Meeting Minutes
EECA CAB and Gilead Sciences

October 23, 2014, Tbilisi, Georgia

Meeting participants

Gilead:

Enrico Magnanelli, Director International Distributor Markets
Graeme Robertson, Director, Access Operations & Emerging Markets
Felipe Rogatto, Associate Director, Medical Affairs HIV, Europe, Middle-East, Australia (EMEA)
Michael Mertens, Senior Medical Project Manager HCV, Europe, Middle-East, Australia (EMEA)
Veronica Krongauz, Medical Project Manager, Russia
Stephen Head, Associate Director, Public Affairs, Europe, Middle-East, Australia (EMEA)

ВЕЩА КАБ:

	Name	Organization	Country
1	Ehtiram Pashayev	Community Association again AIDS	Azerbaijan
2	Yulia Kalancha	PEREBOI.NET.UA	Ukraine
3	Sergey Dmitriyev	All-Ukrainian PLHIV network, Kharkiv office	Ukraine
4	Nurali Amanzholov	Kazakhstan Union of People Living with HIV	Kazakhstan
5	Anahit Arutyunyan	PLHIV Network of Armenia	Armenia
6	Artem Esse	Patients in Control	Russia
7	Natalia Minayeva	My Home NGO	Kazakhstan
8	Denis Maruha	League of PLHIV of Republic of Moldova	Moldova
9	Alexandrs Molokovskis	HIV.LV Association	Latvia
10	Dmitry Sherembey	Patients of Ukraine	Ukraine
11	Tatevik Tatulyan	PLHIV Network of Armenia	Armenia
12	Aisuluu Bolotbayeva	Central Asian HIV Fund	Kyrgyzstan
13	Yurgis Andryushka	Pozityvus Gyvenimas Association	Lithuania
14	Sergey Biryukov	AGEP`C NGO	Kazakhstan
15	Alexey Mikhaylov	ITPCru	Russia
16	Mari Chokheli	Open Society Foundation	Georgia
17	Grigory Vergus	ITPCru	Russia

Moderators: Alexandra Volgina, Denis Godlevsky, Tatyana Khan.

Beginning of meeting. Introduction of participants.

HIV drugs

Stribild: Two phase III trials were conducted in previously untreated patients for comparison with Atripla or atazanavir + ritonavir (ATV/r) + Truvada regimen to review Stribild efficacy.

Stribild has a good virological response when compared to Atripla. Stribild shows a more favourable safety profile and comfortable intake (one tablet once daily) compared to ATV/r + Truvada. Less adverse events as diarrhea (compared to ATV/r), less insomnia, dizziness and abnormal dreams compared to the efavirenz (NB. – included in Atripla).

One more study in which patients that were suppressed on protease inhibitor (PI) and switched onto Stribild. The main reason why the patients wanted to participate in the trial was the simplified therapy regimen. As the result, 94% of the patients switched to Stribild maintained viral suppression in their blood compared to 87% who remained on PI. The advantage of the switch to Stribild was obvious: low incidence of virological failure and no resistance. No new significant adverse events were found in Stribild compared to remaining on PIs; Stribild was associated with less laboratory abnormalities. Stribild is associated with elevation in serum creatinine due to an inhibition of renal transporters of Creatinine, but this does not result in renal failures.

Another trial evaluated the Switch from NNRTI to Stribild. Its goal was to simplify the treatment regimen. Week 48 data showed a numerically higher percentage of patients with a suppressed VL compared to remaining on NNRTIs. Virologic failure was rare and no resistance emerged from those patients failing. As for the previous study, switching to Stribild was associated with a favourable safety profile.

Question: Did people with addictions (alcohol, narcotics) were included in the trials?

Answer: Drug use was not an exclusion criterion. The challenge is to report these data in this subpopulation as many patients don't disclose it.

Question: Is there any data on interaction with opiate substitution therapy (OST)?

Answer: There is data on interaction of Stribild with methadone. No significant deviations were detected.

Company drugs in the pipeline

TAF (tenofovir alafenamide): an enhanced pro-drug of tenofovir. With TAF, more tenofovir is released inside a cell (thus less tenofovir circulates in the plasma, more – in the white cells). This can be related to a more potent activity of the drug, more efficient in viral load suppression compared to TDF, and possibly causing less adverse events.

A new trial compared Stribild (containing TDF) and Elvitegravir/Cobicistat/Emtricitabine/TAF – E/C/F/TAF. In one year, similar number of patients on Stribild and on E/C/F/TAF achieved VL suppression; a lower rate of virological failure is detected. A better renal and bone safety was seeing in the TAF group.

There is one more phase II trial of a combined drug based on PI, darunavir/cobicistat/TAF/emtricitabine. It is being conducted together with Janssen that is responsible for this drug's marketing. No resistance, a more favorable renal and loss of bone profile.

Emtricitabine/TAF (F/TAF): there are two different dosages – 10 mg and 25 mg TAF. The patients studied were transferred from Truvada + third drug to F/TAF + third drug. The outcomes will be available by late 2015 or in early 2016.

Question: What was the third drug?

Answer: This may be any boosted PI, also efavirenz, rilpivirine, etc. TAF is also used for treating Hepatitis B. TAF is considered to be a stand-alone drug with a dosage of 25 mg.

Question: About Stribild – you change the drug for a drug with TAF, are studies with STB still ongoing?

Answer: Stribild phase III is over, but the drug is being studied in specific groups such as female population (the trial is running in Russia), co-infection of hepatitis B and C, interaction with other drugs, for example for treating cardiovascular diseases.

Question: TAF looks like a good drug, especially from the point of view of side effect reduction. Any plans on issuing voluntary licenses on this drug and inclusion in them countries of the region?

Answer: There are agreements with Indian industries and the Patent Pool. On completion of clinical trials, the technologies will be handed over to generic companies. Today some EECA countries are already parties to those agreements.

Comment: This list did not include many countries of the region that badly need this drug. Why?

Company comment: The principle used for choosing countries is low income according to the World Bank classification.

Question: Georgia was included in the TAF agreement, while Ukraine with many people with hepatitis C wasn't. What was the principle?

Answer: The list of countries was offered by the Patent Pool.

Question: Any plans on TAF registration in Moldova?

Answer: The studies will take one more year, after which it will be clear – will the company submit the DMF for the drug's approval by FDA, after which EMA approval will be required. Now it's too early to talk about plans and timeframes for Moldova.

Question: Will the company work with TAF as a single HIV drug?

Answer: Only with a dosage of 25 mg for hepatitis B. For HIV – only as a component of F/TAF.

Question: When the TAF technologies are transferred to Indian companies, will part of the TAF clinical trial data be transferred, which they can potentially use in registration?

Answer: The technology transfer mainly includes a transfer of workflow particulars.

Question: That is, it may happen that generics will do their own trials?

Answer: This depends on regulatory agents. In some countries it's enough to get the innovator drug authorized, while generics may use the data on the innovator drug without doing a trial. It was very quick with Truvada.

Comment: It went real quick with Truvada, as tenofovir had already been registered as a stand-alone drug, while in the case of TAF the company is not going to authorize it separately.

Question: Any plans on Atripla combined with the new TAF?

Answer: No, efavirenz (contained on Atripla) may not be considered a gold standard by some people anymore due to its safety profile (mainly CNS safety).It is expected that patients will soon start taking more tolerable regimens.

Question: In the Baltic countries the company is not very active. What's the company policy on these countries?

Answer: Latvia, Estonia and Lithuania are now under the responsibility of the Polish company office, which is now working on the putting together of the DMF's on the company's ARV drugs. The question about the company plans for the Baltics will be asked to the Polish office representatives at the Glasgow conference (NB. – an answer to this question will be provided in written form).

Comment: When the migrants get back to Latvia, for example from Germany where they got eviplera, they get in a situation whereby they can't get their regimens, since it is not included in the country's compensation list.

Answer: Company priority – ARV drugs authorization in the Baltic countries; for the time being we can't provide any timeframes, but this information will be available in written form.

Access presentation

Russia: for the time being, Viread and Truvada have been authorized, as they are promoted by Delta Medical, and Eviplera promoted by Janssen. DMF's have been submitted for Atripla and Sofosbuvir, and Ambisome (for mycosis). Viread and Truvada have been submitted for inclusion in the Vital and Essential List (NB. – the list is being reviewed).

Azerbaijan: Truvada and Viread have been authorized, an efavirenz generic is available. There are no plans to authorize Atripla.

Question: Why no authorization is planned for Atripla?

Answer: The doctors claim they prefer monocomponents to combination, since it gives them an opportunity to make changes to the regimen in case of adverse events.

Comment: Atripla's authorization in a country doesn't mean its availability. This year BMS (NB. – marketing the drug in the Baltics) has not submitted the drug to the compensation system, nor to establish a maximum allowable price in Latvia or Lithuania.

Company comment: Gilead and BMS have agreed upon price reduction in the Baltics, but BMS faced a number of challenges, including supply logistics-related. We will get in touch with BMS again on this account. The name of the BMS contact person responsible for the access will be provided in written form.

Question: When you say BMS is responsible for the region, do you mean this company makes 100% of its profit in these countries?

Answer: The Atripla market is divided by three companies (Gilead, BMS, MSD), and we are not aware of how the profits are divided.

Question: Does Gilead sustain any damages pursuant to the activities of the two other companies on Atripla sales? Can the company influence the behaviors of BMS and MSD?

Answer: If the drug is selling without any revenues, then yes. About the influence on BMS and MSD – if you have a feedback about their work or complaints which would put Gilead's reputation under threat, we would like to encourage you to send them right over to us, we will try to take measures.

Question: When you say "generic is available", what do you mean? That the generic is authorized in the country or that the generic is brought over by GF programs?

Answer: When we say "generic is available", this means its physical presence in the country, regardless of authorization status.

Comment: All countries for which you indicate that "generic is available", the generic is available via GF programs, which means it's not authorized in the country. By 2017 GF will quit its operations in Armenia, Georgia, Belarus, Kyrgyzstan and other countries of the region, which means the drugs will be procured on state money. Without authorizations for Atripla, Truvada or Viread, these drugs cannot be procured. We ask you not to pay attention to the "availability" of efavirenz in these countries, but please do submit the drugs for authorization because otherwise the patients will not have access to them since 2017.

Comment: That doctors prefer monocomponents – if you ask patients, the opinion will be different; from their point of view - combinations have a tremendous advantage.

Company comment: We fully support the idea of combination drugs and simpler regimens. But there are incidents when monodrugs also have their advantages.

Access presentation: continued

Eviplera market division: Janssen is responsible for the marketing in most countries.

Stribild: the company is working on making the drug available in countries outside of EC.

TAF: plans will be made in the near future.

Cobicistat: as a standalone drug – used as a pharmacokinetic booster for atazanavir and darunavir.

Question: Can cobicistat become a booster for other protease inhibitors that may appear in future?

Answer: Theoretically yes, as well as for integrase inhibitors, but clinical trials must be conducted.

Question: What's the economic benefit of this new booster? There is an analogous booster - ritonavir – it's cheap. What's an additional advantage of cobicistat?

Answer: For the time being, Cobicistat may be used only with atazanavir (BMS) and darunavir (Janssen). Its use as a standalone drug will be limited. BMS has already been submitted for approval as a combined form. About the advantage over ritonavir – it's not better and not worse, this is one more therapeutic possibility and an opportunity to use other different treatment regimens. Cobicistat may be combined with other drugs, while ritonavir cannot be included in other combined forms. Cobicistat has advantages over ritonavir on drug-drug interaction (may be used with methadone, ritonavir may not).

Question: On Atripla authorization in Russia – what will the price be?

Answer: There is no plan for the price, it will be considered after the authorization.

Comment: Gilead is a multibillion dollar company; we have doubts you haven't considered Russia's potential price level.

Question: What's the price of Atripla in Europe? What's the average price of Atripla?

Answer: We have no information on particular countries. The answer will be available in writing.

Comment: We will explain why we asked this question. In EECA countries we often face a situation when the price declared by the manufacturing company is way different from the retail price, despite all stringent in-house policies to struggle with corruption. EECA CAB meetings have more than once displayed a situation when the manufacturing company was surprised to learn the price at which its drugs sold in one or another country of the region. We want to help you.

Company comment: A distributor's price has logistics costs, VAT, etc. Gilead does not adjust their operations, but we will appreciate reports on the company's drugs prices.

Hepatitis C drugs

Here are Gilead's main requirements for hepatitis drugs in the pipeline: high efficacy (VR over 90% in 12th week), good tolerability (minimum side effects from drug-drug interactions), convenience in use (short course, simple dosage), efficient in broad populations (efficacy for all genotypes and all specific populations).

Sofosbuvir (NS5B polymerase inhibitor): the first wave of the trial included sofosbuvir with ribavirin and sofosbuvir with pegylated interferon and ribavirin. Sofosbuvir was approved in the EU for genotypes 1-6. The drug is for oral use, 1 pill once a day. Has a high barrier again resistance and minimum drug-drug interaction; food does not influence the drug's absorption. Over 4000 patients have received the drug for the time being; it is very well tolerated and has no specific adverse events. About specific groups – there is no significant interaction with ARV and OST drugs, immune suppressive drugs. The only drugs contraindicated to be taken with sofosbuvir are Pgp inducers, one of such drugs is refampicin for TB. Often both diseases are concomitant, in which case it's recommended to primarily deal with the TB, then – with the hepatitis.

The trial involved patients from special populations – those who are listed for livertransplant or had had a liver transplant, with decompensated cirrhosis, initial kidney or blood diseases. The generalized data shows that among all these groups and genotypes the clinical efficacy in

12 weeks achieved more than 90%. No resistance was registered. The incidence of quitting treatment was hardly 3%; no further adverse effects were detected.

The drug is authorized in the US, Europe, Turkey, Egypt, Australia. In South America, India, Russia, China, Saudi Arabia it's now being reviewed by authorities. The drug is included in all the standards for hepatitis C treatment.

Question: Were there any pediatric trials?

Answer: There are two studies, including several genotypes . One of them – on sofosbuvir with ribavirin, but since ribavirin may be very toxic for this group, a second trial was started, on sofosbuvir with ledispavir. The data should be available in 2018.

Comment: We would like to encourage you to reject ribavirin as a toxic drug in pediatric clinical trials, and please include people from the patient community into clinical trial designs.

Sofosbuvir + ledispavir (NS5A polimerase inhibitor): approved in the US for genotype 1 and for genotypes 1, 3 and 4 by EMA. The single tablet regimen is taken once daily orally, without ribavirin for most patient groups, food does not interfere with the drug's pharmacokinetics. Over 3000 patients were treated by this drug in clinical trials.

Unlike sofosbuvir, ledispavir can be given to patients with moderate, medium or severe renal and hepatic insufficiency. Those characteristics allowed the inclusion of patients with decompensated cirrhosis and those with transplant.

The company's clinical development program –included >500 patients with compensated cirrhosis and several hundred with deceompensated cirrhosis. The duration of treatment for patients with or without c cirrhosis is 12 weeks to 24 weeks; treatment naïve non-cirrhotic patients can be treated 8 weeks (the US label includes a cutoff of <6 million IU/ml). Patients with advanced liver disease earlier treated must be treated 24 weeks.

The trials ION-1, 2, 3 on genotype 1 studied the hypothesis as to whether the treatment duration may be reduced to 24, 12 or 8 weeks, with or without the ribavirin. According to the results – regardless of the treatment duration and stage of disease, the cure rates achieved 94-99%. Only 36 of 1952 patients on treatment did not achieve SVR. The drug's safety profile: in the ribavirin group the incidence of side effects was higher than in the group without it; the safety profile was very good, the drug was well tolerated (less than 1% of the patients quit their treatment because of adverse events). This combination is not effective for all genotypes.

The company's pipeline includes the drug NS5a-Inhibitor GS5816, for genotypes 1-6. The second phase of the trial includes sofosbuvir and GS-5816. Regardless of the genotype, over 90% of the patients achieved a sustainable virological response. The safety profile is very good, no significant laboratory anomalies, no therapy cancellations. This is a phase III trial (sofosbuvir + GS-5816) that included patients with cirrhosis and decompensated cirrhosis.

The fixed dose combination of ledispavir/sofosbuvir is approved in the US and EU, the others combination is expected to be approved in 2016.

The next wave of trials will look into reduction in treatment length to 8 and 6 weeks. The results will be available by 2016 earliest.

Access to drugs in EECA

Question: Ukraine was not part of the company agreement on issuing a voluntary sofosbuvir license. The country is in an economic constraint. Over 3.5 million people are hepatitis C infected. We believe that the company deliberately kept Ukraine from being included in this agreement, referring to the fact Ukraine was not a middle-income country, to artificially retain the high price of sofosbuvir in Europe. All the other drugs are being sold by Gilead as for a low-income country. There was an official letter sent by the Ukrainian government, no answer was received. Now the decision is made to issue compulsory licenses. Has the company included Ukraine in the voluntary licenses for sofosbuvir, if not – is it ready to support the country in its policy on compulsory licenses?

Answer: The letter from the Ukrainian government is being considered by the company's top management. The voluntary licenses are part of Gilead's strategy to provide for access to drugs. For the time being, Ukraine is not a candidate to be included in the company plans on voluntary licenses. The second part of the company access program is the program to provide availability of innovator drugs. The company will work with the Ukrainian government to make the drug available.

Comment: There's work being done to issue a compulsory sofosbuvir license in Ukraine in the near future. There are three companies that may potentially manufacture it. We believe it's an ethical issue: sofosbuvir's price for the time being is such that the regular Ukrainian will have to work two lives long to pay for a treatment course.

Company comment: This information is very important to us, we will pass it on to the company's top management.

Question: The impression is that the multinational companies have divided their spheres of influence in EU countries. Concerning the Baltics, AbbVie is becoming very active, and its drugs will come out early next year. Are you interested in the Baltics?

Answer: The Polish office is responsible for the Baltics, this allows the company to be more flexible when it comes to submitting DMF's on ARV drugs for hepatitis C treatment.

Question: Anyway, does Gilead have any agreements with companies making analogous drugs (BMS, AbbVie) on market division? And will Gilead work on sofosbuvir in all countries alone, or will its interests be represented by other companies?

Answer: Gilead will work on sofosbuvir. There are no mutual agreements with other companies.

Question: Speaking about the agreement with the Patent Pool on TAF, and Gilead's agreement on sofosbuvir. Georgia is on the list of 112 countries of the TAF's agreement. The company's argument is that Georgia is a low-income country. When it comes to sofosbuvir – Georgia is not on the list of countries on this drug, since it is a middle-income country. Please explain this discrepancy.

Answer: Licensing is not the only mechanism for access expansion the company is using. Another option is direct negotiation with the governments. Yesterday there was a meeting with Ministry of Health of Georgia that dealt with the issue of better access.

Comment: We understand that the company makes a decision on pricing policy based on the World Bank evaluation. As was said already, this data does not reflect the real situation in

EECA countries. Also, you are speaking about the governments. There's no country in the world where the people would be happy with government work. We encourage you to make a humanitarian step and provide access to the drug. Armenia needs it now, not in three years, when the company signs an agreement with our government.

Company comment: The company is working in different countries. You probably know that an agreement is signed with Egypt on a special sofosbuvir price (NB. – 900 US dollars per course). The problem of hepatitis patients is that there are no sustainable international programs on hepatitis C. The company is trying to find a way to convey to your governments the need to start treatment programs.

Question: So the impression is that the drug's price is influenced by GF, political leaders, governments – not its manufacturer. What should we do to make the drug available in EECA countries?

Answer: Patient organizations play a big role trying to communicate this information to the government.

Comment: We all understand that voluntary licenses in poor countries and differential pricing in mid-income countries does not work from the point of view of treatment coverage. Patient organizations play a big role in access advocacy, but we are all from the countries where hepatitis C treatment is financed "from leftovers", so it's very difficult to advocate for a procurement at 84 thousand dollars. We encourage you to change the strategy and give an affordable price by covering more patients.

Question: In Georgia in 2011, pegylated interferon cost more than in other countries. Thanks to the efforts of the patient organizations the price was reduced to the minimum for the region. By our estimates, the negotiation between Gilead and the Georgian government began on May 15, but up to now the company has not met anyone from the Ministry of Penitentiary System which has been implementing the hepatitis C program for almost a year already. Also, thanks to the efforts of the patient organizations, in Ajaria they started a program for free hepatitis C diagnostics on state budget. They also started developing a program on hepatitis C treatment. And it wasn't presented during that negotiation, either. Seems to me not all stakeholders were involved in this negotiation. The government is ready to procure sofosbuvir, if the price is maximum 900 US dollars per course.

Question: Could you send us a spreadsheet with sofosbuvir's authorization status in the countries of the region? Also please tell us in what countries sofosbuvir is patented.

Answer: We can provide the answer in writing after consulting our legal advisors. On Egypt – the patent is not issued yet, though there hasn't been a refusal yet. The epidemic burden in the country is very high, so consensus is expected to be reached in the near future. About Georgia and all stakeholders – we ask you to inform us whom to talk with on access in your countries; we are very interested in cooperation.

Comment: You often mention you are doing negotiations with countries' governments. No EECA country government will procure this drug without a price discount. The average salary in Azerbaijan is 450 Euros. They need cheap generics to make it affordable for individuals.

Question: About Gilead's mechanisms and individual approaches to choosing countries for voluntary licenses: the epidemic penetration in a country should be one of the key criteria. The level of income cannot be interpreted on an ad-hoc basis either, as was the case with

Georgia. You have mentioned some productive meetings with the Georgian government. Could you mention the times, prices and details of these productive meetings?

Answer: The company has held meetings with many other countries: Pakistan, Mongolia, Vietnam, also – negotiations inside the EU and US. About a particular meeting in Georgia – that was a step ahead made to the discussion, with favorable trends for the future. Concrete responses will come a bit later.

Question: Anyway – what's the name of the person in the company who may say what the price will be, what regions will be on patents and what countries will get voluntary licenses for generic production in EECA?

Answer: No clear answer was received.

Comment: Gregg Alton – is he the right contact person?

Answer: No comments.

Question: Can we invite Gregg Alton to this meeting and can we fit into a shareholders' meeting?

Answer: All questions raised today will be passed on to the company management.

Question: EECA CAB sent the company an official letter. Any answer to it?

Answer: We got the letter; we will give you an answer soon.

Question: How soon will that be?

Answer: There will be an answer – both to EECA CAB and to the Ukrainian government. We can't tell you when.

Comment: Since the political situation varies country to country, the company may forever meet with the governments. The only way out is the inclusion of the region's countries in the agreement. We are waiting for an official company answer, we ask you to give one within the next 30 days.

Comment: Here in this room we have people involved in HIV activism over 10 years already. We used to learn working with the media, governments and advocacy. Now the people are learning authorizations, copyrights and patent protection. Compulsory licensing will be available in the near future not only in Ukraine, but also in other countries of the region.

Comment: As you have noticed, all EECA countries are on the same page. Unfortunately, this is not the page Gilead is on. We hope very much that you will deliver this information to company management – along with our pain and hope to get access to company drugs.

Company comment: The company is doing their best to meet the region's needs. We have heard all said above, this information will be made known to our top management.

End of meeting.