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Reportback from the 2017 Conference on Retroviruses and Opportunistic Infections

In this issue of *PI Perspective*, Project Inform reports on data that was presented at this year's CROI, Seattle, WA, from February 13–16, 2017.

cure Cure-based Research

The best HIV cure will be built with us, not just for us

by David Evans, Director of Research Advocacy

Among the world's top scientific conferences on HIV, the Conference on Retroviruses and Opportunistic Infections (CROI) stands among the most prestigious. Only a handful of the top submissions of new scientific data are deemed worthy of stage time. Submissions deemed less worthy are relegated to the poster halls with endless rows of dense text, charts and graphs.

It was in such an inauspicious place that Martin Delaney, Project Inform's founding director, stumbled upon a tucked away poster claiming that an HIV-positive stem cell transplant recipient had gone for months without antiretroviral therapy (ART) with no return of the virus. Recognizing the possibility of the world's first documented HIV cure, Marty hastily contacted the scientist behind the study and in tandem with others set off what is now a furious race to find a cure that will work for many — or something that is a significant step on the way.

Though Marty died in 2009, a little more than a year later, his lifetime of brilliant research activism was recognized not only by the National Institutes of Health — by dedicating its flagship HIV cure research effort in his name — and by CROI — with the placement of a yearly memorial lecture for young scientists.

In February, I had the truly humbling honor to present on the role of the community in HIV cure research at the session named after Marty, who was my friend and greatest mentor. The session, focused on Good Participatory Practices (GPP), was organized by community engagement guru for CROI, Mark Hubbard, and presented jointly along with Stacey Hannah from AVAC, and Deborah Barron

from RFI in Johannesburg, South Africa. No doubt, some of those new investigators probably had the following question when noting our session as part of their training: "What is GPP and why should I worry about it?"

It's not necessarily an unreasonable question. But if HIV cure research can take a cue from prevention research, it grows more clear with each passing day that the community must not merely be involved in helping recruit for trials or review informed consent documents, it must also be involved at the very beginning of the discovery process, to ensure that experimental interventions are worth pursuing, and help to anticipate and plan for how to proceed quickly when things go right, and how to proactively prepare for what to do when things go wrong from a safety, ethical and social stand point.

I use the term "HIV cure research" somewhat reluctantly and have for some time. Social science research — both my own and others — has indicated that for most people living with HIV a "cure" means that the virus is eliminated entirely from their bodies, that an HIV antibody test will be negative, and that they cannot transmit the virus to a sex partner or baby (more on those in a minute). What's more, a cure must also render a person invulnerable to becoming infected with HIV again. I never say never, but it will be a formidable scientific challenge to achieve all four and many scientists now conclude that a much humbler goal for now is to achieve a suppression of the virus to very low levels for extended periods of time without ART.

The case I tried to make at the session, however, is that if the community is not deeply involved now in shaping cure research and how it is implemented, we not only carry the risk of developing a product that does not work for many who need it most or be greatly delayed in doing so, but that we may also harm people unintentionally in the process.

As for the first point, pioneers such as Rowena Johnston with amfAR and Eileen Scully from Johns Hopkins University have demonstrated that cisgender women (people who were assigned female sex at birth and continue to identify as female) might maintain the hidden reservoir of HIV differently than cisgender men due not only to the presence of estrogen and estrogen-like hormones, but also due to the genetic influence of how many estrogen receptors are present on immune cells. We know this, because of research carried out by John Karns — first reported in 2015 — and new research by Scully presented this year at CROI. This means that not only could it be more difficult to poke and wake up the hidden reservoir of virus in cisgender women, but also that interventions designed to do so might not work as well in them, at least during certain periods of the menstrual cycle.

If we don't think carefully and push for HIV cure-related research in women living with HIV now, we might not only fail to develop a product that will work in more than half of the global population of people living with HIV, we might mistakenly discard an effective product due to testing it at the wrong moment in a woman's cycle of hormonal production.

Yet as bad is this sounds, there are further implications that go beyond sex. A majority of people living with HIV globally don't carry strains of the virus that are present in the United States, Western Europe, Canada and other high-income nations where the vast majority of cure research has taken place. Neither the people carrying those other strains, nor their cells and tissue, have received the same degree of scientific scrutiny.

The bottom line, if we fail to equip HIV-positive women and people living with HIV in sub-Saharan Africa and other regions with the tools to participate in shaping and setting priorities and directions of HIV cure research, we could either delay the development of a promising cure strategy or end up with an intervention that is much less useful for a large number of people living with HIV on the planet.

Empowering people living with or affected by HIV with the information, skills and resources to participate in the research process ensures that GPP, a roadmap for comprehensive multi-stakeholder participation, can be followed. I look at GPP as the solution to the ancient fable of the blind men who can only feel different parts of an elephant. To one of the blind men who feels the elephant's leg he is feeling a tree, to another, feeling only the elephant's trunk, it is a thick rope. No one, whether medical scientists, social scientists or members of the community, has the capacity on their own to "see" the whole elephant of a path to a promising cure. GPP helps ensure that we work cooperatively to put the individual pieces together as a whole.

But GPP is also a bit like disaster planning. Even the most rigorous planning can't prevent something bad from happening, but it can minimize the chance of negative outcomes and ensure that if the unexpected occurs, we are ready to limit the damage quickly and effectively. That's what GPP grew out of, a failure to effectively and proactively work with all critical stakeholders in the midst of the controversies and disasters that were spawned when three prevention trials ground to a halt in the mid-2000s.

With HIV cure research, three looming threats have already emerged and we don't yet have answers to them. All are related to what might occur when we interrupt ART in people who participate in studies. Most scientists agree that for now the only way to prove that a cure (or remission) strategy has worked is to stop HIV treatment for some time. This is not without consequences, however. Here are just a few, some of which have already occurred.

Imagine that we take extensive care to ensure that study participants understand that whatever we are testing is highly unlikely to cure them. Quite the opposite, we labor to convince them that it probably won't — at least in the long-term. But even if we are successful at convincing them at the outset of a study, how will they feel if they stop ART and go weeks or months without HIV returning to measurable levels? Will they grow more and more sure that they are cured and how will they respond if the virus does come roaring back?

We're getting so good at identifying people at risk for HIV within the first days after becoming infected, that more and more are being put on ART the same day they are tested. In such people, though we can measure bits of the virus there isn't enough of it to provoke a strong antibody. Thus, they will "test negative" in common parlance. A treatment interruption, however, could and has resulted in the virus levels climbing high enough to provoke the body to generate HIV antibodies. These people now test positive on a standard HIV test, and some of them live in countries where an HIV-positive test result can mean the loss of a job offer or the termination of employment. Testing positive can have even worse consequences, of course.

Finally, multiple studies now confirm that viral suppression from effective ART makes HIV transmission highly unlikely. However, if a person stops ART during a study, we certainly test for a return of the virus often enough to preserve their own health, but what about ART's ability to prevent transmission? If a person has a viral spike, will it be possible to transmit HIV to their partner? If so, how frequently should viral load testing occur? If we test very frequently in a study, how frequently will we need to test when an intervention goes into wider use, and how would we ever do so in countries that struggle to even provide viral load tests at all?

A number of activists such as myself — the vast majority of us being lay scientists — are working with researchers on the technical details of the biomedical research, and we are mentoring and building a new cohort of others who can do the same. However, if these efforts are unlinked to thoughtful planning for the psychological and social impact of a cure intervention going into wide study or being approved, the new intervention might never accomplish what people with HIV most hope for.

At last year's International AIDS Conference, a group of us created a booth in the Global Village, which is open not only to conference goers, but to the local community. Inspired by the thinking of the brilliant Ugandan activist, Moses "Supercharger" Nsuguba, we built a huge cardboard tree trunk and branches, and provided paper leaves and tape to visitors who were asked to write on them the answer to the following question:

"If a cure were found tomorrow, and was available to all free of charge, what would it mean to you or to the people with HIV you love or care for?"

There were so many leaves on the tree by the end of the conference that they extended nearly into the adjacent booths. The answers varied widely, but the most predominant answer by far was related to the concept of freedom — freedom from fear, anxiety, stigma, oppression and isolation.

What this tells me is that we should be aiming for not only a biological outcome or delivery of an HIV cure intervention, but the resulting freedom from all of the things that still afflict our booth's visitors and those they love. Without early and consistent partnership with the community in our efforts to incrementally develop a cure for HIV, one guided by GPP principles, we may never achieve what people with HIV most hope a cure will offer them.

prep Pre-Exposure Prophylaxis

What's Up with PrEP and STIs?

by David Evans, Director of Research Advocacy

Critics have been warning since the concept of oral PrEP was in its infancy that it would lead to major increases in condomless sex among users and a corresponding dramatic spike in sexually transmitted infections (STIs). So far, the data have been inconclusive.

A journal article last year by one of the U.S.'s largest PrEP clinics at Kaiser Permanente of Northern California did find significant increases in STIs after initiation of PrEP in nearly 1,000 recipients. Formal demonstration projects, efficacy studies and even some cohorts have either reported no increases, however, or mixed results. A presentation at the Conference on Retroviruses and Opportunistic Infections (CROI) 2017 in Seattle, Washington, found similarly mixed results.

To investigate this issue, the STI and HIV program in King County, which includes Seattle, looked at data from gay men enrolling in the county PrEP program between September 2014 and June 2016. Condom use was evaluated at PrEP initiation, and then at 3, 6 and 9 months later. STI trends were measured by looking at diagnoses one year before starting PrEP, at PrEP start, and then during the time a person was on PrEP.

Though 218 people started PrEP, complete 9-month data were available for only 108. The cohort was relatively young — on average 30 years old — and while just over half were white, 22% were Hispanic, 10% were Asian or Pacific Islander, 9% were black and 2% were Native American.

The percentage of those saying that they never used condoms for receptive anal sex nearly doubled after starting PrEP but remained below 10% at all time points. Thus, reports of condomless receptive anal sex did increase, which has been reported more consistently. With STI rates, however, it was a more mixed and confusing picture.

Part of the confusion is that number of STI diagnoses increased substantially in the three months *before* starting PrEP — on average the rates almost tripled for all diseases, including chlamydia, gonorrhea and syphilis. This makes the case quite strongly that those for whom PrEP will be most appropriate are those who seek it out or who are offered it.

What is less clear, however, is how to interpret STI diagnosis after starting PrEP. While chlamydia (in general) and rectal chlamydia did increase from 16% to 22% and 15% to 19% respectively over the study period, diagnosis of gonorrhea and rectal gonorrhea stayed the same and early and early-latent syphilis decreased by nearly half.

While these data will certainly not convince PrEP critics that the intervention is being promoted dangerously, they do offer a more sober and less sensational view than an analysis of STI data from PrEP studies published as a commentary in the journal *AIDS* not long before CROI. The authors there claimed that STI rates were more than 10x higher in PrEP users than non- users across several studies or cohort reports, a finding that garnered substantial headlines, social media traffic and press releases from a notoriously anti-PrEP HIV organization in the US.

A rebuttal published in *AIDS* on March 13, 2017, pointed out serious flaws in the earlier analysis and came to the conclusion that while STI rates were higher (about three times higher) in PrEP-users vs. non-users in the same set of studies, this much smaller difference means that the influence of PrEP on STIs is nearly impossible to separate from other confounding factors, including escalating STI rates going back more than a decade in MSM, more frequent STI testing in those on PrEP than those not, and the reality that those most likely to become infected with an STI are also those most likely to seek out PrEP in the first place.

SOURCES:

MA Montano, et al. *Changes in sexual behaviour and STI diagnoses among MSM using PrEP in Seattle, WA*. 2017 CROI, Seattle. Abstract 979.

Harawa NT, et al. *Serious concerns regarding a meta-analysis of preexposure prophylaxis use and STI acquisition*. *AIDS*. 2017 Mar 13;31(5):739-740.

Dapivirine ring for PrEP does not lower effectiveness of hormonal contraception

by Alan McCord, Director of Education

In previous study, certain HIV medications were found to lower the effectiveness of some hormonal contraceptives, including the NNRTI efavirenz (Sustiva). This presented concerns about the experimental NNRTI dapivirine that was already being used as a vaginal ring for PrEP in clinical study. A presentation at the 2017 Con-

ference on Retroviruses and Opportunistic Infections showed that this is not the case with the dapivirine ring.

The Phase 3 ASPIRE study reported in 2016 that the dapivirine ring reduced HIV infections 27% in 2,629 women, half of whom used the dapivirine ring and half of whom used a placebo. However, no data were available at that point about whether the drug also lowered the effectiveness of injected, implant or oral contraceptives and thereby possibly increasing the number of pregnancies.

In ASPIRE, all women had to use a reliable hormonal form of contraception (injected DMPA or NET-EN, implant or oral pill) in addition to the ring, and regular pregnancy tests were done monthly. If a participant become pregnant, the ring was withdrawn for the duration of pregnancy and breastfeeding.

This year's follow-up analysis showed the incidence of pregnancy among the women. There were 117 pregnancies among 114 women (some women had more than one pregnancy during the study). The rate of pregnancy was 0.49 for injected DMPA, 0.58 for injected NET-EN, 0.45 for implants and 30.21 for pills, none of which differed significantly whether a woman received the active dapvirine or placebo riing.

Although the pregnancy rate for oral pills was high and may point to poor adherence, none of these rates differed between the two groups. This led the researchers to conclude that dapivirine given through a vaginal ring did not affect the effectiveness of hormonal contraceptives.

SOURCE:

J Balkus, et al. *Dapivirine Ring Use Does Not Diminish the Effectiveness of Hormonal Contraception*. 2017 CROI, Seattle. Abstract 88.

hiv HIV Care News

Two-drug maintenance regimen controls HIV as well as standard treatment

by Alan McCord, Director of Education

In a late-breaker presentation at the 2017 Conference on Retroviruses and Opportunistic Infections (CROI) in Seattle, data from the SWORD 1 & 2 studies showed that a two-drug regimen of dolutegravir (Tivicay, DTG) + rilpivirine (Edurant, RPV) suppressed HIV as well as various regimens of three or more drugs in people on long-term treatment. This is somewhat remarkable given that the new regimen does not appear to need a booster or an NRTI backbone or protease inhibitor to fully suppress HIV.

Both studies enrolled a total of 1,024 people who had been on their first or second regimen with an undetectable viral load at least a year but with no history of drug resistance or failure. The average time on treatment was four years and average CD4 count at study entry was about 625. Average age was 43, more than 3 out of 4 were men, and 4 out of 5 were white. People with hepatitis B could not enroll.

The studies equally assigned people to either stay on their suppressive 3- or 4-drug regimens or switch to the DTG (integrase inhibitor) + RPV (NNRTI) regimen at study entry. After 52 weeks, the first group will also switch to the DTG + RPV regimen.

The presentation showed that, after the first 48 weeks, 95% of those in both groups maintained undetectable viral loads below 50 copies. There were very slight numerical differences in SWORD 1 (96% for both) vs. SWORD 2 (94% for both), but were statistically not significant.

One person in the DTG + RPV group who was eventually not taking their regimen as prescribed developed detectable viral load and an NNRTI mutation before getting back under 50 copies by re-starting DTG + RPV. No integrase inhibitor mutations were seen in either group.

Serious side effects were uncommon and equal between the groups. A higher rate of mild to moderate side effects were reported in the DTG + RPV group (17%) compared to 2% in the other group. It will be interesting to contrast this difference again after the next switch at 52 weeks to the initial switch.

As for changes in blood fats, very similar rates were seen across both groups for total cholesterol, HDL and LDL cholesterol, total HDL ratio and triglycerides. However, changes in markers of bone health were slightly but significantly better in the DTG + RPV group.

This is very promising news to see a two-drug maintenance regimen suppress HIV at rates similar to 3- and 4-drug regimens. A combination pill will be formulated

for another study, which will include more treatment experienced individuals. Researchers will continue to follow these SWORD 1 & 2 study participants through 148 weeks.

SOURCE:

JM Libre, et al. *Phase III SWORD 1&2: Switch to DTG+RPV maintains virologic suppression through 48 wks*. 2017 CROI, Seattle. Abstract 44LB.

New two-drug maintenance regimen continues to suppress HIV over 144 weeks

by Alan McCord, Director of Education

At the 2017 Conference on Retroviruses and Opportunistic Infections (CROI), results from the LATTE study showed that the 2-drug regimen of the integrase inhibitor cabotegravir (CAB) + the NNRTI rilpirivine (RPV, Edurant) suppressed HIV levels as well as a 3-drug efavirenz (Sustiva) regimen through 144 weeks. The first 96 weeks were partially blinded to establish a proper CAB dose, with the additional weeks of data coming from open-label CAB at the selected dose of 30mg per day. Both CAB and RPV are also candidates for long-acting injected drugs, and the results of LATTE are helping to inform the development of the long-acting products, which will be dosed either every one or two months.

As people with HIV live longer, there's a desire to reduce pill burden and to find easier-to-take, effective regimens. Maintenance regimens have a place in HIV treatment once stable HIV suppression has been established. In another presentation at CROI, the oral combination of dolutegravir (Tivicay) + rilpivirine is also being explored as a maintenance regimen.

LATTE is a Phase II study where roughly 60 people who were new to treatment were randomized to receive either efavirenz + a backbone of 2 NRTIs or one of three different doses of CAB (10mg, 30mg, or 60mg) + 2 NRTIs. At 24 weeks, those on CAB with viral loads <50 copies then switched their 2 NRTIs for RPV, thereby reducing their dosing to two drugs. At week 96, the efavirenz group stopped the study while the three CAB groups were allowed to go onto an open-label phase with the 30mg CAB dose + RPV.

Of the 243 people who were enrolled at the beginning, 96% were male, 38% were non-white and 14% had viral loads >100,000. A total of 138 continued into the open-label phase of weeks 96 to 144.

Among those who started the maintenance regimen of CAB + RPV at week 24, 76% remained suppressed <50 copies HIV RNA at week 144 This analysis included all who continued in the open-label 30mg part of the study, no matter the dose they originally took. Roughly 8% had not reached an undetectable level. Viral failures and drug resistance did occur, with mutations to CAB and RPV in some, but most were found in those on the 10mg maintenance dose between weeks 24 and 96.

Serious side effects were reported in 9% of people on CAB + RPV, affecting a third of them to stop the study. Mild to serious lab changes occurred in 17%, with serious changes in creatine kinase (8%), ALT (1%), lipase (4%) and total neutrophils (3%).

CAB + RPV as maintenance therapy will move into further study with an injected maintenance regimen of both drugs.

SOURCE:

DA Margolis, et al. *Long-Term Safety and Efficacy of CAB and RPV as 2-Drug Oral Maintenance Therapy*. 2017 CROI, Seattle. Abstract 442.

New integrase inhibitor bictegravir s uppresses HIV as well as dolutegravir in first line therapy

by Alan McCord, Director of Education

At the 2017 Conference on Retroviruses and Opportunistic Infections (CROI) in Seattle, 48-week results from a somewhat small Phase 2 study in people new to treatment showed that the Gilead Science's experimental integrase inhibitor bictegravir suppressed HIV levels as well as ViiV's integrase inhibitor dolutegravir (Tivicay). Unlike Gilead's current integrase inhibitor, elvitegravir, bictegravir does not need to be boosted with cobicistat.

The study enrolled 98 previously untreated people, with twice as many taking bictegravir as dolutegravir (65 vs. 33). Everyone also took emtricitabine + tenofovir (Truvada) with or without food. Average viral load was around 30,000, with 15% and 21% of the bictegravir and dolutegravir starting with viral loads above 100,000 respectively. The average CD4 count was roughly 450 for both groups. Nearly all participants were male, and roughly 40% were non-white in both arms. No one with hepatitis B or C was enrolled.

At week 24, 97% of those on bictegravir had suppressed HIV below 50 copies compared to 94% of those on dolutegravir. By week 48, 97% and 91% were suppressed. Though the percentage of participants with full suppres-

sion on bictegravir was numerically higher, the difference was not statistically significant. As for changes in CD4 counts, those who took bictegravir saw an average increase of 258 cells compared to 192 for those on dolutegravir — this was also not statistically significant, despite the large numerical difference.

No integrase inhibitor or NRTI mutations developed in either group.

Both regimens were safe and well tolerated and no serious side effects were seen. Diarrhea and nausea were the most reported mild side effects across both groups (8–12%). Lab abnormalities were similar as well between the groups and occurred in fewer than 10% of the participants. Additionally, decreasing levels in eGFR (a measure of liver health) were similar with -7.0 mL/min in those on bictegravir vs. -11.3 mL/min on dolutegravir.

Larger groups of people will need to be compared in further studies to draw stronger conclusions about meaningful differences in viral suppression, CD4 increases or adverse events. Bictegravir + emtricitabine + tenofovir is being studied as a single tablet regimen in two Phase III studies and as separate pills in two other studies.

SOURCE:

P Sax, et al. *Randomized Trial of Bictegravir or Dolutegravir with FTC/TAF for initial HIV therapy*. 2017 CROI, Seattle. Abstract 41.

Doravirine controls HIV as well as boosted darunavir regimen over 48 weeks

by Alan McCord, Director of Education

In a late-breaker presentation at the 2017 Conference on Retroviruses and Opportunistic Infections, a regimen with the experimental NNRTI doravirine controlled HIV as well as a boosted darunavir (Prezista) regimen with ritonavir in people who were new to treatment. A low rate of resistance occurred in both group but doravirine had better lipid outcomes.

Doravirine may be a promising new option for first-time treatment given its potential in earlier study to suppress HIV with common NNRTI resistance, its low neuro-cognitive side effects, its lack of food restrictions, and its low potential for drug interactions. The currently approved NNRTIs each have qualities that generally restrict their use to later regimens for individuals.

This 48-week Phase 3 study divided 769 people into two regimen groups taken once a day: doravirine + darunavir placebo + 2 NRTIs, or boosted darunavir + doravirine placebo + 2 NRTIs. The 2 NRTIs were either emtricitabine/tenofovir (Truvada, 87%) or abacavir/lamivudine (Epzicom, 13%). All had detectable viral loads above 1,000 and no resistance was present.

Average age was 35 years, 84% were male, 1 out of 5 was African American, and 1 in 10 had an AIDS diagnosis. Average CD4 count was about 425 while 14% were <200 cells. Average viral load was about 25,000, with about 20% having a viral load >100,000 and 4% >500,000.

After 48 weeks, 84% on doravirine and 80% on darunavir were undetectable <50 copies. As for CD4 counts, those who took doravirine had an average change of +193 compared to those on darunavir of +186 cells. None of these differences were statistically significant.

For those who started with viral loads >500,000 or with CD4 counts <50 cells, doravirine appeared to benefit these individuals more than those on darunavir, although the total number of participants with these specific characteristics are too low to draw strong conclusions.

A total of 43 people either did not reach an undetectable level or had gotten to <50 but returned to detectable viral load: 19 on doravirine and 24 on darunavir. However, no NRTI, NNRTI or protease inhibitor resistance mutations were found in these individuals.

Both regimens were safe and well tolerated. Few serious side effects were reported (5-6%) and 2% stopped the study due to side effects. The most common mild to moderate side effects were diarrhea (14% doravirine and 22% darunavir), nausea (11% and 12%), colds (8% and 10%) and headaches (14% and 11%). Rash occurred in about 7% of both groups and neuro-cognitive side effects occurred in about 12%.

Serious lab changes such as cholesterol, glucose, ALT and AST were very low in both groups (1-3%). However, doravirine had less effect (statistically significant) on these types of lipids: total cholesterol, LDL cholesterol and triglycerides.

Doravirine is being developed as a single pill and as a single tablet regimen with tenofovir (Viread) and lamivudine (Epivir).

SOURCE:

JM Molina, et al. *Doravirine is Non-Inferior to Darunavir+ Ritonavir in Phase 3 Treatment-Naive Trial at Week 48*. 2017 CROI, Seattle. Abstract 45LB.

Novel capsid inhibitor may mean a new class of HIV medication is on its way

by Alan McCord, Director of Education

Results from early lab study of a new target for an HIV medication were described at the 2017 Conference on Retroviruses and Opportunistic Infections in Seattle. The potential compounds, called capsid inhibitors, interrupt different steps in the HIV life cycle and appear to be effective against all HIV subtypes and resistance mutations of current HIV medications.

An intact capsid is the structure that encloses HIV's genes and helps the virus to mature. If the capsid is inhibited or incomplete, the virus cannot mature or infect immune cells.

One compound, called GS-CA1, shows qualities that may allow it to be given as a long-acting injected medication (a single injection in rats yielded more than 10 weeks of presence in blood). As this compound moves further into animal and perhaps human studies, it will become apparent if these promising lab qualities translate into reasonable safety, effectiveness and side effects.

SOURCE:

WC Tse, et al. *Discovery of Novel Potent HIV Capsid Inhibitors with Long-Acting Potential*. 2017 CROI, Seattle. Abstract 38.

Ibalizumab is effective at reducing HIV viral load in people with few treatment options

by Alan McCord, Director of Education

In a late-breaker presentation at the 2017 Conference on Retroviruses and Opportunistic Infections (CROI), a new monoclonal antibody drug called ibalizumab reduced viral loads in individuals with multi-drug resistant HIV. The results showed that adding the drug to a failing regimen may help treatment-experienced people who have few options to control their virus.

Ibalizumab is a humanized antibody that attaches to the CD4 receptor to block the HIV life cycle. It is given by IV every two weeks. In earlier study, ibalizumab was effective against a wide range of HIV strains with no evidence of cross-resistance to current HIV drugs.

To be eligible, everyone had to have had a strain of HIV that was still sensitive to at least one drug for their optimized background regimen (OBR), of which nearly half (43%) took the experimental entry inhibitor fostemsavir. Those who were excluded were people with an active AIDS illness, previous use of ibalizumab, recent use of immune system therapy such as steroids and any serious lab abnormality.

The 24-week TMB-301 study enrolled 40 people on stable treatment for at least 8 weeks but with an HIV strain that was resistant to three (53%) or four (35%) classes or all HIV meds (16%). Average time living with HIV was 21 years. Average age was 51, 85% were male and nearly half were non-white. Average CD4 count was 73, nearly half had CD4s <50 and average viral load was around 35,000 with 18% above 100,000.

At study entry, participants stayed on their current regimen. At day 7, ibalizumab IV was given. At day 14, the OBR was added and then ibalizumab IV was given again at day 21 and every other week through 24 weeks.

After the first 7 days of the first ibalizumab dose, 83% saw their viral loads reduced at least by half. By week 24, the average decrease in viral load was 55% for those with a 1 log reduction and 48% for those with a 2 log reduction. In addition, half the participants saw their viral loads drop below 200 copies while 43% dropped below 50.

Small average increases of 15 CD4 cells occurred for those who started with <50 cells. For those with higher CD4s, the average increase was 75–81 cells. There was no evidence that antibodies to ibalizumab developed in any participant, which is possible with a monoclonal antibody.

Nine stopped the study (3 unrelated deaths, 3 withdrawals and 2 lost to follow-up). Most side effects were mild to moderate, and nine patients reported serious side effects.

These are promising results given the growing number of people who face decreasing treatment options due to resistance to many classes of drugs. The expanded access TMB-311 study is now enrolling additional people. A new intra-muscular injection is also being studied.

SOURCE:

S Lewis, et al. *Long-Acting Ibalizumab in Patients with Multi-Drug resistant HIV-1: A 24-Week Study*. 2017 CROI, Seattle. Abstract 449LB.

Substantial statin treatment gap exists for people living with HIV

by Alan McCord, Director of Education

Higher rates of cardiovascular disease (CVD) are well documented in people with HIV infection especially as they age, and using statin treatments with HIV regimens is generally safe and effective. However, in a presentation from a 12-year analysis of the large NA-ACCORD cohort at the 2017 Conference on Retroviruses and Opportunistic Infections, more than half of those who could use a statin to treat their CVD had not received a prescription for it.

Researchers looked at the medical records of more 86,000 people from Jan 2001 to Dec 2013. They used the ATP III Guidelines to assess whether a person was eligible to receive a statin prescription based upon various risk factors such as low and high density cholesterol, triglycerides, Framingham score, diabetes, CD4 counts, viral loads, AIDS diagnosis, age and smoking history. They included those individuals with no prescription at or within 6 months of the indication for a statin prescription.

From their analysis, a large treatment gap had emerged from all of those who were eligible for getting a prescription: between those who had received one (12%) and those who hadn't (88%). The good news is that the rate of statin prescriptions had increased 300% (6% to 18%) over time while the statin treatment gap had declined (73% to 53%). However, still more than 50% of those who could have been prescribed a statin had not received one throughout the 12 years of study.

Those who were less likely to get a statin despite possible benefits from using one were younger people (<40 years), African Americans, current smokers, those with low CD4 counts (<200) and those on a protease inhibitor regimen. Factors that increased the likelihood that a prescription was written included older age (>50 years), being white, MSM, without hepatitis C, higher CD4 counts and undetectable viral load.

These results point to the need for more attention during medical visits to assessing and using documented risk factors for guiding the prescription of statins in those who could benefit from using them.

SOURCE:

KN Althoff, et al. *The Large Gap Between Statin Eligibility and Prescription Among HIV+ in North America*. 2017 CROI, Seattle. Abstract 619.