Meeting Minutes
EECA CAB and MSD

June 30, 2014, St. Petersburg, Russia

Meeting Participants

MSD:

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Tetyana Bilyk, External Affairs Lead, Ukraine and CIS
Will Wooding, Regional Marketing Lead HIV & HCV, EEMEA
Elena Kosminkova, Director, Business Unit, Hepatitis/HIV, MSD Russia
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EECA CAB:

	Name	Organization	Country
1	Andrey Zlobin	Interregional organization Community of people living with HIV	Russia
2	Maria Onufrieva	Interregional organization Community of people living with HIV	Russia
3	Aibar Sultangaziev	Partners' network	Kyrgyzstan
4	Nurali Amanzholov	Kazakh Union of people living with HIV	Kazakhstan
5	Anahit Harutunian	Сеть позитивных людей Армении	Armenia
6	Artem Esse	Patients in control	Russia
7	Iuliia Dragunova	Patients in control	Russia
8	Denis Maruha	Moldova CAB	Moldova
9	Aleksandrs Molokovskis	Association HIV.LV	Latvia
10	Dmitriy Sherembey	Patients of Ukraine	Ukraine
11	Mari Chokheli	OSF Georgia	Georgia
12	Aisuluu Bolotbaeva	Central Asian HIV Fund	Kyrgyzstan
13	Natalia Khilko	E.V.A.	Russia
14	Olga Aleksandrova	ECUO	Ukraine
15	Aleksey Smirnov	PharmActa	Russia
16	Grigoriy Vergus	ITPCru	Russia

Moderators: Alexandra Volgina, Tatyana Khan.

Presentation

The company's hepatitis C portfolio includes boceprevir (BOC), pegylated interferon (PEG-INF) and ribavirin (RBV); vaniprevir (MK-7009) is in phase 3, ; MK-5172, and MK-8742. The results of the 3rd phase are due next year.

Boceprevir

The US and EU have different standards and requirements as to registering pharmaceutical products; that is why treatment durations specified in the leaflets may differ. This applies to boceprevir. In order to optimize the treatment duration, the company has studied treatment outcomes with the triple therapy (PEG-INF/RBV and BOC) and specified the endpoint which can be used for determining the effectiveness of the treatment. This is viral load (VL) <100 after 12 weeks and undetectable VL at week 24. If these parameters are not reached, the therapy has to be discontinued.

Within the phase 3 trial programme, retrospective studies have been carried out evaluating the efficacy of BOC in naïve and experienced patients, as well as in patients who had previously discontinued treatment with PEG-INF alpha-2a and 2b (the results are the same). Also, a study has been carried out comparing the use of erythropoietin (EPO) vs RBV dose reduction as a measure to manage anemia (the results are the same).

In these studies, the researchers looked at the efficacy of the triple therapy to see whether it can be stopped at week 8 (4-week lead-in period with PEG-INF, followed by 4 weeks of triple therapy with BOC). Potential endpoints which can be used include VL less than 1000 IU/mL as well as detectable VL and > 3 log reduction. The results showed that approximately 80% of the patients, who stopped treatment at week 12, could have stopped treatment already at week 8 (SVR not achieved in 9 out of 1307 naïve patients and 4 out of 572 experienced patients).

Today, the following three rules for discontinuing the therapy are used:

- Week 8 – VL ≥1000 IU/mL
- Week 12 – VL ≥ 100 IU/mL
- Week 24 – detectable VL.

Changes to the leaflet will be made within the next few months.

MK-5172 and MK-8742

MK-5172: 2nd generation protease inhibitor (PI), active against genotypes 1, 2, 3, 4, 5 and 6 (pre-clinical studies); effective when treating patients with known resistance to 1st generation PIs.

MK-8742: NS5A inhibitor, active against 1, 2a, 3, 4, 5 and 6 (pre-clinical studies) as a third product.

No drug-drug interactions between those drugs have been found; an attempt has been made to put them into one pill (once-daily).

Phase 2: different treatment durations with different dosages have been tried, with/without RBV. 471 patients have been included in the trials (naïve, without cirrhosis; naïve with cirrhosis; null-responders to PEG-INF/RBV with or without cirrhosis; co-infected with HIV).

After 4 week, the percentage of patients with undetectable VL in the group of naïve patients without cirrhosis was almost 100%. The results have shown that an 8-week course is not enough; a 12- week course has been chosen as a standard course for all patient categories.

For experienced patients with cirrhosis, as well as for null responders either with or without cirrhosis 12 weeks of treatment is enough.

HIV-coinfected patients: inclusion criteria – RAL plus 2 NRTIs, undetectable HIV viral load. 12 weeks, with/without RBV. The results have shown that the regimen with RBV is more effective. Patients taking efavirenz, ritonavir, PIs have been excluded due to a risk of drug-drug interactions (DDIs). 3TC, FTC, TDF, ABC can be co-administered, the rest of the ARVs are being studied.

No clinically significant interactions have been found with methadone, buprenorfine and naloxone.

Question: Have EECA countries been included into these trials?

Answer: Not in phase 1 and 2 trials. In a number of countries, including EECA, regulatory approval is the biggest hurdle.

Phase 3 trials have been started including patients with genotypes 1, 2, 4, 5 and 6, both naïve and experienced. Treatment duration is 12 weeks both with and without RBV, patients with and without HIV. Some patients with chronic kidney diseases are included, as well as patients with grade B cirrhosis; also, the trials include patients with opioid dependence and non-responders to PEG-INF/RBV and triple therapy with 1st generation PIs. Estonia, Lithuania and Russia are among the countries where these trials will be conducted. The 3rd phase trial results might be presented at EASL in Vienna.

Question: What is the percentage of women in the trials?

Answer: Approximately 50%.

Question: When are you planning to launch the products?

Answer: Now it is hard to say, it depends on the country. For instance, in Central Europe it can take from 1 to 4 years.

Question: There are direct-acting antiviral drugs already on the market; in the nearest future, MSD will also launch its DAAs. Maybe, it is better to wait rather than undergo treatment with PEG-INF/RBV?

Answer: It depends on the doctor, we cannot make recommendations.

Question: Given the new drugs entering the market, is the company planning to decrease the price for PEG-INF?

Answer: *MSD declined to comment on potential future pricing decisions.*

Question: Gilead have granted a voluntary license for its hepatitis C drugs to a number of companies for a number of countries. Is MSD planning to do the same?

Answer: *MSD declined to comment on potential future decisions on voluntary licenses.*

Question: Does the company have plans for studying drug-drug interaction (DDI) with cancer and MDR-TB drugs?

Answer: DDI studies will be carried out for MDR-TB drugs; currently, we do not have plans to study DDI with cancer drugs.

Question: Can you provide more detail on the purchase of Idenix with the drug samatasvir?

Answer: We cannot comment on a deal which has not been completed yet.

Access

Question: Last year, Georgia for the first time held a tender for PEG-INF within a pilot national treatment programme. Despite the preliminary agreements made with the company, MSD did not participate in the tender, although the company's participation could have contributed to further price reduction. Is the company planning to participate in the tender at the end of this year?

Answer: We were involved in the negotiations with the Global Fund regarding procurement of drugs for HCV and HIV. As to this particular tender, there was a condition according to which the company had to commit to supplying drugs for the commercial market at the same price as for the GF programme. The policy of MSD is to have differential pricing for public and private sectors. We did contact the government regarding this condition, but they refused to change it; that is why we did not participate.

Question: Will you participate in the tender this year, if the conditions are changed?

Answer: Yes.

Comment from the company: MSD was the first company to decrease the price for PEG-INF in Ukraine. We supplied the drugs tothe MOH for further distribution to the regions ; RBV was provided free of charge. However, MOH did not accept RBV, by terminating the contract with MSD's distributor. At the time of the meeting, this was the status. As of today, the MOH has agreed to accept RBV resolving this issue.

Comment from the company: We have made a decision that MSD will be represented by Berlin-Chemie in the following countries: Armenia, Belarus, Georgia, Moldova, Azerbaijan, Uzbekistan, Turkmenistan, and Mongolia. In the rest of the countries it will be MSD. The contacts of Berlin Chemie will be shared with the participants of this meeting.

Question: What will be the responsibilities of Berlin-Chemie? Only distribution?

Answer: They will have all the rights in the respective countries.

Comment: Such companies, as usual, do not have a culture of working with patient organizations. We ask you to discuss this with Berlin-Chemie and tell them that if we contact them, they will have to answer.

EECA Presentation

PEG-INF is registered in all EECA countries, except Tajikistan and Kyrgyzstan, as we did not have enough economic capacity to register our drugs there. However, the company is looking at opportunities to supply the drugs to the countries where they are not registered (for instance, one-time supply).

Comment: Kyrgyzstan has a simplified registration procedure. We can address our government regarding an accelerated registration procedure. There are many patients who are in desperate need of treatment. The country will soon approve its national hepatitis C treatment guidelines, with PEG-INF/RBV being the preferred treatment regimen. Since Kyrgyzstan is a low-income country, we urge you to register your product at a low price.

Comment from the company: We are ready to cooperate. Kyrgyzstan is on the list of countries eligible for the lowest PEG-INF price.

Comment: In 2013, the company submitted an application to include Victrelis in the national reimbursement programme in Latvia at the price of EUR3048 per package (around 3500 including VAT). Given such price, our government refuses even to consider this application. At the same time, the total turnover of MSD in Latvia in 2013 equaled EUR8.7 mln. You have very high prices for medicines in Latvia. I am not asking for a price reduction in just one country of EU, I am asking you to reduce prices for all the EU countries.

Comment from the company: This question will be passed on to our colleagues responsible for Europe.

Question: In case of PEG-INF, the company justified the high price with the complex manufacturing process of biological drugs. The new drug is chemical. What will the price be?

Answer: We are entering phase 3 trials, and it is too early to speak about the price. By the time our product reaches the market, there will be several analogous products available; competition should drive the price down.

Question: Are you planning to grant a voluntary license for a new product to developing countries?

Answer: At the moment, we are considering options, but the DAA market is hard to predict.

Comment from the company: Based on our experience, the pricing issue is not the key barrier to access. Out of 100% patients with HCV in developing countries only 10% are aware of their status, and only 5% reach the doctor.

Question: In a number of countries, the governments are not interested in scaling up testing to avoid high expenses related to providing treatment. Do you have plans with regard to improving access to hepatitis C testing?

Answer: If a government asks us to provide treatment for a maximum number of patients, we give them the best price. Regarding diagnostics, we do not manufacture tests; however, we do understand the importance of this issue. We support some testing programmes, but within MSD we do not have plans to develop hepatitis C tests.

EECA Presentation, continued

Россия: There is no HCV treatment programme as such, only a programme for HIV/HCV co-infection. The drugs for treating hepatitis C are purchased based on the "left-over" principle. Approximately 35 oblasts have their own hepatitis B and C treatment programmes; the national hepatitis programme is being actively discussed. Russia has national hepatitis C treatment recommendations, which include PEG-INF and 1st generation protease inhibitors. All the three hepatitis C products of MSD are available in Russia: PEG-INF, RBV, and BOC. The first two drugs are included in the Essential Drug List (EDL). An application has been

submitted to include BOC in the EDL. PEG-INF is packaged by R-Pharm and has a local product status. In Russia, MSD is represented by Merck.

Question: Who is in charge of writing the hepatitis C treatment recommendations?

Answer: The group of authors consists of specialists from different institutions. The group operates under the Ministry of Health, and the recommendations will be approved by the Ministry of Health.

Question: The position regarding cooperation of Merck and R-Pharm is still not clear, as the distributor represents both Roche and Merck. We are under the impression that R-Pharm artificially decreases the share of your product in the tenders organized by AIDS Centres given higher prices by Roche. What is your position towards the fact that this company also represents your competitor?

Answer: We consider R-Pharm as one of our global partners. We cannot discuss our commercial relationships with R-Pharm, but we have no influence over the price or the share of our product in the sales.

Comment from the company: if we are talking about the share of our product at all Russian markets, including the retail market, then our share and the share of Roche are about the same.

Comment: The problem is that R-Pharm refuses to communicate with patient organizations. We ask you to discuss this issue with R-Pharm.

Question: You said that PEG-INF in Russia had become more available. We analyzed the government procurement programmes in 2013, and the average price is around USD11,500, which can hardly be called accessible or available. What exactly did you mean by "available"?

Answer: What we meant is that the drug is included in the EDL and can be purchased using the federal money. We also monitor the market and revise our pricing policy each year; unfortunately, the market price is not set by us. The price in the EDL is registered by the Ministry of Health.

Comment: It is the ceiling price which is registered in the EDL; you can sell the product at lower prices. You can also register a lower price, it is not a problem.

Comment from the company: you should remember that there is a whole supply chain influencing the price.

Comment: We would like to mention that BOC was also purchased in Russia in 2013. The average price for the treatment course was approximately USD42,000, which is an extremely high price for the region.

Question: Some regions in 2013 purchased incomplete treatment courses, and we are very concerned about this fact. If the patient does not complete the full course, is there a risk of resistance development?

Answer: Today, we are not talking about resistance in relation to hepatitis C drugs. We are talking about resistance-associated amino acid variants in the virus. Those patients who failed the triple therapy had an increased number of such acids compared to patients who completed the treatment successfully.

We are always trying to underline the following two points when communicating with patient organizations and doctors: 1) the dose of the drugs must not be decreased due to the risk of resistance-associated amino acids, and 2) if a patient misses the doses and the treatment regimen is not complete, then the treatment with the drug should not be re-started.

Ukraine

3 drugs are registered: PEG-INF, RBV, and BOC. PEG-INF and RBV are used in the national treatment programme. We have offered the government a comprehensive partner programme for hepatitis C: we have reduced the price for the drugs, we have offered our assistance in developing a register of patients, as well as training specialists and patients. The patient register, unfortunatelyy, has not been developed yet.We have supported a number of patient organizations, and, also thanks to this support, the concept of the national programme has been created and approved.

Ukraine has local manufacturing facilities. Lumier sells our product Unitron at a reduced price. Also, we have given a special price for the Global Fund programme for treating 100 patients.

Question: The same distributor supplies the drug to another customer, The Ukrainian Academy of Science, at the external price. Do you have any influence over this situation? Is the company planning further price reduction for the national treatment programme?

Answer: Regarding the situation with the Academy of Science, we need to clarify it with our colleagues. Regarding further price reduction – as an option, we can consider supplying some drugs for free together with the products for which the customer pays in the tender. As a result, the price will get lower. However, we need to understand how it will function from the regulatory point of view. Another option is a framework agreement about price reduction. However, the government is not prepared for this step.

Comment: Free supply of products can be perceived differently. From the point of view of local access it looks good, but it does not affect the price. If you do not decrease the price in Ukraine, then there will be fewer opportunities for price reduction in Russia and in other countries for which Ukraine is a reference country.

Kazakhstan

We have close cooperation with the government and patient organizations regarding the national programme. We have offered a price reduction for PEG and training programmes for specialists and patients.

Baltic States

In Estonia and Lithuania, there is 100% reimbursement for naive and experienced patients with hepatitis C and progressing liver diseases and stage 1 fibrosis. In Latvia, there is 75% reimbursement.

Other countries

There is a list of 57 countries in which we sell PEG-INF at a special price (USD40 per vial); Kyrgyzstan and Tajikistan are on this list.

Question: With whom do we have to cooperate to facilitate the registration process in Kyrgyzstan?

Answer: We need interest from the government and information about the situation in Kyrgyzstan which I can hand over to our colleagues in the country office.

Comment: You will receive the data about Kyrgyzstan; however, the company needs to submit the registration dossier. After this, we as a patient community will be able to raise this issue at the national level.

Comment from the company: In any case, we need to estimate the internal resources of the company needed for the registration.

Answer: registration costs 1500-2000 dollars.

Comment from the company: I am talking about the resources needed for preparing the dossier, rather than financial resources. In any case, if the government lets us know that a certain volume of the drug is needed, we will consider this information and offer special conditions.

Question: In Armenia, the drugs are registered, but the price for PEG-INF is very high. What are your plans regarding the pricing policy in this country?

Answer: We have a classification of country pricing policy based on the income level according to the World Bank, disease burden, and national political will in terms of treating HCV. If the government specifies a certain number of patients to be treated, then we can consider special prices.

End of meeting