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ADVANCES IN HIV TREATMENT AND PREVENTION: CROI 2017

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[video transcript]

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- [Narrator] Welcome to The Physician's Research Network. I'm Jim Braun, the course director of the monthly meetings of PRN in New York City. Since our beginning in 1990, PRN has been committed to enhancing the skills of our members in the diagnosis, management, and prevention of HIV disease, as well as its co-infections and complications. We hope this recording of Timothy Wilkin's presentation Advances in HIV Treatment and Prevention: CROI 2017 will be helpful to you in your daily practice and invite you to join us in New York City for our live meetings in the future.

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PRN is a not-for-profit organization dedicated to peer support and education for physicians, nurse practitioners, and physician assistants. And membership is open to all interested clinicians nationwide at our website PRN.org.

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And now, allow me to introduce Tim Wilkin Associate Professor of Medicine in the Division of Infectious Diseases at Weill Cornell Medical College in New York City.

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- [Tim] All right, so we're gonna first talk about prevention. So these are important statistics for all of us to know. The big news is that we're starting to see a decline in the number of infections in the US, which is great. So you can look at the overall rate of decline annually. And so that's nice to see, a significant decline. We see declines in people who acquire HIV through heterosexual contact; declines in intravenous in HIV acquisition through intravenous drug use. But we still overall don't have a decline in men who have sex with men, which is really the heart of the epidemic in this country.

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When we break that down and we look at different age groups of men who have sex with men, we see an interesting pattern. If you look at the 25 to 34, we're actually seeing sort of an increase in HIV infection with more stable rates in other age groups.

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I think one of the more interesting, or actually, more troubling aspects is just the racial breakdown- the racial disparity in the HIV incidence among men who have sex with men. So if you look at the top graph, or the top line, African American men, sort of the really most difficult population to reach with our current prevention technologies, it's really seeing a very steady rate of HIV infection. We haven't really fixed that. Whereas white MSM are seeing a significant decline. So again, black and Hispanic MSM are really not seeing the recent benefits from treatment as prevention and HIV PrEP, where perhaps we are seeing that in white MSM. So, to get at the PrEP issue a huge focus for our national prevention effort is to really reach men of color- MSM of color- and get them onto a PrEP, which is very effective.

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So, this is a study- an observation of cohort study- in Atlanta where they looked at close to 200 men who were eligible for PrEP. And just tried to enroll them into PrEP. So this really took away issues of drug availability, so the PrEP was actually provided through the study. And so you can see, a good proportion of men were interested in PrEP; only 10% said they were not interested. But among the people who were interested, only half of them really initiated PrEP. And then and stayed on PrEP. So really, only about 25% or less of the people who were potentially eligible actually were able to make it onto PrEP and stay on PrEP.

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So if we look at drug use trends, because that can really complicate any kind of prevention strategy, be it PrEP or condom use, if there's a lot of drug use specifically methamphetamine and cocaine use. And we can see that it does it is relatively stable overall but again, we see this troubling increase in crystal meth use among MSM- black MSM- in Washington, DC. And if you've provided care for people using meth, it can be obviously quite challenging.

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So, this is looking at the percentage of HIV infected people who have achieved durable virologic suppression. And this is a broad data from over 600,000 people to try to get the most accurate estimates of how good are we doing at virologic suppression. Does anybody know what the WHO goal is for our country right now for virologic suppression? It's 90 90 90, so if you do the math, that's around 72%. People in a country are supposed to be suppressed and there are some countries in Africa that are getting very very close to achieving that. So how are we doing here in the US? So if we look at a variety of factors- be it sex, race, transmission- you can see that there's varying evidence, just looking at age, for example. Not surprisingly, people who are a little bit older- 45 to 55- generally, are the most likely to be virologically suppressed. Those who are diagnosed more recently are more likely to be virologically suppressed. So these are interesting data that you can look at in more detail. We do see, again, racial disparities. Whites are more likely to be virologically suppressed than Hispanics or blacks. But you can see in all of these categories we're not really achieving that goal of over 70%.

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This is looking at a specific HIV outpatient cohort study, the HOPS cohort. And looking at the percentage of time with viral load over 1,500, so really, what we would want to avoid. And that's really the viral load where you start to have increased risk of transmission. And, you can see that the rates over time, the percentage of time that people are having these higher viral loads, is declining. So this is a specific cohort study, so it's not quite so generalizable to the rest of the country. But those trends are encouraging.

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This is a very interesting study about using combination prevention strategies. So just like we don't treat HIV generally with one drug, we use a combination of approaches. The same is true for HIV prevention. So this is looking at an area in Uganda- Rakai, Uganda- where they looked at a combination of scaling up

treatment as prevention, as well as male circumcision to effective prevention strategies. And what you can see on the right is how they were, what goal they were, what levels they were able to achieve on a population basis for these two strategies. And so in the green bars you can see that they got up to 60% of eligible men being circumcised. And over 60% of HIV positive people on ART. And with those two strategies, together you can see the HIV incidence: this dramatic drop in HIV incidence by close to 50%, or over 50%, showing the potential of using these combination strategies. So in the US, or in other places, it might be a combination of treatment as prevention but also, HIV PrEP, that could hopefully achieve this synergy.

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So this is a pretty specific prevention topic. So if you follow the world of microbicides, there was an interesting study, I think it was last summer, about using tenofovir gel microbicides. And what was very interesting is they found that the microbicide was less effective in women who had vaginal dysbiosis. So bacterial vaginosis, for example, is it's a decrease in your, or increase in your anaerobic bacteria in the vagina, creating an abnormal environment that can put women at risk for HIV transmission. So in those prior studies, it also showed that certain bacteria seemed to take up the tenofovir and actually lead to lower levels. And that was part of the reason that the that there's effectiveness problems. So, these investigators were concerned; well, if that could happen with the topical gel, could it happen with oral PrEP? If you followed the studies on oral PrEP in women in Africa, it's very very challenging. A lot of that is due to adherence, but some of it is also due to difference in drug penetration. So, you start somebody on MSM on PrEP; they're protected after a week, seven days. If you start a woman on PrEP, it takes a month of being on Truvada regularly until she's actually prevented, or has adequate levels. So this study actually showed that the that they did not see a dramatic difference in the effectiveness of the oral TDF/FTC by the vaginal dysbiosis, which is good to know.

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Another study over the coming years, you're gonna see more and more about long acting anti-retroviral therapy- both as treatment and also as prevention. So this is a study conducted by the HPTN 076 looking at monthly injections of rilpivirine, a long acting rilpivirine formulation. And what they found was that they were actually, that they were able to achieve good concentrations of rilpivirine that they think should lead to protection. The study wasn't at all designed for efficacy- it was really safety and tolerability, and PK study. But they did achieve good levels. They also, it was placebo controlled, and they looked at acceptability measures. And, it was interesting. A lot of people said it would definitely use it, would probably use it, would think about using it. And a very small number would say no, they wouldn't use it. So it could be, these injectable long acting formulations could be a nice option for HIV PrEP.

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This is looking at using a long acting injection in acute HIV infection in Macaques. And what they found was that it was that resistance to cabotegravir could develop. So it is important because we're rolling out studies of injectable cabotegravir for PrEP. So, similar to dolutegravir, it’s an injection that you give every two months to prevent HIV infection. We're doing that study at Cornell. We're also doing it at The

Blood Center. Several sites in town- HPTN 083. So this does provide a note of caution that if people break through, or have infection while they're on cabotegravir, they'll likely develop resistance.

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Okay, so this was a very interesting study, just moving away from HIV infection, to other sexually transmitted diseases. This was a study for on demand doxycycline for STI Prophylaxis, sort of a not a PrEP, but an STI PEP post-prophylaxis. So this was done as part of the study of the IPERGAY study, which was a blinded study of intermittent dosing of TDF/FTC. Just as a side note, that's not recommended- intermittent dosing- it's just recommended to have daily dosing. You need to get at least four doses a weekend to be protected for MSM. So anyway, with this study, they also nested into it a study of STI Prophylaxis with doxycycline. So they had high risk, very high risk HIV negative men who have sex with men. And it was a blinded study. So some people got the real doxycycline, some people got a placebo. And the way that they would dose it is that they would take 200 milligrams 24 hours after their sexual exposure. And then repeat a couple doses. So they were only supposed to take it max six doses a week. And so what they found was that it did lower the rate of bacterial infections. So we're just focused on chlamydia, gonorrhea, and syphilis. And so it reduced it significantly by almost 50% reduction in the number of new diagnoses. So when you break down those infections, it was interesting. So that doxycycline- we think of as the treatment for syphilis and we think of it as the treatment for chlamydia. And so you did see nice reductions in those infections. Apparently, doxycycline, I didn't know this, has some activity against gonorrhea. But they actually did not see any reduction in gonorrhea. So reductions in syphilis, and chlamydia, but not gonorrhea. For your post-test. So, it's an interesting strategy. But, I think that there's concerns overall about using antibiotics more broadly just about encouraging resistance. I don't know if we're worried specifically about resisting chlamydia, or syphilis. But, I'm not sure that this is I don't think many people are recommending this strategy in general. But it's something that perhaps deserves a larger study.

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Okay, so moving on to HIV cure. So, there are different stages of acute HIV, so Fiebig I is where you, that very very early stage where you start to get a little detection of HIV and absolutely no antibody response. So it's thought to be, people treat it at the very very earliest part of HIV. I'm sorry, it's actually on the slide. So viral load positive but not even P24 negative. Or still P24 negative. So that's only, I think, about a couple of day window where you start to have viral load but you can't detect P24. So, even treating people at this earliest stage of HIV, if you stop HIV treatment, they rebound and somewhat regularly. So that early treatment alone is not sufficient.

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We all know about Timothy Brown, the one patient cured of HIV. This was a case report of a Allogeneic Stem Cell Transplant actually not CCR5 deleted; it's CCR5 Wild Type transplant, who was continued on ART for about two years post-transplant. When they did a lot of the testing, this patient had some total integrated HIV DNA and some replication competent virus in the peripheral T cells, I'm sorry, that was all negative. And really no evidence of HIV infection. And so after the acute, the analytic treatment interruption, sorry, so that's about 750 days, 250 days so, about eight months that he or she was

undetectable until there was viral rebound. So a really prolonged post prolonged suppression after interrupting therapy. But still an eventual rebound. So you could think of this as a failure but in some ways, those markers that they measured were predictive of having a much much longer time to rebound. So perhaps on the way towards a cure.

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This was a study- a combination study- kind of getting at cure. And so, this was looking at a combination of a vaccine with an HDAC inhibitor, romidepsin, to try to see if that would reduce the reservoir somewhat. And the way that they measured this is by doing a treatment interruption and then measuring the time 'til the viral load rebounds. And so what this found on the left is really the controls where they have, you can see a pretty marked rebound of viremia. Here you have the weeks off of anti-retroviral therapy. And you can see that there's a much reduced rebound of viremia. So just to orient you, this is kind of a confusing graph because this shows the viral load decline as they're starting ART. And then they become suppressed and then they're suppressed for some length of time and then they enter this study. And then it's just kind of cutting out that middle point and then you can see the viremia. So this is basically showing that people rebound, the controls rebound back to their pre-ART set point. Whereas here, you can see that there appears to be a reduction. So perhaps making progress.

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This is looking at another at a TLR7 agonist made by Gilead, that's supposed to promote immune-mediated clearance of HIV infected cells. So this is looking at a monkey model. And so they've found that this was able to reduce the SIV-DNA in the blood, lymph node, and colorectal mucosa in all the animals. And, they did establish that two animals were able to have a stable remission after interrupting the therapy. So, perhaps a promising approach.

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All right. ART. So there were some several interesting ART presentations that we'll talk about, some new drugs that are coming along that are pretty exciting. The first one is doravirine. It took me awhile to learn that, I kept saying doravirine, which doesn't really sound right. But it's doravirine versus darunavir in Treatment-Naïve Study. So, this is just enrolling naïve patients. They're followed for two weeks. And what they found was there was really no appreciable difference between the two groups- the doravirine seemed to function as well as the darunavir ritonavir. The study was a little bit strange because darunavir ritonavir is not really our go-to initial regimen, although I assume this started a few years ago. So it's hard to know how this compares to integrase inhibitors, which would be our preferred choice for initial ART. But it definitely seems to have some activities. Doravirine, I think, it's akin to rilpivirine, or etravirine, that it seems to be active against some resistant and RTI isolets. I'm not sure based on the data they presented exactly where it's gonna fit into our treatment algorithms. But it is effective.

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So they looked at differing sub-group analysis and everybody seemed to, you know, the results were consistent that it seemed to perform as well as the darunavir/ritonavir.

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So this is by viral load. It's by CD4 strata or what NRTIs they paired it with.

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Okay, if we look at resistance really, nothing happened. There were very few people that had true virologic failure. The difference, if you notice, was around 85% success. The 15% that was unsuccessful was mostly people who either missed a particular visit, or perhaps had just a little low level viremia. So they had 19 people that had protocol defined virologic failure. They were able to actually get a genotype result on seven of them. And it was completely wild type. There was only one person who had perhaps a little bit of resistance to the doravirine group, but they actually resuppressed on doravirine so it's not clear that it was clinically meaningful. So, good result.

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And if you look at the adverse events, pretty typical of ART- initial ART studies. Not very many people discontinued due to an adverse event. Only two percent of the doravirine group discontinued due to an adverse event. Some mild GI. Side effects, not clear if that's exactly related to the drug, or not.

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So there's a new integrase inhibitor coming your way, called bictegravir. Why this is particularly interesting is that bictegravir seems to behave, as far as resistance, like dolutegravir. That kind of high barrier to resistance unlikely to develop resistance in clinical practice. It's also made by Gilead and tenofovir alafenamide and FTC are made by Gilead. So then you have this all one pill, once a day, that doesn't, that has the tenofovir alafenamide with the potent integrase inhibitor without that boosting. So it's a very attractive combination. So this was an earlier phase study, it's a phase two study. And they had only 65 people that got the bictegravir as opposed to 33 that got dolutegravir. And they compared the end points. And it's not a very big study, so I wouldn't make any inferences about any differences that you may see. But both arms did really well- very low rates of virologic failure. Or by the end point. So no resistance to any of the study medications in either arm. So the phase three studies for bictegravir have been fully accrued, I think, for awhile. So I don't, I'm not sure when those data will be released. Hopefully this summer. But I can't say for sure. But it's a very attractive single dose tablet regimen, should it come to market.

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And if you look at the adverse events, there really didn't seem to be any noticeable differences between the two groups. They didn't comment on any neuropsychiatric effects, or sleep disturbances. That's the lingering concern with dolutegravir. And if it's a similar drug and a similar class would that happen with bictegravir? So that's something we'll be able to we'll understand more when you have large studies with 1,000 patients, or so.

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So this was a novel regimen that's being studied: dolutegravir rilpivirine. So, it was interesting; this strategy sort of came about because there were two injectables- the bictegravir and rilpivirine- that was

being studied as injectable ART treatment. Then they realized, oh, we got dolutegravir and that seemed to work really well. So then dolutegravir is the potent drug and rilpivirine was also available by pill. So, there have been studies looking at just those combinations. And so these were two large studies of switching from a standard anti-retroviral regimen to dolutegravir rilpivirine. And in at the CROI presentation, they just combined the results and presented them together. So, it took people that were stably suppressed on an integrase and an RTI, PI or 2NRTIs. And then randomized them to either continue their anti-retroviral therapy, or switch to dolutegravir rilpivirine.

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And so as far as the age groups are all pretty typical, pretty high CD4 counts. A nice spread of differing ART regimens that they were on. Most people were on TDF at baseline. And had been on ART for about four years.

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So the outcome slide; everyone did terrific. So 95% of both groups were still suppressed at a year. Most of the people that were not suppressed, it was actually just because they didn't come back for the visit within the required time window. And, true virologic failure was exceptionally rare. So it did achieve the protocol definition of non-inferiority. And so I believe that this is being filed with the FDA and would be, I think the first regimen that has just an indication for switch. So technically you shouldn't start someone on this regimen but you could switch them to it, after they had been suppressed.

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No real mutations, there was one patient who had a minor NNRTI mutation but it wasn't really associated with resistance to rilpivirine and that person resuppressed on the same regimen.

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If you look at the adverse events, it was just kind of a widespread of adverse events. What was important to note was that there were more adverse events on dolutegravir rilpivirine. Remember, one group was on a regimen that they had been on for a while and presumably were stable and tolerating it very well. And then the other group switched to new medications. And so it’s thought that perhaps these, I'm sorry. That these low level adverse events are just what one would expect when switching medicines, you generally keep people on the medicines then they go away.

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So, moving a little bit even more novel is a study called LamiDol. So dolutegravir/3TC. So this was looking at 110 subjects without any history of virologic failure, could not have Hepatitis B because treating with just 3TC and not 3TC/TDF would put you at risk for HPV resistance. So, they were started on their accommodation regimen, whatever they came on. They switched to 2NRTIs and dolutegravir made sure that they were tolerated in the dolutegravir. And then they were followed on dolutegravir/3TC for 40 weeks of follow up. And everyone did great, they were basically all suppressed. There was one virologic failure but no resistance. There were four SAEs but nothing really seemingly related to the medications. So the dolutegravir/3TC is being studied. We did, we participated in a study out of Northwestern looking

at a randomized study of switching it. It will be presented this summer. It seemed to work great. The ACTG completed a study of about 110 people who started dolutegravir/3TC as their first regimen. And, those results should be out within six months, or so. But this is actually of interest and dolutegravir/3TC are manufactured by the same company so this could be a single tablet regimen that could be an option for a simplified or approach for less drugs. So, taking it even further, what about just dropping the 3TC and looking at dolutegravir alone, because it seems to function like a protease inhibitor in that it's very unlikely to develop resistance in clinical practice to dolutegravir.

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So, there's been a bunch of PI monotherapy studies, where you can suppress a lot of patients with it, not everybody. So, there were a few studies of this. And this was a study, this was the formalized study, so they followed people either on a combination ART or dolutegravir monotherapy- switching to either those. And what they found that the rates of people had virologic rebound on dolutegravir monotherapy. By week 50, over 10% of people had had virologic failure. And then among those eight, they got a genotype. And there were three people that developed integrase inhibitor resistance. So really, kind of taking the integrase inhibitors off the table. So kind of a serious resistance outcome. And so based on these limited data, the DSMB stopped the study. Really, this would only be appealing if resistance didn't develop and you could just re-initiate NRTI. So that didn't seem to work. And so the authors concluded that they recommended against dolutegravir monotherapy as an approach.

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I should say there was also a cohort study, a retrospect of chart review of dolutegravir monotherapy that apparently a bunch of people are switched to that and some are in Germany, I can't remember. They also saw the same thing with a lot of failure and resistance.

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So, this is looking additional data from the study of elvitegravir/cobicistat/emtricitabine with TAF, or TDF. And this is just longer term data. And what they found was that there seemed to be a bit more, the benefits of the TAF virologically seemed to be slightly more apparent. So, at three years, 84 suppressed versus 80% suppressed. And it did achieve statistical superiority. I don't know that this really matters very much because we're using TAF really for its side effect profile, or lack of side effect profile with renal dysfunction and the bone density. But it's good to know that the virologic outcomes are good.

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So again, this is looking at the longer term bone density data. So, this is the TAF group, where there was still some loss of bone density. Probably something related to just controlling HIV. But really stabilized as opposed to the much greater bone loss with TDF. And if you look at renal issues there were these renal in the broad class of renal events, all occurring in the TDF group, as opposed to the TAF group.

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Okay. So there was some interesting new drugs. So, if you've been to CROI long enough there's always something really exciting and some of them actually move on to actual drugs that are tested. And some

of them you just kind of never hear about again. But we'll see about the capsid inhibitor. Sorry, so this is, if you remember part of the maturation process is this kind of cleavage and function of caps, so that capsid can form this kind of the structure, the protective structure around HIV. And so they have capsid inhibitors that prevent the assembly of capsid into that 3D structure. And so it becomes this kind of abnormal non-infectious virus in the presence of the capsid inhibitor. And it's always good when you can show pictures to show that the virus is defective. So this is pretty promising, so hopefully it'll enter a clinical trials.

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So this is a little bit more of the detail about the mechanism of action. So it's really this maturation process that the capsid forms, a structure here in green around the viral genome. That the, the capsid inhibitor sort of prevent the assembly of the capsid but they also interfere with the disassembly of the capsid. So kind of a two hit process that could interfere with the life cycle.

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So, this is an interesting study of a monoclonal of an antibody against CCR5. So, this is active against R5 virus that's even ones that are resistant to maraviroc. And so this study was actually looked at just this therapy as monotherapy. And, what they found was that they were actually able to have durable virologic suppression with just this monotherapy of weekly sub-Q injections of this antibody.

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All right. So looking at metabolic events and comorbidities.

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So this was a new analysis from the NA-ACCORD study, which kind of combines a bunch of cohort studies from North America. And it was looking, trying to estimate what were the attributal fractions for traditional risk factors for myocardial infarction versus HIV related factors. Specifically, what was the what were the estimates of the relative contribution to the risk of heart attacks. So interestingly, or maybe expectedly, I should say, that most of the attributal fractions were really to some of our traditional risk factors. Smoking. Uncontrolled hypertension. Hyperlipidemia. And to a lesser extent, these other factors. So having a low CD4 count really only contributed to the end MIs in about 10% of the of the myocardial infarctions, in this event. In this cohort. And same with the the HIV RNA.

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The D:A:D study which brought us the abacavir issue many years ago, looked at the comparison of risk of myocardial infarctions due to darunavir. And what they found was that the, as compared to atazanavir, the cumulative duration of darunavir/ritonavir seemed to raise the rate of myocardial infarction, in a way that was not seen with atazanavir/ritonavir. And so it’s not clear if this is really due to differences in lipid effects. I think they control for that. But, it's, I'm not sure they have the exact mechanism. Other studies have shown that the hyperbilirubinemia from atazanavir actually reduces carotid intimal thickness and carotid progression of that condition. So it could be just that the hyperbilirubinemia was

actually protective against MI as opposed to the darunavir/ritonavir actually being riskier. But it is interesting because that's not the preferred protease inhibitor, right? It's the darunavir/ritonavir.

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So the VA Cohort Study also looked at the Bilirubin and did associate higher levels of Bilirubin with lower risk of myocardial infarctions and heart failures. And this wasn't specific to HIV but people in general.

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So the D:A:D also looked at cancer risk and specifically the cancer risk related to tobacco use. So we all try to get our patients to smoke with varying degrees of success. And so we tried to get across the message that there's many problems that can be avoided if they all stopped smoking. So this gives some actual data about the risk of cancer after smoking cessation. So in this study the reference group here of never smokers is the adjusted rate ratio of one. So no difference. And so if you look at all cancers once you quit, when you quit for less than a year you still have an increase rate of cancer- a relative rate of cancer. And it starts to decline by one to two years. And by five years, you're really approaching that of never smoker. So that's great. So if you look first at smoking related cancer other than lung cancer, what you can see is that the rate approaches by a couple of years. You have basically normalized the rate of that cancer. So great reason to quit smoking. Very exciting. However, we're all really concerned about lung cancer, in terms of smoking. And interestingly, in this study, they did not show a decrease of lung cancer as you've quit smoking. So if you've quit for less than a year versus five years, you still have markedly elevated rate of lung cancer. So, I'm not sure if this is due to somehow a lag time between when you actually have, you're smoking, you have that risk factor, you develop cancer when it's actually diagnosed. It may take quite a while for some of these lung cancers to be diagnosed. But really, the lung cancer risk remains elevated for over five years.

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This is looking at, I briefly mentioned the CNS side effects of dolutegravir. And looking at the rates of discontinuation for these various integrase inhibitors and the incidence of any of these neuropsychiatric effects. And so if you look at the overall discontinuation rates, they're all really quite quite low. Only two to six percent actually discontinue due to any toxicities. If you look at the incidence of discontinuation due to neuropsychiatric effects, again, this did not really show much of a difference between these various regimens. So, two percent for the dolutegravir/abacavir/3TC. No one for the dolutegravir/TDF/FTC, although it's a smaller number. And seems to be pretty similar to the raltegravir. So in this study they really did not find much of a a risk for that.

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If you look at the people who do have the CNS symptoms, this study was looking at the dolutegravir trough concentrations in the blood. So it did seem that those with the CNS symptoms had higher levels of the dolutegravir. So I think we're still really trying to figure out the side effect and how important and what we can do about it.

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This was a study of switching ART in women. So, I believe this is the Wave Study. So these were women that were on TDF/FTC ritonavir/atazanavir, and they got randomized to either stay on that regimen or switch to TAF/FTC regimen. And what they found was that the TAF regimens did have switching to TAF increased the bone marrow density. And that was what was expected. I think why this was important is that there's not a whole lot of data in clinical trials of HIV of women. And so this was really confirming the finding that was in other studies that switching to TAF improves the bone marrow density. They also looked at renal tubular biomarkers or proteinuria. And what they found was that again, there were improvements. You have less tubular secretion, or tubular loss of protein with the switch to TAF as opposed to TDF, which is a good sign. Whether that means that they're gonna be less likely to develop renal failure or renal changes over time- we don't know. But this is a good sign. The one thing about TAF is it does change the lipids a little bit. So you don't have that benefit from TDF of decreasing the lipids overall was the only downside. This is looking at some drugs co-administered with bictegravir. Just some differing drug-drug interactions. I think that there are some issues with Rifampin that will be problematic, which is probably more relevant for the developing countries. But other than that, it seems to do pretty well.

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Okay. This is looking at cobicistat and the interaction with this other medication that I can't really say. But what was interesting is that in this particular for this particular interaction, it did not behave the same as ritonavir. So you couldn't really just extend the ritonavir findings. So that you got more of a drug-drug interaction with using cobicistat as opposed to ritonavir; increase levels that could be clinically significant.

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This was a study looking at switching from darunavir/ritonavir to darunavir/cobicistat, to look at the drug levels. And, what they found was that the darunavir levels, when making that switch didn't really matter. But if you're co-administering that with dolutegravir, you actually started to get an increase in the dolutegravir levels with the cobicistat as opposed to the ritonavir. Again, saying that there could be some subtleties with these two boosters and the drug-drug interactions that we should be aware of.

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This was a study of out of South Africa that was looking at treatments for high grade CIN, or HSIL. And they use quite commonly cryotherapy, because it's just easier to implement than LEEP therapy for a number of reasons. And what they found was that cryotherapy was less effective. So women were more likely to get recurrent HSIL after LEEP. Not terribly relevant for our setting because it's extremely rare for women to be treated with cryotherapy for HSIL here in the States.

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That's a little potpourri of topics from the meeting.

[Video End]