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CONTENTS

EDITORIAL

This issue of HTB includes diverse news and reports that cover a surprising and disturbingly wide ground. Even though this was expected to be a quiet month, there is a lot to report.

The recent BHIVA Autumn conference included news about a UK case of potential HIV eradication.

The meeting also launched the new joint BHIVA/BASHH UK PrEP guidelines which are now online together with feedback from the open consultations.

Our coverage from the 9th HIV and Ageing Workshop held last month is thanks to NATAP.org who were involved in cofounding the meeting and whose own coverage includes more than 40 reports.

Other articles includes Richard Jefferys analysis of cure research from AIDS2018 and news that the fixed-dose combination of dolutegravir/3TC has now been submitted to both the EMA and FDA - based on results from the GEMINI studies presented at AIDS2018.

BHIVA and BASHH also collaborated on a survey of sexual health services which provided a disturbing picture of the impact of funding cuts. These leading organisations representing doctors and other health workers involved in sexual health report services that are over-stretched and at breaking point.

Postive news from South Africa includes the first HIV positive trasplant (to a child that was HIV negative.

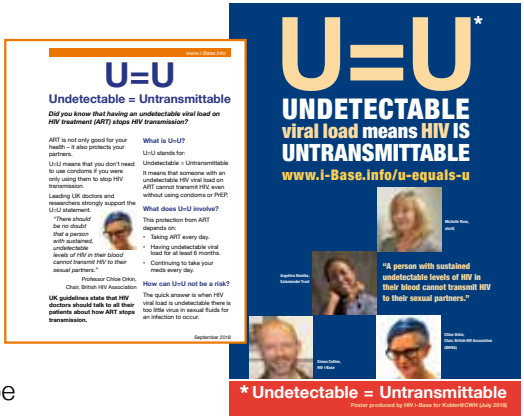
Finally, we highlight the shocking murder of an HIV positive activist in Greece which is now the focus of a community campaign for justice.

The next issue will report from the upcoming HIV Treatment for Prevention (R4P) and Glasgow conferences.

SUPPLEMENTS

U=U resources for UK clinics: free posters, postcards and factsheets

Please continue to order these free resources.



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Last year we launched a funding appeal to help i-Base continue to provide free publications and services.

Your help has been inspiring – and we hope this support will continue during 2018. If 1000 people support us with £5 a month we will be on course to meet our shortfall.

All help is appreciated.

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CONFERENCE REPORTS

BHIVA Autumn Conference, 2018

4 – 5 October 2018, London

The annual BHIVA Autumn conferences always include an exciting programme of expert speakers in a largely single-track meeting. This is an important meeting to continue to support.

Although this is not an abstract-driven conference, and the sessions are not webcast, slides are available online from many of the oral presentations.

https://www.bhiva.org/Autumn2018Presentations

Unfortunately, slides are not posted for many of the sessions, which is a pity given the quality of the presentations, and that the results are in the public domain after they have been presented.

The short reports in this issue are:

- Second case of HIV eradication
- BHIVA/BASHH guidelines for PrEP
- Other selected talks

Second case of potential HIV eradication

Simon Collins, HIV i-Base

One of the highlights of the BHIVA Autumn Conference, slipped in as a couple of slides at the end of the meeting, was that the UK might have a second potential case of HIV eradication (although this is one of the presentations is one that is not online). [1]

The case involves an HIV positive man who has undergone successful allogeneic stem cell transplantation from an unrelated donor homozygous for CCR5 delta-32 deletion.

ART was stopped 15 months post transplant following ethics approval and for the subsequent 12 months HIV has been undetectable by all methods including proviral DNA outgrowth and integrated and total HIV DNA in CD4 cells.

Further details will be presented to a future medical conference.

Reference

Gabriel I. Bone marrow transplants. BHIVA Autumn conference, 4-5 October 2018.

New UK PrEP guidelines 2018

Simon Collins, HIV i-Base

The conference included the launch of the new PrEP guidelines (jointly produced by BHIVA and BASHH) with a presentation from Alison Rodger, co-chair of the writing group, on the issues that generated most discussion for the group and comments from the open consultations. [1]

This included the recommendations on use by adolescents, transgender people and during pregnancy, and the schedules for monitoring (more frequently renal monitoring for adults older than 40).

It also includes starting and stopping PrEP in terms of time to protection and coverage and management in cases of confirmed or uncertain HIV infection.

A more detailed summary of the guidelines is included later in this issue of HTB and the full guidelines are now online. [2, 3]

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2. Collins S. UK launches PrEP guidelines. HTB. (19 October 2018).
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https://www.bhiva.org/file/5b729cd592060/2018-PrEP-Guidelines.pdf (PDF)

Other selected talks at BHIVA Autumn 2018

Simon Collins, HIV i-Base

There were of course many other important talks at the meeting and the following are a few where the slides are available online.

Other selected talks included Paul Holmes on HIV dementia [1] and Shimu Khamlichi on psychological management [2] with invited lectures on HIV and ageing by Caroline Sabin [3] and the gut microbiome by Caroline Le Roy [4].

The community session at the conference was on the future of local clinical and community services, many of which are being cut due to lack of secure funding. This discussion included a comment by Yusef Azad from NAT that an early result from the current PHE Positive Voices survey is a significant drop in HIV positive people accessing support services over the previous 12 months. This has more than halved from 35% to 14% in the two years since the previous survey, without any evidence that need for these services has fallen.

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CONFERENCE REPORTS

9th International Workshop on HIV and Ageing

13 – 14 September 2018, New York

This year the annual Workshop on HIV and Ageing was held in New York from 13 – 14 September.

Although i-Base were unfortunately not able to attend the meeting we include four reports from NATAP.org which has been the leading organisation raising the importance of HIV and ageing.

Many of the materials from the workshop are available online.

http://www.infectiousdiseasesonline.com/event/workshop/9th-international-workshop-hiv-aging-2018/

Webcasts

http://www.infectiousdiseasesonline.com/hiv-aging-2018-webcasts

Presentations

http://www.infectiousdiseasesonline.com/hivaging2018-presentations

NATAP coverage

More than 40 reports and conference slides are also posted to the NATAP website:

http://www.natap.org/2018/AGE/AGE.htm

Reports in this issue of HTB are:

- Detectable viral load quadruples odds of recurrent falls in older men with HIV
- More than 40% of HIV group has hepatic steatosis, regardless of age
- Associations of loneliness with cognitive function and quality of life (QoL) among older adults living with HIV - 18% lonely quite often
- Physical function worse in older women than men with HIV, despite better CD4 recovery

Detectable viral load quadruples odds of recurrent falls in older men with HIV

Mark Mascolini , for NATAP.org

Having a detectable viral load quadrupled odds of recurrent falls in a large analysis of older men with or without HIV in the Multicenter AIDS Cohort Study (MACS). [1]

Taking diabetes or depression medications, taking efavirenz, and having peripheral neuropathy also boosted odds of falling in this 2-year study, but HIV did not emerge as a fall risk factor.

Falls and fall risk factors are frequent in older people with and without HIV. A prior study of 359 HIV positive men and women 45 to 65 years old identified female gender, diabetes, antidepressants, sedatives, opiates, didanosine, exhaustion, weight loss, and balance difficulties as the strongest independent predictors of falling in the past 12 months. [2]

A prospective study of 967 HIV positive men and women at least 40 years old determined that frailty independently raised odds of recurrent falls 17-fold, while pre-frailty almost quadrupled odds of recurrent falls. [3]

The new analysis involved men 50 to 75 years old enrolled in the Bone Strength Substudy of the MACS, which tracks HIV positive men who have sex with men (MSM) and HIV negative MSM at risk for HIV. Researchers recorded new falls in real time over a 2-year period. They used multinomial logistic regression to identify predictors of falling in an analysis that adjusted for HIV status, age, race, study site, enrollment period, body mass index, illicit drug use, peripheral neuropathy, and diagnosis of and medications for depression, diabetes, and hypertension.

Compared with the 379 HIV negative men, 279 HIV positive men were younger (61.1 versus 62.4 years, $p < 0.001$), included a lower proportion of whites (71% versus 82%, p=0.001), had a lower body mass index (25.2 versus 26.1 kg/m^2, p=0.004), had higher diabetes prevalence (18% versus 12%, p=0.034), and used depression medications more (30% versus 18%, $p <0.001$). About 45% of men with or without HIV used illicit drugs. Most men with HIV, 91%, had a viral load below 50 copies.

Dividing study participants into subgroups of 23 HIV positive men with a detectable viral load (viraemic), 256 HIV positive men with an undetectable viral load, and 379 men without HIV, the researchers determined respective single-fall rates of 13%, 22%, and 22%. Recurrent fall rates in those three groups were 35%, 18%, and 17%. About 10% of recorded falls led to injury and almost 5% caused fracture.

Men with HIV reported having a pet as a reason for a fall more than men without HIV (9.4% versus 3.8%, p=0.008). Among all men, those with poor balance confidence and slower time to rise from a chair proved more likely to have recurrent falls.

Multivariate analysis did not link HIV infection to higher odds of falling, but 3 variables emerged as independent predictors of falling in the combined HIV positive and negative group: taking diabetes drugs, peripheral neuropathy, and illicit drug use. Five variables independently predicted recurrent falls in the combined HIV positive and negative group: taking diabetes drugs, taking antidepressants, peripheral neuropathy, illicit drug use, and every additional 5 years of age.

Among men with HIV, a detectable viral load (versus an undetectable load) independently predicted 4-fold higher odds of recurrent falls. Four other variables independently predicted recurrent falls: efavirenz use (about 4-fold higher odds), taking diabetes drugs (about 4-fold higher odds), peripheral neuropathy (about 2-fold higher odds), and illicit drug use (about 2-fold higher odds).

The researchers suggested their findings support fall prevention through physical activity, antiretroviral adherence, transition to nonefavirenz regimens, and counselling about pets, kerbs, and other physical hazards.

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More than 40% of HIV group has hepatic steatosis, regardless of age

Mark Mascolini, NATAP.org

In a study of 168 US adults with HIV, 39% of those 50 or older and 49% of younger people had hepatic steatosis (fatty liver disease), a nonsignificant difference. [1]

Compared with younger people with steatosis, older people with steatosis were more likely to be women, to have cirrhosis, and to have HIV infection longer.

Fatty liver disease – defined as 5% or greater hepatic steatosis – remains highly prevalent in HIV populations with and without hepatitis virus coinfection. A US study of 62 HIV positive adults with elevated aminotransferase while taking antiretrovirals but without chronic hepatitis infection found that 34 (55%) had nonalcoholic steatohepatitis determined by liver biopsy and predicted by insulin resistance and obesity. [2]

Using a hepatic steatosis index based on transaminases, body mass index, gender, and presence or absence of diabetes in 796 Canadian patients with HIV but without chronic hepatitis, a Montreal team charted a steatosis incidence of 6.9 per 100 person-years. [3]

Researchers from University of Texas Health in Houston and other centres noted that, as a metabolic inflammatory disease, fatty liver disease has the greatest impact on morbidity and mortality via cardiovascular disease, not progressive liver disease.

To learn more about steatosis prevalence, risk factors, and biomarkers in people with HIV, these investigators enrolled 168 people in a cross-sectional study. All participants underwent FibroScan to determine controlled attenuation parameter (CAP, a steatosis measure) and liver stiffness measurement (LSM, a fibrosis and cirrhosis indicator).

The researchers defined significant hepatic steatosis as CAP greater than 260 dB/m. They used quantile regression to determine factors associated with CAP. A subset analysis presented at the HIV and Ageing Workshop compared outcomes in people 50 or older with outcomes in younger people.

The study group was 58% male, 31% female, and 11% transgender women. There were 90 people 50 or older and 78 younger than 50. Overall age averaged 51 years, body mass index 29 kg/m^2 (near the top of the overweight range), CD4 count 640, time with HIV infection 14 years, and time taking antiretrovirals 9 years. About 96% of the group was nonwhite.

Significant steatosis affected 39% of people 50 or older and 49% of the younger group. Among people with steatosis, average CAP was marginally and nonsignificantly lower in the older group (256 versus 266 dB/M, p >/= 0.05), while LSM was nonsignificantly higher (worse) in older participants (6.1 versus 5.4 kPa, p >/= 0.05). Average body mass index was similar in older and younger people with fatty liver disease (32.9 and 31.5 kg/m2, p=0.45).

Older participants with fatty liver disease were more likely to be female than younger patients with fatty liver disease (43% versus 29%, p=0.005). The older group with fatty liver disease had a higher cirrhosis prevalence than the younger group with fatty liver disease (14% versus 0%, p=0.02), and the older group with fatty liver disease had a marginally higher HCV frequency (29% versus 12%, p=0.08). The older and younger groups with fatty liver disease did not differ significantly in current smoking, hyperlipidaemia, or diabetes.

Two HIV variables differed significantly between older and younger people with fatty liver disease: The older group had a significantly longer duration of HIV infection (average 16 versus 12 years, p=0.009) and significantly more years on antiretroviral therapy (average 12 versus 7 years, p=0.0003). But the older and younger groups with

fatty liver disease did not differ significantly in current CD4 count, viral load below 50 copies, history of AIDS, or type of antiretroviral therapy. Nor did the older and younger groups with fatty liver disease differ significantly in an array of markers: adiponectin, hs-IL-6, PCSK9, FGF21, fetulin A, or FABP-4.

Compared with older people without fatty liver disease, older individuals with fatty liver disease were more likely to be obese (average body mass index 32.9 versus 26.5 kg/m2, p <0.0001) and to have higher fetulin A, a liver-derived blood protein that inhibits insulin receptor tyrosine kinase associated with insulin resistance [4] (average 836 versus 665 ug/mL, p=0.003). Older people with fatty liver disease tended to include a higher proportion of Hispanics and to have higher rates of cirrhosis and high triglycerides but less prevalent cardiovascular disease.

The researchers underlined obesity as a major clinical factor tied to hepatic steatosis in older people with HIV. Preventing and treating obesity in older and younger people, they proposed, are crucial to preventing hepatic steatosis with advancing age.

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Associations of loneliness with cognitive function and quality of life (QoL) among older adults living with HIV - 18% lonely quite often

Mark Mascolini, NATAP.org

Younger people with HIV more often lonely than their elders

Many consider loneliness an affliction most common in the elderly, but a study of 836 HIV positive people in Canada found loneliness more likely in the youngest age group studied, those 35 to 45. [1]

Almost 1 in 5 people in the overall study group reported feeling lonely “quite often,” while almost half said they were “sometimes” lonely. HIV stigma, depression, and waning cognitive function can contribute to loneliness in people with HIV infection. A study of 914 HIV positive men and women over age 50 in New York City found that 39% had symptoms of major depression that could be predicted by increased

loneliness, increased HIV-associated stigma, decreased cognitive functioning, reduced energy, and younger age. [2]

Loneliness predicts coronary heart disease and stroke in the general population. [3]

To get a better understanding of loneliness prevalence and predictors in middle-aged and older people with HIV, Canadian researchers analysed data collected at the first visit for Positive Brain Health Now, a longitudinal study of HIV positive people in care at 5 outpatient clinics. All participants were 35 or older and had HIV infection for at least one year. No one had dementia or a known central nervous system disorder.

The investigators determined loneliness prevalence by asking one question: Do you find yourself feeling lonely: quite often, sometimes, or almost never? They rated cognitive function on the B-CAM battery of cognitive tests and the PDQ perceived deficit questionnaire. The researchers used proportional odds regression and multiple linear regression to estimate the strength of associations between loneliness and other conditions after adjustment for age, sex, and education.

The 836 participants who enrolled between October 2013 and June 2016 were mostly (85%) men with an average age of 52 years (standard deviation 8.3). Almost three quarters of participants, 71%, were Caucasian. While 148 people (18%) felt lonely "quite often," 383 (46%) "sometimes" felt lonely and the rest almost never felt lonely. These loneliness rates did not differ between women and men. But the study linked several factors to a higher likelihood of loneliness: insufficient funds (37.0% quite often lonely, 18.7% sometimes lonely, 7.3% never lonely, $p < 0.001$), more HIV-specific symptoms (average 5.1, 4.6, 3.8, $p < 0.001$), and lung disease (16.9%, 19.9%, 11.8%, $p < 0.05$).

Average age was significantly younger in people who felt quite often lonely (51.2) or sometimes lonely (52.5) than in those never lonely (54.4) ($P < 0.05$). Compared with older people, those 35 to 45 proved significantly more likely to report loneliness ($P < 0.05$).

Statistical analysis identified several sociological and psychological factors that may contribute to loneliness: stigma (21.1% quite often lonely, 13.4% sometimes lonely, 6.0% never lonely, $p < 0.001$), having fewer than 5 close people (71.0%, 51.2%, 29.9%, $p < 0.001$), having no plans or goals (23.8%, 9.8%, 7.2%, $p < 0.001$), not working or volunteering (34.5%, 31.1%, 22.9%, $p < 0.05$), and SF-36 scores [4] for pain, vitality, and physical function.

Four lifestyle factors predicted loneliness: fewer hours of physical activity (average 7.0 quite often lonely, 8.1 sometimes lonely, 9.8 never lonely, $p < 0.001$), seldom active (37.4%, 22.1%, 19.9%, $p < 0.001$), more TV hours weekly (18.4, 15.4, 14.6, $p < 0.05$), and opioid use independently of pain (14.6%, 10.4%, 5.4%, $p < 0.05$). Current smoking did not differ significantly by loneliness status.

Compared with people who almost never felt lonely, those who felt lonely sometimes

or quite often consistently had worse emotional and mental health outcomes including cognitive ability, stress, depression, anxiety, and outcomes reflecting self-rated health, health-related quality of life, and overall quality of life.

The researchers noted that results may not apply to everyone with HIV because the study group consisted largely of men and Caucasians. They also stressed that loneliness – a discrepancy between desired and actual level of socialisation – is not the same as isolation. That distinction could bear on the greater loneliness identified in younger people.

The investigators concluded that almost two thirds of these middle-aged and older adults felt lonely sometimes or quite often. They proposed that "interventions to engage people in socially meaningful activities, shown to be effective for loneliness in other conditions, should be developed for older adults living with HIV."

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Physical function worse in older women than men with HIV, despite better CD4 recovery

Mark Mascolini

Older women with HIV had significantly worse physical function and quality of life than older men, according to analysis of 1126 people in the Modena HIV cohort [1]. Women's worse physical function contrasted with their better CD4 recovery and lower cardiovascular disease rates and risk than men.

Researchers in Madrid and Modena who conducted this study noted that women represent 20% to 30% of people with HIV in developed countries. As HIV populations age, they face growing risks of comorbidity and quality-of-life challenges. Yet few large studies address diverse clinical and behavioural differences between older women and men with HIV.

To address these issues, researchers from two Madrid universities and the University

of Modena conducted this retrospective analysis of consecutive patients older than 50 attending the Modena HIV clinic between June 2016 and May 2018. Besides recording clinical characteristics and comorbidities, the researchers measured body composition, assessed physical function with the Short Physical Performance Battery (SPPB), measured walking speed, and determined quality of life with EQ-5D-5L. [2]

The study involved 1126 HIV positive people over 50, 284 of them (25%) women. Women did not differ significantly from men in median age (55 years overall), years with HIV infection (25), nadir CD4 count (195), or proportion with an undetectable viral load (76%). But several clinical factors did differ between women and men, favoring women:

- Median current CD4 count: 758 in women versus 699 in men (p=0.03).
- Median CD4/CD8 ratio: 1 in women versus 0.84 in men (p=0.0001).
- No alcohol use: 80.6% of women versus 66.5% of men (p=0.0001).
- Mild or intense alcohol use: 19.4% of women versus 33.5% of men (p=0.0001).
- Cardiovascular disease: 2.8% of women versus 11% of men (p=0.0001).
- Hypertension: 38.7% of women versus 60.3% of men (p=0.0001).
- Diabetes: 11.6% of women versus 22.9% of men (p=0.0001).
- Sarcopenia (age-related muscle loss): 41.2% of women versus 47.1% of men (p=0.08).

Women had a worse history of more advanced HIV infection, including AIDS wasting, and a worse kidney failure rate:

- CDC stage B or C HIV infection: 57.8% of women versus 52.4% of men (p=0.001).
- History of AIDS wasting: 21.1% of women versus 8.9% of men (p=0.0001).
- Kidney failure: 33.1% of women versus 17.9% of men (p=0.0001).

Women and men did not differ significantly in rates of smoking, abnormal lipids, chronic obstructive pulmonary disease, lipodystrophy, cirrhosis, vitamin D insufficiency, osteoporosis by DEXA scan, AIDS malignancies, or non-AIDS malignancies.

SPPB-measured physical function and EQ-5D-5L-measured quality of life were significantly worse in women than men:

- SPPB below 9: 11.5% of women versus 5.6% of men (p=0.002).
- EQ-5D-5L: 0.87 in women versus 0.90 in men (p=0.02).

Walking speed did not differ significantly between women and men. But moderate or severe pain was more frequent in women (23.9% and 3.9%) than in men (13.7% and

3.1%) (p=0.001).

Women reported more exhaustion. Exhaustion (rarely: <1day/week) was reported by 56% of women vs 68% of men. BUT, exhaustion 1-2d/week was reported by 33% of women vs 25% of men. Exhaustion 3-4 d/week was reported by 9% of women vs 5.8% of men. Always or almost always exhaustion (5-7 d/week was reported by 3 women (1.1%) and 2 men (0.2%).

The Madrid/Modena investigators stressed that, although women had better CD4-cell recovery with antiretroviral therapy than men, and less cardiovascular disease and cardiovascular risk, women had worse physical function and quality of life than men. They proposed that "older HIV positive women have special characteristics and the assessment of physical function in this group seems to be crucial."

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ANTIRETROVIRALS

Dolutegravir/lamividune FDC submitted to EMA and FDA

Simon Collins, HIV i-Base

On 17 October 2018, ViiV healthcare announced that the dual-drug fixed dose combination FDC) of dolutegravir/lamivudine had been submitted to the US FDA. [1]

Submission is based on results from the phase 3 GEMINI studies in treatment naive participants that were presented at the AIDS 2018 conference in July. [2, 3]

These results showed dolutegravir/3TC to be non-inferior to triple therapy using dolutegravir plus tenofovir-DF/emtricitabine.

The FDA submission included a priority review voucher which shortens the decision timeline to six months. These vouchers are bought and sold by companies and enable a faster review process.

The dolutegravir/3TC FDC was submitted to the EMA on 14 September 2018. [4]

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CURE RESEARCH

Post-AIDS 2018 updates on HIV cure research

Richard Jefferys, TAG

In the aftermath of the 22nd International AIDS Conference (AIDS 2018), which took place in Amsterdam in July, there has been some reflecting on the challenges facing the HIV cure research field.

The presentations that garnered the most news coverage described disappointing study results, but there were also nuggets of novelty and encouragement to be found amidst the sea of data on offer. Please see the earlier post for links to relevant conference sessions, many of which now have video and/or slides available. [1]

The RIVER trial

The most widely reported findings came from a clinical trial in the UK known as RIVER (Research In Viral Eradication of HIV Reservoirs), available as a webcast. [2, 3]

Participants with primary HIV infection were randomised to receive a standard

antiretroviral therapy (ART) combination plus the integrase inhibitor raltegravir or ART plus raltegravir along with a therapeutic HIV vaccine regimen and a short course of the HDAC inhibitor vorinostat (a candidate HIV latency-reversing agent). The primary purpose was to evaluate whether the vorinostat and vaccine combination—a version of the proposed "kick & kill" approach to depleting the HIV reservoir—had a significant effect on HIV reservoir measures compared to ART.

As described in detail in multiple online reports, the size of the HIV reservoir—as assessed by both total HIV DNA and the viral outgrowth assay—remained equivalent between the two arms. Presenter Sarah Fidler pointed out some possible caveats, such as the relatively short follow up time, but the data appear to rule out any significant effect by this particular kick and kill combination.

The researchers cited several potential explanations: the latency-reversing activity of vorinostat may be suboptimal, and there is uncertainty as to whether the HIV-specific T cell responses that were successfully induced by the vaccines were targeting parts of the virus most likely to be displayed by infected cells after latency reversal. As is emphasised in much of the coverage, the study itself should not be considered a failure because it provided a clear answer to the question it was designed to address. The interventions were also found to be safe and no participants withdrew.

The results echo a theme that has been sounding recently in HIV cure research: randomised controlled trials are required to rigorously evaluate the potential of candidate interventions, and positive results from single-arm exploratory trials (which tend to compare results to baseline values or historical controls) need to be interpreted with caution.

Studies published over the past year that have reached a similar conclusion include randomised controlled evaluations of a therapeutic vaccine combination [4] and single doses of the candidate latency-reversing agent romidepsin [5].

Vedolizumab

The second piece of unwelcome news related to vedolizumab, an antibody that targets the alpha4/beta-seven integrin, a protein involved in CD4 T cell trafficking to the gut that may also facilitate HIV entry into target cells. In 2016, an experiment in SIV-infected macaques generated excitement when administration of vedolizumab was associated with control of viral load after ART interruption. [6] Human trials were initiated relatively quickly because vedolizumab is already FDA approved as treatment for ulcerative colitis and Crohn's disease.

During a talk at the conference on HIV remission, Anthony Fauci from the National Institute of Allergy and Infectious Diseases (NIAID) provided a glimpse at the data from the first of these trials, and sadly the results did not mirror the published macaque study. While it appeared that one or two participants displayed some evidence of viral

load containment after an analytical treatment interruption (ATI), the majority did not. [7, 8]

Fauci suggested the variations in viral load levels were similar to those his group has observed in placebo recipients in prior trials, and were not indicative of any effect from vedolizumab. At least two other clinical trials involving the antibody are ongoing, so additional results will be forthcoming. [9]

In a separate presentation, Michele DiMascio put another dent in the optimism that had surrounded vedolizumab by reporting that an attempt to repeat the original results obtained in SIV-infected macaques had failed. This time, there was no evidence of vedolizumab-induced SIV control. The reasons for the divergent outcomes are unclear, but may relate to the type of SIV used in the experiments, which has a mutation in the nef gene. [10]

Reservoir targeting

A number of presentations described novel approaches for targeting the HIV reservoir, highlighting the amount of work that is underway to try and improve upon the interventions tested to date.

Isa Munoz-Arias and colleagues from UCSF and Merck reported that a number of FDA-approved chemotherapeutic drugs have HIV latency-reversing activity in laboratory studies. [11]

In some cases the magnitude of the effect was demonstrated to be greater than the combination of bryostatin and romidepsin, which has previously been shown to be among the most potent latency-reversing strategies in vitro. The effects were not associated with significant T cell activation or CD4 T cell death (although it's important to note that this does not mean the drugs are without side effects - those are described on their labels). [12]

A total of 12 FDA-approved chemotherapies were found to reverse HIV latency via a variety of novel pathways, suggesting new avenues for exploration beyond the current candidates, which primarily comprise HDAC inhibitors. The details of the presentation can be found on the NATAP website [13] (which often does more to make information public than conferences themselves), and it was also covered by i-Base. [14]

The research group of Wen Kang debuted data from a small, uncontrolled pilot study of the HDAC inhibitor chidamide, which is approved in China as a cancer therapy. [15]

Kang described evidence that the drug had stimulated production of HIV RNA in seven individuals on ART, and may have slightly reduced HIV DNA levels. However in the Q&A after the talk Sharon Lewin noted that the various possible markers of activity that were analysed did not appear to necessarily correlate with each other. A larger randomised controlled trial that should provide more definitive results is now ongoing. [16]

Tim Henrich from UCSF followed up on work published earlier this year in PLoS Pathogens identifying CD30—a cell surface molecule known for its association with lymphoma—as preferentially expressed on HIV-infected CD4 T cells. [17]

In the paper, the researchers describe an individual with HIV who exhibited undetectable viral RNA and DNA levels after receiving therapy for lymphoma including brentuximab vedotin, an anti-CD30 antibody-drug conjugate. Unfortunately the individual died after cancer recurrence so no further investigation was possible.

Henrich's conference abstract reports the identification of a second person with HIV who received brentuximab vedotin as part of treatment for lymphoma (now in remission). [18]

Three weeks after administration of the first dose, HIV RNA was reduced to undetectable from a previous level of 7,359 copies per million CD4 T cells (a greater than 3 log reduction). HIV DNA levels fell by 42%. The individual is now being followed longitudinally.

This research opens up the possibility of targeting CD30 as a means to deplete the HIV reservoir, and in addition to brentuximab vedotin there are also CD30-specific chimeric antigen receptor (CAR) T cells in development that are already being studied in clinical trials for cancer. [19]

An interesting presentation by Sarah Joseph from the University of North Carolina at Chapel Hill outlined an effort to establish when viruses enter the latent reservoir. [20]

Using complex phylogenetic analyses, Joseph uncovered evidence that in most individuals studied, the majority (~72%) of the replication-competent latent HIV reservoir was most closely related to viruses circulating in the year prior to ART initiation. In contrast, only 5% was derived from virus replicating during the first year of infection.

A paper published in the journal eLife in 2016, [21] involving ten participants, reported similar results, although Joseph also pointed out that a much smaller study presented at the conference by Zabrina Brumme (subsequently published in PNAS) reached different conclusions, finding more diverse dates of establishment of the reservoir. [22]

Joseph's data suggests that latently infected cells tend to be shorter-lived during untreated infection, with ART initiation triggering the formation of the bulk of the long-lived HIV reservoir. The implication for therapeutic strategies targeting the reservoir is that there might be a window of opportunity to intervene at the time ART is started (currently, almost all clinical trials involve testing candidate therapies in individuals after ART has suppressed viral load). This idea could potentially be explored in the SIV/macaque model.

HIV control off ART

Participants in the VISCONTI cohort represent the best known and most widely cited examples of post-treatment control of HIV replication. In 2013, when Asier Sáez-Cirión and colleagues published a detailed report in PLoS Pathogens, the cohort comprised 14 individuals. [23]

Updates have been fragmented since that time, occurring at various conferences, and as yet there have been no follow up publications as thorough as the original paper (at least that I'm aware of - for the sake of disclosure I should note that I chided the investigators about this situation in a public comment to the PLoS Pathogens article in 2017). [24]

At AIDS 2018, Laurent Hocqueloux and colleagues presented a poster on factors associated with loss of post-treatment controller status that included an update on the VISCONTI cohort. The study also offered results from analyses of inflammatory biomarkers, which I've not seen described previously. [25]

A total of 24 post-treatment controllers have now been added to the VISCONTI cohort; all started ART during primary infection and then interrupted after a median of 3.5 years of treatment. During subsequent follow up (current median of 12 years), five (21%) have restarted ART, four due to increasing viral load and one as a result of a head and neck cancer diagnosis.

These five participants were among seven who experienced one or more viral load measurements above 400 copies/ml during monitoring; none of the 17 who remained below this viral load level restarted ART (a highly statistically significant difference). The fact that the individual who developed cancer was in the former group, despite not reinitiating ART based on viral load criteria, may raise concern that prior exposure to detectable HIV viraemia was a risk factor for cancer development. Whether remaining on ART would have been associated with lower risk is an unanswerable question. This conundrum illustrates that firm conclusions about the clinical benefits of post-treatment control compared to continuous ART cannot be drawn until post-treatment control can be induced in sufficient numbers of people to allow a randomised comparison.

Overall, CD4 counts and CD4:CD8 ratios have remained stable in the cohort with medians not significantly different between the time of ART interruption and last follow up. Individual plots are not shown in the poster, however, so it's unclear if declines occurred in participants who experienced viral load increases.

Encouragingly, the majority of VISCONTI cohort members have maintained viral loads below 50 copies/ml, and levels of three inflammatory biomarkers – IP-10, sCD163 and sCD14 – were not significantly different between these post-treatment controllers and healthy HIV negative individuals (see figure 6 in the poster).

In a separate oral presentation, Asier Sáez-Cirión showed evidence that certain immune response genes are associated with post-treatment control in the VISCONTI

cohort, and may be mediating their effects—at least partly—through superior natural killer (NK) cell activity against HIV (unfortunately neither slides or video of this presentation are available on the conference website). [26]

Lisa Chakrabarti described an investigation of potential mechanisms of HIV control in a different population: elite controllers participating in the ANRS CODEX cohort. The researchers focused on HIV Gag-specific CD4 T cell responses, and found that CCR5 expression was lower among elite controllers compared to a control group of people with HIV on ART. [27]

The lower CCR5 expression by Gag-specific CD4 T cells was associated with reduced susceptibility to HIV infection, suggesting this may contribute to elite controller status. The results may offer support to efforts to protect virus-specific CD4 T cells from HIV infection using gene therapies that ablate CCR5 expression (or otherwise attempt to protect the cells from HIV entry), an approach being pursued by researchers at the defeatHIV collaboratory. [28]

Analytical treatment interruptions (ATIs)

A controversial component of research working toward achieving post-treatment control of HIV is the use of ATIs.

A systematic review of past studies involving ART interruptions could help shed light on the safest approaches to conducting ATIs in clinical trials, and Jillian Lau and colleagues from Alfred Hospital and Monash University in Melbourne, Australia delivered just such a review as a poster presentation at the conference.

Their work is now in press at a journal and will hopefully be published soon.

Source

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TREATMENT ACCESS

UK government funding cuts leave sexual health and HIV care at 'breaking point'

BHIVA/BASHH press release

Surveys of members of the British Association of Sexual Health and HIV (BASHH) and the British HIV Association (BHIVA) provide new evidence of pressure on over stretched sexual health services and a sector at 'breaking point'.

Access to sexual health and HIV services has been dramatically reduced as a result of changes to the funding and organisation of sexual health services since 2013, according to the medical professionals providing care. Over half (54%) of respondents to a survey of members of the British Association of Sexual Health and HIV (BASHH) reported decreases in the overall level of service access to patients over the past year, with a further 16 per cent saying that access had significantly decreased. In a parallel survey of members of the British HIV Association (BHIVA), three quarters (76%) of respondents said that care delivered to patients in their HIV service had worsened.

With Public Health England (PHE) data showing a 13 per cent increase in attendance of sexual health services between 2013 and 2017 (PHE, June 2018,) it is not surprising that nearly 80 per cent of BASHH respondents (79%) said that they had seen an increased demand for services in the past 12 months. Budgetary pressure means that this demand cannot always be met: more patients are now either turned away or redirected to other parts of the health system. Six in ten (63%) per cent of BASHH respondents said that they had to turn away patients each week, with 19 per cent saying that they were having to turn away more than 50 patients on a weekly basis. While most were offered the next available appointment, 13 per cent said that patients were referred to another sexual health provider and four per cent that they were redirected to primary care. Clinicians responding to the survey report that many of the patients who are being turned away have symptoms of potential infection.

Reduction in prevention, cytology and mental health services

Both surveys revealed significant reductions in services such as the delivery of HIV prevention activities, outreach to vulnerable populations, cervical cytology and psychosexual health services. Three quarters of BHIVA members (75%) said that there had been an impact on access to HIV prevention advice and condoms, with 63 per cent saying access had been reduced; 44 per cent of BASHH members said that HIV prevention services had decreased. Almost half (47%) of BASHH members reported

reductions in the provision of cervical cytology functions, reflected by BHIVA members, who also said that cervical screening had been halved (reduced access reported by 49.5%). This is of particular concern in the context of a fall in national cervical screening coverage and the higher risk of HPV related cancer in women with HIV.

More than 40 per cent (42%) of BASHH respondents reported reduced provision of psychosexual health care, mirrored by a similar number (41%) of BHIVA members, who said that access to psychology input for HIV related mental health problems had been reduced. This is despite the higher risk of mental health issues the HIV population faces. Nearly half of BASHH members (47%) also said that care for vulnerable populations had reduced.

STI screening and HIV testing

More than 40 per cent (41%) of BHIVA members said that access to sexual health screening had been reduced, despite HIV positive people being at greater overall risk of sexually transmitted infections. BASHH members gave a mixed response, with 29 per cent of respondents reporting reductions in STI testing in the past year and 27 per cent increased testing. The BASHH response regarding HIV testing was similarly mixed, with 21 per cent saying there was a decrease and 26 per cent an increase.

The BHIVA survey showed that it is becoming more difficult for people to test for HIV, with 35 per cent of respondents reporting that there is now reduced access to testing in their own location. Although 58 per cent of services offered outreach testing, with a quarter of respondents (26%) saying that it was offered locally in another service, more than half (52%) said access to testing in outreach settings was also reduced. Almost half (47%) of BASHH respondents reported increases in access to online testing in the last 12 months, but it is not yet available in all locations. Although some respondents were optimistic about its role in helping to manage the growing demand for services, others expressed concerns about poor implementation, and suggested it was taking the focus away from face-to-face services.

Funding cuts have also drastically reduced the output of third sector organisations, such as charities and community groups, who have traditionally helped to plug gaps in services with HIV testing, advice and peer support. Nearly 40 per cent of BHIVA respondents said that peer support was no longer offered by their service, with 28 per cent of those that still do saying access to it had been reduced. 70 per cent said that overall the remaining third sector support had worsened, with services stripped back to basics or simply closed down completely.

PrEP availability and reproductive health

The roll-out of the PrEP programme through the IMPACT trial has led to increased availability. Over 70 per cent (71%) of BHIVA respondents said that PrEP is now either available from their service or offered locally by another service (17%) and over 70 per cent (74%) of BASHH respondents reported increased delivery. However, provision

remains mixed with 28 per cent of BHIVA respondents saying access is improving, 25 per cent saying it had been reduced, and 11 per cent saying PrEP was not currently on offer locally.

At the same time almost a third (32%) of BASHH respondents reported decreased provision of reproductive health and contraception and a similar percentage (34%) of BHIVA respondents also reported reduced access to these services.

Impact of separation of HIV and GUM on staff and services

Changes since 2013 have in many areas led to previously fully integrated clinics that were able to provide a range of services from a single location now being divided between differently funded suppliers. Patients, particularly people living with HIV, may not be willing or able to travel elsewhere and staff may not be able to access records from other services.

Funding cuts have led to staff not being replaced with a knock-on effect to those remaining and to the level of service they can offer. For example, the loss of Health Advisers and nursing staff can limit support for patients. More than a quarter (27%) of BHIVA respondents reported that access to partner notification has been affected, yet this is a key method of increasing testing of people at a higher risk of HIV transmission. Although the majority of services (64%) still maintain counselling for the newly diagnosed, close to 30 per cent said that access is reduced.

Staff morale has been affected, with more than 80 per cent (81%) of BASHH survey respondents saying that staff morale had decreased in the last year, with almost half (49%) reporting it had greatly decreased. Respondents to both surveys cited the damaging impact sustained budget cuts were having on staff, as well as the pressures and stresses experienced by retendering, restructuring and the loss of experienced colleagues. Some describe the situation as being “at breaking point” and nearly all are worried about the future: more than 90 per cent (92%) of BASHH respondents said that they were worried, or extremely worried, about the future delivery of sexual health care in England.

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BHIVA/BASHH press release. Government funding cuts leave sexual health and HIV care at ‘breaking point’. (28 September 2018).

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Brazilian court suspends patent on hepatitis C medicine sofosbuvir

MSF press release

On 24 September 2018, a Brazilian Federal Court suspended a patent granted to US pharmaceutical corporation Gilead Sciences for the oral hepatitis C drug sofosbuvir.

The patent had been granted to Gilead the week before by Instituto Nacional da Propriedade Industrial (INPI), the Brazilian patent office. However, given the impact this granted patent would have on public health and on the government's budget, the court has suspended the patent and ordered the patent office to review its ruling, opening up the possibility for companies in Brazil to produce affordable generic versions of sofosbuvir. Key patents on sofosbuvir have already been rejected in China, Egypt and Ukraine, and decisions are pending or being appealed in several other countries including Argentina, India, Thailand and Russia.

Sofosbuvir is an oral, direct-acting antiviral drug that is safer, more tolerable and more effective than older hepatitis C treatments. Sofosbuvir forms the backbone of most hepatitis C treatment combinations, but sofosbuvir and its key companion drugs are priced out of reach for people who need them in many countries, including Brazil. About 700,000 Brazilians have the disease but no access to treatment due to its high price.

The Brazilian government has set the goal of eliminating hepatitis C by 2030, but with treatment at current prices, it´s very likely that budget constraints will limit the scope of national treatment plans. Therefore, it´s essential that competition among generic manufacturers is allowed, in order to lower prices and save more lives.

source

MSF press statement. Brazilian court suspends Gilead's patent on hepatitis C medicine sofosbuvir (26 September 2018)

https://msfaccess.org/brazilian-court-suspends-gileads-patent-hepatitis-c-medicine-sofosbuvir

TREATMENT GUIDELINES

UK PrEP guidelines now online (2018)

Simon Collins, HIV i-Base

New guidelines for using PrEP in the UK were launched last week at the BHIVA conference and cover all aspects for using oral PrEP.

The guidelines**,** jointly produced by BHIVA and BASHH (professional organisations that specialise in HIV and sexual health), include recommendations on assessment for PrEP, dosing, monitoring, adherence, access (including online) and cost-effectiveness.

The strong evidence for efficacy and safety includes use during pregnancy and for transgender people.

The guidelines emphasise that there are no potential interactions between PrEP and feminising or masculinising hormones but also recognise that there are limited data on efficacy for vaginal (frontal) sex. Daily dosing is recommended for both trans men and trans women.

Safety concerns from daily TDF/FTC in adolescents include 1.5 – 2.0% reduced bone mineral density at the hip and spine from daily PrEP for a year. Routine monitoring is not recommended unless indicated by a high FRAX score.

Monitoring for kidney function is essential and was discussed in responses to the consultation draft documents. Although a mild decline in renal function is common and generally reversible after PrEP is stopped, it has a higher risk for older people (defined as being older than 40). For example, if eGFR is 60-90 mL/min/1.73 m2, the guidelines recommend annual monitoring in people younger than 40 years but every six months in those aged above 40. If baseline eGFR is < 60 mL/min/1.73 m2, PrEP should only be used on a case by case basis.

Time to protection after starting PrEP is based on whether the protection is for anal or vaginal sex. For anal sex, this is after a double-dose 2-24 hours (based on the IPERGAY study) and for vaginal sex this is after seven days of daily dosing.

Similar times after the last exposure are recommended for stopping PrEP: two daily doses for anal sex and seven daily doses after vaginal sex.

HIV testing is recommended every three months. Results that indicate suspected HIV infection should be interpreted with a regional expert. If seroconversion is suspected, the guidelines recommend intensification to ART in people still on PrEP and not restarting PrEP in people who are already off PrEP.

Baseline screening for hepatitis C (HCV) is recommended for gay men and others

at risk as part of the full STI screening with three-monthly monitoring for HCV and bacterial STIs (chlamydia, gonorrhoea and syphilis).

Buying PrEP online is also supported, using advice from the community websites iwantprepnow.co.uk and prepster.info.

PrEP should be discussed on a case-by-case basis for risk factors other than sexual transmission. There are also limited data on efficacy on HIV transmission when the exposure route is from shared drug injecting, including slamming.

C O M M E N T

These first pragmatic guidelines are important for establishing the strong clinical evidence for routine use of PrEP in the UK.

The guidelines are also important for covering many aspects where data is limited. As such, they should be routinely updated as new results become available.

The guidelines were produced with a large degree of professional and community involvement, It is also welcomed as good practice that all comments from the open consultations are also available online.

Reference

BHIVA/BASHH guidelines on the use of HIV pre-exposure prophylaxis (PrEP), 2018

https://www.bhiva.org/PrEP-guidelines

https://www.bhiva.org/file/5b729cd592060/2018-PrEP-Guidelines.pdf (PDF)

OTHER NEWS

HIV positive mother is living donor to negative child: HIV is considered an acceptable outcome of liver transplant

Simon Collins, HIV i-Base

In a first from South Africa, researchers from University of the Witwatersrand, Johannesburg, report results from a successful liver transplant from an HIV positive mother to her HIV negative baby. Although there is evidence that the child has become HIV positive, this was an acceptable and better outcome to not having the transplant.

The results are detailed in an open-access fast-track article in the journal AIDS. After more than a year of follow-up, both the donor and recipient are healthy, without complications. [1]

The case involved a 13-month old baby with end stage liver disease due to progressive obliterative cholangiopathy (biliary atresia). The child had been added to the waiting list for a deceased donor liver transplant when a 7-month infant. Although the mother wanted to be considered for a living donor, this was initially declined (due to international transplant guidelines).

Both parents are HIV positive and the mother had been diagnosed before pregnancy, with a CD4 count of 169 cells/mm^3. The mother used ART before, throughout, and after pregnancy (efavirenz, lamivudine, tenofovir-DF). The baby received standard prophylaxis for 6 weeks and was exclusively formula fed – and was confirmed HIV negative.

Although the expected waiting list time was about seven weeks, the child was still waiting almost six months, before being urgently admitted to intensive care with life-threatening complications. The mother repeated her request to be a donor and this was urgently considered and approved by the institutional review board. Factors affecting the decision were the mother having an undetectable viral load for >6 months, a CD4 count >200 cells/mm^{3}and no active co-infections or complications. Both parents consented to the transplant operation.

The transplant was reported as standard, although post-operative recovery for the child was complicated by pneumonia and an epigastric collection requiring surgical drainage. Oral corticosteroids and tacrolimus were continued in the child for six months afterwards when corticosteroids were weaned. The child remains on oral tacrolimus only, dose-adjusted with therapeutic drug monitoring and has since been well with normal catch-up growth.

HIV prophylaxis for the child with integrase-inhibitor-based ART (raltegravir, lamivudine, abacavir) was started before the transplant, throughout recovery and has been continued since. However, although HIV viral load testing remained negative, indeterminate antibody results at day 225 using western blot showed antibodies only to Gag and Pol (but not Env) indicating potential HIV seroconversion in the child. The positive antibodies might also be linked to the donor organ however.

Ultrasensitive viral load (PCR) tests have been negative, with no proviral HIV DNA in plasma PBMCs or CD4 cells.

No complications have been reported for the mother.

So far these short-term results are extremely promising in terms of the transplant but disappointing that the baby may have become HIV positive. Future management includes continuing HIV treatment for the child.

C O M M E N T

This is the first report of an HIV positive living donor to an HIV negative recipient. Although the transplant was a success and it has been a life-saving operation, the child is likely to now be HIV positive.

Part of the risk evaluation for the transplant included the recognition that with optimal HIV treatment, the benefits to the child, even with a possibility of HIV infection, outweighed the risks.

The management of the child by continuing on ART is clearly essential. The potential for latently infected cells in the donor organ to remain active for many years, perhaps decades, will make lifelong ART in the baby the most likely management plan for many years.

Early and continuous use of ART throughout might have the potential to eradicate HIV at some point in the future. However, this is likely to still require many years of viral suppression on ART and the only way to test for this possibility would be to stop HIV treatment as part of a very carefully controlled protocol. There should be no urgency to try this.

Unfortunately, HIV viral rebound has nearly always been reported even when ART prophylaxis is started in very early infection. This will complicate the timing of any future decision to stop ART.

South Africa has allowed HIV positive donors to recipients who are also HIV positive since 2008. [2]

The US only allowed HIV positive people to receive organ transplants from HIV positive donors in 2016, but only in cases where the donor had died. [3]

HIV negative recipients of organs from an HIV positive deceased donor have been reported in a case where initial HIV screening was missed. [4]

Reference

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LGBT HIV activist Zak Kostopoulos murdered in Athens: campaign calls for justice

Simon Collins, HIV i-Base

European HIV treatment activists are calling for justice after the murder of the Greek human rights activist Zak Kostopoulos in central Athens on the afternoon of Friday 21 September 2018.

Early reports included that Zak Kostopoulos's HIV status and sexuality were a factor in his attack and in the lack of police investigations.

The following information is compiled from a new release from the European AIDS Treatment Group (EATG).

On Friday 21 September, Zak Kostopoulos, died as a consequence of brutal beatings in Athens Greece. Zak was an HIV positive, sex positive, queer, human rights activist and defender, also raising awareness performing as drag queen Zackie Oh.

We are mourning him, shocked at the lynching that led to his death, the way in which the police officers acted and the public discourse that was constructed and spread to legitimise the violence perpetrated. We have been dismayed at the way in which the investigation has been carried out by Greek authorities.

The footage of the attack indicate that Zak was inflicted inhuman and degrading treatment that amounts to torture. We call all relevant Greek authorities for a swift, thorough, independent and impartial investigation into the events so that the perpetrators of the violence are brought to justice. The examination ought to take into consideration the motivation of the perpetrators.

We ask for due process and respect for the deceased, who if he were living would be presumed innocent. We call on the authorities to ensure the rule of law and respect for human life so that similar tragic events are not allowed to occur again.

Timeline regarding the death of Zak Kostopoulos

The incident took place on the afternoon of Friday 21 September 2018 between 14.00 and 15.00 in the centre of Athens, near Omonoia square.

Media reports from Friday evening reported that a thief died after trying to rob in a jewellery store. A video surfaced that shows the alleged thief to be beaten up by two unidentified persons while trying to escape the store. On Saturday 22 September, it

was announced that the person was Zak Kostopoulos, an LGBT, HIV activist, also performing as drag queen Zackie Oh.

Rumours started circulating in Greek about the person being under the influence of substances, carrying a knife, entering the shop to rob. Mainstream media constructed the narrative of a junkie trying to break in and steal. Fringe media also referring to as faggot, AIDS-patient, 'he was asking for it', 'it served him right'.

This is when LGBTI, drag queen groups, community lawyers and civil society actors started to openly question the version provided by media. On Sunday, it was claimed that Zak Kostopoulos had entered the shop to escape a fight at the café nearby by where he was.

A discussion that remains low in media priorities: the brutal beating up of a person which amounts to inhumane, degrading treatment and torture as well as self-justice is unacceptable. This discussion is mainly put forth by community and citizens in social media.

On Sunday, one of the two persons who attacked Zak, was put under investigation and has been released under restrictive measures since then. The second person involved in the assault, a neighbouring real estate store owner with links to extreme right groups, was identified on Wednesday and was put under investigation on Friday. He has also been released under restrictive measures.

On Monday 24 September, the coroners reported that the first autopsy was inconclusive regarding the cause of the death and that toxicological and histological examination results will be available later.

On Thursday 27 September, a video surfaced showing eight policemen holding Zak down to handcuff him exerting excessive violence. The events in this video follow chronologically those from the first one. The Minister of Citizen Protection – in charge of the police – stated that they will investigate the case thoroughly.

On Friday, investigation concluded that there were no fingerprints in a knife that allegedly Zak was carrying. Media reported that a knife was found outside the store and it was thrown in the store after by an unknown person. A witness claimed that it was a food knife that Zak found from the café opposite and used to protect himself while he was held down.

On Wednesday 3 October a third video surfaced. This video comes from the CCTV of a store nearby. The events chronologically precede those of the previous videos. It shows three people bullying Zak in the pedestrian street before he seeks refuge to the jewellery store.

Further information

Media reports, including other calls for justice and links to the online video footage are included in the reference article below.

For further information, please contact: communication@eatg.org

#JusticeForZak

#EATGForZak

#ZakKostopoulos

Reference

EATG press statement. We call on the authorities to ensure that justice for Zak Kostopoulos is done. (1 October 2018).

http://www.eatg.org/news/we-call-on-the-authorities-to-ensure-that-justice-for-zak-kostopoulos-is-done