United Kingdom
Community Advisory Board (UK CAB)
HIV treatment advocates network

CAB 29
01 May 2009

Minutes of meeting

Contents:

Presentations for the May meeting are online:

http://www.ukcab.net/may09/index.html

Programme:

09:30 - 10.00	Registration, refreshments and expenses
10:00 -10:05	Welcome and Introductions
10:05 – 11.00	Introducing the HIV Vaccine Advisory Board Ken Legg, MRC and St Mary's Hospital
11:00 - 11:15	Refreshment Break
11:15 - 12:30	Resistance Explored – interactive workshop: Simon Collins Company pre-meeting: Simon Collins
12:30 - 14:00	Lunch
14:00- 15:00	GSK, abacavir, pipeline drugs and merger
15:00 - 15:15	Refreshment Break
15:15 - 16:00	Updates, Feedback & AOB
16:00	Close

Attendees:

Name	**Organisation**	
Alastair Hudson	iPPF – Stigma Index UK	London
Angeline Marang	HIV i-Base	London
Badru Male	CHAT	London
Ben Cromaty	North Yorkshire AIDS Alliance	Yorkshire
Brian West	Waverley Care	Edinburgh
Elijah Amooti	The African Eye Trust	London
Jeff Ukiri	Black Health Agency	Manchester
Jo Murray	National AIDS Trust	London
Jo Robinson	Terence Higgins Trust	London
Joram Barigye	THT - Woking	Woking
Lucy Stockpool-Moore	IPPF – Stigma Index UK	London
Memory Sachikonye	UK CAB	London
Pamela Mahaka	London	London
Richard Blackburn	The Brunswick Centre	Halifax
Samuel Serunjogi	London	London
Sepo Young	NHS Dumfries and Galloway	Stranraer
Simon Collins	HIV i-Base	London
Svilen Konov	HIV i-Base	London
Toju Cline-Cole	Terence Higgins Trust	London
Walter Zonke	HIV i-Base	London
Zhana Books	London	London

Meeting co-chairs: Badru Male, Sepo Young
Minutes: Memory Sachikonye
Apologies: Michael Marr, Gus Cairns, Mohamed Jowata

Introducing the HIV Vaccine Advisory Board, Ken Legg, MRC and St Mary's Hospital

Why is there no effective HIV Vaccine?
This presentation covered reasons why is there still no effective HIV vaccine. This included a brief HIV vaccine history and explained why 25 years later there is still not effective vaccine that has been licensed and scientists cannot envisage one becoming available in the next 10 years.

Current situation
- Scientists are trying to target the envelope protein that HIV uses to attach to the CD4 cells, but this protein is different from person to person and this limits any vaccine to the strain used to develop the vaccine. They are also working on the more stable parts of the protein and trying to boost the response using an extra component that helps present the vaccine called 'adjuvants'.
- Next target is to stimulate the T-cell response of the long term non-progressors, hoping to control of viral load. As the celluar response was mainly to core proteins, not envelope the bodies response is unlikely to be quick enough to prevent infection.
- Working on ways to broaden the core and envelope cellular response and also looking on ways for better techniques to measure the cellular immune response.
- Thai Phase III trial is exploring a combination regime with an avian vector prime and protein boost. The first two futility analyses suggest the trend is in the right direction, report will be out in late 2009.

Questions:
Q: Everyone's HIV is different, does that affect the way the vaccine is developed? Do you have to develop individual vaccines?
A: The virus mutates so much that a patients' virus from 10 years ago, will be the same today. This is why researchers are trying to make the vaccine work on the parts that don't alter, the envelop on the outside. By the time your immune system has kicked in, it is too late, we need a general vaccine that will destroy anything that comes along.

Q: Therapeutic or preventative vaccine trials?
A: Therapeutic vaccines could be used to come off treatment; preventative ones are still a challenge, with no successful results from any trials.

Comment: Need an open access transparent site of all trials in the UK on VaccNet.
Q: What is the timeline for this site to be set up?
A: Around September 2010.

Q: Any prospect from bone marrow transplant in Germany - vaccine ideas?
A: Don't know much about that. This is the process where the doctors replaced the patient's stem cells that now generate new immune cells with cells that HIV can't affect. It's not an easy process; there is a 30% chance of dying.

The full list of ongoing work on vaccines in the UK is available on the slides.

HIV Vaccine Advisory Board
Jo Robinson is the UKCAB HIV Vaccine Advisory Board member. The board is being set up in support of the future trials and to initiate a CAB specifically for HIV vaccines. Board will include

members of the HIV community, VaccNet network and trial team members. Role of the board is to help in the development of the protocols and recruitment strategies for trials.

Need for advocate input
It was agreed that it is important for UK CAB to be involved in anything that the MRC does, as this will inform the general public and volunteers better about ongoing trials. UK CAB was also urged to be involved in other trials such as rectal microbicides, there is need to develop a formal link.

Discussion:
Q: - Is there a need /role for such a board?
A: It is important for UKCAB to be involved in anything that the MRC does. Recruiting volunteers is difficult, needs commitment and an understanding of the risks and impacts on individual health care providers. Have the sense of the HIV sector and UKCAB being involved so as to be able to inform the general public. Public needs to understand that they are not going to be exposed to HIV. This would then stop onward transmission and no new infections.

Q: Would it be a good idea to be involved?
A: It is good to be involved early on in the development of study design and protocols rather than just be asked to review a final version.

Q: How many people should be on it?
A: Preferably at least two; one already recruited and would have one more to be mentored.

Q: With other general trials, I been told its confidential and cannot be discussed elsewhere, makes it difficult to discuss in a community environment.
A: UKCAB involvement can help map out what volunteers can talk about, develop trust, and work it out together with MRC. There is lots of ongoing other work in other trials such as rectal microbicides, etc. I would like the CAB to be linked into that kind of work. Need to develop formal link.

HIV and Drug Resistance: Simon Collins, HIV i-Base

Simon Collins led an interactive workshop on facts and questions related to resistance (Rx), a great chance for all members to participate.

The discussion involved each person contributing a fact or question relating to resistance.

Facts about Resistance (Rx):

a. Rx is related to genetics. A virus has genetic material similar to other living organisims: plants, bactgeria, animals and humans. Every living thing can evolve with each new generation. Although the HIV structure is very small compared to human DNA, it reproduces very, very quickly and mutated and evolves with each cyle.
b. HIV makes errors when reproducing. It doesn't copy itself exactly and some of these errors (called mutations) will stop drugs working

c. Resistance can stop drugs stop working
d. Resistance is permanent. This means you can't go back and re-use a drug later, or use similar drugs. The only exception is 3TC or FTC where the resistance also makes the virus weaker and this reduces viral load.
e. Resistance tests only give information on the drugs you are taking when the test is run.
f. Resistance causes viral load to go up (because the drugs are not longer working).

g. Cross-resistance means that resistance to one drug can also mean resistance to other drugs in the same class (PI, NRTIs, NNRTIS and integrase inhibitors etc)

h. Every HIV+ person should have Rx test before starting treatment – so as to ensure the person doesn't have a resistant strain at infection and doesn't rely on drugs that will not be active.
i. Prevalence of resistance in newly diagnosed people in the UK varies: up to 15% have one resistant mutation. Multidrug resistance to 2 or more classes is still relatively low (in less than 2% of new diagnoses)
j. Structured Treatment Interruption (STI)– can lead to Rx. If you need to stop treatment, talk to your consultant. This is because different drugs leave the body at different speeds and can leave you on monotherapy (ie only one active drug) which will increase the risk of resistance. A recent study form Steve Taylor suggests hatever treatment you are on – switch to Kaletra, goes through Rx zone quickly. Some drugs are far more vulnerable to Rx, PIs more solid in terms of Rx, some NRTIs are more sensitive to Rx.
k. In other parts of the world, the main cause of Rx is due to interuptions in drug supply – where hospitals or pharmacy run out of stock.
l. Resistance is important in the options to prevent Mother-To Child prevention – mothers get resistant to nevirapine from one single dose. This is why the recommendation is generally to use triple therapy to all pregnant women.

Questions about Rx:

a. How adherent do you need to be to prevent resistance?
   A: 100% is best guide. Anything less is just luck. Everyone occasionally misses or is late with a dose, but if this happens regularly (every week) then the risk of resistance is much higher, There is usually a window period fo 1-2 hours for most drugs.
b. How and when should one have Rx test?
   A: i) On diagnosis (to check you don't have a resistant strain)
   ii) Before starting treatment (if you have been at risk of reinfection)
   iii) If viral lad doesn't drop by one log within one month of starting treatment
   iv) Before making any treatment change if your viral load is detectable.
c. Can you request Rx test if you have been on the same medication for a while with an undetectable viral load and have no problems?
   A: There is no point You, need a VL of at least 500 copies/mL for the test to work. If VL is undetectable, by definition, you do not have Rx.
d. Treatment interruptions/break – any hope?
   A: This is a research area. The largest interruption study (SMART) showed that generally being on treatment protects you form many serious illnesses, including heart disease, liver failure etc.
e. Co-infection: can treatment for one virus impact on the drugs use to treat other viruses?
   A: Only if the same drugs works on both viruses. Some hepatitis B drugs also treat HIV (tenofovir, 3TC, FTC). 3TC resistance to hepB is different to HIV because it involves different chances in the structure of each virus. This is a specialist area. Everyone should have a Hep B test yearly.
f. What specific drugs can use if you need to take an STI?
   A: Switching to a boosted PI for a month when you stop an NNRTI-based combination is probably safest..
g. Is it possible to have caught HIV 10 years ago, get diagnosed today and have Rx?
   A: This is much less likely, Resistance could only be to drugs that were available 10 years ago, and would be difficult to detect. You could have been reinfected within that time though.
h. What happens to Rx over time?
   A: Resistant virus is not as fit as non-resistant virus (called 'wild-type) If you are not taking

treatment, or you stop taking the treatment you are resistant to, then wild-type virus takes over and becomes the main virus. However, even though you may not be able to test it, resis itant virus remains in small quantities (called 'archived' virus).

i. If you have been on 4 failed regimes, are there chances that you are resistant to 3 regimes?
   A: Yes, this is very likely..
j. What is the risk then if you pass this to someone else or are reinfected with resistant virus.
   A: The importance of the risk of reinfection is much more serious with greater Rx. Transmission risk is relative to VL; if low less risk but is worse if you have a sexual transmitted infection. The SWISS statement recognized that VL may always not be undetectable, and maybe detectable in genital fluids.
k. What is Genotype and phenotype testing?
   A: There are 2 types of Rx tests:
   i. Genotype (molecular) —blood sample is multiplied many times and then the structure of the virus is looked at to see if HIV has changed sequence; results are given as leter:number:letter i.e. M414L, K103N. The number is the junction on the virus genome that has changed. The first letter is the amino acid that should be there and the last letter is the amino acid that it has changed to.
   ii. Phenotype (biological): a sample of your HIV is put in a test tube and drugs are added to see how much virus is produced. Results are given as –flod change (relative to wild-type). i.e 4-fold resistance means that four times the concentration of a drug was need to have the same impact on reducing viral replications, Different dugs have different phenotypic cut-offs for whether the virus is still sensitive or resistant.
l. Do HIV drugs treat both HIV-1 and HIV-2?
   A: Most do, but some drugs (notably NNRTIs) do not HIV-2.

The question about swine flu was raised and it was explained that it is different from the seasonal flu. It's a new strain and the vaccine is yet to be produced. The UK-CAB forum has a link to resources to information about dealing with swine flu.

Company pre-meeting
It was a time to briefly review the drugs manufactured by GSK: AZT, abacavir, amprenavir, 3TC and the combined formulations of Combivir, Kivexa and Trizivir. Members could relate to this and be able to ask the pharma the issue of abacavir and heart disease still remains topical. It was necessary to raise issues to GSK about the DAD study results. It is important for UK CAB to meet with the companies that manufacture the drugs we take.

GSK, Abacavir, pipeline drugs and merger with Pfizer – Dr Michelle Moorhouse

As with all CAB meetings with companies, this started with one minute silence to remember those who had not lived long enough to benefit form today's treatment and for those people who currently have no access to treatment.

GSK merger with Pfizer is to create a company that is more sustainable and broader in scope that either company's individual business with equity split of GSK- 85% and Pfizer – 15%. Discussions are still ongoing about the details so this information is preliminary.

The main meeting focussed on the GSK response to abacavir and cardiovascular (CV) (heart disease) data.

GSK have been transparent with the DAD results of 2008 with more data presented at CROI 2009. Patient safety is paramount, CV risk should be evaluated and managed as part of the assessment for each patient, consistent with the BHIVA guidelines.

Relative risk and absolute risk should also be taken into account. GSK is working with scientists to further understand the data and its implications, and is also undertaking further investigations to seek greater clarity on the CV risk signal reported for abacavir. They also ensure that health professionals are fully aware of the data.

GSK said they had stopped marketing abacavir for new sales, but based on the latest EMEA statement this may now change.

Discussion:

Q: Is it just abacavir or all drugs that contain abacavir component.
A: Both abacavir and the formulations that contain abacavir (Kivexa and Trizivr).

Q: Does 1.9 relative risk result mean you take all your risks and double it?
A: You need to take an individual's total risks into account. This is then doubled, but it your absolute (actual risk) is very low, doubling this is also very low.

Q: Would you advise anyone to switch from abacavir?
A: This is an individual situation that you need to ask for assessment from your doctor.

Q: Does taking abacavir and other things like coffee change the rhythm of heartbeat , do these have an interaction?
A: No evidence has been found of changing heart rhythm.

Q: What are heart attack symptoms?
A: Very severe pain in the chest on the left sid;e sometimes goes up to the jaw of arm and feeling you are going to die.

Q: Why do I get breathless when I run a short distance, I do not smoke?
A: We can't engage in personal issues; recommend you raise issue with your doctor.

Q: Most members in this meeting have not been offered a CV risk by their doctors. Are GSK doing anything to prompt doctors to do this?
A: Sales people are going out since DAD data to encourage doctors to do CV risk.

Q: Why hasn't this got through to clinics, even a year later?
A: GSK is trying their best to encourage doctors to do CV risk assessments.

Q: Other people do not understand the CV risk, its adding more distress to the HIV they have already. What about the long-term risks?
A: GSK ran long-term clinical trials, data has been reviewed and nothing came through showing heart attack risk.

Comment: Clinical trials - 48 week in a young population is unlikely to see any risk, even if there is one, should look at long-term effects.
A: Drug development takes about 10years before it goes for clinical trials. Clinical trials set up to compare drug efficacy. Other indicators will come out the trial. There are specific reasons. Any side effects should be submitted to doctor and should be sent to GSK.

Q: what are about absolute risk - vs relative risk being - on abacavir ?

Comment: *From a satellite session at BHIVA, there was a study on someone who had had a heart attack and still on abacavir. This is surely the highest predictor of a future heart attack and isn't included in Framingham, It was disturbing to see GSK include the recommendation that an individual patient with a history of heart disease should still continue on abacavir. For people with high CV risk, D:A:D showed this risk is doubled with abacavir. Generally speaking people enrolling in clinical trials are generally at low risk and should be excluded from trials.*
A: Will take this on board to GSK.

Q: How do you advise your patients in your clinic?
A: I offer a 6-monthly risk assessment, but because of demographics (South Africa) it has not been necessary. If a patient doesn't have any other treatment option, then I would explain available options and risks. Some patients say they do not want to switch.

Q: How long before an assessment whether to withdraw the drug?
A: DAD cohort had 517 heart attacks and 192 of these were on abacavir. We have no plans to take it off the market. Too many people rely on abacavir, provided they are informed of risk. Everyone must have a CV risk assessment. Some doctors may just want an easy option to switch.

Comment*: Should restrict abacavir to older patients, look at age factor.*

Comment*: BHIVA satellite symposium would have been a perfect opportunity to inform doctors of CV risk, but the session wasn't centered on this. Instead it includes one case study that was probably inappropriate.*
A: GSK not marketing abacavir for new sales, based on EMEA advice, still ongoing dialogue with customers.

Q: Do you have any studies to look at the DAD results?
A: A study in health volunteers is being developed to look at pure drug effect.

Q: Any other studies on HIV being a CV risk factor itself, what's your feeling?
A: Don't know how to factor it, as I cannot put a number on it. Risk is higher when not on HIV treatment.

Q: How many people have confidence to challenge their doctors?
Q: Will doctors honor up to putting you on the wrong treatment?

Summary:
- **GSK is working to try and understand the mechanism of abacavir, it about patients and not money.**
- **GSK is not marketing abacavir for new sales.**

There was not enough time to discuss the rest of the issues, Pipeline Drugs and Pfizer merger. The slides will be uploaded on the UK CAB website.

Feedback from CROI – Simon Collins

Members urged to watch the presentations online.

Q: What is my risk from using or not using treatment?
The meeting looked the charts on the "When to start" from the BHIVA guidelines treatment booklet showing comparative 6 month risk, delayed vs immediate. These let you look at the risk of becoming ill based on your latest CD4 and viral load results, and importantly, by age (i.e. 25, 35, 45 and 55). They show the risk when on treatment compared to not being on treatment and being on treatment reduces the risk at every point Risk increase with age, meaning it is more important to start treatment as you get older.

HIV and the brain – there is an article in the current HTB, it is a new and important area of research.

HIV risk in pregnancy – studies from South Africa have shown women being HIV negative at beginning of pregnancy and testing positive later. Other studies shoed importance of earlier treatment during pregnancy.

New boosters – 3 new formulations coming through, Gilead 4-in-1 pill, Abbott formulation that doesn't need refrigeration and an early compound from Sequoia.

Swine flu and HIV Treatment of flu can improve symptoms. General good hygiene is recommended.

Q: Any interactions with ARVs?
A: None with Tamiflu or Relenza but the Liverpool drug interaction site has a new detailed interaction chart.

More information available from:

www.hiv-druginteractions.org

i-Base answered an online Q&A on this:
http://www.i-base.info/qa/?p=814

Information from the US Centre for Disease Control:
HIV/AIDS Update - Interim Guidance--HIV-Infected Adults and Adolescents: Considerations for Clinicians Regarding Swine-Origin Influenza A (H1N1) Virus
http://www.cdc.gov/swineflu/guidance_HIV.htm

An online PowerPoint update on the current swine flu outbreak. This is a good source of information - what it is, how many people have gotten sick, how to protect yourself (pay particular attention to clean hands), etc. It is updated daily:
http://www.pitt.edu/%7Esuper1/lecture/lec34601/index.htm

BHIVA feedback - no time for feedback, slides to go on website.

AOB

Next meeting date changed to 31July 2009