UK-CAB
HIV treatment advocates network

CAB 47: HIV and cancer
12 April 2013

Contents:

Presentations from the April meeting are all available to download at:
http://www.ukcab.net/2013/04/ukcab-46-hiv-malignancies/

Members attending

	Name	Organisation	Destination
1	Albert Biete	Baltus Healthcare	Derby
2	Badru Male	CHAT	London
3	Ben Cromarty	North Yorkshire AIDS Action	Yorkshire
4	Bryan Teixeira	Personal	London
5	Damian Kelly	George House Trust	Manchester
6	David Rowlands	Baseline Magazine	Birmingham
7	Elijah Amooti	African Eye Trust	London
8	Emma Hudson	The Brunswick Centre	Huddersfield
9	Evelyn Joseph	Personal	Sheffield
10	Garry Brough	THT	London
11	Gertrude Wafula	Personal	Manchester
12	Godwyns Onwuchekwa	Personal	London
13	Gus Cairns	NAM	London
14	Helen Byarugaba	The Brunswick Centre	Huddersfield
15	Jeff Ukiri	Personal	Manchester
16	Jo Josh	Body and Soul	Redhill
17	Mark Platt	Personal	London
18	Memory Sachikonye	UK-CAB	London
19	Michael Marr	Waverley Care	Edinburgh
20	Paul Clift	Kings College Hospital	London
21	Paul Decle	Forum Link	London
21	Robert Fieldhouse	Baseline Magazine	Birmingham
23	Roger Pebody	NAM	London
24	Roy Trevelion	Personal	London
25	Silvia Petretti	Positively UK	London
26	Simon Collins	HIV i-Base	London
27	Susan Cole	National AIDS Trust	London
28	Virginia Cucchi	Bloomsbury Patients Network	London
29	Zhana Books	Africa Health Forum	London

Apologies: Fabiola Bayavuge, Larry Gurney, Mike Mpofu, Tsepo Young, Angelina Namiba

London :17 Out of London :12
Male :19 Female: 10

Programme

Chair: Ben Cromarty Timekeeper: Emma Hudson	
09.30 – 09.50	Registration, refreshments and expenses
09.50 – 10.00	Welcome, introductions, UKCAB updates
10.00 – 11.00	CROI feedback
11.00 – 11.30	Merck Sharp & Dohme (MSD) pre-meeting
11.15 – 12.15	**Introduction to HIV and cancer** - Simon Collins
12.15 – 13.30	Lunch – Strada restaurant
Chair: Gertrude Wafula Timekeeper: Albert Biete	
13.30 – 15.00	**HIV and cancer: monitoring, screening and treatment** - Prof Mark Bower, National Centre for HIV Malignancy, Chelsea & Westminster Hospital
15.00 - 15.30	**Break**
15.30 – 17.00	**Company meeting:** Merck Sharp & Dohme (MSD)
17.00	Meeting close

UK- CAB updates

- The UK-CAB steering group is still looking for more members, attendees were encouraged to speak with current members and consider applying.
- A reminder for the 30 April deadline for applications for the Methodological and Statistical Issues in Clinical HIV research was announced.
- The UK-CAB advocacy development course will run in autumn, further information to be provided.

CROI feedback

BHIVA convened seven best of CROI feedback meetings in March. The first was held in London with subsequent regional meetings in Birmingham, Haydock, Wakefield, Newcastle, Edinburgh and Cardiff. Garry chaired the London meeting and gave feedback on the London feedback session; three other members at the meeting had attended from around the country.

The big news was the functional cure, with focus on the Mississippi baby, with more scepticism on the facts as most babies born to HIV-positive mothers receive only a prevention course of ART. This typically involves fewer drugs and less frequent dosing. Full treatment is then given only after a positive diagnosis. In the case of the Mississippi baby, the newborn was put on the more aggressive regimen even before the tests came back showing that the child was HIV positive. The doctor did so out of the concern over the possibility of mother-to-child transmission, as the mother's HIV-positive status was only discovered to doctors while she was in labour. Following the baby's diagnosis six days later, full ART treatment was maintained, drug withdrawal was never planned. But after 18 months on the regimen, the child was lost to follow up for five months and when she returned the virus not rebounded. The key to the baby's functional cure, researchers believe, was probably the unconventionally aggressive treatment administered to the newborn in the first days of life: a trio of antiretroviral agents given twice daily starting from around 30 hours after birth. By giving these drugs before the infant had the chance to develop any memory T cells, the place where HIV goes to hide, may have prevented the virus from establishing the latent reservoir that make any efforts at fully eliminating HIV from the body very complex.

The VISCONTI study of 10 men and four women most of who were infected in the late 1990s. All patients started treatment early and were on treatment for up to three years. They have since been off ART for 4 to 10 years. This is a treatment interruption study, mathematical models showed that they could have functional cure and HIV could come back. The challenge is to make this happen in chronically ill people. This is not useful to anyone living with HIV long term.

There were several encouraging studies in the HCV pipeline concerning the safety and effectiveness of new HCV drugs used in combination without interferon. Current HCV therapy is based on pegylated interferon and ribavirin. These drugs don't always work and can cause unpleasant side effects. Research results showed that an interferon-free combination of drugs that work directly against HCV can achieve a 90% cure rate. The study involved people with genotype 1 infection. Other research showed that a two-drug combination of direct-acting drugs could achieve high rates of sustained virological response (SVR, considered a cure) in people with the easier-to-treat genotype-2 HCV. Another combination of three drugs being developed by Bristol-Myers Squibb cured over 90% of patients with genotype 1 infection after 12 weeks of treatment. Most of these interferon-free combinations will need to be studied in larger trials before they are licensed for use. Nevertheless, it seems likely that HCV treatment consisting entirely of direct-acting agents will be a reality within a few years.

Silvia Petretti highlighted the presentation on CVD monitoring of HIV patients vs general population. CVD in people with HIV is very different and she expressed concern that GPs in the new NHS may not be trained for this. Statins are widely prescribed in general population to lower cholesterol and reduce immune inflation. The question is which branded and generic statins are safe for HIV patients if they have high lipids and what are the drug-drug interactions with ART? There is concern about lack of data on statins.

There is also concern on the use of aspirin to lower CVD risk in people with HIV. One member had a lifetime experience of taking aspirin for rheumatoid arthritis as an anti-inflammatory. This does not have the same effect and no one seems to be anything in the fragmented NHS.

Gus Cairns fed back on the PrEP:

- PrEP had disappointing results due to lack of adherence in the VOICE trial where adherence was reported as 90% yet only 28-29% who had measurable drug levels in their blood, and only 22% of women using tenofovir microbicide. There is need to look into the social drivers that affect PrEP adherence as this does not take into account of behaviour and social circumstances. Adherence in negative people is lower due to perception of risk. There will be further subs-studies to come out VOICE to look at these issues.
- Use of condoms in anal sex - first estimate of the efficacy of condoms in preventing HIV transmission during anal sex since in the EXPLORE study. It found condoms stop seven out of ten anal transmissions, the same efficacy found by an earlier study. However, it also found that *sometimes* using condoms is not effective at preventing HIV infection, and that long-term 100% condom use is a minority behaviour: only one-in-six gay men actually managed to maintain it over the three- to four-year time frame of the analysis. One ongoing problem in assessing the effectiveness of different HIV prevention methods is that anal sex between men and anal sex between women and men is under-studied. There isn't enough data on rectal viral loads and their effect on transmission, or on whether HIV treatment reduces transmission via anal sex as well as it does for vaginal sex. This shows that 100% condom use is difficult to maintain and sometimes is no better than never.
- PREP: Nanoparticles and long acting formulations - Development of slow release and long acting formulations is critical. TMC 278LA and GSK744LAP are currently in development GSK744 and TMC278 can be made as nanosuspensions because the drug molecules have specific attributes that permit such an approach - not the case for many other ARVs. GSK744 half-life in the nanoparticle suspension ranged from 21 to 50 days after a single injection of various test doses in 56 HIV-negative volunteers. GSK744LAP appears to be a promising next-generation PrEP agent suitable for monthly to quarterly injections

Pipeline:

- New Tenofovir (TDF) formulation (Alafenamide, TAF) showed less damaging effects on markers of renal function compared with TDF, explaining that the kidneys are exposed to approximately 90% less TDF using the new formulation.

More information on ARV pipeline, long-acting formulations from CROI available here:
http://i-base.info/htb/21069

MSD pre-meeting

Robert Fieldhouse led the MSD pre-meeting and the meeting agreed on the following agenda for MSD.

- Safety – any post marketing report on muscle problem on Raltegravir patients.
- MK1439 resistance profile from CROI.
- TDF-like nuke – co formulation?
- Back up intergrase?
- Raltegravir pricing.
- What so you perceive the impact of Dolutegravir?
- Role for 3TC+new TDF+Raltegravir
- Any update on extended release formulations/injectables?
- Raltegravir in pregnancy.
- NNRTI sparing – raltegravir+darunavir+etravirine
- Update on current studies
- HDAC inhibitors
- HCV drugs in the pipeline

Introduction to HIV and cancer – Simon Collins

Cancer is a complex specialised condition that has generally been seen as an age-related disease and therefore the highest risk being in the elderly. With HAART, HIV patients are now surviving into old age. There is a more than 75% risk for people getting cancer in a lifetime and for HIV patients, how much of this is a natural ageing process? There are a lot of cancers; many are treatable with high remission rates if treated early. Individuals should be self aware of any changes in their bodies and importantly get early screening for better treatment outcomes. Some cancers however are not treatable and people should make the most of their lives in such cases.

There is still a lot of research in cancer treatment, unlike HIV; it does not have data for modified treatment combinations. There is nothing precise in cancer treatment, no data, and no markers for cancers like viral load in HIV. It is guesswork on whether the cancer responses to treatment with a long treatment timeline. Most cancer symptoms are similar to side effects you get from HIV, it is important to listen to what your body is telling you. With HIV, it is best to switch drugs till you have something that you are comfortable with. Cancer treatment can be long with horrible side effects that may include changes of life style. It is however important to prioritise one's health.

Relative vs absolute risk
Is cancer independent risk from HIV? This is difficult to know, the risk in HIV positive patients vs HIV negative shows higher rates but must be adjusted for ages of reduced the differences in incident. There are higher rates reported from some people with HIV at an earlier age, data showing how the lack of adjustment for the younger age of HIV positive compared to general population cohorts, can explain studies that previously suggested HIV positive people might age 20-30 years earlier than HIV negative people.

The common sense approach for broad screening is not always supported by evidence. Screening for cancer aims to find cancers as early as possible, when the chance of cure is highest. Sometimes screening can find changes that would lead to cancer if they were not treated. Cancer screening aims to prevent cancer or detect it at a very early stage.

Activist role:
Simon's aim was to get members to become confident enough to ask Mark Bower a question when they have problem for which they might seek his expert opinion.

Q: Does late cancer diagnosis relate to HIV patients or other issues?
A: It could be off the individual's radar; just not monitoring their personal health.

Comment: Sometimes when you monitor yourself you still have to convince your GP to look for cancer as most HIV patients get it when they are young.

Comment: Bowel cancer screening has been successful through a lot of publicity and campaigns.

Comment: Cancer is age-related. E.g. breast cancer campaign is aimed mainly at young women whereas the highest risk is in women over 75.

Q: Is there any advice you can give such as not smoking, diet?
A: Cancer risk is increased by life style. There are over 200 types of cancers -viral cancers, genetics cancers, environmental, etc. Outcome of treatments depends on the type of cancer. As activists we should be asking our HIV specialists to speak to cancer specialists.

Q: Should gay men only be screened for anal cancer?
A: Anal cancer in gay men is as common as cervical cancer was in women before the use of the Pap smear, the test used to screen for precancerous spots on the cervix. The human papilloma virus (HPV), which also

causes genital warts, causes both types of cancer. Pap smears, which have saved the lives of many women, should also be used to look for anal cancer in gay and bisexual men.

Q: Should we worry about drug-drug interaction between HIV drugs and cancer drugs?
A: Expert care is essential; you need to be sure of the doctor treating you. That's why it is important for HIV specialists to speak with cancer specialists in such cases.

Q: Are you likely to have more risk if you are HIV positive?
A: There is no comparative group for HIV negative people, therefore difficult to say.

Comment: It is important for clinicians to communicate; I had breast cancer and the clinicians at the cancer hospital made a mistake and gave me 10 times the dose of the drug. It was picked up early; otherwise it could have been fatal.

HIV and cancer: Monitoring, screening and treatment - Prof. Mark Bower

What is the community feeling about the HIV care for people with cancer? The balance between: should everyone be treated in one centre where all the expertise is and probably better outcomes or should there be treatment in smaller centres? What criteria should be put in e.g. breast cancer criteria has ended up in NICE guidelines with no evidence and has become law. This was the decision of doctors and with very little user involvement and has resulted in some centres being shut down.

In London Great Ormond Street specialises in children's cancer and The Royal Marsden for adults. Generally mothers will travel miles with their children for best treatment. The other side of the argument is around pancreatic cancer which is incurable. Rather than travelling miles, patients would rather be looked after nearer home, as they would be spending more time in the hospital. Care differs by different cancer types.

BHIVA guidelines now accredited by NICE, the cancer guidelines we write are very important. Community input is very important as opportunity for community, patients, careers and clinicians to organize the service before the new commissioners tell us what to do. It is very powerful to have community input into guidelines. Prof Bower would like community input into the BHIA guidelines for 2013.

HIV infection is associated with three AIDS-defining malignancies (Kaposi's sarcoma, high-grade B-cell non-Hodgkin's lymphoma and invasive cervical cancer) as well as an increased risk of a number of other malignancies. The clinical care of patients with these tumours requires a multidisciplinary approach drawing on the skills and experience of all healthcare professional groups. Moreover, optimal care can only be achieved by the close cooperation of oncologists, haematologists and HIV physicians, and unless all these clinicians are intimately involved in the care of patients it is likely that the outcome will be less favourable. Patients with HIV-associated malignancies should therefore only be managed in a centre dealing with large numbers of patients with these tumours.

The three AIDS defining malignancies:
- Cervical Cancer
- Kaposi sarcoma
- Non-Hodgkin lymphoma – including primary cerebral lymphoma

Cervical cancer
There is a controversial argument on whether cervical cancer is more common in women living with HIV or not. It is important that they be screened regularly for this disease. Studies have suggested that Pap test abnormalities are more common among HIV positive women and that HPV DNA tests may not be as effective as Pap tests in screening these women for cervical cancer.

What defines an AIDS-related cancer? Is it co-related to a deteriorating CD4 count? Large number of cancers that occur in HIV positive people do not co-relate with CD4. There are a lot of cancers that are not disappearing with the use of HAART.

Kaposi Sarcoma (KS)

KS can affect both the skin and internal organs. The most common initial symptom of Kaposi's sarcoma is the appearance of red or purple patches on the skin. The patches then grow into lumps known as nodules. KS is caused by the human herpes virus type 8 (HHV-8). The virus is also sometimes referred to as the Kaposi's sarcoma associated herpes virus (KSHV). HHV-8 is a common virus, and as many as 1 in 20 people possibly have the virus in their body. In most cases, HHV-8 doesn't cause any noticeable symptoms. The majority of people with the virus won't go on to develop KS.

However, certain groups of people who are vulnerable to the effects of HHV-8 go on to develop KS. KS often affects people whose immune systems have been severely weakened by HIV. During the 1980s, about one in five people with HIV or AIDS developed KS. With the introduction of a range of HAART in the 1990s, the number of people with HIV who were affected by Kaposi's sarcoma fell by about 90%.

KS is an uncommon complication of organ transplants. In England, an estimated one in every 200 people who have an organ transplant develop KS. The immunosuppressants may further weaken the immune system making the person more vulnerable to the HHV-8 virus. Adjusting a person's dosage of immunosuppressants can usually successfully treat this.

In the UK, KS treatment outcome is usually relatively good when compared to other types of cancer. It is important for people with people with HIV-related KS get access to HAART early on in their HIV diagnosis their outlook will also be relatively good, and the condition will often go into remission (the symptoms will go away). If not, chemotherapy and radiotherapy can also relieve symptoms. KS mortality has gone down, but it is important to realise that a complete cure for all types of KS isn't always possible, and there's a chance that the condition could reoccur in the future.

Endemic African KS

This is common in parts of Africa and is one of the most widespread types of cancer in that region, accounting for 1 in every 10 cases of cancer in Africa. The condition is particularly widespread in Uganda, the Congo (both the Democratic Republic of the Congo and the Republic of the Congo) and Zambia. Many people from sub-Saharan Africa are also infected with HIV as well as HHV8. Therefore, it is highly likely that many cases of so-called 'endemic' African Kaposi's sarcoma were and are, in fact, due to undiagnosed HIV infection. 'Endemic' African KS that is not HIV-related is thought to develop as a result of a pre-existing genetic vulnerability to the virus that causes it.

Epidemiology suggests sexual transmission; the number of sexual partners increases risk. KS is more common in gay men and in the pre-HAART era it was suggested HIV caused it. There are number of older men in the UK are getting KS. In people living with HIV, transmission is similar to glandular fever which is predominantly transmitted through saliva.

Staging of KS – this a description of how far the cancer has spread, based on the results of physical exams, biopsies, and imaging or other tests:
T (tumour) status
T0 (good risk): Localised tumour
T1 (poor risk): The KS lesions are widespread. One or more of the following is present:

- Oedema (swelling) or ulceration (breaks in the skin) due to the tumour
- Extensive oral KS: lesions that are nodular (raised) and/or lesions in areas of the mouth besides the palate (roof of the mouth)
- Lesions of KS are in organs other than lymph nodes (such as the lungs, the intestine, the liver, etc.). Kaposi sarcoma in the lungs is a particularly bad sign.

I (immune system) status
The immune status is assessed using a blood test known as the *CD4 count*.

- I0 (good risk): CD4 cell count is 150 or more.
- I1 (poor risk): CD4 cell count is lower than 150.

Treating KS
Treatment is determined by staging. Patients with early stage KS - T0, I0-1:

- HAART is given and 80% of patients do not need any other treatment for KS over 10 years of follow up. It takes three to six months for the KS lesions to shrink on HAART.
- Intralesional vinblastine - an injection on the lesions effective and useful treatment for KS.
- HAART may be followed by courses of radiotherapy or chemotherapy.

Late stage KS – T1, I0-1

- HAART and chemotherapy with liposomal anthracyclines and paclitaxel.

Immune reconstitution inflammatory syndrome (IRIS)-KS occurs frequently in HAART-naive individuals with HIV-related KS. Those with a higher CD4 count appear more susceptible but have a decreased subsequent rate of increase in their CD4. This is reflected by KS progression following the start of HAART.
A proportion of patients with HIV who subsequently receive HAART show deterioration in their clinical status, despite control of viral load and decreased CD4. KS gets worse with IRIS which occurs secondary to an immune response against previously diagnosed infections. There are different incident rates of IRIS-KS in different countries.

Most HIV positive patients who have recurring KS will have gone through a lot of treatment. This is where patient participation in treatment choice is very important. Does the patient what to have chemo or not? If KS keeps coming back despite good HIV control, do you want to have chemo now or later?

Chemo injections only treat local points and its mainly cosmetic. If a patient has multiple nodes on various parts of their body, it is up to the patient if they want injections or not. They can choose to go on the usual drugs that treat KS including a topical cream.

Discussion:
Q: We have discussed treatment in HIV positive people, how do you treat HIV negative people?
A: HAART will control KS in more than 80% of people long term. HIV negative patients are not treated with HAART but get chemotherapy. There are studies that showed good response from ART on HIV negative patients. This is controversial and the patient has to be involved.

Q: Is there any explanation why fully suppressed HIV positive men (mainly) are getting KS in the UK?
A: Patients with fully suppressed HIV do get KS; this is usually in older MSM. This may be due to the effects on ageing on the immune system. Some will require continuous chemotherapy. There is an enormous amount of work required to check and analyse a large cohort to determine cause and incident rates.

Q: Are there a lot of KS cases in HIV negative MSM?
A: The cases seen in HIV-negative men were less aggressive and rapidly-progressing than those in people with HIV. I have a cohort of about 10 who have been referred to me. I have done numerous tests on their immune system and have never found any abnormalities. None of them have had any opportunist infection malignancies. However they tended to be more aggressive than in the originally described type of KS which is seen most often in men of Mediterranean origin, and occurred at an older age – around 50 years.

Q: Can KS be transmitted from mother to child?
A: This could be referred to the Ugandan study where 10% of infants had KS, but it is difficult to separate the two, as KS can be present in breast milk.

Q: There people with high CD4 on treatment, suppressed viral but still get KS?
A: Unable to tell how it happens, could be ageing and very difficult to control. Difficult to research whether it is anything to do with previous low CD4 cells and takes a lot of time to analyse data prospectively.

Q: Can KS be transmitted genetically?
A: It is mainly through sex, especially in MSM, but doesn't explain how many heterosexual African men and women and their children acquire this common infection with HHV-8. Therefore HHV-8 may be passed on by some other means, e.g. through saliva. This means that kissing could spread the virus.

Q: Could viral suppression recur in KS?
A: Chronic KS treatment – if it keeps coming back despite good HIV treatment.

Q: Do you use topical chemo on lesions?
A: Yes an injection into the lesion, especially for cosmetic purposes, but this is not a long term solution.

Q: Would you inject say 20 lesions?
A: The injections are painful, but there are creams that could be used

Lymphomas
There are over 100 types of lymphomas, HIV patients get lymphomas in the brain, but these are now very rare and also body lymphomas. Lymphomas occurring in HIV-positive patients are usually aggressive. In the pre-HAART era survival was three months for patients with HIV-related lymphoma. It is estimated a number of people who are HIV-positive will ultimately develop lymphoma. Although both Hodgkin and non-Hodgkin lymphomas may occur in HIV patients, non-Hodgkin lymphomas are more common and include diffuse large B-cell, Burkitt's/Burkitt-like and primary central nervous system lymphoma.

Burkitt's Lymphoma (BL)
This is an is an extremely fast growing form of non-Hodgkin's lymphoma that originates from a subgroup of white blood cells called B lymphocytes of the immune system. There are three main types of Burkitt's lymphoma: sporadic, endemic and immunodeficiency-related disease. 25% of HIV patients get BL and immunodeficiency-associated BL may also occur in people who have had an organ transplant and are taking medicines to suppress their immune system so it doesn't reject the donor organ. The disease may affect the jaw, central nervous system, bone marrow, bowel, kidneys, ovaries or other organs. BL is potentially curable. Endemic Burkitt's lymphoma is found mostly in Africa and is often associated with the Epstein-Barr virus (EBV).

Chemotherapy is the main treatment for BL. Chemotherapy is the use of anti-cancer (cytotoxic) drugs to destroy cancer cells. It is usually an intensive treatment and involves staying in hospital for weeks at a time. A monoclonal drug called rituximab can be given in addition to chemotherapy. Some people may have stem cell treatment.

Diffuse Large B-Cell Lymphoma (DLBCL)
Diffuse large B-cell lymphoma (DLBCL) is a common type of non-Hodgkin lymphoma and is a cancer of the B-cells. DLBCL can occur at any time between adolescence and old age. The most common age to be diagnosed is around 60. It is slightly more common in men than in women.

The first sign of the condition is often a painless swelling in the neck, armpit or groin, caused by enlarged lymph nodes. Sometimes lymph nodes in more than one part of the body are affected. In some people, DLBCL doesn't begin in the lymph nodes but develops in another part of the body instead. This is called extranodal disease. The most common place for DLBCL to develop outside of the lymph nodes is the stomach or bowel, but any area of the body can be affected. The lymphoma may spread to various organs in the body such as the liver, lungs or bones. Some people experience a loss of appetite and tiredness.

Other symptoms, known as B symptoms, include night sweats, unexplained high temperatures and weight loss.

The stage of non-Hodgkin lymphoma describes how many groups of lymph nodes are affected, where they are in the body, and whether other organs such as the bone marrow or liver are involved.

Chemotherapy is the main treatment for diffuse large B-cell lymphoma. The type of chemotherapy you have will depend on the extent of the lymphoma and other factors, such as your age and general health. The most widely used combination treatment is called the R-CHOP regimen. This is made up of the chemotherapy drugs doxorubicin, cyclophosphamide and vincristine, the steroid prednisolone, and a monoclonal antibody called rituximab. Other treatments include monoclonal antibody therapy, stem cell transplant, radiotherapy and steroid therapy.

Sometimes there is a risk of developing scar tissue in the affected lymph nodes after treatment for DLBCL. The scar tissue can make it difficult to assess whether or not there are still lymphoma cells in the lymph nodes. A scan known as a PET scan may be used after treatment is finished to check if any active lymphoma are still present.

It is important to note that some chemotherapy drugs can damage healthy cells and cause side effects such as nausea and vomiting, reduced appetite, hair loss and mouth sores. Damage to healthy immune cells may also put lymphoma patients undergoing treatment at risk for infection. Doctors can prescribe medicines to offset these effects. Since chemotherapy may cause infertility, this should be discussed with your doctor, prior to starting therapy. Sperm banking is generally recommended in men and measures to attempt fertility preservation in women may be considered. It is essential that birth control be used during treatment.

Q: Would you find great to modify the HIV regimen in IRIS-KS?
A: Yes with boosted PIs.

Q: What expertise and understanding is available at C&W?
A: There are joint meetings between cancer and HIV specialists and have all good data on NHL.

Q: Is it worth investing in joint clinics for the future?
A: Yes is it, the epidemic is growing due to the ageing HIV population.

Q: What are chances of survival when diagnosed with pancreatic cancer and have your pancreas removed?
A: 5% of patients survive.

Q: The GPs will be taking so much of our care and will they be knowledgeable and prepared to deal with all the cancers related to HIV?
A: That's the worry, they should be.

Q: Do you recommend use of aspirin for cancer?
A: Yes, it has been seen to work especially for colon cancer.

Q: Prof Bower can be used as referral informally; how could this benefit CAB member living outside London? Is there a role for us as an activist organization?
A: I highly recommend input into the BHIVA guidelines, especially on the designation of services.

Q: If somebody has a cancer, how do they get in touch with Mark Bower, any ideas? The CCGs do not know how to deal with someone who has HIV and cancer.
A: It is therefore important to have community input into the BHIVA guidelines.

Comment: Anal cancer screening is the most controversial topic; there is no data support what is being offered. Those doing it and offering it believe in it. Treatment for AIN caused regression. None of those studies show that it works. Cervical and anal cancer screening is screening for pre-cancerous cells and if treated will stop them progressing into cancer.

Comment: Prof Bower does not want to come to the conclusion that screening has made any difference. How come women are not tested for anal cancer? Anal cancer is more common in women than men.

Community involvement: Members asked to email Simon Collins or Prof. Bower with input into configuration of cancer services into the BHIVA guidelines.

Company meeting: MSD

Pipeline
Raltegravir is being still developed into a once daily formula. MSD were asked to also consider the size of the new drug as the current drug is large and they said they would take that into consideration.

A fixed dose combination of Raltegravir + emtricitabine + 3TC is also being developed.

Doravirine (MK-1439): Phase 1 and II studies
Darvirine is an NNRTI that demonstrated robust antiviral activity and good tolerability in a small clinical study of 7-day monotherapy. In the double-blind, placebo-controlled study of 18 treatment-naive patients with HIV divided into three even groups - first group took 25mg of Doravirine; the second 200 mg of the drug; and the third a placebo. All participants took one dose per day as a monotherapy for seven days. Viral load levels fell steadily for people taking either dose of Doravirine, whilst remaining stable for placebo recipients. At day seven of treatment, HIV viral load declines were similar in the 25mg and 200mg dose arms. Doravirine was safe with few side effects, not related to the drug. Pre-clinical studies showed that Doravirine has enhanced activity against HIV strains with certain other common NNRTI resistance mutations (including K103N and Y181C). Unlike the widely used NNRTI efavirenz (Sustiva), it appears to have low potential for central nervous system (CNS) toxicity. PK data showed that it is rapidly absorbed with no food interaction. There was no data on renal toxicity.

CMX157 was purchased from Chimerix and is more than 300 times more potent than Tenofovir. It can also be used to treat hepatitis B virus. The drug structure decreases circulating levels of Tenofovir, lowering exposure and thereby reducing the potential for renal side effects. In safety trials it was highly active against all major subtypes of HIV, including strains that fail to respond to all currently available NRTIs.

EFdA is an NRTI which targets the main HIV enzyme responsible for viral replication. In laboratory tests, human cells treated with EFdA can still become infected with HIV, but the compound stops the virus from replicating and spreading. Compared to microbicides that contain the same or related antiretroviral drugs such as Tenofovir,it provided a much longer-term barrier to HIV infection, up to days whereas other microbicides last hours. EFdA also has a low toxicity against normal cells, and it is active against a broad spectrum of HIV subtypes is probably the most potent HIV inhibitor discovered so far. This is the molecule that should and will move forward as a microbicide.

Q: We support both the Doravirine once daily dosing and low dosing, could the dose go lower than 20mg?
A: It is likely to come with some drug-drug interaction with other drugs; it is always safe to work with nothing lower than 25mg.

Q: With a potential weekly drug, are you likely to have a dual weekly NRTI dosing?
A: This is what we are hoping for provided all other factors are in place.

Q: Are you able to tell how much you paid for them the Chimerix and Yamasha licenses?
A: Price did not come into the UK team. Ben Yellowlees to look at it and feedback to the CAB.

Prevention strategy:

- Vicriviroc + MK-2048 is being developed into a vaginal ring that could stay inside the woman for up to a week. MSD are trying to incorporate a contraceptive agent into vaginal ring.
- Vorinostat has been seen awaken latent cells but has have safety concerns, more research needed.

Comment: A weekly pill is fantastic, but risks adherence in older patients who may forget all together.
A: We may produce a forgiving pill that would stay in the body for longer periods, but may not good for everyone.

Q: Does the contraception in vaginal affect women's periods?
A: It is too early in development to look into that.

Q: Are you considering rectal microbicides similar to the vaginal ring?
A: Yes, but still in animal models.

Q: Does CMX157 have renal effects?
A: There is currently no data on this, but could have less effects compared to Tenofovir.

From the CAB agenda:

Q: Could you give us an update on Raltegravir and muscle toxicity?
A: Patients in the study were on PIs that changed stomach PH and caused increased absorption of Raltegravir.

Q: Will there be Raltegravir co-formulation with 3TC?
A: As fixed dose combination is the patient preference, we are working on that.

Q: How safe is Raltegravir in pregnancy?
A: There is currently no data at the moment on safety, doctors interested as it has rapid viral load decrease when used in pregnancy, but not available post partum.

Q: Any update on nuke sparing studies?
A: The study is currently running in Africa on patients who have failed first line and looks promising. It is part of the NEAT study.

Q: How expensive is Raltegravir in the African study?
A: When a trial stops patients will get drugs for six months post-trial. MSD will commit to provide the drug at $1/day or lower. MSD's position is that no one should manufacture the drug lower than them and would rather sell it no profit through voluntary licensing.

Q: Why are you doing trials in Africa where the drugs are not available/accessible?
A: Raltegravir is now licensed in several African studies. We have discussions with MRC who talk to various African governments in ensuring continued access.

Hepatitis C drugs

Pipeline
MK5172 is a multiple dose study will assess the safety, tolerability, pharmacokinetics and pharmacodynamics of MK-5172 in Genotype (GT) 1 and GT3 in co-infected participants. It is a once a day

drug with other drugs for 12 weeks and should achieve clear HCV. MSD said they would soon start trials with HIV co-infected participants.

Comment: Raltegravir use in UK - MSD has lowered price for the NHS, depending on the treatment centre with patients using Raltegravir, it can be reduced below the cost of PIs. There is uptake up in Scotland, Ireland, and North West. London and the south are still low after the London drug prescribing process. MSD should try to find a way to engage at local level with relevant authorities. If Raltgrevir costs less than Efavirenz, they should discount it a bit more to sell more, must realize that NHS is all price-driven.

Next meeting

Topic: Transition from paediatric to adult services
Date: 12 July 2013