Wednesday 4th March 2015

Contents

Raised risk of kidney disease with some ARVs

Photos from CROI 2015, by Robb Cohen www.RobbsPhotos.com. Thanks to the International Antiviral Society-USA

Three antiretroviral drugs are associated with a slowly increasing rate of kidney disease over time, according to an analysis from the large D:A:D observational cohort. They are tenofovir, boosted atazanavir and boosted lopinavir.

Researchers examined the risk of developing chronic kidney disease – eGFR below 60 ml per minute – in individuals whose kidney function was normal when they entered the cohort. Estimated glomerular filtration rate (eGFR) is an indirect measure of the amount of blood that the kidneys filter per minute and is a test used to assess kidney function. Data were included on 23,560 people during an eight-year period.

Overall, the risk was low – fewer than 1% of participants (210 people) developed chronic kidney disease.

As expected, several factors were associated with kidney disease – older age, high blood pressure, hepatitis C, diabetes, cardiovascular disease, having previously had a low CD4 count and having injected drugs.

But there were also associations with the use of some antiretrovirals, with an increasing risk the longer a person was taking the drug. The incidence was 2.2% after six years taking tenofovir; 4% after six years of boosted atazanavir; and 4% after six years of boosted lopinavir.

After adjusting for other risk factors for kidney disease, each year on tenofovir was associated with a 12% increase in the relative risk, each year on boosted atazanavir with a 27% increase and each year on boosted lopinavir with a 16% increase.

In contrast, abacavir wasn't associated with an increased risk, nor was taking other protease inhibitors. But there weren't enough data to examine any other drug individually.

Although chronic kidney disease remains uncommon and more influenced by 'traditional' risk factors than antiretrovirals, doctors are likely to take these data into consideration when choosing antiretrovirals, especially for people who have other risk factors for kidney problems.

Related links

Read this news story in full on aidsmap.com

View a webcast of this presentation

Financial incentives did not help the treatment cascade in American cities

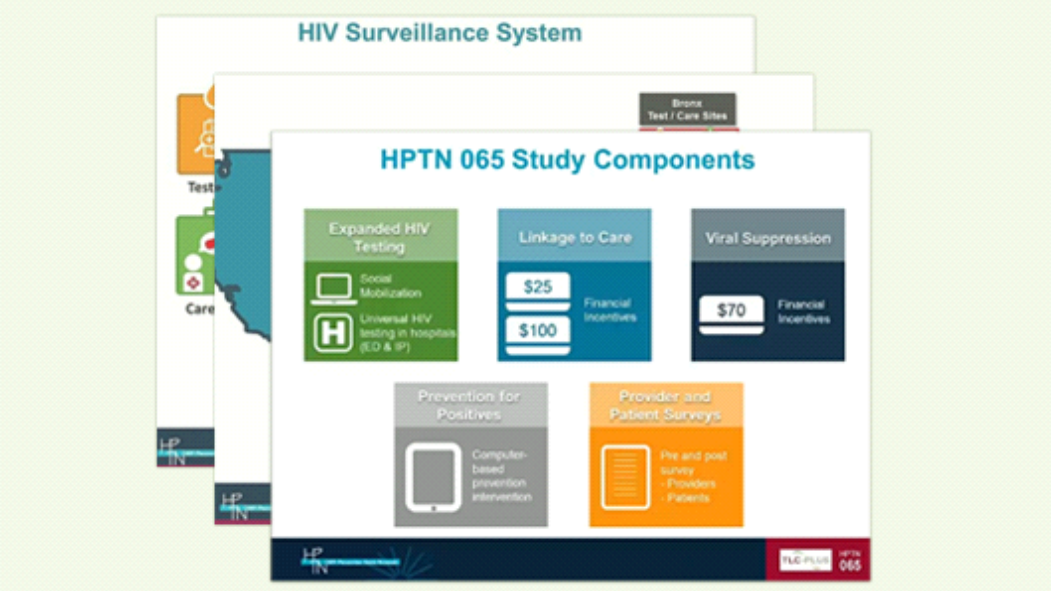


Image from the presentation by Wafaa el-Sadr, at CROI 2015.

An American study which offered individual patients financial incentives to present themselves for HIV care after testing, to stay in care, and to maintain an undetectable viral load did not succeed in its main aims and with most patients. But the intervention did improve results at some smaller and under-performing services, the conference heard.

Financial incentives have previously been shown to be effective in engaging drug users with healthcare. And financial incentives have improved HIV outcomes in some African studies.

The study was conducted in two urban areas beset by poverty and social problems, Washington DC and the Bronx in New York City. Several dozen HIV testing sites and HIV care providers were randomised to either continue with their usual standard of care, or to offer financial incentives. Individuals who had just been diagnosed with HIV would receive US$25 if they presented for care within three months, with an additional $100 if they completed a care plan with their doctor. They would further receive $70 every three months if they attended and were virally suppressed.

However, the financial incentives made no statistically significant difference to the proportion of people presenting for care within three months, nor to the proportion who were virally suppressed. There was a small (8%) but statistically significant increase in the proportion of patients who attended at least four out of five clinic visits.

The greatest improvements were seen in services that previously had especially poor performance – these tended to be small and under-resourced services. The researchers believe that financial incentives may still have a potential role in improving the treatment cascade in specific locations and populations.

Related links

Read this news story in full on aidsmap.com

View a webcast of this presentation

Cancer, lung cancer and smoking

Panel including Elizabeth Yanik and Matthias Egger, at CROI 2015. Photo credit: Robb Cohen www.RobbsPhotos.com.

The incidence of cancers is very high in Americans over the age of 65 who are living with HIV, despite the widespread use of antiretroviral therapy, according to data presented at CROI. The risk of cancer may be linked to both HIV and ageing.

Researchers collected data from 5% of those using Medicare (the national health insurance programme for people aged 65 and older in the US) between 2002 and 2009, with linked data

from a cancer registry. There were data on over 450,000 people, including a few hundred who had been diagnosed with HIV.

Overall, within five years 10.2% of the older adults living with HIV were diagnosed with a cancer. In absolute terms, the largest numbers of cases were of prostate cancer and lung cancer. But rates of prostate cancer were no higher in men living with HIV than in other men.

But the rates of some cancers were significantly higher in people with HIV than other people. This applied both to AIDS-defining cancers (for example, non-Hodgkin's lymphoma, hazard ratio 3.0 and Kaposi's sarcoma, hazard ratio 79.2) and other cancers already reported to be more common in younger people living with HIV (for example anal cancer, hazard ratio 32.4 and lung cancer, hazard ratio 1.5).

A second study analysed cancer rates in over 39,000 Americans living with HIV, excluding those cancers which are AIDS-defining. Almost 600 participants in the study were diagnosed with a non-AIDS-defining cancer during a ten-year period, with lung cancer being the most common. The researchers wanted to calculate how much non-AIDS cancer can be attributed to smoking rather than other HIV-related risk factors (the population attributable fraction).

They found that 37% of cancers would be avoided if people with HIV had the same rates of smoking as the general population. Smoking was, by far, the most important modifiable risk factor – more than avoiding immune suppression below 200 CD4 cells/mm^3, detectable viral load or hepatitis infection.

Patrick Mercie presenting at CROI 2015. Photo by Liz Highleyman, hivandhepatitis.com

While the research underlines the importance of programmes which help people living with HIV quit smoking, the conference heard results from a randomised trial of the smoking cessation tablets varenicline (*Champix/Chantix*). Smokers living with HIV in France either received varenicline or placebo for twelve weeks, in addition to smoking-cessation counselling.

The drug helped significantly more people to stop smoking, but after 48 weeks only 17.6% were not smoking, compared to 7.2% of those receiving the placebo. These rates are comparable to those previously seen for HIV-negative people using varenicline, bupropion (*Zyban*, *Wellbutrin*), nicotine replacement products such as patches, or counselling alone. No intervention has been shown to work for more than about one-quarter to one-third of people who use it. Combining interventions might be more effective than any single method used alone.

Related links

Read *Study finds high rates of cancer among older people living with HIV*

View a webcast of this presentation

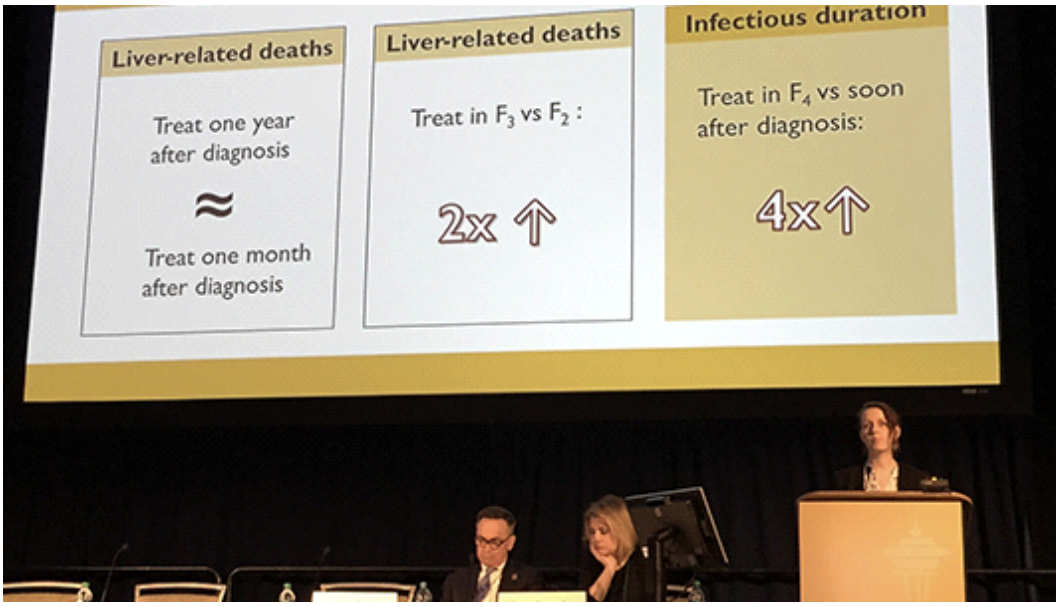
Read *Smoking is the biggest risk factor for non-AIDS-defining cancers in people living with HIV*

View a webcast of this presentation

Read *Varenicline helps people with HIV stop smoking, but success rate remains low*

View a webcast of this presentation

Delaying hepatitis C treatment leads to liver cancer and death



Cindy Zahnd presenting at CROI 2015. Photo by Liz Highleyman, hivandhepatitis.com.

If people with hepatitis C and HIV co-infection delay taking hepatitis treatment until they have advanced liver disease, they remain at risk of liver-related complications and death, according to a modelling study.

During the era of interferon-based therapy for hepatitis C, experts generally recommended that patients put off treatment until they experienced liver disease progression. Although new hepatitis C drugs are more effective and have far fewer side-effects, their high cost has led to restrictions on their use, with some insurers and public payers only covering treatment for the sickest patients.

The mathematical model was based on data on men who have sex with men in Switzerland.

It found that if treatment with new hepatitis C therapies was begun within a year of diagnosis, 2% of patients would eventually have HCC (a type of liver cancer) and 3% would die of liver-related complications. There was no advantage to beginning therapy within a month of diagnosis rather than a year.

However, if treatment was delayed until patients had severe liver fibrosis (stage F3), 8% would get HCC and 10% would die of liver-related complications. Moreover, a delay until liver cirrhosis (stage F4) would increase the proportions to 20 and 25% respectively.

Of note, the risk of these serious events did not fall to zero, even after successful treatment with modern therapies. Most of the events would occur *after* hepatitis C had been cured in patients who had previously had severe fibrosis or cirrhosis.

Delays in taking treatment would also have an impact on the length of time that patients were infectious. This would be around 5 years in a person treated within a year, more than 15 years if delayed until severe fibrosis, and nearly 20 years if delayed until cirrhosis.

The findings support earlier initiation of treatment, before significant liver damage occurs. But a second study suggested that, at the moment, almost half the Americans living with hepatitis C have severe fibrosis or cirrhosis. These cases are concentrated in the 'baby boom' generation, those currently between 50 and 70 years of age.

Related links

Read this news story in full on aidsmap.com

View a webcast of this presentation

Questions about maraviroc for PrEP

Julie Fox presenting at CROI 2015. Photo by Liz Highleyman, hivandhepatitis.com.

Whereas most PrEP (pre-exposure prophylaxis) research has focused on tenofovir/emtricitabine (*Truvada*), researchers are exploring other antiretroviral agents in various forms (e.g. pills, gels, vaginal rings).

In particular, the entry inhibitor maraviroc in tablet form *(Celsentri/Selzentry)* is being tested in a phase 2 trial. Maraviroc could be an attractive option because it acts at an early stage, blocking HIV from attaching to the CCR5 co-receptor that HIV typically uses to enter cells – other antiretrovirals interfere with viral replication after HIV has already entered a host cell.

Moreover, there is hope that new formulations of PrEP may be able to achieve high levels of the drug in vaginal and rectal tissues after a single dose. This could allow for event-driven or 'on-

demand' PrEP.

However, the conference heard findings from a laboratory study, showing that a single dose was not enough. A few hours after taking maraviroc, tissue samples from the rectum and vagina were taken by biopsy and were subsequently exposed to HIV.

While high concentrations of the drug in tissue were observed four hours after taking the dose, these dropped off soon afterwards. Most importantly the antiviral protective effect was limited.

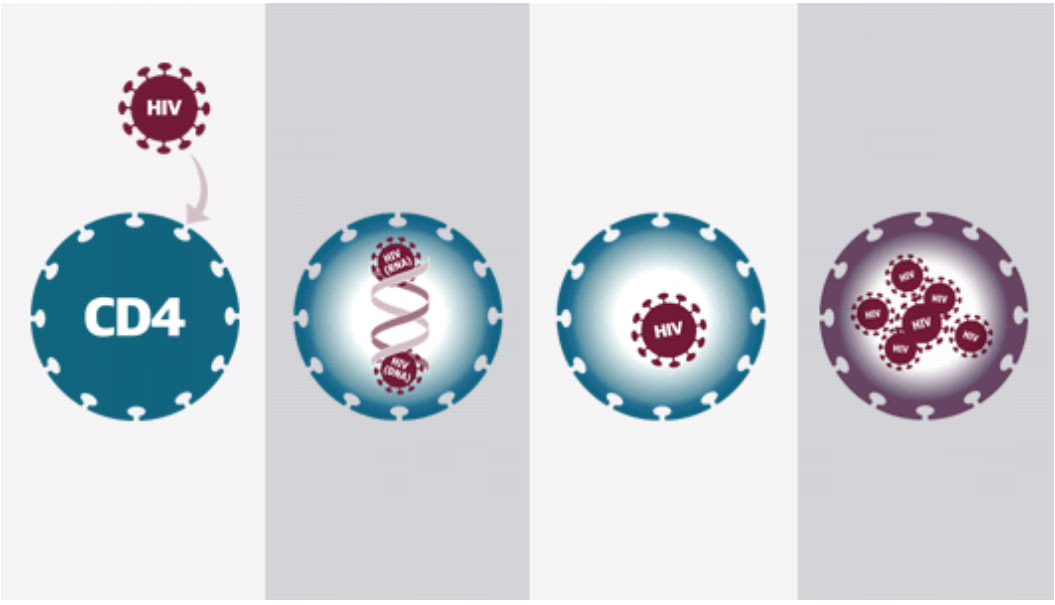
However, some researchers question whether these laboratory analyses are a reliable guide to actual performance in living people. And the study cannot tell us about the protection afforded by multiple doses of maraviroc.

Related links

Read this news story in full on aidsmap.com

View a webcast of this presentation

BMS-663068, new drug for treatment-experienced people



Detail from the NAM leaflet *How treatment works*, showing different stages of the HIV lifecycle targeted by antiretroviral drugs. See www.aidsmap.com/thebasics

Encouraging 48-week results from a phase 2b trial of Bristol-Myers Squibb's BMS-663068 (fostemsavir) were presented at CROI.

It belongs to a new class of drugs – attachment inhibitors. BMS-663068 binds directly to the gp120 protein that makes up part of the 'spikes' on HIV's outer surface, thereby preventing viral attachment and entry into CD4 T-cells. CCR5 blockers like maraviroc (*Celsentri*/*Selzentry*) and fusion inhibitors like enfuvirtide (*Fuzeon*) work at slightly later steps; BMS-663068 is active regardless of whether an HIV strain uses CCR5 or CXCR4 co-receptors.

The study enrolled 254 treatment-experienced people, most of whom had had treatment failure on first- or second-line therapy and had problems with drug resistance. Two-in-five participants had a CD4 cell count below 200 cells/mm^3. With recruitment in many middle-income countries, more women, black people and individuals with HIV subtypes other than B took part than in

some other studies.

Participants were randomised to receive BMS-663068 (in one of four doses, either once or twice daily), along with raltegravir and tenofovir. Those in the control group took ritonavir-boosted atazanavir, raltegravir and tenofovir.

After 48 weeks, response rates were similar – between 61 and 82% of those taking BMS-663068 had an undetectable viral load (with variation by dosing schedule), compared with 71% in the atazanavir arm. The new drug was generally safe and well-tolerated at all doses tested.

Analysis of potential drug-drug interactions suggests that BMS-663068 can be safely taken with darunavir and/or etravirine, without the need for dose adjustment. These drugs are widely used by treatment-experienced people.

Related links

Read this news story in full on aidsmap.com

News coverage on aidsmap.com

We hope you have found our news reporting from CROI 2015 useful.

You can find all our coverage online at www.aidsmap.com/croi2015 including:

- all our news stories
- our conference bulletins in English, French, Spanish, Portuguese, Italian and Russian
- news from other sources, selected by our editors.
- a selection of tweets from the conference.

Please do share links and information with your colleagues and networks.

And remember, we publish news all year round and there are lots of ways of keeping in touch with us:

- Sign up for one of our regular email bulletins, such as *HIV prevention news: Europe* (once a month), or *HIV update*
- Download an aidsmap news app for iPhone or android
- Find us on Facebook or follow us on Twitter.

Related links

Visit www.aidsmap.com/croi2015

Support our work

This message from one of our supporters made us smile! As a charity we rely on donations to continue our work and are so grateful for every gift we receive, no matter how big or small.

We believe passionately that independent, clear and evidence-based information lies at the heart of empowering people to make decisions about their health and live longer, healthier, happier lives.

If you can feel you can support our work with a donation, you can do so online at www.aidsmap.com/donate.

Thank you.

Related links

www.aidsmap.com/donate

Connect with NAM on Facebook: Keep up to date with all the exciting projects, latest achievements and new developments that are going on in the world of NAM.

- Follow NAM on twitter for links to hot off the press news stories from our editors covering key developments and conferences as they happen. Our news feed is linked to www.twitter.com/aidsmap_news and we also tweet from www.twitter.com/aidsmap.
- Follow all the conference news by subscribing to our RSS feeds.

For more details, please contact NAM:
tel: +44 (0)20 7837 6988
fax: +44 (0)20 7923 5949
email: info@nam.org.uk
web: www.aidsmap.com

NAM Publications
Registered office: Acorn House, 314-320 Gray's Inn Road, London, WC1X 8DP
Company limited by guarantee. Registered in England & Wales, number: 2707596
Registered charity, number: 1011220