PDF created June 29, 2025, 11:59 am

Expert Interviews

National HIV Curriculum Podcast

Initial ART Regimens Considerations: A Discussion

November 19, 2024

Season 1, Episode 18

The three National HIV Curriculum Podcast editors share their perspectives on recent guideline changes to initial ART choices for treatment-naïve individuals with HIV, practical considerations for first line and alternate ART regimens, and the impact of M184V mutation.

Topics:

- ART
- HIV
- M184V

Brian R. Wood, MD
Professor of Medicine
Division of Allergy & Infectious Diseases
University of Washington

Disclosures

Disclosures for Brian R. Wood, MD
None

Jehan Z. Budak, MD
Assistant Professor of Medicine
Division of Allergy & Infectious Diseases
University of Washington

Disclosures
Disclosures for Jehan Z. Budak, MD
None

Aley G. Kalapila, MD, PhD
Associate Professor of Medicine
Division of Infectious Diseases
Emory University School of Medicine
Grady Health System

Disclosures
Disclosures for Aley G. Kalapila, MD, PhD
None

Transcript

Read along with the audio or jump to a particular chapter.

In this episode:

- Introduction
- Guideline Changes Rationales
- First-Line ART Options
- Insurance Impact on Tx
- Alternate ART Regimens
- M184V Mutation Impact
- Closing
- Credits

---

introduction**[00:00] Introduction**

Hello, everyone. I'm Dr. Brian Wood from the University of Washington in Seattle. Welcome to the National HIV Curriculum Podcast. This podcast is intended for health care professionals who are interested in learning more about the diagnosis, management, and prevention of HIV.

As background, the recommended antiretroviral regimens for treatment-naïve individuals with HIV have evolved over the years. National guidelines have been updated recently, and today I will be joined by two experts who will discuss reasoning behind the most recent guideline updates and also their experience choosing a first antiretroviral regimen in clinical practice.

Dr. Jehan Budak is assistant professor of medicine at the University of Washington in the Division of Allergy and Infectious Diseases. She serves as assistant medical director for the Madison Clinic, our Ryan White-funded HIV primary care clinic at Harborview Medical Center. She also serves as Director of the HIV Pathway through the Internal Medicine Residency and associate editor for the National HIV Curriculum. Welcome, Jehan.

Dr. Budak

Thank you. Hi.

Dr. Wood

I'm also joined by Dr. Aley Kalapila, who is associate professor of medicine at Emory University. She's a clinical provider at Ponce de Leon Center, a Ryan White-funded outpatient HIV clinic in Atlanta, Georgia. And she attends on the inpatient infectious disease consult service at Grady Memorial Hospital in Atlanta. She also serves as an associate editor for the National HIV Curriculum, and I'm honored to be joined by Aley today. Welcome.

Dr. Kalapila

Hi Brian. Hi Jehan. Thanks for having me.

Dr. Wood

It is great to see you both. I'm really looking forward to this conversation. I'm honored that we get to sit and chat together. The focus, as I mentioned, is going to be on initial ART [antiretroviral therapy] and recent changes to the Department of Health and Human Services guidelines. So, let's dive right in.

guideline-changes-rationales**[01:50] Guideline Changes Rationales**

Dr. Wood

The Department of Health and Human Services (or HHS) guidelines for selecting ART for treatment-naïve adults or adolescents with HIV, focusing really first on those who have never received injectable cabotegravir for PrEP: That section was recently updated and there was a major update to these guidelines. The guidelines panel removed the combination tablet, dolutegravir-abacavir-lamivudine (DTG-ABC-3TC) from the list of recommended options. So, as a first question, Jehan, could you take us through why you think the panel removed that option from first-line and why that option has fallen out of favor?

Dr. Budak

So, I think one, I am happy to see that it was moved off of the initial start because I don't know about you all, but I cannot remember the last time that I started anybody on abacavir-lamivudine-dolutegravir. I certainly have patients who are still on it. I remember starting them on it way back in the day, but recently I have not started somebody on it. Practically speaking, I'm not really using it on a day-to-day basis. My understanding of the reasons why it was likely removed from that initial start is one, sort of logistically, the need for an HLA-B*5701 test, which can at best take a week, at worst, take three weeks to come back. And so, before initiating, so especially in the era of trying to start ART as soon as possible, without having that information, it's hard to do that.

And then I think, my guess is, that perhaps more so was the sort of the association with cardiovascular disease. I know that's been a thing for a long time; that there have been some big studies showing association with cardiovascular disease. But my guess is that that was the perhaps the nail in the coffin of why it's no longer something to start. And I think I personally was also moved by the subanalysis, if you would say, from the REPRIEVE study where they showed that people who used abacavir had, to me, so much more adverse cardiovascular events. And again, I know that there's a lot of association and it's not necessarily causation, but when we have other things and there is so much association with cardiovascular disease, that's my understanding why. I think in the small print it said those two reasons, but my guess would be that it was more so the latter as to what led for it to be there.

Dr. Wood

So, it sounds like your clinical practice was moving that direction anyway. Aley, how about your practice?

Dr. Kalapila

So, I agree with Jehan that probably the two biggest factors that I'm aware of, at least, led to the change in the guidelines was because of the need for the HLA-B*57 testing, which often takes a while for it to come back. And we're trying to do rapid ART initiation, oftentimes on patients who are newly diagnosed. And then also, of course, the cardiovascular effects of abacavir. I will tell you that it was a regimen that I used to use quite frequently since I've been now in Atlanta for like almost a decade. It's hard to believe how time flies. And, you know, we had a fair number of patients, and tenofovir alafenamide (TAF) was not available. And we see a lot of advanced HIV in Atlanta. We also see a lot of HIVAN [HIV-associated nephropathy] in Atlanta, which would preclude the use of TDF (or tenofovir disoproxil fumarate). And so oftentimes I was trying to get a single-tablet regimen that was integrase inhibitor-anchored to avoid drug interactions. And so, this [dolutegravir-abacavir-lamivudine] often used to be a good choice. So, I definitely have used it previously. But

yes, with the availability now of bictegravir, you know, single-tablet bictegravir-tenofovir alafenamide-emtricitabine (FTC), I've kind of fallen out of having to use it again, especially because more so of the need to wait for the HLA-B*57 testing to come back before we can actually use it. So that being said, I do think that there might still be a role for it. I don't know. Like, again, if you have someone with really bad CKD [chronic kidney disease] and you can't use TAF, even if the GFR is less than 30, and you have some time to wait and they really want to be on a single-tablet regimen, you could start with something else and then switch over to the 3TC-abacavir-dolutegravir regimen.

And then I think another time that you could consider using it is also to mitigate drug interactions, right? So, if you see patients who need to be on a rifamycin for whatever reason, there's issues with a lot of the rifamycins be it for LTBI[*latent tuberculosis infection]* or disseminated MAC [mycobacterium avium complex] with tenofovir alafenamide in particular. And so sometimes this is also a convenient way to kind of bypass that, at least for a temporary period of time until they have done with the treatment of whatever other thing is causing the drug interaction. So, I think those two probably are like the biggest reasons why I would consider using that regimen.

Dr. Wood

Thanks, Aley. Jehan, what would you add?

Dr. Budak

I think I was more curious, Aley, as you were talking was in a TAF era, when was the last time you started somebody on abacavir-lamivudine-dolutegravir?

Dr. Kalapila

Oh, hardly ever. Although, I think if I think about my inpatient time, that probably there have been moments when I have done that to give someone a triple-drug regimen that is obviously fully active, that when they don't have other contraindications to being on it. And, more often than not, in the inpatient side when I've had to do it, it is because of drug interactions, and combined with plus/minus CKD issues it's come into play.

Dr. Wood

I appreciate you both outlining your own practice and why it seems that the guidelines panel got away from this 3-drug combination option. I'll share from my own practice. Like you, I have not started anyone on this option for a very long time. There was an era when we were checking B5*701 on almost everyone, and we were prepared to prescribe this option for almost everyone, if any CKD developed. But now with other new options with all the concerns about the drugs that you both raised, plus it's also a *huge* pill and I don't find people tolerate it very well. And now there's such robust data for dolutegravir and lamivudine dual therapy, including in the setting of M184V mutation and other things, it's hard for me to come up with very many scenarios where I would reach for this option.

first-line-art-options**[07:56] First-Line ART Options**

Dr. Wood

So, let me turn to, if you're not reaching for that, what do you reach for? And so, what I'd really like to hear is what tends to be the first ART regimen you reach for someone who has never taken ART before? Again, someone who has never had cabotegravir as PrEP before either. This list of options is now relatively short. The HHS guidelines really list three, the bictegravir-TAF-emtricitabine (or FTC) option that Aley mentioned or dolutegravir with TAF-FTC or TDF-FTC or TDF-3TC. And then there's the 2-drug option dolutegravir-lamivudine (or dolutegravir-3TC). So, practically speaking, how do you make that decision? Aley, will you start?

Dr. Kalapila

Yes, sure. So, I think in the era of having a single-tablet bictegravir-tenofovir alafenamide-emtricitabine, it is always my first go-to. It's a single-tablet regimen, it's dosed once a day, it's highly potent, it has a high barrier to resistance. All things I look for. And it is pretty well tolerated. And, unlike 3TC-ABC-dolutegravir, it is actually a smaller pill. So, I think that probably for me is like my first go-to, especially when I have concerns about patient's adherence to sometimes the TAF-FTC plus DTG combination is also convenient. They're two small pills once a day. But sometimes I think for patients who have, say they have housing insecurity, unable to store pills in a safe place, I think it's just easier when you have to think about you just have to take one pill. I've had situations where patients might take one and not the other because they get confused. So, I think for all those reasons, that's probably my first choice that I reach for.

Dr. Wood

Jehan, is your practice similar?

Dr. Budak

Yes. My practice is quite similar to Aley's. I will discuss with the patient at first, what is it that they're hoping for in a medication? What's important to them: pill burden, pill size, side effects, etcetera. And then, I will give them the three options of bictegravir-TAF-emtricitabine or TDF-FTC plus dolutegravir or TAF-FTC plus dolutegravir, and mention the pros and cons of each of these medications. And one of the things that I'm definitely counseling about is the potential for weight gain. And then, I kind of see what the patient is feeling based on that, and then we'll make a decision out of one of those three options together with some shared decision-making.

Dr. Wood

Thank you for that, Jehan.

insurance-impact-on-tx**[10:31] Insurance Impact on Tx**

Dr. Wood

How much are you finding insurance approval and cost to be a barrier to your first-line option and how does that play into your decision-making around initial ART? Aley, is insurance coverage for BIC-TAF-FTC a challenge for you or not an issue?

Dr. Kalapila

So that is a great question. Coming from a state that does not have Medicaid expansion and also in the last year, the other thing that I have noticed is that more and more of our patients are being encouraged by my hospital system to sign up for the ACA [Affordable Care Act]. And oftentimes they end up getting onto a lower tier plan, which makes this extremely complicated. So, in the immediate instance when someone doesn't have any health insurance at all, and it's going to take them some time to get enrolled in the state-funded like AIDS Drug Assistance Program (or ADAP), we are able to get a patient assistance application that will sort of be the bridge. And for that, that's pretty easy to get it for BIC-TAF-FTC. But once they get onto ADAP, it is on the ADAP formulary. And then for lower tier insurance plans, at least in the recent past, I have not had a terribly difficult time getting it approved. And I think some of that is because it is first-line. It hasn't been too complicated to get it approved or at least to get it through a prior authorization. But yeah, it is something I have to think about, like all the time.

Dr. Wood

Thanks, Aley. Jehan, what's your recent experience with that?

Dr. Budak

Yeah, I mean unfortunately, Brian, to your point, this is reality and a lot of what we have to do is dictated by one's insurance coverage or lack thereof, unfortunately. And as you and I both know, having worked in Washington state up until January 1st, 2023, BIC-TAF-FTC was not even on the state formulary. And so, we could not give it for any of our patients on Medicaid, which was very frustrating. Now, however, we can, and so I have been offering that switch to anybody who is on a 2-pill combination of either TDF-FTC or TAF-FTC and dolutegravir versus switching to BIC-TAF-FTC. And it's interesting. I don't know about you both in your experience, but I feel like half of people are like, “yes, please let me get to a single-tablet regimen.” And the other half are fine with just their two pills. And again, it really is dependent on the patient and the person.

Dr. Wood

Absolutely. And coming back to choosing a first ART regimen, if there's no coverage for BIC-TAF-FTC, where are you going after that? Jehan, what's your backup option?

Dr. Budak

My backup options are either TDF-FTC plus dolutegravir or TAF-FTC plus dolutegravir.

Dr. Wood

Got it. Thank you, Jehan for outlining that. Aley, are you prescribing dolutegravir-lamivudine, which is dolutegravir-3TC, a 2-drug combo pill as a first regimen?

Dr. Kalapila

So, honestly, no, and for a couple of different reasons. So, I see a fair amount of NRTI (nucleoside/nucleotide reverse transcriptase inhibitor) resistance and so I'm nervous. I mean usually it's an M184V, which I know we're going to get to in a couple of minutes, but so I'm often at times having to wait for the genotype data. I also see a lot of advanced HIV and a lot of opportunistic infections. So, it again gets very challenging because these patients often have very high viral loads, which can also be a contraindication because you can't prescribe it if someone has a viral load greater than 500,000 copies. And, I actually also see a fair amount of hep B coinfection as well. Another reason for why I can't prescribe that.

Actually, I think it has been harder in my experience to get the dolutegravir-lamivudine regimen approved through ADAP and private insurance. I don't think it's impossible, but I think that also has been a little bit more of a challenge. So, I think for all of those reasons, for me personally, it's one of the big reasons I haven't reached for that 2-drug regimen and have just gone straight to BIC-TAF-FTC.

Dr. Wood

Thanks, Aley. And those are great reminders that per the guidelines, dolutegravir-lamivudine is an option as a first regimen, but it's recommended to only prescribe it if the viral load is below 500,000. A person absolutely should be confirmed to not have hepatitis B, and it would not be a fully active regimen with hepatitis B. And, that is one regimen where it is recommended to have your genotype resistance results in hand, which is very different scenario, as was mentioned, than we usually want to do. We're often reaching for first ART before the genotype results return. So, Jehan, it is an acceptable option, but are you reaching for it as a first regimen?

Dr. Budak

Never. Not yet. And, presumably, at some point I will, but I'm not there yet. I think you've heard me talk about this before in clinic when we're sitting next to each other, and I think there's just a lot of things we don't know about a person when we first meet them. And for me, if somebody is going to be on a 2-drug regimen, I like to know that they're adherent and that they will be taking their meds. And so, for me, I've only used those 2-drug oral options for switch and not for start. Plus, I can't do a rapid start on someone if I don't have their genotype.

To Aley's point is about logistics. Again, not having started anybody on it, but whenever I'm doing 2-drug oral combinations, I've had issues with insurance coverage for the branded combination and I've had to separate the two. Yeah. It is what it is.

Dr. Wood

So, sounds like it is not either of your preferred options for an initial ART regimen, but maybe a consideration for switching later on once the viral load is suppressed.

alternate-art-regimens**[16:00] Alternate ART Regimens**

Dr Wood

So, Aley, if I can come back to you, we talked about the recommended regimens for most individuals with HIV. There is also a table of other initial regimens to consider for certain clinical scenarios. This includes things like regimens that are NNRTI (non-nucleoside reverse transcriptase inhibitor)-based, regimens with boosted darunavir, now dolutegravir-abacavir-lamivudine, as we talked about. I'm just wondering, are you ever reaching for one of those options for a first regimen, such as an NNRTI-based or boosted Darunavir-based option?

Dr. Kalapila

Again, I think I would probably reach for it if someone had been on injectable cab [cabotegravir], for instance, for PrEP and they seroconverted, then I think that would be an indication, right, to be on a protease inhibitor (PI)-anchored regimen. I think also in certain circumstances, if I'm trying to keep them on a once-a-day regimen and you have to give them, again, a rifamycin is probably the most frequent time that I have to deal with this situation because we, again, see a fair amount of disseminated MAC, and so dosing of dolutegravir gets a little bit complicated, the TAF issue gets complicated. So, I can see why there might be circumstances to avoid drug interactions, particularly where I might reach for one of these other oral options in an effort to simplify the regimen to at least keep it once a day and/or keep it as single-tablet regimen. And, of course, insurance, right? That's the other big thing too. But again, most of these times also, I usually would like to wait for resistance data to come back, certainly to use NNRTI-anchored regimens. A PI based-regimen, if I have to use it, again, because of the high barrier to resistance and its potency, that’s another one I would be happy to do a rapid start if I could not use an integrase inhibitor-anchored first-line.

Dr. Wood

Got it. Jehan, I'd like to hear from you if you are ever reaching for those options. And I wonder if you could also reiterate or give more detail into this scenario of if someone has ever received injectable cabotegravir in the past. So, let's consider that scenario too. Then, what are you reaching for and what do the guidelines recommend?

Dr. Budak

I'll touch on that first. So, Aley was mentioning too that if somebody came in on long-acting injectable cabotegravir for PrEP (or preexposure prophylaxis) and developed HIV, then we would want to use a darunavir-based regimen, and so probably TAF FTC, cobi [cobicistat]-darunavir as a single-tablet option. And, that is

also what the guidelines recommend is that if that happens, there is concern for INSTI [integrase strand transfer inhibitor] resistance and so thus you would not want to use an INSTI and would use a PI-based regimen while waiting for some more data (i.e., a genotype). And so, I have not personally been in that scenario where someone has come to me previously on injectable cabotegravir for PrEP, but that's what I would do consistent with the guidelines if I was in that scenario.

And then as far as other options, I do offer a doravirine-based regimen upfront for someone for whom weight gain is a concern. And, in which case, I would do a single-tablet regimen of TDF-3TC, and doravirine because I think that it is the most weight-neutral. I think many of us think that it's the weight-neutral. So, that is something that I would reach for. That's probably the fourth most common thing I start.

Dr. Wood

Aley, have you reached for doravirine in that situation before?

Dr. Kalapila

I have not yet, actually. The times I've reached for doravirine, it's because there's been a lot of issues related to resistance. So, these are patients who are like highly experienced and have now developed integrase inhibitor resistance and I can't give protease inhibitors for whatever reason, but I haven't yet considered giving doravirine.

Dr. Wood

Certainly, a controversial area in which we are waiting for more data. And I think this is great to hear some differences in opinion and practice. Sounds like we all reach for similar options for most individuals, for initial ART. Sounds like for all of us, bictegravir-TAF-FTC for its simplicity, potency, high barrier resistance, it tends to be our preferred option. But then, you've brought up a lot to consider in terms of insurance, in terms of the priorities for the individual, in terms of potential side effects, drug interactions. So, this is great.

m184v-mutation-impact**[20:20] M184V Mutation Impact**

Dr. Wood

Aley, let me just ask you. Let's say you start your preferred option, bictegravir-TAF-FTC, you're starting before the genotype resistance result returns, and then you get the result and there's an M184V mutation. Do you make any changes?

Dr. Kalapila

Yeah, this happens very frequently for me in clinical practice. And so, I typically don't. I think there was a time when we knew a little bit less about the M184V mutation, and probably early on in my clinical practice, like 10 years ago, I used to intensify the regimen, oftentimes adding on a protease inhibitor. But, and now we know that we have a lot of great data that show that M184V, even though it causes this phenotypic resistance to 3TC, FTC, it doesn't actually translate clinically. And also we know that it influences sort of the in vitro susceptibility and makes the virus kind of hypersusceptible to drugs like tenofovir. So, I think in those cases we now know that these patients do very well with…as long as your anchor drug is potent and bictegravir is certainly a very potent integrase inhibitor. And so, I don't feel the need to intensify the regimen.

Dr. Wood

Jehan, I see you nodding your head in agreement.

Dr. Budak

Yes. I'm vigorously nodding my head. Yeah, I totally agree with Aley. I think in a pre-2019 era, there was concern with use of just two nukes and an INSTI with regards to an M184V. But then once we got the DAWNING subanalysis that was shared at CROI in 2019, and I just remember that because it was my first CROI, and then subsequent to that, we've had more data and then including another big RCT [randomized controlled trial] with regards, especially like the NADIA trial, which is where we know that we can use two nukes and an INSTI with an M184V.

What I've taken away from those two trials is that you can still fail and develop INSTI resistance and that it's harder to develop PI resistance. But that being said, I trust them. And so now I think if I were in that scenario and I had somebody viremic coming in, I started them on this, I subsequently get an M184V. I would just say, come back in, as you would, in a month or so, let me check your viral load. And then I don't think I would make any changes unless that sort of repeat viral load was still elevated and the sort of viral decay wasn't what I expected.

Dr. Wood

Great. Sounds like you are largely in agreement on that topic. And I will just add, I do the same.

closing**[22:41] Closing**

This has been such an excellent discussion. There's more we could talk about, but I really want to thank you both for sharing your time and expertise and for participating in this episode on starting ART. And I look forward to future conversations with you both.

Dr. Budak

Thanks, Brian. Bye, Aley.

Dr. Kalapila

Bye.

credits**[23:00] Credits**

Transcripts and references for this podcast can be found on our website, the National HIV Curriculum at www.hiv.uw.edu. The production of this National HIV Curriculum podcast was supported by Grant U10HA32104 from the Health Resources and Services Administration of the U.S. Department of Health and Human Services. Its contents are solely the responsibility of the University of Washington IDEA program and do not necessarily represent the official views of HRSA or HHS.