

UK CAB

HIV treatment advocates network

CAB 39: London HIV drug prescribing and Hep C 8 July 2011

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Presentations are all available to download for the July 2011 meeting at:
<http://www.ukcab.net/2011/08/uk-cab-39-presentations/>

Members attending

No	Name	Organisation	Destination
1	Adebisi Alimi	Migrant African MSM Network, Europe	London
2	Albert Biete	Personal	Derby
3	Angelina Namiba	Positively UK	London
4	Angeline Marang	HIV i-Base	London
5	Ben Cromarty	North Yorkshire AIDS Action	Yorkshire
6	Brian West	Waverley Care	Edinburgh
7	Claudia Stoicescu	Harm Reduction International	London
8	Damian Kelly	George Hose Trust	Manchester
9	David Rowlands	Baseline Magazine	Birmingham
10	Elijah Amooti	The African Eye Trust	London
11	Emma Rezel	London School of Hygiene and Tropical Medicine	London
12	Fabiola Bayavuge	Black Health Agency	Manchester
13	Georgina Robson	The Haemophilia Society	London
14	Gertrude Anyango-Wafula	Black Health Agency	Manchester
15	Godwyns Onwuchekwa	Homerton University Hospital	London
16	Jeff Ukiri	Personal	Manchester
17	Jet Lengalenga	Personal	London
18	Juliet Bosa	Guys and St Thomas NHS	London
19	Mark Platt	Personal	London
20	Memory Sachikonye	UKCAB	London
21	Michael Marr	Waverley Care	Edinburgh
22	Paul Clift	King's College/UKCAB	London
23	Richard Oakley	Personal	Stevenage
24	Robert Fieldhouse	Baseline Magazine	Birmingham
25	Robert James	Brighton Clinic	Brighton
26	Roger Pebody	NAM	London
27	Silvia Petretti	Positively UK	London
28	Simon Collins	HIV i-Base	London
29	Stewart Murau	Personal	Manchester
30	Tsepo Young	NHS Dumfries and Galloway	Stranraer
31	Virginia Cucchi	Personal	London

Speakers:

Yusef Azad, National AIDS Trust

Dr Sanjay Bhagani, Royal Free Hospital

Apologies:

Mark Mpungu, AAEGRO

Gus Cairns, NAM

Programme:

Chair: Ben Cromarty	
09:30 – 10:00	Registration, refreshments and expenses
10:00 – 10:15	Welcome, introductions, UKCAB updates
10:15 – 10:30	Introduction to London HIV drug prescribing – Simon Collins, HIV i-Base
10.30 – 11.00	NAT Response to London HIV drug prescribing – Yusef Azad, NAT
11:15 – 11.30	Break
11:30 - 12:00	Moderated discussion on London HIV drug prescribing
12.00 – 12:30	BHIVA standards of care document: community input – Roger Pebody, NAM
12:30 - 14:00	Lunch
Chair: Silvia Petretti	
14:00 - 15:15	Hepatitis C - what next? - Dr Sanjay Bhagani
15.15 - 15.30	Break
15:30 – 16:00	UKCAB AOB
16.00	Close

The meeting observed a moment of silence on the recent passing away of a UKCAB member, Maurice Hebert. A celebration of his life was to be held on 14 July at the Riverhouse in Hammersmith.

Introduction to London HIV drug prescribing - Simon Collins, HIV i-Base

Simon Collins gave an input summarising the position and highlighting some significant issues for the HIV community.

He stressed the importance of understanding the background to this:

- NHS budgets have effectively been frozen for 2011 and probably 2012, so there is no allowance for inflation, currently around 5%.
- Furthermore, for the NHS in general, and for HIV specifically, it is also clear that the number of people accessing treatment is growing. So there was a need to find a way to make the London drug budget go further.
- Since nearly 20% of the London drug budget is for HIV drugs, then clearly this is a key area of interest.

In London, all the NHS trusts work together to purchase drugs at an advantageous price from the pharmaceutical companies. As a result, they probably achieve the lowest price for drugs in the UK. Whilst this may be advantageous for London, as treatment activists, we might want to question this – prices in the rest of the UK are possibly higher as a result of the low pricing in London – is this really equitable nationally? Why is there not a national drug price? (Clearly, London resists this idea, as they would end up paying more for their drugs).

So the London commissioners arranged a bidding process for HIV drugs for the next 2 years. The process did involve community representation, but because the discussions were commercially sensitive, there has been some concern from the community that they did not really get to be involved until after the event. A cornerstone of the process was that price would be considered only if the drugs being considered were clinically equivalent – taking drug A versus drug B is clinically the same – so then if drug B is cheaper, we would go with that.

Despite concerns about the process, the outcome for London may not be too bad. A saving of £8M was the target, and this can be achieved in the large part by switching the recommended regimen for new ART-naïve patients from Atripla (Truvada and efavirenz) to Kivexa and efavirenz. This involves taking 2 pills once a day rather than 1 pill once a day, which was not considered to be a significant drawback for HIV-positive people. Since Kivexa contains abacavir, care must be taken for those HIV-positive persons who have hypersensitivity to abacavir (a test is available for this) and for those with any risk of cardiovascular disease (CVD) such as age, family history of CVD, smoking and lifestyle.

There may be some switching of regimen for some people who have already started treatment, and it is this area that is of particular concern. The view of many advocates is that patients should be switched for clinical reasons, not financial ones. Deciding on whether or not a particular regimen is truly equivalent for an individual is complex, and needs to take full account of the HIV-positive person's experience on the drug with regard to side effects. Equivalence should not be restricted to control of viraemia, but needs to take into account the side-effects.

There are also psychological and emotional issues involved when patients switch drugs. HIV-positive people are concerned that switching may be harmful: if a treatment is working well, why take the risk of switching to something new and unknown? As advocates, we may need to help HIV-positive people understand that switching HIV regimens, if done properly under the care of a clinician, is simple and in many cases can offer benefits. Perhaps we need to produce a simple leaflet highlighting switching?

Already, though, there are anecdotal cases being reported where patients have been switched without being told why, or even that they have been switched – they only saw that that the drugs they got from pharmacy were different. We need to ensure that any switch of regimen is only done after a discussion with the clinician, and with patient consent.

NAT response to London HIV drug prescribing – Yusef Azad, National AIDS Trust (NAT)

Yusef Azad is the Director of Policy and Campaigns at [NAT](#). He acknowledged that NAT did not have the treatment expertise of UKCAB or i-Base, but rather, focuses more on policy. The concern is that NAT have achieved a reasonable result from a flawed process, but in future, there is need to be sure that the process is a good process.

The issues in future might be more acute: what if there are then generic drugs at a fraction of the cost? What pressures would there be then to switch regimens?

The issue of drug costs for London needs to be looked at in the context of three wider issues:

- i. The consortium was handed a flat budget. But policy-wise, who decides on this number for the HIV drug budget? Is keeping it flat sustainable? Is there actually enough funding for HIV as numbers continue to rise?
- ii. There was an issue with regard to service costs, and a push to move to home delivery for HIV drugs, saving VAT. What other aspects of wider HIV care may be considered? Should the focus not be on better rather than cheaper?
- iii. If in the long term, we want to have a lower treatment budget, surely there needs to be more focus on prevention?

The process used was done in good faith and done reasonably well, although it is clear that there was not a full and transparent discussion with the HIV community. As the community we need to be very clear about the principles driving the process. In any decision taken at the very least there must be no harm done, and ideally, some good should be done, and there must not be a focus just on price. If the process was indeed flawed, then we need to challenge it now, so that it is better next time.

NAT has some concerns about the outcome, not so much with treatment-naïve patients but more with the issue of switching stable patients onto a new regimen. A possible further outcome of a process such as this every two years is that there might be a different “winner” from the commissioning process, resulting in switching again. Are we happy with a scenario where there may be switches dictated by price every two years?

There have been few clear assurances about the process of switching and the degree of patient involvement in switching. It should be made clear that switching will only occur with patient consent, and that in any discussion about switching between patient and clinician, the discussion needs to be clear and without bias, outlining pros and cons, and also raising the pricing issue.

No individuals or groups who may be regarded as “easy targets” for switching should be so targeted by clinicians struggling to meet their financial goals.

It is also not clear what the financial (or other) sanctions might be for clinics not hitting their targets. There are already examples of poor practice with regard to switching. How do we in the HIV community respond to this?

It is clear that this is a difficult process. NAT and the UKCAB need to ensure that next time round, the process is clearer and improved; that there is much better communication about the process; and we need to deal with any specific issues arising from the analysis of this process.

There is need for better communication and cooperation between the various HIV organisations.

Moderated discussion - Simon Collins, HIV i-Base

1. NAT did not involve directly the UKCAB in their response, agreed on better and clearer involvement in future to give a broader HIV voice. Meeting also acknowledged that Commissioners' communications has been difficult and contributed to problems. NAT are seeking much more detail about the process, with a view to improving it next time round.

Action: Should we have a working group?

2. Should there not be some survey done to see how patients feel about switching and also about 1 versus 2 pills a day?
3. Many patients now only see their doctor annually – how will this impact on the take-up of the drug deal, and what might the impact of that be on hitting targets? Some allowances for this kind of thing were made in the assumptions underlying the deal.
4. People are concerned about switching in general. We as advocates need to support anyone who for whatever reason is contemplating switching.

Action: We need to provide information and reassurance about how to switch safely.

5. The NHS has a poor track record for implementing change, and their record on patient involvement is not great either.
 - a. **How can we keep track of what is happening? Should there be some audit of the process?**
 - b. **What is the impact of the idea of treatment as prevention?**
6. We need to have a way of collecting information about poor practice, and a way of collating it and feeding it back to the commissioners. We also need to understand what the savings are based on.

Action: Currently, it appears that several organisations are collecting feedback – we need to find a way of collating all this without duplication.

7. Clinical outcomes are paramount on the new commissioning process; there is concern on how this process will influence the new BHIVA guidelines that are from 2008 and may not be current best practice.

Action: As treatment activists, we need to recommend to BHIVA to provide six-monthly updates from a live e-document rather than wait 3-4 years before a new guideline is issued.

8. About 85% of the drugs prescribed in the NHS are generic. Within the next few years, efavirenz, nevirapine, saquinavir and 3TC will come off-patent.

Q: What if there is then generic pricing – at a tenth of the current cost; how would we respond to that and would be it OK to take 3 pills vs 1 a day?

9. HIV is no longer being treated as 'special' and we need to strike a reasonable balance between being too understanding and accommodating. Whilst we should not be overambitious, we do need to set a high target – not just "no harm" but "better care". We need to get to bottom of how this process is working, being realistic and sensitive to cost pressures.
10. NAT wrote to Claire Foreman with their concerns and got an answer in two weeks while UKCAB waited over two months.

Action: Follow up and document outcomes, how do we collate the data and whom do we send it to?

BHIVA standards of care document: community input – Roger Pebody, NAM

Roger Pebody is the community rep on the BHIVA standards committee and led the discussion on updating the BHIVA standards of care document to have input from a wider range of people. Recommendations for update from the community were:

1. Importance of good referral pathways - to other medical services, psychosocial support, voluntary sector, social care.
2. Document needs to clarify the nature of links with primary care.
3. Auditable standard: number of patients who have a personalised care plan.
4. Support for the 'spoke and hub' model, but concern that it's unclear at present whether clinicians know they are working for a unit or a centre? Lack of clear naming of these.
5. Example of haemophilia services pointed out - specialist centres are designated; there are auditable standards; if a specialist centre doesn't meet these standards, the clinician's professional body recommends to commissioners that the centre is stripped of its 'specialist' status.
6. Support for robust/meaningful targets, especially in relation to patient experience.
7. Importance of monitoring for co-morbidities, diseases of ageing.
8. Auditable standard: proportion of patients starting therapy in line with guidelines.
9. Culturally appropriate support services.
10. Endorsement of standards document by DH will be important.
11. The standards document should be 'translated' into a patient-friendly resource, explaining what they can expect.

HCV – where next? – Dr Sanjay Bhagani, Royal Free Hospital

Dr Bhagani is a doctor in Infectious Diseases/HIV Medicine and General (internal) Medicine at the Royal Free Hospital in London. He has a specialist interest in the management of HIV in-patients with complex multi-system and opportunistic infections and patients with viral hepatitis co infections. His presentation was on the principles of where hepatitis C (HCV) is going in the next few years, and where we may be in the next 10 years.

HBV can be kept under control by your immune system; HCV is curable but not HIV and 10-15% of patients who get HCV spontaneously clear it. Response to treatment is measured by change in HCV viral load at different time points. The most sensitive tests can detect >5 copies/ml. The standard drugs used for treat HCV are pegylated-interferon (PEG-INF) - injection with ribavirin (RBV) – oral tablet. There is a genetic variation in HCV treatment; studies show that Asians are better than Africans at responding to PEG-INF treatment.

HCV treatment definitions:

- **SVR** (Sustained Virological Response) - when there is no HCV detectable in the blood six months after a person completes HCV treatment – which can be regarded as a cure, and it is an indication of long-term remission.
- **SVR-12:** - there is no hepatitis C virus detectable in the blood 12 weeks after completion of HCV treatment. However, if you HCV viral load hasn't dropped by week 12, chances of getting SVR are very slim.
- **RVR** (Rapid Virological Response) – there is no detectable hepatitis C virus in the blood after 4 weeks of treatment. An RVR is a good indication of SVR, but it is not as accurate for predicting who is unlikely to have SVR. Therefore, HCV treatment should not be discontinued if there is no RVR. RVR is mainly used in research.
- **EVR** (Early Virological Response) - HCV viral load has dropped by 99% (2 logs), or is undetectable after 12 weeks of HCV treatment. An EVR is a good predictor of the ultimate response to HCV treatment. If a person does not have an EVR, their chance of SVR is very low (1-4%). Usually, HCV treatment is discontinued in people who do not achieve an EVR.
- **ETR** (End-of-Treatment Response) - no detectable hepatitis C virus in the blood at completion of HCV treatment. ETR is usually higher than the SVR rate, because the HCV may reappear in a person's blood after completion of HCV treatment.

Despite the failure to achieve SVR with PEG-INF in non-responders patients, treatment may slow the progression of HCV to cirrhosis, although this has not been shown for certain.

HCV genotypes:

- 1, 2, and 3 are widely distributed throughout Western countries and the Far East (Japan, China, Taiwan, Thailand). In the UK, there are over 300 000 HCV cases and half are genotype 1.
- 5 and 6 are mainly confined to South Africa and Southeast Asia
- 4 is predominant in the Middle East and Central Africa

An online resource, [Prometheus index](#), can be used to predict SVR after treatment of HCV with PEG-INF plus weight adjusted ribavirin. It is as good as a FibroScan and is free in the UK as it is unlicensed. People who carry a particular type of the IL28B gene have a good chance of achieving SVR when treated with PEG-INF.

The future of HCV treatment:

An improved understanding of the HCV life cycle has identified several potential targets to interrupt HCV replication. These newer anti-HCV agents in development target several viral enzymes, such as the NS3/4 protease inhibitors, NS5A inhibitors and NS5b polymerase inhibitors.

Two PIs boceprevir (BOC) and telaprevir (TPV) used to treat HCV genotype 1 and 2 are in Phase III and have been approved in the US but not yet in Europe. European approval is expected maybe around August 2011 at the earliest.

TPV and BOC are inhibitors of HCV NS3/4A serine protease and will be the first direct acting agents (DAAs) for treatment of patients with chronic HCV. The treatment provider must effectively manage dosage and adherence to the regimen to avoid emergence of resistant variants of HCV. Close monitoring of patients, awareness of drug interactions, management of known TPV and BOC side effects, and strategies for reduction or discontinuation of individual drugs in the treatment regimen will be critical to ultimate success of triple therapy.

These with other new therapies in development are very likely to transform the treatment of HCV, hopefully allowing viral eradication to be the "norm" for all HCV patients, irrespective of baseline factors such as age, race, viral load, or genotype.

During the study, TPV was taken three times a day (every eight hours) with a fatty meal. As it was a short trial, lipids were not measured which is a concern for long-term health. Patients were given alarm clocks to help with adherence, which is usually a big problem.

Patients going onto the BOC were treated for four weeks PEG-INF/RBV to provide antiviral activity prior to introduction of BOC to enhance virologic response, reduce risk of resistance and predict response to BOC-based triple therapy.

Results from phase II and III trials indicate that triple therapy with TPV or BOC in combination with PEG-INF/RBV increases SVR rates from about 40% to nearly 75% in HCV treatment naïve patients with HCV genotype 1. This triple therapy is also effective in treatment experienced patients especially relapsers, but also null responders.

TPV-based triple therapy is more effective to PEG-INF/RBV in achieving SVR. Patients achieving eRVR can cease PEG-INF/RBV treatment at 24 weeks without compromising SVR, although 12 weeks of TPV may be superior to 8 weeks.

BOC-based triple therapy is more effective than PEG-INF/RBV in achieving SVR. Pre-treatment with PEG-INF/RBV response predicts likelihood of SVR but a third of patients with <1 log₁₀ decrease in HCV achieved SVR. Patients with eRVR can stop treatment at 28 weeks. Anaemia is common and often requires treatment.

Side effects/safety

- Boceprevir – anaemia and dysgeusia (bad taste in the mouth).
- Telaprevir - rash, anaemia, pruritus (severe itching, often of undamaged skin) and nausea.

Resistance

- HCV develops resistance when exposed to PI monotherapy after 24 hrs of exposure and addition of IFN decreases emergence of these resistant variants. The question raised was whether HCV would persist after you stop therapy and yes, at a low level.

TPV and BOC increases SVR in both treatment naïve and treatment experienced patients. African Americans respond less well to triple therapy, but still higher than PEG-INF/RBV. TPV and BOC have the potential to shorten therapy duration.

Challenges:

- Side effects: rash, anaemia, dysgeusia, anal pain
- Viral resistance will require careful monitoring. Protease inhibitor must be stopped at initial sign of resistance. Adherence must be emphasized.
- Drug-drug interactions need to be checked before proceeding with treatment.

Future questions on HCV treatment:

- Optimal management of HIV, post-transplant, non-1 genotypes?
- Twice vs. thrice daily dosing?
- Should all patients have IL28b testing?
- Which IFN – a or 2b?
- Which PI is better?
- Other pipeline:

- NS5B polymerase inhibitors
- NS5A inhibitors
- Direct Acting Agents (DAA) combinations

More information about HCV pipeline drugs can be found at: <http://i-base.info/htb/15222>

Q & A

Q: HIV co-infection trials are not interesting to pharma, shall we put pressure?

A: Pressure should come from government.

Q: What percentage of HIV-positive gay men in London have HCV?

A: 10%

Q: There is vitamin D deficiency in HCV patients on PEG-ING/RBV response

A: Studies have shown higher responses in Europe and US.

Q: What is in the HCV drug pipeline?

A: Standard of care is about to change; all future studies should use BOC and TPV rather than PEG-INF/RBV as comparative.

Q: Of the two licensed drugs, which do you think is better?

A: TPV is probably advantageous due to shorter treatment time and no anaemia side effects.

Q: Will there be access issues in terms of cost and where the patient lives?

A: NICE are putting together a treatment algorithm.

Q: How can you communicate that resistance can develop in 24hrs on PI monotherapy to the patient effectively?

A: This can be done by telling patient that they need about 85% adherence and there is need to provide adherence support.

Q: Is lack of adherence due to poor life style?

A: Most HCV patients are not used to taking meds compared to HIV patients, it is a completely different group of patients.

Q: Is there any new data PEG-ING/RBV and conception?

A: There is still no new data and should be avoided by women planning to conceive before starting treatment.

Comment: In Manchester have no follow up; there is no adherence support especially in migrant communities. It is therefore important to engage doctors dealing with mono infections

Note: The [drug interactions website](http://www.hiv-druginteractions.org/) also has a section on HCV, link: <http://www.hiv-druginteractions.org/>

Dr Bhagani was asked to talk about kidney and liver transplants in HIV positive people.

Kidney and liver transplants are no longer contraindicated as in the past. Transplants amongst HIV positive patients are safe. There are legal barriers in other countries, but not in the UK. Recipient could be affected if donor is on different HIV drugs. There have been higher kidney transplant rejections in HIV patients compared to HIV negative ones. In liver transplants, there have been cases of HCV recurring.

Q: Any key conditions to look out for when deciding on a donor?

A: Its mainly age, health history, CVD and diabetes.

Q: For a patient in stage 4 of CKD; could you switch to raltegravir in preparation for an imminent kidney transplant? Will you need to stay on raltegravir after the transplant?

A: The drug switch is usually soon after transplant for 6 months as that is when rejection is highest, then switch back to usual therapy.

Q: There is lack of info on drug-drug-interactions, how can we share more info on the new drugs?

A: The community needs to ask pharma to start acquiring data for drug-drug-interactions during phase 1 trials.

Comment: There has been NO new drug for TB since 1972 yet there are so many in the pipeline for HCV.

Next meeting:

Topic: Gender and HIV research

Date: 21 October 2011