Meeting of ViiV Healthcare and EECA CAB,

October 5, 2011, St. Petersburg, Russia

MINUTES

Participants:

From ViiV Healthcare:
Jean-Marc Steens – Medical Director, ViiV Healthcare International
Andrey Polyakov – Medical Director of ViiV Healthcare Russia.
Evgeny Bukin –Vice-MD of ViiV Healthcare Russia.

From EECA CAB:

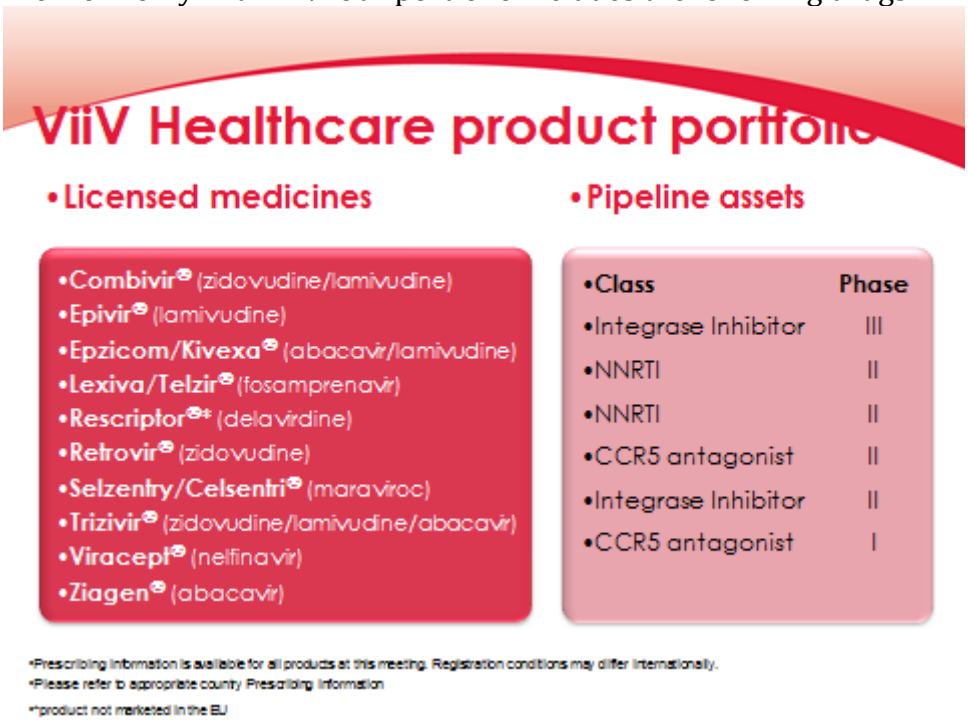
Svilen Konov	ECAB
Andrey Zlobin	Russian CAB
Denis Godlevskiy	ITPCru
Dmitry Sherembey	Ukrainian CAB
Natalia Leonchuk	ECUO PLHIV
Ekhtiram Pashaev	Caucasus Sub-Region
Grigoriy Vergus	ITPCru
Inna Boyko	Ukrainian CAB
Ivan Varentsov	EHRN
Vladimir Osin	ITPCru
Elena Khodanovich	Belorussian CAB
Vyacheslav Vasilyev	Estonian CAB
Albert Zaripov	Tatarstan CAB
Alexey Kropinov	All-Russian Union of PLHIV
Eugenia Kalinichenko	Central Asia Sub-Region
Sandris Klavins	Baltic States Sub-Region
Lyudmila Untura	BUM Sub-Region (Belarus, Ukraine, Moldova)
Irina Teplinskaya	EHRN

Moderator: Anastasia Solovyeva

Presentation 1. Jean-Marc Steens.

ViiV Healthcare was established 2 years ago by GlaxoSmithKline and Pfizer and has a broad portfolio of ARV medications. The main focus of the company is patients. The legal environment in which the company operates has changed. 10 years ago, the issue of confidentiality at meetings with patients was the issue of trust. Now, however, the company has to go through numerous legal procedures in order to be able to share information.

There are 34 million of people living with HIV (PLHIV) in the world, and their number is continuing to increase in the countries represented at this meeting. In terms of development of new medications, we have achieved considerable success; however, it is necessary to meet the demand of the patients both for treatment and prevention, as there is evidence proving that treatment is prevention. Patient organizations must promote this idea further. Mother-to-child transmission of HIV (MTCT) can be prevented and reduced by 2/3 using very simple methods; however, much still remains to be done in reality. The patients also play a very important role in this in terms of realization. The number of people receiving ARV is 7 million, but a greater number of people need treatment.
We work only with HIV. Our portfolio includes the following drugs:

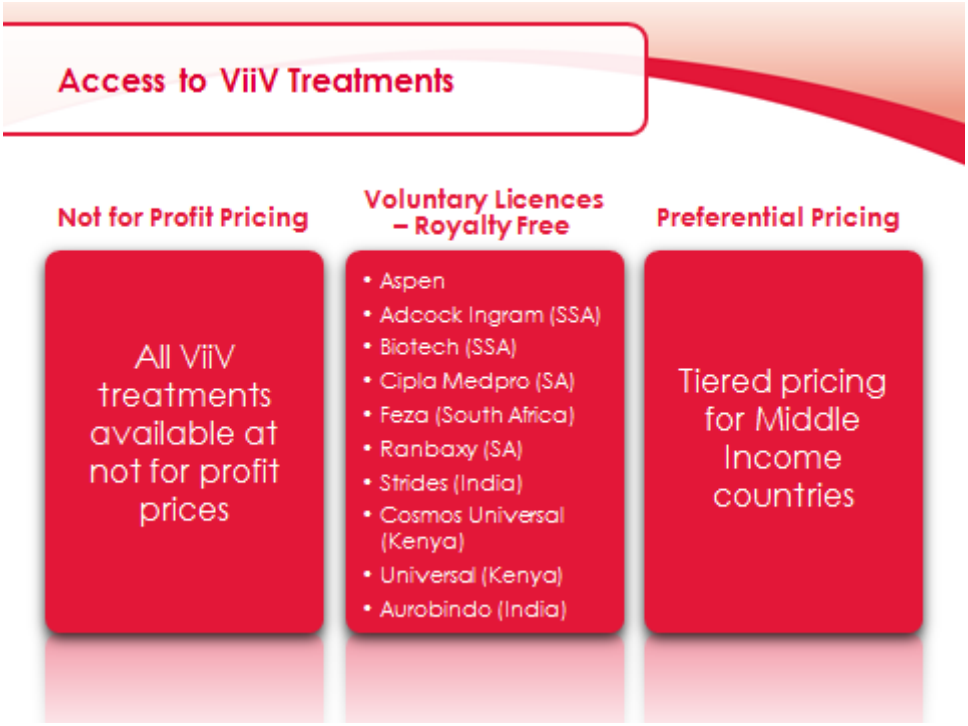


We need new research and we need to seek for resources to finance our research.

New medications:
II 572 – we are keeping the research phase schedule and are expecting good results. We are worried about people being overenthusiastic about this product.
NNRTI – the research is put on hold, but it does not mean it is over.
New CCR5 antagonist, Integrase Inhibitor, which may change the dynamics of HIV treatment, can be administered once daily, maybe once a week in the future or even with greater intervals. It is tested in humans for the first time.

Strategic goals: right medications for every patient.
The company does not agree with WHO that one solution can suit everybody. In terms of HIV/TB co-infection, one medication cannot suit all patients. We think that the needs of every patient must be taken into account, and that treatment must be optimized. The needs of all

patients are different. Treatment accessibility is very important. It is important that the drugs reach the patients, and there is no single solution for this problem.
Changing the treatment paradigm means reducing the treatment load on the patient, that is administering the drug once a week or even once a month. We used to concentrate on the virus, but those who start treatment early never recover the immune system fully. Maybe, in our research we used to focus too much on the virus itself, and not on recovering the immune system. We need to investigate how we can recover the functions of the immune system.
ViiV Healthcare follows certain principles for availability: in less developed countries we offer non-commercial pricing. The products in the pipeline will also be available at such prices. Voluntary licenses have been granted to the following companies: Aspen, Cipla, Ranbaxy, Aurobindo etc.



Portfolio of new integrase inhibitors: Combivir+Maravirok 572 fixed-dose combination (FDC).

QUESTION: You mentioned a list of voluntary licenses; there are none for companies in our region. Have you ever negotiated about issuing voluntary licenses for products in Phase 3?

Jean-Marc: We issue licenses to companies working in least developed countries, and only for registered products. Between 2000 and 2005 we had to stop trials of certain products due to toxicity issues. It is important for us to conduct the trial till the very end and make sure the product is both effective and safe.

QUESTION: Is it true that ViiV Healthcare plans to launch 1 new product per year, and that you plan to issue voluntary licenses as soon as possible? In Ukraine, there are manufacturing facilities for ARV medications. Is it possible to use this principle for the products already developed by Pfizer and Glaxo?

Jean-Marc: Most products are covered by the licenses already issued. We issue licenses for registered products, and registration can take some time depending on the country. Some products have a more complex administration procedure than others. Maravirok requires a tropism test. If the country cannot provide such tests, we will not issue a license. So, we look at the technical capacities inside the country. The most important thing is that patients receive treatment. Voluntary license is just one option to achieve that.

QUESTION: You mentioned investing your profit into new research. Are you investing into the development of AIDS vaccine?

Jean-Marc: If Glaxo does make a vaccine, it will be in cooperation with ViiV Healthcare. 20 years ago I used to say that in 10 years time we would be able to make something, but now I am not that certain. It is difficult to develop a safe and efficient vaccine. The efficacy level was very low. Glaxo Biological invests a lot into developing vaccines; however, the success is very little.
Andrey Polyakov: If we compare vaccines with microbicides, the effectiveness of microbicides is much higher. Taking ARV for prevention purposes is even more effective. Now, let us look at the ethical side of the trial. In order to make a 90% effective vaccine, I cannot even imagine what kind of cohort we can enrol. In terms of eliminating the virus, there has been some progress. We have the Berlin patient who underwent a stem cell transplant with a particular genetic defect known as Delta-32, preventing the virus from entering the cells. ViiV Healthcare does not develop products itself; instead, it invests into scientific research of Glaxo and Pfizer.

Presentation 2. Products

Abacavir + Lamivudine (Kivexa)

Myocardial infarction. 3 years ago there was a research looking at the number of infarctions and PIs causing increase of lipid concentration. The results of this survey were predictable. There research studied the connection between Abacavir and cardiovascular diseases. The scientists discussed the risks of developing cardiovascular diseases.

Till now, no specific factors have been revealed showing what exactly causes cardiovascular diseases. We cannot say that the issue has been resolved completely, but the FDA analysis was very thorough and didn't reveal any linkages between Abacavir and the increased risk of cardio-vascular diseases..

Availability of hypersensitivity tests in the regions:

Jean-Marc: One of the side effects of Abacavir is hypersensitivity reaction. Usually, this reaction developed on day 14 of clinical trials, and did not appear after day 40. Only 2-3% of the patients develop hypersensitivity, but the health consequences can be very serious.
The cause of the reaction was HLA 5701; trials were conducted in the west. In some countries, for instance, in Africa, only 0.1% of the patients developed hypersensitivity. It was recommended to look at the reaction (rash). Taiwan also has a very low percentage of patients developing hypersensitivity.

Andrey Polyakov: In Russia, we work with doctors on how to diagnose hypersensitivity. There are special printed educational materials. There is a local hypersensitivity test under development. It is based on polymerase chain reaction, and most laboratories in the Russian Federation (RF) are capable of performing these tests. It is 10 times cheaper than the analogous tests in developed countries. A year ago, the Ministry of Health (MH) registered this diagnostics method and included the test into the list of tests eligible for state purchasing; however, due to unknown reasons, the test is not being purchased under the National Project. In Ukraine, such tests are also available, and there is a possibility of supplying them from Ukraine. The information about the other countries is not available. ViiV Healthcare Russia used to deliver the tests free of charge to the regions in need, but it cannot guarantee that this practice will be continued.

QUESTION: Is the test supplied for every patient in the region starting abacavir?

Andrey Polyakov: There is no such policy, but the doctors are recommended to perforrm hypersensitivity tests. There is a system of pharmacological surveillance. Thus far, no deaths related to hypersensitivity have been registered. An epidemiological research has been conducted, showing that 4% of the patients develop hypersensitivity.

Maraviroc

Jean-Marc: Maraviroc is a new drug which is increasingly used in different countries. It blocks receptors on the surface of CD4 cells. In North America and Australia, the drug is used only for experienced patients. In Russia, we are planning to find out whether the drug will be effective for naïve patients using a special tropism test, which is similar to a resistance test. Since the technology is similar to a resistance test, this tropism test for Maraviroc can be easily included into the list of tests already available. The earlier we start to use Maraviroc, the higher the probability of successful treatment is.

Maraviroc and Kombivir

Clinical trials have been conducted for these two drugs, and we are planning to manufacture a FDC (Maraviroc + Kombivir). In future, we have to conduct trials for Maraviroc and Kivexa during 3-4 years.

QUESTION: Why was RF chosen as a place for conducting these trials? And why Kombivir?

Jean-Marc: There results of trials involving Maraviroc and Kombivir are already available. The number of patients receiving Kivexa is not big. We chose RF because most naïve patients start with Kombivir, and it is not planned to switch to Kivexa. We are also planning to promote this combination in other countries (Asia and Latin America).

Andrey Polyakov: The company is against the “one pill for all” strategy. The local tropism test was a priority. Genotype testing is cheaper, and this method is being implemented on the basis of the tests already available in cooperation with our partners in RF. Phenotype tests (HLA tests) will be compared to genotype tests (genotype tests will belong to the Institute of Epidemiology, their cost being approximately $100).

QUESTION: Have you conducted trials on interaction between Maraviroc and methadone? Are you planning to supply Maraviroc to Azerbaijan?

Andrey Polyakov: There have been no such trials in RF, they are forbidden here. Maraviroc is a cytochrome inductor, so interaction is possible.

QUESTION: Will tropism tests be supplied free of charge like the hypersensitive tests? What is the cost of these tests? Maraviroc is promoted in RF for naïve patients, but we have no mandatory treatment guidelines, and there are concerns that it may be prescribed due to non-medical indications.

Andrey Polyakov: Yes, tropism tests will be supplied, but their cost is high ($1500). We have only received the Marketing Authorization, and it is difficult to say when it will appear. First, we need to obtain permission for naive patients. In the US guidelines, this drug is not yet even an alternative, it is an back-up option. In 2013, in theory, we will obtain permission for supply, and there will be a recommendation to use it in a limited number of patients.

QUESTION: Example: In St. Petersburg, Kivexa is purchased in increasingly larger volumes. There was a patient who was not offered Abacavir tests upon prescription. We also failed to explain the difference between Efavirenz side effects and Abacavir hypersensitivity to the doctors.

Andrey Polyakov: Stokrin and abacavir is another field where training for doctors and patient0s is needed. You can prescribe Abacavir without a test, the doctor can cancel the prescription. However, it is not possible to prescribe Maraviroc without a tropism test (it is stated in the leaflet). Fuzeon was prescribed in one of the republic in order to increase lymphocyte concentration. Tropism test introduction will be decided upon through meetings with MH and consultations with experts.

Jean-Marc: What do medical experts do in pharmaceutical companies? They compare the instructions for drug products with the norms in specific countries. We will not supply Maraviroc to countries where there are clinical contraindications (absence of tropism tests). The advantage of the medical division in ViiV Healthcare is that they do not allow the commercial department to interfere.

QUESTION: Is there interaction between Maraviroc and other ARVs? Use of Maraviroc in pregnant women?

Andrey Polyakov: There is interaction with PI and NNRTI, Maraviroc dosage increase is needed. The results were presented at the Rome conference. The effect on the foetus is not known; however, there have been no special trials.

Jean-Marc: If a woman taking Maraviroc gets pregnant, we enter her data in a special register; there have been no problems thus far, we are monitoring the situation.

QUESTION: Are there paediatric forms of Maraviroc? Are you planning to negotiate with WHO on renewal of the protocols for the countries of the regions using WHO protocols?

Jean-Marc: We have already started discussion with WHO, about Kivexa, for instance. We are planning to register Maraviroc in all countries where GSK are present. There is a liquid form for children from 2 to 6. However, trials of paediatric forms start only after the trials of the adult form. The WHO guidelines considers one treatment regimen, which may not suit all patients, we are working on once-daily forms. Negotiations on renewal of guidelines are being conducted; the new draft will be available only next year. We want to provide them with as detailed information as possible.

Andrey Polyakov: It will not be possible to establish a network of laboratories capable of working with tropism tests in developing countries. There is a high risk that Maraviroc may not appear in CIS countries.

QUESTION: Maraviroc is registered in our country, but the information leaflets are not available. Can we get access to the leaflet beforehand? Are you planning trials of Maraviroc and Kivexa? What will the price for Maraviroc be?

Andrey Polyakov: It is possible to obtain the leaflet. Yes, we are planning to conduct a trial of Maraviroc and Kivexa. FDC (Maraviroc and Kombivir) will cost the same as Maraviroc alone. The price will not be as high as the price for Raltegravir, for instance. The price for Kivexa has gone down dramatically, and the price for Maraviroc will be acceptable.

Jean-Marc: Phase 3 is underway, involving naïve patients, 800 people in total. The patients are in week 24, so far the product appears to be safe.
VIKING study, involving patients resistant to Raltegravir. We add 572 to optimize treatment.

FDC Abacavir + 3TC and 572. Administration 1 tablet/once daily, which is convenient for the patients. The effect of the drug is as we planned, there are no problems in terms of interaction with Abacavir.

Dolutegravir paediatric program. We cover 4 age groups. We prefer to wait till we get effectiveness results for adults before starting with children.

Andrey Polyakov: It is mainly RF that takes part in the Dolutegravir research. We are not taking part in the latest trial, as Atripla is not registered in Russia. We take an active part in the Spring study, Sailing, and are planning to take part in the Viking study. Adverse effects are registered centrally. I don't have the information about clinical trials of Dolutegravir in other countries.

Jean-Marc: This drug does not require any tests prior to prescription. There are many trials looking at drug-drug (DD) interaction. There are many drug products that must be taken 2 hours after or 6 hours before taking Dolutegravir. In terms of DD interaction we can see that it is a good product. We have looked at interaction with TB medications, with Methadone, at the effects in patients with genitourinary system dysfunction, and also at the effect the drug has on hidden reservoirs. This list is not complete, there may be additional trials.

QUESTION: Are you planning to conduct a trial on interaction of Dolutegravir and Hepatitis C medication? Do the trials that are being conducted include patients with Hep C? Interaction with street drugs is a very urgent issue for our region.

Andrey Polyakov: There are no clinical trials on interaction with street drugs. Dolutegravir can be used with tenofovir. There have been no trials including buprenorfin, we are planning to conduct a trial with Methadone in the nearest future. Not used with Etravirine. IDUs are a very difficult group in terms of monitoring, it is impossible to enrol them in the study. This might rather be an exclusion criterion. It is better to study this interaction in real practice.

Jean-Marc. NNRTI 761
We are developing 2 similar products. The most popular are such products as Efavirenz. Efavirenz has certain side effects on the central nervous system, and we see resistance to NNRTI.
The first drug product is Relsivirine, in phase 2, developed by Pfizer.
The second product is 761, developed by Glaxo. There were side effects associated with seizures. We decided to stop the trial and find out the cause of the seizures before we start using the product. The trials of many drug products that are available on the market now have been suspended due to similar reasons. If the experts decide that it is not our drug product that causes these symptoms, we will continue the trials.
Andrey Polyakov: We think that Russia will take part in Phase 3 of Relsivirine.

Andrey Polyakov: Social Responsibility.
Positive Action is the only programme of ViiV Healthcare for vulnerable groups. There are 65 projects in 63 countries of the world. Most programmes are focused on Africa and South-Eastern Asia. In Russia, there are projects in Chelyabinsk and St. Petersburg; we also have projects in Armenia and Azerbaijan.

Positive Action For Children Fund has the budget of 50 million British pounds. The programme is aimed at preventing MTCT. Russian organizations are not included in the programme so far.
In 2010, we supported 11 organizations from 9 regions of RF. The company allocates funds for AIDS centres, for delivery of medications. 11 million roubles have been allocated this year for social projects and AIDS Centres.

ACCESS

Andrey Polyakov: The company has a clear mission: Voluntary licenses for countries with limited access, special pricing for countries with middle income. The company will consider the possibility for further reduction of prices, including prices for Kivexa.

QUESTION: Are you planning to establish your facilities in the countries of the region?

Andrey Polyakov: Yes, on the territory of RF. Now we cannot name any potential partners. This includes almost the whole portfolio.

QUESTION: Do you want to grant a license to manufacturers in Ukraine? And under what brand can the drug products be manufactured if granted a voluntary license?

Andrey Polyakov: Under ViiV Healthcare brand name. We have not yet considered manufacturing in Ukraine. We do not see a big need for manufacturing in the Ukraine. According to the estimates, the products manufactured in Russia would be 20% cheaper.

QUESTION: Would you be interested in joint procurement?

Andrey Polyakov: It could lead to lower prices. However, every country has its own rules regarding registration of drug products. There is an issue of packages: Every country has its own requirements.

QUESTION: Do you involve patients in trial planning?

Jean-Marc: Yes, patients in Europe, Latin America take part in discussions. Sometimes we change the trial after consultations with patients. We try to take into account discussion with patient organizations.

QUESTION: When conducting clinical trials, do you develop 1 protocol for all countries? Our countries would like to participate.

Jean-Marc: You can be included into this process. However, this applies to new programmes, not the current trials.

QUESTION: Are ViiV Healthcare at the final stage of negotiations with the Patent Pool?

Jean-Marc: The negotiations have been successful thus far, at the next meeting our colleagues would be able to tell you about the results.

QUESTION: We ask you to consider including EECA as a region eligible for taking part in Positive Action for Children programme We would also like to have a person who could answer questions concerning the whole region, not only Russia.

Jean-Marc: There is a board responsible for approving the applications. EECA would be included next time.

Anastasia Solovyeva:
The remaining questions for ViiV Healthcare:

1. Interaction of Maraviroc and Methadone
2. Pricing policy and dialogue with people responsible for it
3. Difficulties the company faces when registering products in our region
4. Plans on manufacturing products in EECA
5. We would like to obtain information about clinical trials beforehand and be involved in the process
6. Reaction of the company towards excessively high prices
7. Map of the company's offices in the region, responsibilities
8. Access to the clinical trials database in the region
9. Details on Maraviroc study in Russia
10. Slides in Russian
11. Information on all patents in the countries of the region
12. Detailed information about projects in Azerbaijan and Armenia (Rostropovich Foundation): Purpose, objectives, who realizes what.

Jean-Marc: We were impressed by the level and the maturity of questions, it is good to have such communication.
Andrey Polyakov: We are very grateful for inviting us to this meeting.

The meeting is over