.

And, of course, the third pillar on innovation, research, and, you know, developing new tools and making use of them at the earliest opportune time to provide care.

So with this in mind, I just want to take us through what it is countries should pay attention to or should consider while implementing a bedaquiline-based regimen. And this is, in general, before we discuss about countries' experience, I think, again, based on what Dr. Ndejka has presented on is quite critical. And this is not to say that -- it has to put into consideration or into perspective the different context as far as this is concerned.

Important first is to consider the evidence available and the recommendations. And evidence could be from multi-centered clinical trials. It could be from case studies. It could be perfect operational research or observational data that is based on the country's experience. And really what's happened is that an assessment to evaluate the quality of evidence is done by reviewers or guideline developers who will critically look -- who need to look at the quality of evidence and decide whether recommendations need to make or guidelines need to be implemented.

Of course, beyond reasonable doubt that there's significant benefits to the patient that if you were to withdraw or withhold this drug from a patient, you're actually taking away their right to treatment when there is compelling evidence that that drug or that patient will actually benefit.

And then, of course, value and preferences within the context. Consideration in terms of our resources have -- available resources and we do know globally in a world where resources are scarce it is important -- look at what resources are available to actually implement [Inaudible: Background noise overpowering voices.]

Then, of course, we have the feasibility and acceptability and equity of the implementation. So basically it's a view and this is what you should all consider. And we're really waiting to see what is likely to recommend of what South Africa's evidence have shown in terms of compelling evidence that, indeed, use of bedaquiline over the injectable actually has better outcomes compared to when you do not use bedaquiline.

And so this is just to show the levels if you have very high certainty level on the evidence that you have further research is unlikely to change our confidence in the estimate of effect the evidence has. So we hope that as this is being considered on whatever certainty level it falls, we at least can see from routine or programmatic data that, indeed, there's actually better outcomes of patients' experience when using bedaquiline.

So evaluating the evidence, it is important that the country does a situational assessment or analysis to determine the capacity they have to implement the injectable-free regimen.

And key -- and I'm glad Dr. Ndejka brought up -- is the decentralization -- models of care is very important. And particularly because a decentralized model of care is actually key when you plan to scale up. It's a lot easier to scale up when you have a decentralized model of care than when you have a centralized. However, in the event that you have very limited systems to support decentralization, then initially -- provide central review or central coordination so that you have an enclosed system that you can easily monitor until you build up confidence and plan to decentralize.

But over and above, I don't think that -- well with the bare minimum requirements of quality parameters that need to be set, it is possible to still decentralize as long as you have evidence that your system is water tight and taking care of patients.

So the other thing to critically look at is the resource capacity in terms of the numbers. We know at the health sector staffed -- and this is the global picture. So we have to critically look at how many healthcare workers do intend to involve or do you want to help us to -- what is the critical mass that you require for you to implement an injectable-free regimen? And this is because of bedaquiline.

And further to that, besides the numbers, you also need to look at the capacity or the expertise of these healthcare workers. In the event that the capacity is limited, then you need to plan for capacity building, capacity reinforcement in terms of knowledge, experience, expertise so that you have all healthcare workers -- patients with the right capacity to manage these patients.

And this is critical because management of drug-resistant TB is not a one-man show. This is a condition that requires a multi-disciplinary approach when managing because we do know that these patients do not only present with one particular challenge but present with a myriad of challenges that require different specialties to address. And this is very, very important.

When it comes to quality of care management, and this is very, very important, I think Dr. Ndejka has done justice to this particular parameter in terms of you need to ensure that you have a bare minimum package that you need to offer this patient. What is it that we know at the very least is adequate for our patients to benefit in the event that we want to implement? And once that is listed it becomes very easy to say this is for our patients, this is how we want to monitor. And we must have this in place before we run it out.

Again, it is in the context of the country based on, again, the availability of resources, although the quality of care indications should not change much because ultimately the

outcome indicators are either favorable or unfavorable and they are looking towards parameters that ensure the treatment of quality of care and have favorable outcomes for our patients.

And availability and infrastructure and resources. This we do know that in the past [Inaudible: Background noise overpowering voices.] the fear that we do not have adequate infrastructure or resources to scale up or implement the bedaquiline rollout in full because of challenges in monitoring these patients due to the fact that caution was given that bedaquiline may cause QT prolongation.

However, I am glad that Dr. Ndejka explicitly allayed these fears by telling us that there were actually very minimal adverse QT prolongation of above 450. That is quite encouraging. And to further say that out of the cohorts that had been initially given bedaquiline during the cohorts in the trial, they actually had other co-existing conditions or comorbidity that led to the death or accentuate the adverse effects experienced. And it was not truly because of the bedaquiline.

And this gives countries confidence that, indeed, there is no fear that we must have water tight -- we should not create barriers to wide access because of fear that this drug will cause adverse reactions and for that it still requires us to put in place a very robust monitoring system. Nonetheless to still look at what the effects of this drug has to the patient until such a time that we have gathered enough evidence and by doing this, we are also pulling enough data or enough evidence to give us more confidence that, indeed, this drug is -- should not be afraid of using this drug on our patients.

Another factor to consider is the procurement and supply chain management. In some countries or regions, these drugs must be registered by the regulatory bodies. However in some countries, certainly the one that procure through the global drug facility, are exempted and can still use the drug in country. So you also have to ensure that at least you understand the status or the conditions given by the regulatory bodies in the country so that you can ensure that the drug is registered in that country.

Further to that, accessibility in terms of costs is another key issue that Dr. Ndejka also brought up. I think this is now where we really need to ensure that we put up a global campaign to ensure that the drugs actually are not costly. Because as it is, I think the drug costs about $900 per dose. That is quite expensive. Especially resource-limited countries or setups. And so there is need for political commitment in terms of locating funds. And at the global level ensure that we have enough bodies or enough muscle to lobby for this drugs, at least for the price of this drug to be reduced so that we are able to procure them and avail them to patients. So that the cost does not become an inhibitive factor as far as that is concerned.

So again, reforecasting and quantification because want to implement those already certain amounts of drugs. Of course, again, you do not want to waste the resources so you really have to coordinate what you have in country and quantify really on how far or how much or how long that will take you vis-a-vis what is in the pipeline. And then see what you had ordered for -- or procured earlier, whether it can be actually switched, switch the orders for kanamycin and replace with bedaquiline. At early stages if that can be done, it should be done in good time just so that you don't end up with wastages, don't end up with political time of using citizenry -- well taxed -- of course, over and above patients' care comes first and the issue of cost should not be a major issue.

So, of course, we also need to lobby. We need to lobby and endorse this particular

regimen to subject matters experts to give the opinion to give the contribution, and to really have input from the patients, community, and civil society organization.

Now, the civil society organization is a very key element or a key body when it comes to implementation of the injectable free regimen and the adoption of the new molecules as a whole. And it would be paramount that they actually create the good will -- the push within organizations and compel institution that supports to say the injectable-free regimen because we appreciate that there are some societies or some regions in global that are sending the idea that this would lead into discussions of what is the cost benefit analysis what are the losses we are looking at.

So of course over and above at how many money it costs to treat a patient vis-a-vis quantifying for the patient's life or value of a patient life. You cannot put a price to the life of a patient.

So I think the civil society really, really needs to actually be robust and aggressive and ensure that they have a critical mass pushing, at the global level, pushing at the country level, and ensuring that the implementation or the endorsement takes place much faster and sooner. And of course the government plays a critical role because it passes as law in the favor of the citizens.

After all that is done there's a need for a meticulous rollout plan. And this, of course -- after considering all that we have discussed, you need to now look -- the strength in country, in the program, look at the opportunities and the low-hanging fruits that you can tap in, as well as potential threats that can shed light on how to roll out the strategy. So it could be an approach where select sites actually [Inaudible: Background noise overpowering voices.] given to the patients can actually implement.

So, again, the rollout strategy is left after considering the situation in country of the PMDD program. And if the country is confident enough that they can roll out on a full scale. Then it would be good.

[CART NOTE: please mute your microphone if you are not speaking]

Where there is a limited capacity, of course an approach would be more applicable.

Ok, as far as capacity building is concerned, would be very important. At the national level you need capacity to ensure that you have all of those parameters or factors coordinated in a similar manner to ensure that the infrastructure, the healthcare worker, the centers of excellence, the clinical teams can handle the implement of the free regimen.

And from Dr. Ndejka's experience, they have brought all the healthcare workers to play a critical role. They all are very important and they need to capacity build so that they have enough confidence that when you roll out this injectable-free regimen, we'll have a seamless operational or implementation [Indiscernible].

Important to note at the national level they also require support from, you know, other partners or other institutions to also help them set up. And this is very important because countries also need to be told that they are doing the right thing and this is what they need to do in addition to what they are already doing or it could change that way and for you to achieve favorable outcomes.

I think it is important to highlight that there is no sequence in order of which this can be done. All of this can take place simultaneously. So you look at your commodity or your procurement and supply management, you look at all of those advance systems we've just discussed. They can be done at the same time. Review of guidelines and curriculums can be developed and aligned within the road map or within the considerations just so that you have

them in place at the right time.

So there is no practical order in terms of how making this presentation. All of this can take place simultaneously or, again, depending on what's the country -- capacity in terms of -- what their weaknesses or what their potential threats could be.

So the critical elements as we implement an injectable-free regimen is to ensure you have a robust monitoring and evaluation system. You have to enlist the cohorts and say this is the number of patients we initiated on this regimen, this is the duration of treatment, this is the interim outcomes. And you're confident that if you look at the interim outcomes before completion of treatment, you're able to take action in good time.

And subsequently, at the end of treatment you can actually ensure, just as Dr. Ndjeka assured us earlier, that from the programmatic data they were actually able to see that use of bedaquiline conferred data, outcomes for XDR-TB patients compared to the ones not initiated on bedaquiline. That I'm sure took a robust evaluation system to pick that from programmatic data as opposed to operational research. So robust data monitoring and evaluation system is very critical when implementing this regimen.

Over and above, an oversight to the implementing countries, regions, facilities is very important just so that you can touch base and ensure that if there are any operational issues, implementational issues, are actually troubleshoot -- can actually troubleshoot before -- the foreseeable, you can troubleshoot what is actually happen organize could hamper the operation towards the regimen.

And so continuous support and mentorship is very, very important. And, of course, documenting the experience is very, very important. And this cannot be over-emphasis because had it not been that South Africa had documented what the experience was I don't think the world would have drawn its attention towards what you're seeing today. And thus very important that even at the global level and at the national level that we do provide -- we do provide quarterly reviews or frequent, monthly reviews could be shared again on experiences in the country.

I think in conclusion I want to say [Inaudible: Background noise overpowering voices.] compelling and undisputable evidence from what South Africa has shown the world that bedaquiline-based regimen actually is very, very beneficial to the patients with the treatment successes of from 23% to 73%. I don't know what other compelling evidence we would wish to see in practice to convince us further that this regimen actually, bedaquiline-based regimen, actually compels us to think about adopting it very fast.

And the call for us today is to ensure that, especially resource-limited countries, that we do not have to wait for us to fulfill -- to have a practical system for us to adopt this regimen. It could be on an operational basis until WHO makes recommendation it could be on an individual basis based again on clinical physicians.

But I think it is imperative that we begin to think about critically how to implement the injectable-free regimen and borrow from South Africa. Because at the end of the day, we want to offer patient-centered care at the earliest opportunity possible and not withhold treatment for later as we wait for more evidence. So the main focus today is patient-centered care, diagnosing the patient early, early treatment, and social support in good time so that we have happy families and happy population at different points.

So also to finally say that, again, we have to look at the context. We do know that South Africa's context is fairly, well, can say advanced compared to other countries in the region. So it is important that you look at your country context. Try and see what is its limits.

We can tap on as the low-hanging fruit to ensure that with the bare minimum available resources we still give our patients the best opportunity.

Ladies and gentlemen, with that very brief presentation, think I want to end there and hand this over to the coordinator.

Thank you very much.

>> MARCUS LOW: Thank you very much, Doctor. That was very informative. I'm glad to hear that you're taking the South African data seriously and that you are thinking about these matters so seriously in Kenya. I think even though implementing a new regimen is complex, I think, you know, that's not an excuse or that will never be an excuse for inaction. I think hopefully as we've seen in Kenya and South Africa, if the political will is there, we can deal with all the other issues.

So I'm aware we're going a bit over time so please bear with us. Our next speaker is definitely someone worth listening to. She knows better probably than most of us do.

If we make guidelines, the figures can't tell us what it means to lose some of your hearing, for example, and when we decide. So one of the leading TB advocacy organizations here in South Africa. So with that, over to you.

>> PHUMEZA TISILE: Thank you, Marcus. As Marcus said, [Inaudible] I am from South Africa but unfortunately I was a victim [Inaudible: Audio garbled]

>> I think we lost you. Are you still with us?

>> PHUMEZA TISILE: I went to the nurse and the nurse was talking, I know this because [Indiscernible] and I couldn’t make out what the nurse was saying. [Inaudible: Background noise overpowering voices.] In the other department they played sounds. I heard some, I didn’t hear some so I need to go to the doctor again. Confused as to what it happening so the doctor had to explain. Things change. The doctor had to do [Indiscernible] talking which was weird because I could not hear my own voice. The doctor explained I am deaf and reason was the kanamycin injection and she mentioned that [Inaudible: Background noise overpowering voices.] and that there was nothing that they could do. So I was told, pre-XDR

[CAPTIONS PAUSED: Inaudible due to garbled audio]

In 2013, I was given a drug that stopped my XDR. Because I was sharing my story, I was traveling, people knew my story. I googled cochlear implants. They are very expensive, close to $40,000 U.S. dollars and in South Africa [inaudible]

We did a fundraising and now I can hear again using cochlear implants. But I am one in many people who are deaf who are lucky enough to have access to those funds. And I am also likely to be given an opportunity again [Indiscernible]. Many don't get that chance. It's like the end of your life. And [Indiscernible] forced to things like they say cannot change. [Indiscernible]

Anyway I am also part of TB Proof advocating for injection-free regimen, we wrote my patient choice pledge for no more injection. I think we should thank Dr. Ndjeka alongside with the Ministry of Health [Indiscernible] listening to patients' voices and doing something about it.

Lastly, I think other countries would learn a lot from South Africa and most importantly patient voices should be heard so that such news, too, can be celebrated all around the world.

I think I'm done. Thank you.

>> Thank you, Phumeza, that was powerful to hear your story and I want to echo your call for others to [Indiscernible] so we can celebrate around the world. No more deafness caused by

injectable medicines that don't seem to work very well for TB.

Marcus, did we want to make any final remarks or should we have Khairunisa go over some of the questions?

>> MARCUS LOW: If people want to stay on, I think we should keep going until half passed if that's acceptable but understand if some people dropped away. I think this is an important discussion to have. So I'd say let's continue.

>> Thank you so much, Phumeza, Dr. Ndejka, and Dr. Omesa. This is the co-technical lead of the Global TB Community Advisory Board. And I'll be assisting by asking some of the questions some of you posed in advance of the call -- this webinar, rather, and also as you're posing.

One of the questions to Dr. Ndejka is: Would the bedaquiline containing regimen -- how will it be adapted for children and pregnant women? If you could kindly answer that.

And then -- yes, and with regards to Kenya -- so I'll be asking some of the questions. You can jot them down, please, and then answer. When will Kenya procure bedaquiline, Dr. Omesa?

And then back again to Dr. Ndejka. How are you monitoring bedaquiline resistance or what is your relapse rate with this bedaquiline-injectable-free regimen?

And then what is the effectiveness -- talked about the effectiveness in the XDR patients. Thank you for that.

Echoing the call on need to prioritize patients over cost -- for instance, for you, Dr. Omesa and Dr. Ndejka, are there enough resources available to rule out bedaquiline? And how would you advocate -- also answer this question, how can we advocate for reasonable cost of the regimen -- I am aware that the company that produces bedaquiline has reduced the price to $400 for six months but is this reasonable enough for low and middle income settings or limit reed source settings?

And then --

>> Could we maybe pause and answer those questions before moving on?

>> Yes.

>> Sure. Dr. Ndejka, please, go ahead.

[No Audible Response]

>> Dr. Ndejka, I think you're still muted if you're trying to speak.

>> DR. NORBERT NDEJKA: Ok. Can you hear me know?

>> Yes. Loud and clear, thank you.

>> DR. NORBERT NDEJKA: So our laboratory services monitoring the resistance to bedaquiline has been done for some time now. Maybe we could get more details from Dr. Ismail. So this is happening routinely now.

We received the donation for 200 patients, initial bedaquiline for 200 patients. [Indiscernible] countries that received [Indiscernible: Multi-voice overlap]

Way before GDF. So we've been buying at the price almost $900 U.S. We had budgeted moving forward to spend approximately $900 U.S. to patient but now with the reduction it means that we can really put more patients, you know, double what we had planned for and so cost is not really a big issue.

But I'm also hoping that there will be more usage around the world. Because if more countries use definitely or were country to buy $400 U.S. if more countries [Indiscernible] that is a problem.

In terms of children with bedaquiline, the regimen for children will give bedaquiline

up to the age of 12. Below that nobody knows how much bedaquiline should be given. So the options for the injection-free -- we agree [Indiscernible] if we can't give to others.

So options include delaminid. Bigger hospitals have delaminid access. We are running a delaminid program at this point in time. So most of our bigger sites have delaminid available. That will be used. Experts have advised that in the absence of delaminid one could use [pass] if really it has been shown to be susceptible and you don't have anything. Really that comes like third option. They spoke of linezolid, I'm sorry. So delaminid, [pass], and add linezolid,. So these are the options.

But the use of amikacin in our program overall we realize that resistance happens. Some patients might not be responding to other molecules. So we need to keep amikacin. To those patients where the non-injectable choice is suitable, perhaps one might need amikacin. But this is debatable. We're not too sure whether people will accept that. But it's something that is a big challenge here, given the decision we've taken. But if your patients are not tolerating this non-injectable, what do you do with them? So they could still be very, very limited space for this agent.

But I also know that there are issues -- it's possible to administer an injectable without a needle. So this is something that we also have in mind if it comes to such options. Maybe we can talk about it another day. It's possible to administer this. If you have a very small number of patients, it can be more costly but that is an option. It can be done. I know it is possible. It’s happening for diabetics, why not for MDR-TB patients.

So that, in short what I can say -- now, pregnant women, we've been giving bedaquiline to pregnant women. We are monitoring very closely. They get individualized regimen with the guidance of experts -- would send to committee and then the committee would review and then recommend dosage or recommend another one.

One of the things that we have picked up since using bedaquiline is the better one compared to what we used to give before. Remember we used to give capreomycin to pregnant women. We now know that basically that was the problem. So bedaquiline is better than what we used to give the capreomycin although we never got kanamycin anyway. But we used to give capreomycin in other concoction which were not really very good. So pregnant women are going to get bedaquiline. Children below 12, to options include: Up to 12 options include linezolid. In very rare cases you can make a regiment and consider kanaymic but this option is theoretical.

>> Thank you, Dr. Ndejka.

Dr. Omesa, would you like to comment on when Kenya would procure or widely use bedaquiline and what's your thoughts about the price of bedaquiline, how we can -- in terms of advocacy. And then I'll pass it on.

>> DR. EUNICE OMESA: Thank you so much. Just to address the first question when will Kenya procure bedaquiline, it is important for me to highlight at this point that Kenya is currently benefiting from a donation of bedaquiline. So the issue of cost right now is not a prohibitive factor towards access.

But we do know once this donation comes to an end at some time in 2020, they will be required to buy these drugs. And I think as Dr. Ndejka mentioned earlier, we really do need to start thinking about how, when, if we plan to scale up, we are going to address the prohibitive costs that bedaquiline brings onboard.

I think first thing we need to do is we need to advocate at a global level so that we all speak in one voice. And how do we do this? I think once we pool together for a procurement

would address some of these issues so that in the event that South Africa wants to procure, Swazi wants to procure, Lesotho, Kenya, Uganda, Tanzania and so on and so forth it would actually lower the costs. Because as it is, $900 actually is a significant amount of money. And as I mentioned earlier, it should not quantify the value of life again based on this cost. But it's something we need to critically look into if we want to scale up the implementation.

So Kenya's experience as far as bedaquiline is concerned is that we have had experience in country in the use of bedaquiline. It's just that we have not been able to scale up. And this is because we have challenges in this terms of decentralizing. However, we have a very clear roadmap on how we intend to do this. An assessment has actually shown that the steps that we need to undertake towards ensuring that we have a scale up on bedaquiline, we actually elicit it to patients that success is a commodity.

Needless to say, there is no patient in this country who falls within the eligibility criteria for bedaquiline. So far in the pipeline, in country, we have bedaquiline. We do call downs based on, again, on the focus that we have done.

We have initiated at least 30 patients on bedaquiline. I know it's not a significant compared to what South Africa has done. But I think to us it's more of a learning lesson. A point to benchmark from South Africa to now be confident and say that the direction to take and actually that is a direction to take.

And I want to also highlight today that just recently the technical working group -- actually in those injectable free regimen. We now seek to take this a scale higher to the TB in the country and have this body also endorse so that we have that critical pool and a good way to continue lobbying for the same.

Yes, we need support in terms of infrastructure, in terms of capacity building. We need assistance in terms of, you know, centers, institutions well equipped to ensure that patients, once initiated, are able to monitor.

So as it is, I think we are ok until 2020 when the bedaquiline program actually comes to an end. And for now there's no patient to go without bedaquiline if there is one who needs bedaquiline today.

I think that's my humble submission.

Oh, yeah, the other question was how would you advocate for use? Evidence never lies numbers don't lie. So if we use the evidence that's already South Africa is showing and also basically in country, the initiative on bedaquiline, all of these patients have actually had good outcomes with the exception of one patient who was co-infected. And that clearly shows us that even in a resource-limited setting and with a few number of patients on bedaquiline, there's still a lot of benefits -- I mean visible evidence that's truly, indeed, this drug actually has favorable outcomes to our patients.

So I think critical use of data and evidence out there would be a very strong tool to lobby. And, of course, such platforms and forums and engagements with the civil society, engagements with partners will help in the scaling up.

Khairun, I think that is my humble submission. I want to believe that I've answered those questions

>> KHAIRUN: Thank you. What about Phumeza, do you think, first of all, price is fair and how would you advocate for decrease in price for the bedaquiline injectable-free regimen? Thanks.

>> PHUMEZA TISILE: It's actually quite easy. First in those decision making, patient voices are needed. We cannot decide for someone [Indiscernible] cannot call people a subject, degrading terms like subject, cases, and objects and think that you are doing something

[garbled] patients should be at the forefront of those decision making things.
And I don't see what's the point of making drugs for people [Indiscernible] civil society compared with people who do [Indiscernible] drugs. And [Indiscernible] advocates to patients taking the drugs. And in all doing that we can have a winning team and TB can be eradicated.
>> KHAIRUN: Thank you so much. I think I'm going to ask one last question. We will be sharing the presentation through the various platforms but the question is, for those who have suffered hearing loss in both Kenya and South Africa from TB treatment, what services are available and what support mechanisms exist?

And with that, I apologize we are not able to ask all of your questions but we hope to keep the conversation alive.

Dr. Omesa and Dr. Ndejka, thanks.
>> DR. NORBERT NDEJKA: Ok. Can I quickly go ahead?

In terms of the services available, like I said, a very large network of hearing tests. TB program also able to, you know, convince some of our partners to provide equipment to the facilities, some of the facilities. We notice that the portable [Indiscernible] that we give actually the main odometers in major parts of South Africa. So it's a really critical that we continue to do that.

So despite the fact that we are doing all of these changes in the regimen, we will continue to do hearing tests because we know that hearing and HIV is also a problem for hearing. Definitely there will be a decrease but we don't think you see your hearing challenges come 0%. Want that to be 0%. And the one way to know is now 0% is to continue monitoring at least for the next six months or 12 months.

So we are very serious about that. We provide hearing aids but I must say hearing aids most of the time are useless. Efforts is that we still -- right now we're planning to buy more devices to deploy so that hearing test is done. Because we've been told that six months after you stop the injectable or even 12 months, some individuals, the damage could still be happening. So we want to be very serious with prevention. And then also hearing aids.

We are also collecting data on patients in a require cochlear implants. We want to approach some of our partners so that we could get more patients, you know, to benefit from this because we believe that this although it is expensive it is cheaper than legal sue. We have to be ahead of legal suit if they sue you, you pay millions; so why not spend those millions in making people better before they take you court. So this is what we have in mind. And I'm saying this because there are no generalists here.

But I must say our short regimen we studied last year. Most of our data is really on the long regimen. Short regimen last year. Some of our promises that we haven’t kept last year, September. So we don't have outcome from Cape Town. We have preliminary outcomes from the few province that their outcomes looks very much in line with what we have been seeing. But we need to continue to collect data. And hopefully next year we can present more evidence on this short regimen with bedaquiline.

Thank you.
>> KHAIRUN: Thank you so much. And quickly, Dr. Omesa before we wrap it up, what support are Kenyans who go deaf because of injectables -- what kind of support do they get?
>> DR. EUNICE OMESA: Ok, thank you, Khairun. I think just to quickly respond, first we try our best to ensure that patients are monitored throughout the tests. We can pick audio-toxicity before patient actually goes deaf. We have at least one audiometry machine in every country in this country, and so access to the same is actually paramount so that the patients are

monitored adequately.

When it comes to ability of management of patients once they become deaf, unfortunately in Kenya the cost of cochlear transplant is quite, quite high. And unless the patient has an insurance cover or has the national health social cover, it then becomes quite a challenge to ensure that they are able to receive hearing aids or cochlear transplants.

Again, those are some of the issues we are really trying to address, especially right now where we have universal health coverage as an agenda for the president just so that our patients -- in the event that they go deaf, which is an unfortunate and unprecedented side effect, they're actually able -- can actually support them by providing them with hearing aids.

All and above that, I think we also provide rehabilitative or economic cushioning for these patients because, again, it affects their normal way of life. It means they will not be able to conduct their routine -- not able to go on with their normal lives. So enrollment on the economic cover to relieve them of the taxes they pay, the disability assessment is also one of the ways as a country we ensure that our patients are able to not really be compensated but at least make it a lot lighter because there are benefit package that come along with that particular assessment.

So it is utmost responsibility and are committed to that, to ensuring that at least no patient goes deaf while on treatment. And my trust and hope is that moving forward, once we adopt this injectable-free regimen, patients actually will be able to face the adverse reaction that can be prevented with the implementation of the injectable-free regimen.

So I'm excited on behalf of my country and really, really pushing towards seeing that we roll out or actually at least have our heads rolling and thinking. We already initiated that talk. We are at advanced stages. And very soon I think you will hear that we have a plan towards the implementation.

>> KHAIRUN: Thank you so much, Dr. Omesa.

With that, I hand us back over to Marcus. Thank you, everyone.

>> MARCUS LOW: Can you hear me?

>> Yes, we can.

>> Now we don't hear you, Marcus.

>> MARCUS LOW: Sorry. Sorry.

So just a few words in closing. I think we've had a very rich discussion today. I think we all understand that it's not trivial to introduce a new medicine and to do it properly. But right now the reality is that in most countries people are still being given injections. People right now are having to undergo those painful injections every day. People are losing their hearing. Most of them won't get hearing aids or cochlear implants.

So you know, the clock is ticking. We need to fix this quickly. I think, you know, five or 10 years ago the evidence was unclear and there was some excuse for treating people in this way. But times have changed. And, you know, if anyone still disputes the evidence, the question I would ask is: What would you do if you had MDR-TB? I think the vast majority of us will not want to take the injections and I think that should be the test.

My hope is certainly that the WHO will see it that way. I'm actually quite constant given the strong data from South Africa that they will recommend an injectable-free regimen. [confident not constant] and after that there's a moral obligation on governments to make it happen and to stop unnecessary suffering. And that's really what it's about.

So, on that note, thank you very much to our three speakers, Dr. Ndejka, Dr. Omesa, and Phumeza Tisile. Thank you to TAG, to DR-TB, to my TB CAB colleagues,

organizers, Khairun helping with the questions, and Safiqa Khimani and Erica at TAG for helping. Thank you to everyone who tuned in and especially those of you who are still here who stayed till the end amount apologies for running over. And for those who tried to join last time, apologies for that being canceled.

With that thank you very much. Have a good day. And let's keep this going. It's important.

Thanks.