UK-CAB

HIV treatment advocates network

UK-CAB 41: HIV and TB

20 January 2012

Contents:

Presentations are all available to download for the January meeting at:
http://www.ukcab.net/2012/01/cab-41-tb-and-hiv/

Programme:

Chair: Roger Pebody	Timekeeper: David Rowlands
09:30 – 09:50	Registration, refreshments and expenses
09:50 – 10:00	Welcome, introductions, UKCAB updates
10:00 – 11:15	**TB and HIV: Screening and treatment** – Dr Santino Capocci, Royal Free Hospital
11:15 – 11.30	**Break**
11:30 – 12.15	**TB-HIV: Strengthening Community Response** - Gitau Mburu, Int. HIV/AIDS Alliance
12:15 – 12.45	**Company pre-meeting on TMC207** - Polly Clayden, HIV i-Base
12:45 - 14:00	Lunch
Chair: Polly Clayden	Timekeeper: Damian Kelly
14:15 - 15:30	**Company meeting**: Janssen
15.30 - 15.35	**Break**
15:35 – 16:00	**UKCAB London drug survey feedback** – Mark Platt
16.00	**Close**

About the speakers:

Dr Santino Capocci is a research registrar at the Royal Free Hospital looking at tuberculosis and lung disease in people living with HIV. He trained in Nottingham and London and attended the London Short Course in Tropical Medicine and Hygiene in 2006. He worked at medical school with the International Federation of Medical Students and was a founder of Marrow, an outreach project recruiting students to the Anthony Nolan Bone Marrow register. He went on to train in General then Respiratory Medicine and has presented at the European Respiratory Society, British Thoracic Society and British HIV Association.

Gitau Mburu – is the Senior Advisor for HIV and Health Services at the International HIV AIDS Alliance, an International organization that supports communities to respond to HIV in 36 countries globally. Gitau has worked in a variety of settings in developing countries with PSI, IRC and MSF, mainly in HIV and TB treatment and care as well as primary health care. Gitau received his medical degree from the University of Nairobi, Diploma in Tropical Medicine and Hygiene from the London School of Hygiene and Tropical Medicine and Masters in Public Health from the University of Edinburgh. He is a member of the Kenya Medical Association, a fellow of the Royal Society of Tropical Medicine and a member of the TB/HIV working group of the WHO STOP TB Partnership.

Members attending

	Name	Organisation	Town
1	Adebisi Alimi	HIV i-Base	London
2	Albert Biete	Personal	Derby
3	Andrew Shamboko	Personal	Liverpool
4	Badru Male	CHAT	London
5	Ben Cromarty	North Yorkshire AIDS Alliance	Yorkshire
6	Blake Smith	THT London	London
7	Brian West	Waverley Care	Edinburgh
8	Damian Kelly	George House Trust	Manchester
9	David Rowlands	Baseline Magazine	Birminghman
10	Eunice Sinyemu	Personal	London
11	Fabiola Bayavuge	Black Health Agency	Manchester
12	Gertrude Wafula-Anyango	Black Health Agency	Manchester
13	Godwyns Onwuchekwa	Personal	London
14	Jeff Ukiri	Personal	Manchester
15	Jonathan Ssentamu	Waverly Care	Edinburgh
16	Li Marhaban	HIV i-Base	London
17	Mark Platt	Personal	London
18	Maxwell Madzikanga	Faith in People with HIV	Leicester
19	Memory Sachikonye	UKCAB	London
20	Michael Marr	Waverley Care	Edinburgh
21	Paul Clift	King's College Hosp/UKCAB	London
22	Polly Clayden	HIV i-Base	London
23	Robert Fieldhouse	Baseline Magazine	Birmingham
24	Roger Pebody	NAM	London
25	Silvia Petretti	Positively UK	London
26	Stuart Murau	George House Trust	Manchester
27	Susan Cole	National AIDS Trust	London
28	Tsepo Young	NHS Dumfries & Galloway	Stranraer
29	Vivian Lewis	Footprints	Leicester
30	Winnie Sseruma	Christian Aid	London
31	Zhana Books	Africa Health Forum	London

Apologies:
Emma Hudson, The Brunswick Centre, Halifax
Tendai Ndanga, Ffena (AHPN), London
Anne-Marie Shields, The Brunswick Centre, Halifax

Introduction

Memory introduced the meeting by highlighting that:

- Tuberculosis (TB) is an infectious disease that is caused by a bacterium called Mycobacterium tuberculosis. TB primarily affects the lungs, but it can also affect organs in the central nervous system, lymphatic system, and circulatory system among others.
- One-third of the world's population is currently infected with the bacteria that causes TB, and anyone infected has a 10% chance of suffering from TB during their lifetime. This is propelled by global poverty, the AIDS epidemic, and drug resistance.
- People with weakened immune systems are especially at risk of developing TB. People living with HIV, for example, are ten times more likely to develop TB and often live in resource-limited settings where TB infection is also more prevalent.
- Sub-Saharan Africa is has the highest rates of HIV/TB co-infection; 30-50% of the population is infected with TB, compared to 5% in the west.
- Economic breakdown in former Soviet Republic has led to rising TB rates and high levels of multi-drug resistant TB (MDRTB) (including some EU countries). Population movement results in infection movement within the EU.
- In the UK new TB cases fell by 5% in 2011 (HPA annual report 2011), although one in 20 patients don't complete treatment. Most cases occur in major cities, particularly in London.

Current first-line TB treatment is nearly half a century old. TB treatment is six months. Treatment is a two-month course of a combination of four antibiotics (isoniazid, rifampicin, pyrazinamide and ethambutol), followed by a four-month course of a combination of 2 antibiotics (isoniazid and ethambutol). For patients who are erratic or inconsistent in taking with the treatment develop drug resistance, yielding deadlier, more difficult to treat disease.

Only with faster, better and affordable cures for TB can millions of lives be saved and reverse this global epidemic that kills around 1.4million people each year. The hunt continues, therefore, for a drug that can treat TB faster and kill the bacteria that survive treatment with existing antibiotics.

TB and HIV: Screening and treatment – Dr Santino Capocci

Dr Santino Capocci is a research registrar at the Royal Free Hospital looking at tuberculosis and lung disease in people living with HIV.

One-third of the world population is estimated to be infected with TB. The global incidence of TB peaked around 2003 and appears to be declining slowly. According to the World Health Organization (WHO), in 2010, 8.8 million individuals became ill with TB and 1.4 million died. Both these statistics reflect a decline compared with prior years.

In 2010 in the UK, a total of 8,483 cases of tuberculosis were reported, a rate of 13.6 cases per 100,000 population. London accounts for 40% of TB in the UK. Newham borough in London has the highest TB rates and risk in the UK. Compared to the rest of the world, Cape Town in South Africa still has one of the highest rates in the world.

Dr Santino spoke about the natural history of TB and why it remains such a problem. Most people are exposed to TB in their lifetime but do not have active TB; i.e. latent TB. Patients with latent TB are not infectious; it is not possible to get TB from someone with latent TB. The main risk is that approximately 10% of these patients will go on to develop active tuberculosis at a later stage of their life if their immune system is compromised by diseases such as HIV, or during the ageing process, malnutrition or in past living in degrading accommodation such as concentration camps.

HIV highest factor of developing active TB, despite CD4 bring fairly normal. Pulmonary TB affects lungs and extra pulmonary TB occurs outside the lungs. The latter can be treated using the same combination of antibiotics as those used to treat pulmonary TB. Treatment course for extra pulmonary is up to 12 months, rather than the six-month course. Screening of family members of a patient with active TB is important. The aim of screening in public health settings is to diagnose active TB, subclinical TB (absence of TB symptoms) and latent TB.

TB treatment

The standard course treatment for TB is for six months. After taking the medicine for two weeks, most patients are no longer infectious. However, it is very important that they adhere to their treatment and complete the whole course of antibiotics. The patient is considered cured at six months (although there is still a relapse rate of 2 - 3%). For latent tuberculosis, treatment involves either taking a combination of rifampicin and isoniazid for three months, or isoniazid on its own for six months.

BHIVA guidelines recommend starting treatment as soon as possible on co-infected patients with a CD4 below 100. For CD4 above 100 to 350, the patient could wait two months after starting ART to start TB treatment and those with CD4 over 350 are the discretion of the consultant.

TB meningitis is TB infection of the meninges - the system of membranes that envelop the central nervous system (CNS). It is the most common form of CNS TB and has a high mortality rate. The treatment of TB meningitis is isoniazid, rifampicin, pyrazinamide and ethambutol for two months, followed by isoniazid and rifampicin alone for a further ten months. Steroids are always used in the first six weeks of treatment (and sometimes for longer). Treatment must be started as soon as there is a reasonable suspicion of the diagnosis.

Dr Santino presented some case studies of HIV-TB co-infected patients and discussed each case study on each diagnosis and treatment; shows that TB sometimes presents with no symptoms.

- Case 1 was a patient with subclinical TB, which was first diagnosed as pneumonia.
- Case 2 patient had disseminated TB (that has spread from the lungs to other parts of the body through the blood or lymph system), also developed IRIS.
- Case 3 was a woman with latent TB diagnosed after her husband developed TB.

Problems of talking ART and TB treatment at the same time were also highlighted:

- Drug-drug interactions especially with PIs were common.
- Increased side effects from both treatments.
- High pill burden.
- Reduced patient adherence.
- Immune reconstitution disease (IRIS).
- Delaying treatment often results in high risk of major opportunistic infections and death.

Isoniazid Preventative Therapy (IPT)

In South Africa, isoniazid can be used to prevent TB. IPT is available in public clinics for people living with HIV. IPT reduces a person's risk of developing active TB. The study looked at the effect of IPT on mortality in a population of South African adults, predominantly male, for three years. The study compared outcomes in those who received IPT and those who did not. Individuals were eligible for ART if they had a CD4 count below 250 without symptoms or if they had a CD4 count below 350. The study showed a significantly lower mortality rate for those who received IPT; the risk of death was approximately halved if an individual received IPT in addition to antiretroviral therapy.

TB screening

TB is diagnosed using the TB skin test, chest x-rays, and lab tests. In the UK two skin tests are on the market; the T-spot and the Tuberculin Skin Testing (TST).

The T SPOT TB blood test stimulates T-cells, is a rapid and accurate diagnosis of active and latent TB. It is the first test that reliably detects (up to 95%) of TB infection in people who are most vulnerable to developing active TB. The test is much faster and gives results within 24 hours allowing physicians to treat those who test positive before they actually develop TB and become infectious to others. It is an accurate and effective tool for controlling the spread of TB.

Tuberculin Skin Testing (TST)

Is done by injecting a measured amount of TB protein (antigens) called purified protein derivative (PPD) under the top layer of skin on the inner forearm. If a person has ever been exposed to the TB bacteria, their skin will react to the antigens by developing a firm red bump at the site within two days. This is a good test for finding a TB infection and mainly targeted among high-risk groups. It is often used when symptoms, screening, or testing, such as a chest X-ray, show that a person may have TB. A tuberculin skin test cannot tell how long the person has been infected, or whether the TB is latent or active. A bump of 10mm or more is considered positive especially in recent immigrants (< 5 years) from high-prevalence countries. A bump of 15mm or more is considered positive in any person, including persons with no known risk factors for TB.

A TST is done to find people who have TB, including:

- People who have been in close contact with someone known to have TB.
- Health care workers who are likely to be exposed to TB.
- People with TB symptoms, such as an ongoing cough, night sweats, and unexplained weight loss.
- People who have had an abnormal chest X-ray.
- People who have had a recent organ transplant or have an impaired immune system, such as those with HIV.

A TST should not be done for people who:
- Are known to have TB.
- Have had a previous severe reaction to the TB antigens.
- Have a skin rash that would make it hard to read the skin test.

Q: Could you get a false-positive reading? Yes, this could be due to:
- Infection with non-tuberculosis mycobacterium.
- Previous BCG vaccination.
- Incorrect method of TST administration.
- Incorrect interpretation of reaction or bottle of antigen used.

False-negative reading to the TST could be due to:
- Cutaneous anergy (the inability to react to skin tests because of a weakened immune system).
- Recent TB infection (within 8-10 weeks of exposure).
- Very old TB infection (many years).
- Overwhelming TB disease.
- Very young age (less than 6 months old).
- Recent live-virus vaccination (e.g. measles and smallpox).
- Some viral illnesses (e.g., measles and chicken pox).
- Incorrect method of TST administration or interpretation of reaction .

GeneXpert
GeneXpert is a new cartridge-based, automated diagnostic test that can identify MDR-TB resistant to rifampicin in about two hours compared to up to four weeks from traditional screening. It picks up two out of three tests done for MDR-TB that would otherwise be missed using the microscope. It makes TB diagnostic fast and simpler for active TB. The limitation is its cost, which may be prohibitive for a disease that principally affects poor people in resource-limited settings. There is need to lobby the manufacturers to lower the price so it can be rolled out widely.

Due to time constraints, these were not discussed:
- Interferon Gamma Release Assays (IGRAs) for the diagnosis of latent TB
- Use of IGRAs in detecting active disease in HIV
- Drug interactions when treating TB
- IPT and ART in reducing the risk of reactivation of latent TB

Q&A

Q: How easy is it to get good positive sputum from the patient in case study 1?
A: In this case he was coughing, so it was easy, not all smears are culture positive. If the affected person is unable to produce sputum, a bronchoscope may be used to collect fluid during a procedure called a bronchoscopy. In children, gastric washings may be collected. Depending on symptoms; urine, and washings from the site of suspected infection, cerebrospinal fluid (CSF), other body fluids, or biopsy tissue samples may be submitted for smear and culture.

Q: Would you have any idea how long a person might have had TB before they become ill?
A: You cannot tell and it's hard to know. The person could have had latent TB and then seroconverted later.

Q: How long does TB culture take to get a result?
A: The culture can take up to six weeks.

Q: Can the patient start TB treatment while waiting for cultures?
A: TB treatment is often started before getting sputum culture results. All four drugs are given while waiting for the results of the sputum culture.

Q: As a doctor working in a TB clinic, how often do you get screened?
A: We take precautions when treating patients with active TB. If a colleague is diagnosed active TB, then all staff get screened. People coming to work or stay in the UK for more than six months are screened for latent TB.

Q: How much does the TST test cost?
A: It costs around £13, mainly the cost of the nurse doing the test; there is an HPA test for £24 for up to £80 in private hospitals.

Q: Does TB clear after 6 months? Can a patient be re-infected?
A: As long as the person completes their treatment, they will be cured. Re-infection is possible if they are exposed to active TB again, risk drops by half is they stay on isonazid.

Q: Is the old BCG vaccination injection useful for a certain period in your life?
A: The BCG vaccine is 70-80% effective against the most severe forms of TB, such as TB meningitis in children. It is less effective in preventing respiratory disease, which is the more common form in adults.

Q: Does TB mutate?
A: TB can mutate, due to irregular or overuse of antibiotics, thus making it resistant to the very antibiotics used to treat the disease. There are reported cases of very resistant TB in India.

Q: Can you get TB from cows and other animals such as badgers?
A: The TB that affects animals is called bovine and can be spread to humans but it is not very likely. Bovine causes currently less than 1% of cases of TB in humans. With modern living conditions, better sanitation and the widespread use of pasteurisation/cooking, making risk to humans negligible. Humans however can get bovine TB by:

- *Closely breathing or inhaling air contaminated from an infected animal (which is not practical).*
- *Drinking unpasteurised milk from an infected cow or eating raw or undercooked meat from an infected animal.*
- *Handling infected meat in the dressing and processing of animal carcasses, especially if hands aren't washed carefully prior to consuming food.*

Q: Would it wise to recommend that HIV patients in high prevalent countries be tested for TB as well?
A: The WHO recommendations that HIV patients should be screened for TB and they are working hard on rolling that out.

Q: When do people get TB of the bone, intestines, etc? Is there a high proportion of these cases?
A: Extra pulmonary TB happens when the infection moves from the lungs to other parts of the body. There are cases and often difficult to diagnose, a lumbar puncture is performed to diagnose TB meningitis.

Q: What are the TB treatment side effects?
A: Most common side effects of TB drugs include nausea or vomiting, loss of appetite; jaundice (yellow colour to skin and eyes), rash and dark urine. All TB medications can be highly toxic to the liver. Severe side effects should be reported to the clinic immediately.

Q: Is MDR-TB a problem in London/UK?
A: There is 1-2 % in London and lower in the rest of the country.

Q: Is TB screening and treatment in children different from adults?
A: We use the same methods and sometimes use gastric washing to get sputum cultures. Risk of TB infection is higher in children who have no BCG vaccination in high prevalent areas.

Q: Is there anything gender specific on women – pregnancy, contraception?
A: Treatment usually involves isoniazid, rifampicin, and ethambutol for 9 months. If the TB bacteria cannot be killed by any of these first-line medicines, then other medicines and a longer treatment time may be needed.

- *WHO recommends pyrazinamide for treatment of pregnant women who have TB. Pyrazinamide is seldom used in the United States because of safety concerns.*
- *Streptomycin is not used to treat TB in pregnant women, because it may cause birth defects.*
- *The safety of second-line medicines for a developing foetus is not known. A pregnant woman with MDR-TB or is co-infected with HIV should talk to her doctor about the safest treatment options.*
- *Breast feeding - women being treated for active TB with first-line medicines can continue to breast-feed. The small amounts of medicine that get into the breast milk do not appear to harm the baby. It is recommended that breast-feeding women should also take vitamin B6 during TB treatment.*
- *Contraception - rifampicin makes contraceptive pill less effective.*

Q: Is TB a disease of poverty?
A: TB is one of the three top causes of avoidable death in poor countries.

Q: Is there a periodic testing for patients who did not have TB at HIV diagnosis?
A: UK guidelines recommend testing once, but a patient can request for screening if they have been to a high prevalent country or exposed to someone with active TB.

Q: HIV, TB and HCV co-infection treatment problems?
A: There is a high risk of high side effects and doctors should take into account drug-drug interactions to avoid hepatotoxicity.

Strengthening community response to TB-HIV – Gitau Mburu

Gitau Mburu is the Senior Advisor for HIV and Health Services at the International HIV AIDS Alliance, an International organization that supports communities to respond to HIV in 36 countries globally. He is a member of the Kenya Medical Association, a fellow of the Royal Society of Tropical Medicine and a member of the TB/HIV working group of the WHO STOP TB Partnership.

Gitau presented on how the UK community can help raise awareness of TB. UK Epidemiology:
- 9600 number TB cases diagnosed a year.
- 85% target for TB treatment completion rate and 82.1% achieved completion rate.
- People not born in UK are 21 times more likely to develop TB.
- 1989 overseas visitors regulations list TB as one the diseases that is exempt from paying for foreign visitors.
- WHO have a global plan to eliminate TB by 2015.

The risk factors for TB in the UK are the country of birth, race, age and HIV. The specific vulnerable groups include prisoners, asylum seekers and refugees, homeless people, IVDUs and support staff who with these communities.

TB and HIV co-infection
There is a lot of HIV activism in the community and none for TB. TB cases vary across regions and boroughs, with London being the worst affected. The meeting discussed what works to strengthen surveillance and diagnostics at community level:
- There should be integrated screening of TB and HIV.
- There is need to strengthen treatment support, adherence of TB and HIV drugs. Treatment defaulters should be followed up and offered community support. There should be an improvement in contact tracing especially testing for children of TB patients.
- Most cases are late presenters; there is need for community outreach nursing.
- Community integrated support services should be decentralised to poor, marginalised and vulnerable populations.
- TB and HIV influence other social and economic determinants, so it is important to educate and empower these communities - inform, invest, engage and empower!
- There should be collaboration and partnerships to support TB-HIV co-infection.

Q & A:

Q: Is there stigma around TB; the voice of TB is harder to hear, why is adherence poor?
A: There is a difference in delivery methods. There is not much TB information compared to HIV and there is almost no TB treatment competency. It is difficult to get funding for TB literacy; there should have the same activism as HIV in all countries, response to TB has been made difficult.

Q: What prevention measures are best for family and community levels?
A: If a patient is diagnosed with active TB, it most likely that they may have infected those they live with. At community level, it's about overcrowding, stay in hospital isolation if required.

Q: Is there a country case study on the global elimination of TB by 2015?
A: The roadmap was written by WHO, I have no answer at the moment, I will research and feedback.

Q: Russia and Ukraine are high TB spots, are they included as vulnerable communities?
A: I mentioned those countries as immigrations to the UK, including IVDUs.

Q: How are GPs sensitised about diagnosing TB? Should the community be engaging the private sector?
A: GPs need to be aware of the surveillance systems but they do not understand the system and do not do notification properly. I have no knowledge or experience of engaging private providers outside the NHS.

Q: What can communities do in preventing an air borne disease without stigmatizing and discrimination?
A: Communities should educate people to practice good cough etiquette (covering of mouth); there is need for another TB campaign to raise awareness of symptoms by using messages communities can identify with.

Comment: There are lots of materials for symptoms on cough etiquette that are in picture form and should be put up in public places, including the tube, etc.

Q: What do physicians do with difficult TB patients who are likely to spread active TB; do they get detained?
A: The hospital can be put those patients in isolation. The community should make educate them on the importance of being isolated to prevent TB transmission.

Comment: TB Alert are running workshops on TB awareness in the UK for World TB Day, information in available from their website and attendees were encouraged to sign up for workshops.

Company pre-meeting for Janssen – led by Polly Clayden

The meeting set the agenda for Janssen:

- What are Janssen's TB drugs? There have no been new drugs or funding for over 60 years.
- Early Bacterial Activity (EBA) how that's defined by Janssen? Time to sputum culture conversion with MGIT to see two consecutive negative tests in each culture, 25 days apart.
- MDR-TB patients
- Update on bedaquiline (TMC 207); any HIV patients in trials, how many, interactions with ARVs?
- Has Janssen considered testing new drugs together with Otsuka?
- Update on Expanded Access Plan.
- What is Janssen's paediatric development programme?
- Any changes in pricing for darunavir?
- How much funding has Janssen committed into research?
- Why Janssen refused to join the patent pool?

Company meeting with Janssen - Dr Michael Aboud, Medical Lead, Virology

A minute's silence was observed in memory of those who were and are unable to benefit from advances in treatments and who are unable to access treatment today.

Dr Aboud's presented on the treatment of TB explaining that the standard TB treatment is a six-month course of antibiotics but the duration and drugs used may vary according to a patient's age, type of TB infection, and whether they have been treated before. Treating TB takes longer than treating other types of bacterial infections because the bacteria that cause TB grow slowly, and die slowly. The standard six-month course of treatment consists of two phases. The intensive phase is first phase and lasts two months. The continuous phase is the second phase and lasts four months.

During the intensive phase, patients are normally administered a combination of four antibacterial medications: isoniazid, rifampicin, pyrazinamide, and ethambutol. These drugs are taken on a daily basis. The medications work by disrupting the functioning of the bacteria that cause tuberculosis. Isoniazid and ethambutol inhibit the formation of the bacterial cell wall. Pyrazinamide prevents bacterial growth, while rifampicin makes the bacterium unable to produce vital proteins. Rifabutin is another medication that is sometimes used in place of rifampicin during the intensive phase, but rifampicin is more widely used because of its cheaper cost. These medications are used in combination rather than alone in order to prevent the development of resistant strains of bacteria. Adherence and completing treatment are important to prevent resistance to TB drugs.

A question was raised the cause MDR-TB and he said it was either by acquisition, treatment failure of prior therapy or non-adherence. He explained that MDR-TB treatment could last up to two years.

Bedaquiline (TMC207) update:

- Active on drug-sensitive TB (DS-TB), MDR and XTR-TB
- Proof of concept in early bacterial activity (EBA) in one week.
- Increases culture conversion by approx 40% in 8 week trial in MDR-TB patients
- Shorter MDR-TB treatment from 24 months to six months (possible??)
- TMC207 has better treatment response in patients with no lung cavities.
- Side effects reported were evenly distributed across treatment groups.

PK data:

- Taking with food increases the drug exposure by two-fold in the body – metabolised by CYP3A4.
- When administered with rifampicin it decreases TMC207 efficacy by 50%.
- TMC207 has no interaction with nevirapine.
- Kaletra increases efficacy by 22% (also ketoconazole, an antifungal).
- Long term elimination of half-life; could this mean shorter treatment??
- The phase II study (C208) compared an optimised background regimen plus either placebo or TMC207 and the primary endpoint was culture conversion. There was faster culture conversion in the patients on TMC207 by 24 weeks. In secondary analyses, average time to culture conversion was 12 weeks; at 24 weeks 79% of TMC207 patients had converted to sputum-negative. Side effects were distributed evenly over the two groups.
- There were no serious study drug-related side effects nor were there clinically significant differences in laboratory results. QT prolongation (heart beat measurement) was seen on the TMC207 patients, but there were no adverse events associated with this nor were there any prolongations greater than 500 milliseconds.

TMC 207 safety, efficacy and tolerability: (C209 study)
The study was over two years in smear-positive MDR-TB patients; there was an 80% response rate at 24 weeks. Resistance to more drugs was associated with poorer response rates. Patients with no lung cavitations also responded better as did patients on three or more potentially active drugs. The most frequent side effects were nausea, arthralgia (pain in the joints) and hyperuricaemia (high uric acid levels in the blood). About 2% of the patients stopped TMC207 due to an adverse events.

A Phase III superiority study (C210) is planned with 600 patients. The primary endpoint is intended to be relapse-free cure at 15 months and a final analysis will also be done at 21 months.

MGIT (Mycobacteria Growth Indicator Tube) is a system another way to test for the resistance of TB bacteria to certain TB drugs. MGIT determines whether or not TB bacteria will grow in the presence of TB drugs. If the bacteria grow, then they are resistant to the drugs, because the drugs could not stop their growth, in not, the TB drugs work. In this case, researchers and health care workers say the bacteria are 'susceptible' to the drugs.

Paediatrics - the company considering a paediatric trial of 60 children to examine PK and safety.

Expanded Access Programme is a available in countries that have a mechanism to authorise pre-approval access of unregistered medicines, patients with pre-XDR or XDR TB at what the company describes as validated centres can obtain TMC207. In countries where this is not feasible, such as China, Russia and Lithuania, an expanded access trial is planned. However, by the end of 2011 fewer than 30 patients had accessed the drug via compassionate use or expanded access.

Q: Are there any studies on interaction with efavirenz?
A: No yet.

Q: Do patients who do not achieve negative sputum at 12 weeks get more resistant?
A: They may be technically well, but do not have data on that.

Q: There is not much difference on treatment at 18 weeks why settle for 24 weeks?
A: MDR-TB treatment is for 24 months and cannot make it any shorter.

Q: Are there any guidelines for treatment of MDR-TB?
A: WHO has guidelines that are not set in stone as different areas/countries have different settings?

Q: What happens to patients who fail after 24 weeks?
A: No answer yet, patients will be followed for 18-24 months.

Q: How was adherence in the study; 3 times a week?
A: There is no adherence data. Conversion rates were 50% at 8 weeks.

Q: What is reason behind developing TMC207 study endpoints?
A: It is a dramatic improvement for MDR-TB. Globally should be made available to people who need it at an affordable price, still being investigated.

Q: What benefit of TMC207 to the TB patient?
A: It could shorten the treatment time of MDT-TB.

Q: In the TMC207 study, 5% of patients has HIV co-infection, do you have numbers of success rate?
A: The study has small numbers and cannot make conclusions from that.

Q: There is no gender balance in the studies, shouldn't you try to include equal numbers?
A: Men get TB more than women.

Q: When will the study show reduced treatment time?
A: TMC207 phase III study will be for 9 months.

Q: How quickly are you going to collaborate with Otsuka for co-formulation with their pipeline drug delamanid?
A: I do not know.

Comment: Both companies don't have plans and that is bad news, makes sense to collaborate as learnt from HIV drugs.

Brief updates were presented for other studies:
NEAT
MODERN
Etravirine switch studies
Sense

Darunavir
The MONET study found boosted darunavir monotherapy maintains undetectable viral load as well as standard combination ART. There is a concern that the penetration of protease inhibitors into the CNS may not be sufficient to prevent replication of HIV, more research if needed to monitor psychiatric or CNS side effects.

- Dosing - will soon be a single 800mg pill (approved in the US) and will be about 30% less the size of the original pill.
- Studies with Gilead's booster, cobicistat, if successful, could mean co-formulation with new Gilead quad pill.
- Developing a second pill combining darunavir, cobicistat, Emtriva, and an investigational new form of GS 7340.

Comment: More people would use darunavir if it were less expensive, current preference is kaletra.
A: The price of darunavir was reduced by 25% since June 2011 from $3 to $2.50. Patients do have a voice within Janssen.

Q: How quickly would prices change if it were a EU buying scale instead of current UK style?
A: We do understand the economics but we have only been in HIV business for 6 years.

Rilpivirine:

- Rilpivirine is an NNRTI approved in 2011. Small tablet - adult dose once daily single 25 mg tablet for treatment naïve patients with a viral load less than 100k. It has to be taken with food.
- Side effects: depressive disorders (depressed mood, depression, mood altered, negative thoughts, suicide attempt, suicidal ideation), rash, nausea, liver problems.
- Resistance to rilpivirine is closely linked to less than perfect adherence and is likely to result in resistance to other NNRTIs including nevirapine or efavirenz. For this reason it is not recommended to use if you are not adherent.
- Rilpivirine is included with tenofovir and FTC in a fixed dose single pill formulation called Complera.

Q: Have you had any reported problems with rilpivirine on dietary advice; restrictions?
A: Diet is not specified, only recommended to take with a meal, not prescriptive about calories or quantity.

Patent Pool:
The meeting requested an explanation from Janssen's Ronan Collins on the company's recent decision to the Medicine Patent Pool. Janssen do not to allow licensing of its antiretroviral products as part of the international collaboration to enable sustained and affordable access to latest HIV medicines in poor countries. The community are not happy with Janssen's decision and feel there is not a very good case for not joining and think there is scope and room for the patent pool to work. Janssen promised to will provide an answer about their decision back to the UKCAB, in a week after the meeting. Janssen is still doing other things in terms of access in resource-limited settings, with EPA in 112 countries since June 2011.

Q: Is the decision on the patent pool a definite NO?
A: Currently YES, we are doing it in the way we feel is appropriate.

Comment: The people who will benefit from the patent pool are the people who buy your other products from Johnson and Johnson.

UKCAB London drug prescribing survey feedback – Mark Platt

Mark reported that the survey went live and is been run on several UKCAB members' website. Results to date show that:

- Home delivery is having a big impact.
- 37% of patients have been switched.
- 60% of survey respondents were aware of the changes.

The concern was that given the number of patients in London, the response numbers were still low to have a complete picture. Most of the patients in London do not have Internet access and it was suggested to have a paper version that would reach that demographic. Mark is still trying to get a paper version of the survey that can be completed at various organisations/patient groups during support group sessions, etc. He currently has a quote for £60/1000 copies, which the meeting agreed, was reasonable and could be paid by the CAB. Logistics on distributing the form and ensuring its completed and sent back were discussed. Distribution will be through support groups and patient groups; the form will have a freepost address. Another suggestion is to email printable version to organisations that would hand them out to service users to complete and return. Could the i-Base freepost address be used?

Mark is still to meet with Claire Foreman to establish if the LSCG can contribute to the printing costs.The meeting appreciated Mark taking the survey forward and would also like a deadline on completing the survey. Mark suggested three months in time for BHIVA spring conference, but could run for 6 months. The survey could be used as an example within the EU community groups.

Q: There are patients who do no even know the name of the drugs they are taking, how do we deal with those?
A: The questionnaire will have pictures and names of tablets.

Q: We are getting requests from media on when preliminary data will be presented, any idea on how to handle these?
A: All queries should be directed to Mark or Mem, we own this data and decide on when we present this data.

Q: Level of survey awareness in the community about the changes is low and there are patients who do not access support groups, how will we reach out to them?
A: There is a question in the survey to address this and room for comment.

Next meeting

Date: 13 April 2012
Topic: Diagnostics