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PHARMACOECONOMIC ANALYSIS OF SOFOSBUVIR FOR THE TREATMENT OF CHRONIC HEPATITIS C (GENOTYPE 1) IN THE RUSSIAN FEDERATION

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Abstract: The objectives of this study were to determine the most advantageous antiviral therapy option for chronic hepatitis C (CHC) (peginterferon alfa + ribavirin (PegIFN + RBV) 48 weeks (F0–F4), peginterferon alfa + simeprevir + ribavirin (PegIFN + SMV + RBV) 24 weeks (F0–F4), peginterferon alfa + sofosbuvir + ribavirin (PegIFN + SOF + RBV) 12 weeks (F0–F4), dasabuvir + ombitasvir/paritaprevir/ritonavir (Dasabuvir + Ombitasvir/paritaprevir/ritonavir) 12 weeks (F0–F3) and dasabuvir + ombitasvir/paritaprevir/ritonavir + ribavirin (Dasabuvir + Ombitasvir/paritaprevir/ritonavir + RBV) 12 weeks (F4)) among treatment-naïve and treatment-experienced patients (HCV genotype 1) based on the comparison of cost-effectiveness ratios and economic outcomes (“budget impact” analysis) from implementing the treatment strategy PegIFN- α + SOF + RBV instead of PegIFN- α + RBV, PegIFN- α + SMV + RBV and Dasabuvir + Ombitasvir/paritaprevir/ritonavir. Model-based pharmacoeconomic analysis has been conducted. The cost-effectiveness analysis showed that independently of the former treatment experience of CHC (genotype 1) patients the combination PegIFN- α + SOF + RBV was a predominant regimen as compared to PegIFN- α + RBV and PegIFN- α + SMV + RBV. In the groups of patients without cirrhosis and with cirrhosis the highest QALY value was noted for Dasabuvir + Ombitasvir/paritaprevir/ritonavir and Dasabuvir + Ombitasvir/paritaprevir/ritonavir + RBV combinations, respectively. Also a smaller cost-effectiveness ratio (CER) relative to the two above regimens was noted for PegIFN- α + SOF + RBV. In the group of treatment-naïve patients without cirrhosis incremental cost-effectiveness ratio (ICER) of Dasabuvir + Ombitasvir/paritaprevir/ritonavir vs PegIFN- α + SOF + RBV was higher than willingness-to-pay threshold (WPT), whereas in the group of patients with cirrhosis ICER Dasabuvir + Ombitasvir/paritaprevir/ritonavir was lower than WPT.

+ RBV vs PegIFN- α + SOF + RBV
Using “budget impact” analysis it was shown that switching to PegIFN- α + SOF + RBV from PegIFN- α + RBV regimen will involve extra direct costs for antiviral treatment (AVT), but will lead to a reduction in medical aid costs to the patients not reaching SVR, patients with CHC complications and, as a consequence, will lead to a reduction in cumulative medical costs. Moreover, transition from PegIFN- α + SMV + RBV, Dasabuvir + Ombitasvir/paritaprevir/ritonavir and Dasabuvir + Ombitasvir/paritaprevir/ritonavir + RBV to PegIFN- α + SOF + RBV will lead to a reduction in both AVT costs and cumulative medical costs.

Keywords: Chronic hepatitis C, genotype 1, liver cirrhosis, antiviral therapy, cost analysis, effectiveness analysis, “cost-effectiveness” analysis, “budget impact” analysis.

According to WHO, about 110 million people worldwide are living with chronic hepatitis C (CHC) infection, most of which are unaware they are infected [1, 19]. According to expert estimates, in the Russian Federation there are more than 4 million infected people [3]. At the 2016 World Health Assembly the first Global Strategy on viral hepatitis was adopted. The strategy aims to eliminate viral hepatitis C (HCV) by 2030.

For a long time the standard of care for CHC patients was dual treatment with pegylated interferon (PegIFN) and ribavirin (RBV). However, the first-gen-

eration direct-acting antiviral drugs (DAAD) became available in 2011, which significantly increased the effectiveness of treatment. Then the second-generation DAAD increased the probability of achieving the clinical endpoint — getting sustained virologic response (SVR) in 90–100 % of cases independently of treatment experience, cirrhosis, viral genotype and HIV co-infection [1]. Achieving SVR in 99 % of cases is deemed to complete recovery from HCV [9]. Besides, in the absence of cirrhosis at the onset of treatment achieving SVR makes it possible to normalize liver function, i. e. to stop the progression of the disease and prevent the development of life-threatening conditions (for example, hepatocellular carcinoma [HCC]) [9].

The progression of CHC is accompanied by a gradual increase in the need for medical aid and, accordingly, an increase in medical expenditures and social transfers (for example, sick leave payments and disability benefits). In 2010, annual expenses on medical care for one CHC patient totaled 3,375 rubles, after progression to compensated cirrhosis (CC) — 15,188 rubles and after progression to decompensated cirrhosis (DC) — 71,634 rubles [4]. Since the majority of CHC patients belong to the 20–40 age group, the state (society) incurs substantial economic losses (indirect costs) in the form of GDP loss. In 2010, overall economic burden from acute hepatitis C and CHC totaled 48.47 billion rubles, of which medical aid provided on an outpatient basis and in hospitals accounted for 35 % [6].

Materials and methods of research

The objective of this study was to determine the most advantageous option of antiviral drug treatment of CHC (peginterferon alfa + ribavirin (PegIFN + RBV) 48 weeks (patients with fibrosis F0–F4), peginterferon alfa + simeprevir + ribavirin (PegIFN + SMV + RBV) 24 weeks (F0–F4), peginterferon alfa + sofosbuvir + ribavirin (PegIFN + SOF + RBV) 12 weeks (F0–F4), dasabuvir + ombitasvir/paritaprevir/ritonavir (Dasabuvir + Ombitasvir/paritaprevir/ritonavir) 12 weeks (F0–F3) and dasabuvir + ombitasvir/paritaprevir/ritonavir + ribavirin (Dasabuvir + Ombitasvir/paritaprevir/ritonavir + RBV) 12 weeks (F4)) among treatment-naïve and treatment-experienced patients (HCV genotype 1) based on cost-effectiveness analysis and budget impact analysis.

Hence, two scenarios of pharmacoeconomic analysis were proposed:

- Scenario 1 — in the subgroup of treatment-naïve patients;
- Scenario 2 — in the subgroup of treatment-experienced patients.

The study was conducted using a combined pharmacoeconomic model. The logical-mathematical tools of the model combined both “decision tree” and Markov models. The model time horizon used was 100 years. The duration of one cycle was one year.

The study strategy hypothesized that a group of patients (Table 1) included in the model simultaneously took AVT treatment course according to one of the regimens analyzed. Thereafter the Markov model was used to simulate the disease progression (CC, DC, HCC, liver transplantation [LT]) and death of patients (Figure 1). If the patients were initially at stage F0–F3 and achieved the clinical endpoint — sustained virologic response (SVR) — it was pre-

sumed that no progression could occur. In all other cases the probability of progression was not zero (Supplement 1) [25-32].

The discount rate for costs and effectiveness was 3.5 % starting from the second year of a model.

Description of a group of patients used in the model

The model (target) group of patients was represented by averaged treatment-naïve CHC patients (HCV genotype 1). The description of the group was based on the results of the analysis of the published data on CHC morbidity patterns in the Russian Federation for the period of 2011–2015 (Table 1).

Table 1. Description of a group of patients used in the model

Indicator	Value		Source
	Scenario 1	Scenario 2	
Number, people	3119	108	[3, 21]
Percent of male patients, %	51,7		[5]
Average age, years	42,8		
Persons taking injection drugs (PID), %	16		
Distribution of patients by fibrosis stages, %			
F0	38		
F1	24		
F2	17		
F3	9		
F4	12		

Effectiveness analysis

The effectiveness analysis was conducted using the above pharmacoeconomic model. Based on a surrogate endpoint (SVR), transition probabilities (probabilities of disease progression, probabilities of death) and utility values (numerical values of the endpoint — Quality Adjusted Life Years [QALY]) — were calculated. In order to determine the SVR values for each AVT regimen under consideration a search and analysis of the published data of the clinical studies (CS) have been conducted [7, 10, 11, 12, 13, 14, 15, 16, 17, 18].

Since no data on direct comparison of the regimens of interest were found, the methodology of naive indirect comparison of effectiveness has been used. For this purpose CS data were retrieved, systematized and analyzed by their design, effectiveness criteria used, and number and description of patients. As a result, it was possible to identify the most comparable CS to be used as the sources of data for a comprehensive pharmacoeconomic analysis. At the same time it was hypothesized that the existing heterogeneity of the groups of patients in the selected CS could be neglected.

The SVR data used in the pharmacoeconomic study are summarized in Tables 2 and 3.

Table 2. The results of naive indirect comparison of CS results across AVT-naïve CHC patients

Name of AVT regimen	SVR, %					Source
	Genotype 1					
	F0	F1	F2	F3	F4	
PegIFN-α + RBV (48 weeks)	57	57	57	41	41	[14]
PegIFN-α + SMV + RBV (12 weeks – SMV 24 weeks– PegIFN-α and RBV)	84	84	84	68	68	[15]
PegIFN-α + SOF + RBV (12 weeks)	91	91	91	91	81	[13, 16, 17]
Dasabuvir + Ombitasvir/ paritaprevir/ritonavir (12 weeks) ¹	95	95	95	95	-	[11]
Dasabuvir + Ombitasvir/ paritaprevir/ritonavir + RBV (12 weeks)	-	-	-	-	94	[19]

¹ In accordance with the instruction for medical use registered in the Russian Federation, in the group of CHC genotype 1a patients the regimen of Paritaprevir/r/ombitasvir/dasabuvir can be applied only in combination with RBV. However the published CS data were found that stated that Paritaprevir/r/ombitasvir/dasabuvir was applied in a specified group of patients without RBV and demonstrated high efficacy, which made it possible to use the SVR data for Paritaprevir/r/ombitasvir/dasabuvir without RBV (12 weeks) in the present study for a mixed group of genotype 1a and 1b patients.

Table 3. The results of naive indirect comparison of CS results across AVT-experienced CHC patients

Name of AVT regimen	SVR, %					Source
	Genotype 1					
	F0	F1	F2	F3	F4	
PegIFN-α + SMV + RBV (12 weeks – SMV 24 weeks – PegIFN-α and RBV)	82,0	82,0	82,0	73,0	73,0	[15]
PegIFN-α + SOF + RBV (12 weeks)	79,0	79,0	79,0	79,0	-	[12, 18]
Dasabuvir + Ombi- tasvir/paritaprevir/ ritonavir ² (12 weeks)	100	100	100	100	-	[8]

² SVR data has been found only for the group of genotype 1b patients

Figure 1. The pharmacoeconomic model diagram representing the sequence of events during simulation

Cost analysis

In the cost analysis the account was taken only of the costs related to the medical aid to CHC patients (Figure 2). To obtain the data on the amounts and structure of the costs we used the tariffs of the Federal Obligatory Medical Insurance Fund (for Moscow and Moscow region), medical aid provision standards and in their absence the expert opinions (Table 4).

The prices of medicines included in the analysis were determined taking into account the regulatory requirements related to the strategies of clinical-economic studies, the rules of pricing and procurement for the medicines included in the list of essential drugs: Russian Federation Government Resolution of August 28, 2014 No. 871 "On Approval of the Rules for Compiling Lists of Medicines for Medical Use and the Minimum Range of Medicines

Figure 2. Breakdown of the costs taken into account in the present study

Table 4. Medical aid costs taken into account in the present study

Stages	Costs, rubles		Source
	SVR not achieved	SVR achieved	
Fibrosis			[22, 23]
F0: Year 1	3 427	1 533	
F0: Year 2+	3 427	-	
F1: Year 1	3 427	1 533	
F1: Year 2+	3 427	-	
F2: Year 1	3 427	1 533	
F2: Year 2+	3 427	-	
F3: Year 1	3 427	1 533	
F3: Year 2+	3 427	-	
F4: Year 1	43 172	19 638	
F4: Year 2+	43 172	19 638	
Decompensated cirrhosis			[22, 23]
Year 1	111 499	-	
Year 2+	111 499	-	
HCC			[22, 23]
Year 1	158 499	-	
Year 2+	20 832	-	
Liver transplantation			[22–24]
Year 1	939 142	-	
Year 2+	593 759	-	

Table 5. Data on the prices for the medicines included in the analyzed CHC AVT regimens

international nonproprietary name [INN]	PegIFN-α-2a	PegIFN-α-2b	cplIFN-α	SMV	RBV	Dasabuvir + Ombitasvir/paritaprevir/ritonavir	SOF
Dosage	180 mcg/0.5 ml No. 1	120 mcg/0.7 ml No. 1	200 mcg/1 ml No. 1	150 mg No. 28	200 mg No. 120	No. 28	400 mg No. 28
Price per pack (with VAT)	9 607	9 491	5 649	228 157	2 101	317 786	186 000
Source	[2]					[6]	Maximum sale price planned for registration by the manufacturer

Necessary for Medical Aid"; Federal Law of April 12, 2010 No. 61-FZ (revised on July 13, 2015) "On the Circulation of Medicines" (with amendments and supplements enforced on July 24, 2015); Federal Law of April 5, 2013 No. 44-FZ (revised on July 13, 2015) "On the Contractual System Used by Federal and Municipal Governments to Procure Goods, Works, and Services" (with amendments and supplements taken effect since August 13, 2015).

Prices of the medicines used in the compared regimens were obtained (in the presence of duly registered maximum sale price for the medicine) from the State Register of Maximum Sale Prices with VAT. In the absence of a duly registered maximum sale price for a medicine the price used in the present study was a median value of the average statistical price for actual purchases (by the data of electronic auctions for the purchase of medicines for the state and municipal needs) for the generic medicines for the period from January 1, 2016 to October 21, 2016 (Table 5).

Prices for other included medicines (which were included in the structure of direct medical costs but not compared in this study) were derived from the portal <http://www.pharmindex.ru/>, the calculated price for a medicine was an average statistical median value of wholesale prices or (in the absence of such) an average statistical median value of retail prices.

Results — Scenario 1: AVT-naïve CHC patients

As a result of effectiveness analysis it was established that in the group of HCV-infected (genotype 1) patients without cirrhosis and with cirrhosis the maximum values for Life Years Gained (LYG) and Quality Adjusted Life Years (QALY) corresponded to Dasabuvir + Ombitasvir/paritaprevir/ritonavir and Dasabuvir + Ombitasvir/paritaprevir/ritonavir + RBV regimens, respectively (Table 6).

The cost analysis showed that in the group of HCV-infected (genotype 1) patients without cirrhosis and with cirrhosis the smallest cumulative costs per 1 patient correspond to PegIFN-α + SOF + RBV regimen (Table 7).

From the perspective of "cost-effectiveness" analysis the best ratio in the group of HCV-infected (genotype 1) patients without cirrhosis and with cirrhosis corresponds to PegIFN-α + SOF + RBV regimen (Figure 3).

Since the cumulative costs were lower while the effectiveness was higher, then in comparison to PegIFN- α + RBV and PegIFN- α + SMV + RBV the regimen PegIFN- α + SOF + RBV was predominant, therefore no ICER calculations have been conducted.

For Dasabuvir + Ombitasvir/paritaprevir/ritonavir (characterized by higher costs and greater effectiveness) and PegIFN- α + SOF + RBV regimens when used for patients without cirrhosis ICER was higher than willingness-to-pay threshold (WPT) calculated by the method recommended by WHO (1,597,618 rubles) – 5,310,259 > 1,597,618. In turn, for Dasabuvir + Ombitasvir/paritaprevir/ritonavir + RBV (characterized by higher costs and greater effectiveness) and PegIFN- α + SOF + RBV regimens when used for patients with cirrhosis ICER was lower than willingness-to-pay threshold (WPT) calculated by the method recommended by WHO (1,597,618 rubles) – 366,707 < 1,597,618.

Table 6. Results of effectiveness analysis: Scenario 1

Name of AVT regimen	QALY	
	F0-F3	F4
PegIFN- α + RBV	12,20	8,25
PegIFN- α + SMV + RBV	12,79	9,70
PegIFN- α + SOF + RBV	13,06	10,44
Dasabuvir + Ombitasvir/paritaprevir/ritonavir	13,11	-
Dasabuvir + Ombitasvir/paritaprevir/ritonavir + RBV	-	11,13

Table 7. Results of cost analysis: Scenario 1

Name of AVT regimen	Cumulative costs, rubles		Cumulative costs per 1 patient, rubles		Cumulative costs of AVT, rubles		Cumulative costs of management of patients not reaching SVR, rubles		Cumulative costs of management of patients reaching SVR, rubles		Cumulative costs of medical aid to patients with complications of CHC, rubles	
	F0-F3	F4	F0-F3	F4	F0-F3	F4	F0-F3	F4	F0-F3	F4	F0-F3	F4
PegIFN- α + RBV	2 099 537 244	463 142 466	765 010	1 237 542	1 848 347 969	252 047 450	53 056 104	88 629 569	2 212 222	44 779 476	195 920 948	77 685 971
PegIFN- α + SMV + RBV	2 590 039 969	528 622 697	943 735	1 412 508	2 483 328 965	338 635 768	20 477 899	48 070 274	3 291 089	74 268 400	82 942 015	67 648 255
PegIFN- α + SOF + RBV	2 015 879 203	447 604 318	734 528	1 196 023	1 963 723 976	267 780 542	10 859 402	28 541 725	3 636 181	88 466 770	37 659 644	62 815 280
Dasabuvir + Ombitasvir/paritaprevir/ritonavir	2 742 957 765	-	999 454	-	2 710 066 307	-	6 515 641	-	3 780 030	-	22 595 787	-
Dasabuvir + Ombitasvir/paritaprevir/ritonavir + RBV	-	542 361 901	-	1 449 220	-	372 857 635	-	8 712 737	-	102 883 577	-	57 907 952

Figure 3. Results of “cost-effectiveness” analysis: Scenario 1

Table 8. The results of “budget impact” analysis: Switching from PegIFN-α + RBV to PegIFN-α + SOF + RBV

Cumulative costs of AVT, rubles		Cumulative costs of management of patients not reaching SVR, rubles		Cumulative costs of management of patients reaching SVR, rubles		Cumulative costs of medical aid to patients with complications of CHC, rubles								Cumulative costs, rubles		Cumulative costs per 1 patient, rubles	
						Patients who progressed to F4		Patients who progressed to DC		Patients who progressed to HCC		Patients who progressed to LT					
F0-F3	F4	F0-F3	F4	F0-F3	F4	F0-F3	F4	F0-F3	F4	F0-F3	F4	F0-F3	F4	F0-F3	F4	F0-F3	F4
will increase by 115,376,007	will increase by 15,733,092	will decrease by 42,196,703	will decrease by 60,087,843	will increase by 1,423,959	will increase by 43,687,294	will decrease by 106,617,506	will not change	will decrease by 25,726,037	will decrease by 6,602,219	will decrease by 3,746,148	will decrease by 824,860	will decrease by 22,171,614	will decrease by 7,443,612	will decrease by 83,658,041	will decrease by 15,538,148	will decrease by 30,483	will decrease by 41,519

Table 9. The results of “budget impact” analysis: Switching from PegIFN-α + SMV + RBV to PegIFN-α + SOF + RBV

Cumulative costs of AVT, rubles		Cumulative costs of management of patients not reaching SVR, rubles		Cumulative costs of management of patients reaching SVR, rubles		Cumulative costs of medical aid to patients with complications of CHC, rubles								Cumulative costs, rubles		Cumulative costs per 1 patient, rubles	
						Patients who progressed to F4		Patients who progressed to DC		Patients who progressed to HCC		Patients who progressed to LT					
F0-F3	F4	F0-F3	F4	F0-F3	F4	F0-F3	F4	F0-F3	F4	F0-F3	F4	F0-F3	F4	F0-F3	F4	F0-F3	F4
will decrease by 519,604,989	will decrease by 70,855,226	will decrease by 9,618,498	will decrease by 19,528,549	will increase by 345,092	will increase by 14,198,371	will decrease by 30,269,968	will not change	will decrease by 7,392,140	will decrease by 2,145,721	will decrease by 1,003,339	will decrease by 268,079	will decrease by 6,616,923	will decrease by 2,419,174	will decrease by 574,160,766	will decrease by 81,018,379	will decrease by 209,208	will decrease by 216,485

Table 10. The results of “budget impact” analysis: Switching from Dasabuvir + Ombitasvir/paritaprevir/ritonavir to PegIFN-α + SOF + RBV

Cumulative costs of AVT, rubles		Cumulative costs of management of patients not reaching SVR, rubles		Cumulative costs of management of patients reaching SVR, rubles		Cumulative costs of medical aid to patients with complications of CHC, rubles				Cumulative costs, rubles		Cumulative costs per 1 patient, rubles	
						Patients who progressed to F4	Patients who progressed to DC	Patients who progressed to HCC	Patients who progressed to LT				
F0-F3	F4	F0-F3	F4	F0-F3	F4	F0-F3	F0-F3	F0-F3	F0-F3	F0-F3	F0-F3	F0-F3	F0-F3
will decrease by 772,078,274	will increase by 4,493,546	will decrease by 148,809	will increase by 10,530,695	will increase by 2,528,813	will increase by 378,318	will increase by 2,145,475	will decrease by 752,150,236	will decrease by 264,926					

Table 11. The results of “budget impact” analysis: Switching from Dasabuvir + Ombitasvir/paritaprevir/ritonavir + RBV to PegIFN-α + SOF + RBV

Cumulative costs of AVT, rubles		Cumulative costs of management of patients not reaching SVR, rubles		Cumulative costs of management of patients reaching SVR, rubles		Cumulative costs of medical aid to patients with complications of CHC, rubles				Cumulative costs, rubles		Cumulative costs per 1 patient, rubles	
						Больные, которые перешли в F4	Больные, которые перешли в ДЦ	Больные, которые перешли в ГЦК	Больные, которые перешли в ТП				
F4	F4	F4	F4	F4	F4	F4	F4	F4	F4	F4	F4	F4	F4
will decrease by 108,700,440	will decrease by 108,700,440	will decrease by 14,913,938	will not change	will increase by 2,253,861	will increase by 281,590	will increase by 2,541,095	will decrease by 98,025,086	will decrease by 253,197					

The sensitivity analysis conducted for the results of the present PEA demonstrated that the greatest effect on the cost-effectiveness ratio is produced by the variables “Medicine price”, “Probability of SVR achievement” and “Average age of patients”. In other words, when the values of the specified variables were changed by a set percent (+/- 10 % was used in the analysis), the value of the costs-effectiveness ratio underwent the greatest change.

It is worth noting that in different patient models the effect of the variables varied. It was also established that independently of the treatment regimen analyzed in the groups of patients initially ranked as F0–F3 the greatest effect was produced by the variables “Medicine price” and “Average age of patients”. In the group of patients initially ranked as F4 the greatest effect was produced by the variables “Probability of SVR achievement” and “Medicine price” (Figures 4 and 5).

Results — Scenario 2: AVT-experienced CHC patients

The effectiveness analysis demonstrated that in the group of HCV-infected (genotype 1) patients without cirrhosis and with cirrhosis, the maximum values of Quality Adjusted Life Years (QALY) corresponded to Dasabuvir + Ombitasvir/paritaprevir/ritonavir and Dasabuvir + Ombitasvir/paritaprevir/ritonavir + RBV regimens, respectively (Table 12).

The cost analysis demonstrated that in the group of HCV-infected (genotype 1) patients without cirrhosis and with cirrhosis, the minimum cumulative costs per patient correspond to PegIFN-α + SOF + RBV and Dasabuvir + Ombitasvir/paritaprevir/ritonavir + RBV regimens, respectively (Table 13).

From the perspective of “cost-effectiveness” analysis the best ratio in the group of HCV-infected (genotype 1) patients without cirrhosis and with cirrhosis corresponds to PegIFN-α + SOF + RBV and Dasabuvir + Ombitasvir/paritaprevir/ritonavir + RBV regimens, respectively (Figure 6).

Since in the group of patients with cirrhosis the cumulative costs were lower while the effectiveness was higher, than in comparison to PegIFN-α + SMV + RBV the regimen Dasabuvir + Ombitasvir/paritaprevir/ritonavir + RBV was predominant, therefore no ICER calculations have been conducted.

For Dasabuvir + Ombitasvir/paritaprevir/ritonavir (characterized by higher costs and greater effectiveness) and PegIFN-α + SOF + RBV regimens when used for patients without cirrhosis ICER was lower than willingness-to-pay threshold (WPT) calculated by the method recommended by WHO (1,597,618 rubles): 513,276 < 1,597,618.

Table 12. Results of effectiveness analysis: Scenario 2

Name of AVT regimen	QALY
	F0-F3
PegIFN-α + SMV + RBV	12,78
PegIFN-α + SOF + RBV	12,78
Dasabuvir + Ombitasvir/paritaprevir/ritonavir	13,23

Figure 4. Results of analysis of CER sensitivity to changes in variables in Scenario 1 in the subgroup of patients without cirrhosis

Figure 5. Results of analysis of CER sensitivity to changes in variables in Scenario 1 in the subgroup of patients with cirrhosis

Table 13. Results of cost analysis: Scenario 2

Name of AVT regimen	Cumulative costs, rubles	Cumulative costs per 1 patient, rubles	Cumulative costs of AVT, rubles	Cumulative costs of management of patients not reaching SVR, rubles	Cumulative costs of management of patients reaching SVR, rubles	Cumulative costs of medical aid to patients with complications of CHC, rubles
	F0-F3	F0-F3	F0-F3	F0-F3	F0-F3	F0-F3
PegIFN- α + SMV + RBV	89,422,810	944,909	85,632,033	771,663	111,717	2,907,398
PegIFN- α + SOF + RBV	71,727,302	757,925	67,714,620	873,745	108,851	3,030,086
Dasabuvir + Ombitasvir/paritaprevir/ritonavir	93,588,349	988,926	93,450,562	0	137,786	0

Figure 6. Results of “cost-effectiveness” analysis: Scenario 2

When switching to PegIFN- α + SOF + RBV from PegIFN- α + SMV + RBV the cumulative costs per one patient in the group without cirrhosis will decrease by 186,984 rubles (Table 14).

And when switching to PegIFN- α + SOF + RBV from Dasabuvir + Ombitasvir/paritaprevir/ritonavir the cumulative costs per one patient in the group without cirrhosis will decrease by 231,000 rubles (Table 15).

The sensitivity analysis demonstrated that the greatest effect on the cost-effectiveness ratio is produced by the variables “Medicine price”, “Probability of SVR achievement” and “Average age of patients” (Figure 7).

Table 14. The results of “budget impact” analysis: Switching from PegIFN- α + SMV + RBV to PegIFN- α + SOF + RBV

Cumulative costs of AVT, rubles	Cumulative costs of management of patients not reaching SVR, rubles	Cumulative costs of management of patients reaching SVR, rubles	Cumulative costs of medical aid to patients with complications of CHC, rubles				Cumulative costs, rubles	Cumulative costs per 1 patient, rubles
			Patients who progressed to F4	Patients who progressed to DC	Patients who progressed to HCC	Patients who progressed to LT		
F0-F3	F0-F3	F0-F3	F0-F3	F0-F3	F0-F3	F0-F3	F0-F3	F0-F3
will decrease by 17,917,413	will increase by 102,082	will decrease by 2,865	will increase by 89,318	will increase by 19,059	will increase by 4,840	will increase by 9,471	will decrease by 17,695,508	will decrease by 186,984

Table 15. The results of “budget impact” analysis: Switching from Dasabuvir + Ombitasvir/paritaprevir/ritonavir to PegIFN- α + SOF + RBV

Cumulative costs of AVT, rubles	Cumulative costs of management of patients not reaching SVR, rubles	Cumulative costs of management of patients reaching SVR, rubles	Cumulative costs of medical aid to patients with complications of CHC, rubles				Cumulative costs, rubles	Cumulative costs per 1 patient, rubles
			Patients who progressed to F4	Patients who progressed to DC	Patients who progressed to HCC	Patients who progressed to LT		
F0-F3	F0-F3	F0-F3	F0-F3	F0-F3	F0-F3	F0-F3	F0-F3	F0-F3
will decrease by 25,735,942	will increase by 873,745	will decrease by 28,935	will increase by 2,047,635	will increase by 491,714	will increase by 73,562	will increase by 417,176	will decrease by 21,861,046	will decrease by 231,000

Figure 7. Results of analysis of CER sensitivity to changes in variables in Scenario 2 in the subgroup of patients without cirrhosis

Conclusions

Therefore, the cost-effectiveness analysis showed that independently of the former experience of CHC (genotype 1) patients, the regimen PegIFN-α + SOF + RBV was predominant in comparison to PegIFN-α + RBV and PegIFN-α + SMV + RBV regimens. In the subgroups of patients without cirrhosis and with cirrhosis the highest QALY value corresponded to Dasabuvir + Ombitasvir/paritaprevir/ritonavir and Dasabuvir + Ombitasvir/paritaprevir/ritonavir + RBV regimens, respectively. Also a smaller CER relative to the two above regimens was noted for PegIFN-α + SOF + RBV. In the group of AVT-naïve patients without cirrhosis ICER_{Dasabuvir + Ombitasvir/paritaprevir/ritonavir vs PegIFN-α + SOF + RBV} was higher than WPT, whereas in the group of patients with cirrhosis ICER_{Dasabuvir + Ombitasvir/paritaprevir/ritonavir + RBV vs PegIFN-α + SOF + RBV} was lower than WPT.

The “budget impact” analysis showed that switching to PegIFN-α + SOF + RBV from PegIFN-α + RBV will require extra direct AVT costs, but will lead to a reduction in medical aid costs for the patients not reaching SVR, medical aid costs for the patients with CHC complications and consequently to a reduction in cumulative medical costs. Moreover, switching to PegIFN-α + SOF + RBV from PegIFN-α + SMV + RBV, Dasabuvir + Ombitasvir/paritaprevir/ritonavir and Dasabuvir + Ombitasvir/paritaprevir/ritonavir + RBV will lead to a reduction in both AVT costs and cumulative medical costs.

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