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COMPARATIVE PHARMACOECONOMIC ANALYSIS OF LONG-ACTING LANREOTIDE USED IN ACROMEGALY THERAPY WITHIN CONDITIONS OF THE RUSSIAN FEDERATION HEALTH CARE SYSTEM

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The aim of this study is to conduct a comprehensive pharmacoeconomic evaluation of the use of long-acting subcutaneous lanreotide gel compared to alternative drugs, for the treatment of acromegaly.

Materials and methods. Based on the literature data, a treatment model with a 1-year outlook was developed, a cost-effectiveness analysis (CEA) in pharmacoeconomics and a sensitivity analysis of changes in the model parameters were carried out. Direct medical costs for the annual therapy course were calculated. The data on the medicines costs were taken from the register of marginal prices of the State Register of Medicines.

Results. According to the unified Russian registry of the pituitary-hypothalamic tumors area, the achievement of remission in the acromegaly patients using lanreotide, a long-acting gel for a subcutaneous administration, compared to the long-acting octreotide, is 51% vs 24%. During the first year of treatment with octreotide, the total pharmacotherapy costs were lower than with lanreotide (RUB 225,496.07 vs RUB 574,451.84). According to the results of the cost-effectiveness analysis for one achieved case of remission, the advantage of using lanreotide over long-acting octreotide was revealed (RUB 1,251,870.56 versus RUB 1,431,005.31). The sensitivity analysis demonstrated the model's stability to increases in the lanreotide price (up to +18%), decreases in the octreotide prices (up to –22%), increases in the transsphenoidal adenomectomy prices (up to +59%), and decreased lanreotide remission rates (up to –12%).

Conclusion. Although the treatment costs analysis showed lower total per year costs of the treatment with long-acting octreotide compared to lanreotide, the calculation of the cost-effectiveness ratio per remission showed that lanreotide had been superior to long-acting octreotide.

Keywords: acromegaly; lanreotide; octreotide; cost-effectiveness analysis; treatment costs

Abbreviations: MP – medicinal product; SSAs, somatostatin analogues; IGF-1 – insulin-like growth factor-1; QOL – quality of life; STH – somatotropic hormone; VAT – value added tax; TM – trade margin; RCT – randomized clinical trial; CT – clinical trial; HTMC – high-tech medical care; AEs – adverse effects; RR – relative risk; CI – confidence interval.

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СРАВНИТЕЛЬНЫЙ ФАРМАКОЭКОНОМИЧЕСКИЙ АНАЛИЗ ПРИМЕНЕНИЯ ЛАНРЕОТИДА ПРОЛОНГИРОВАННОГО ДЕЙСТВИЯ ДЛЯ ТЕРАПИИ АКРОМЕГАЛИИ В УСЛОВИЯХ СИСТЕМЫ ЗДРАВООХРАНЕНИЯ РОССИЙСКОЙ ФЕДЕРАЦИИ

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Цель. Проведение комплексной фармакоэкономической оценки применения препарата ланреотид гель для подкожного введения пролонгированного действия по сравнению с альтернативными препаратами для терапии акромегалии.
Материалы и методы. На основании данных литературы была построена модель лечения с горизонтом 1 год, проведен фармакоэкономический анализ затраты-эффективность (CEA) и анализ чувствительности к изменениям параметров модели. Прямые медицинские затраты были рассчитаны на годовой курс терапии. Данные о стоимости лекарственных препаратов были взяты из реестра предельных цен Государственного реестра лекарственных средств.
Результаты. По данным единого Российского регистра опухолей гипоталамо-гипофизарной области, достижение ремиссии у пациентов с акромегалией при использовании ланреотид, гель для подкожного введения пролонгированного действия в сравнении с октреотидом пролонгированного действия составляет 51% против 24%. Общие затраты на фармакотерапию в течение первого года при использовании октреотида были ниже, чем при использовании ланреотида (225496,07 руб. против 574451,84 руб.). По результатам анализа «затраты-эффективность» на один достигнутый случай ремиссии было выявлено преимущество применения ланреотида перед октреотидом пролонгированного действия (1251870,56 руб. против 1431005,31 руб.). Анализ чувствительности продемонстрировал устойчивость модели к увеличению цены на ланреотид (до +18%), уменьшению цены на октреотид (до –22%), увеличению цены на транссфеноидальную аденомэктомию (до +59%) и снижению частоты ремиссий на ланреотид (до –12%).
Заключение. Несмотря на то, что анализ затрат на лекарственные препараты показал меньшие общие затраты на годовой курс терапии октреотидом пролонгированного действия в сравнении с ланреотидом, при расчёте коэффициента «затраты-эффективность» на один достигнутый случай ремиссии было выявлено преимущество применения ланреотида перед октреотидом пролонгированного действия.
Ключевые слова: акромегалия; ланреотид; октреотид; анализ затраты-эффективность; затраты на лечение
Список сокращений: ЛП – лекарственный препарат; АСС – аналоги соматостатина; ИФР-1 – инсулиноподобный фактор роста-1; КЖ – качество жизни; СТГ – соматотропный гормон; НДС – налог на добавленную стоимость; ТН – торговая наценка; РКИ – рандомизированное клиническое исследование; КИ – клиническое исследование; ВМП – высокотехнологическая медицинская помощь; ИФР-1 – инсулиноподобный фактор роста-1; НЯ – нежелательные явления; ОР – относительный риск; ДИ – доверительный интервал.

INTRODUCTION

Acromegaly is a severe neuroendocrine disease caused by a chronic hyperproduction of a somatotropic hormone (STH) in individuals with a completed physiological growth [1]. Due to the development of various complications, the disease is accompanied by a progressive disability, a reduced life expectancy, and an increased mortality risk [2].

Somatostatin analogues (SSAs) are the most common pharmacological treatment option for acrome-

galy. According to the current clinical guidelines [1], the main indication for the SSAs prescription is the adjunctive therapy while maintaining a disease activity at the end of the surgery [3, 4]. SSAs are also used as the first therapy line for small adenomas. In this group, the most common drugs are octreotide and lanreotide [4]

The problem of the therapy resistance in the acromegaly patients is widespread in the clinical practice [5]. To date, about 50% of the acromegaly patients do not achieve biochemical remission when using standard SSAs doses [3]. One of the possible ways to overcome the resistance is to increase the dose or reduce the interval between the injections.

To improve the therapy effectiveness, Russian and international experts also recommend an intragroup replacement of octreotide with lanreotide [5]. In the SSAs group, octreotide is older, while lanreotide is more modern. A number of studies note its better tolerability, a higher percentage of successful injections and, as a result, the achievement of a better control over acromegaly [4].

Lanreotide is a natural somatostatin analogue, able of suppressing the growth hormone secretion due to its pronounced tropism for human somatostatin receptors SSTR [6, 7]. It exists in the usual form (Somatulin®, injections once per 14 days, practically not used at the moment), and in a more convenient prolonged form (Somatulin® Autogel®, injections once per 28 days) [7].

A significant price of SSAs and lanreotide, in particular, is worth notifying. In the study published by Lesén E. et al., in 2013, the annual costs of the SSAs therapy in Sweden were valued at 13,500 euros [8]. In the article by Orlewska E. et al., the annual average costs of therapy with lanreotide (Autogel, 120 mg) in Poland were valued at 12,187 euros [9]. In the analysis by Biermasz N.L. et al., the costs of the SSAs therapy in the Netherlands were reported as €16,500 for octreotide (Sandostatin® LAR, the mean dose of 24 mg/4 weeks) and €23,000 for lanreotide Autogel [10].

No similar studies have been conducted in the Russian Federation. To carry out a competent and reasonable distribution of the healthcare budget, this fact highlights the importance of a comprehensive assessment of different options for the acromegaly treatment.

THE AIM of this study is to conduct a comprehensive pharmacoeconomic evaluation of the use of long-acting subcutaneous lanreotide gel compared to alternative drugs, for the treatment of acromegaly.

To achieve the aim, the following tasks were set:

1. A comparative review of the clinical efficacy and safety of lanreotide, a long-acting subcutaneous gel, for the acromegaly treatment, vs long-acting octreotide.

2. Direct costs calculations for the acromegaly treatment with lanreotide and octreotide within the framework of the Russian healthcare system, as well as for the surgical treatment (transsphenoidal adenomectomy) in case of a failure to achieve remissions.

3. Developing a pharmacoeconomic model to assess the relationship between the prescription of lanreotide and the costs of acromegaly therapy using mathematical modeling.

4. The sensitivity analysis of the selected model to changes in the primary parameters.

MATERIALS AND METHODS

In order to analyze the effectiveness and safety, a search for the information on randomized clinical trials in the following electronic resources – Cochrane Library; Medline eLIBRARY – was made.

The search was performed on September 28, 2021. It included publications with a statute of 10-year limitations with the following keywords: “lanreotide” OR “octreotide” AND “clinical effectiveness” OR “clinicaloutcomes” AND “acromegaly”; “lanreotide” OR “octreotide” AND “clinical efficacy” OR “outcomes” and “acromegaly”.

According to the primary search query, 902 publications were found in the Medline database; 0 in the Cochrane Library database; 12 – in the eLibrary. A further selection was carried out according to the PRISMA criteria (Fig. 1). When reviewing the literature, the following publications were selected:

1) Review by Qiao N. et al., 2020 [11]; 2) Review and meta-analysis by Leonart L.P. et al., 2018 [12]; 3) Review by Abu Dabrh A.M. et al., 2014) [13]; 4) Review by Marko N.F. et al., 2012 [14]; 5) RCT by Bernabeu I. et al., 2020 [15]; 6) RCT by Guistina A. et al., 2017 [6]; 7) RCT by Annamalai A.K. et al., 2013 [16]; 8) RCT by Gariani K. et al., 2013 [17]; 9) RCT by Li Q.Z. et al., 2012 [18]; 10) RCT by Carmichael J.D. et al., 2012 [19]; 11) RCT by Tutuncu Y. et al., 2012 [20]; 12) CT by Salvatori R. et al., 2017 [21]; 13) CT by LANTERN, An Z et al., 2017 [22]; 14) CT by PRIMARYS, Caron P.J. et al., 2016 [23]; 15) Data from the Moscow Register, Antsiferov M.B. et al., 2020 [24]; 16) Data from the unified Russian registry of tumors of the pituitary-hypothalamic system, Belaya Zh.E. et al., 2020 [2].

The original somatulin medicinal preparation – Somatulin® Autogel® (Ipsen Pharma, France) – gel for a subcutaneous (s/c) administration of the long-acting drug in the doses of 60 mg, 90 mg and 120 mg, was chosen as the study drug (SD).

For a comparative analysis, octreotide preparations that are most commonly used in acromegaly patients in clinical practice were selected: Sandostatin-LAR® original preparation (Novartis, Switzerland), generic preparations Octreotide-depot® (Pharmsynthesis, Russia) and Octreotide-long® (Nativa, Russia) in the doses of 10 mg, 20 mg and 30 mg.

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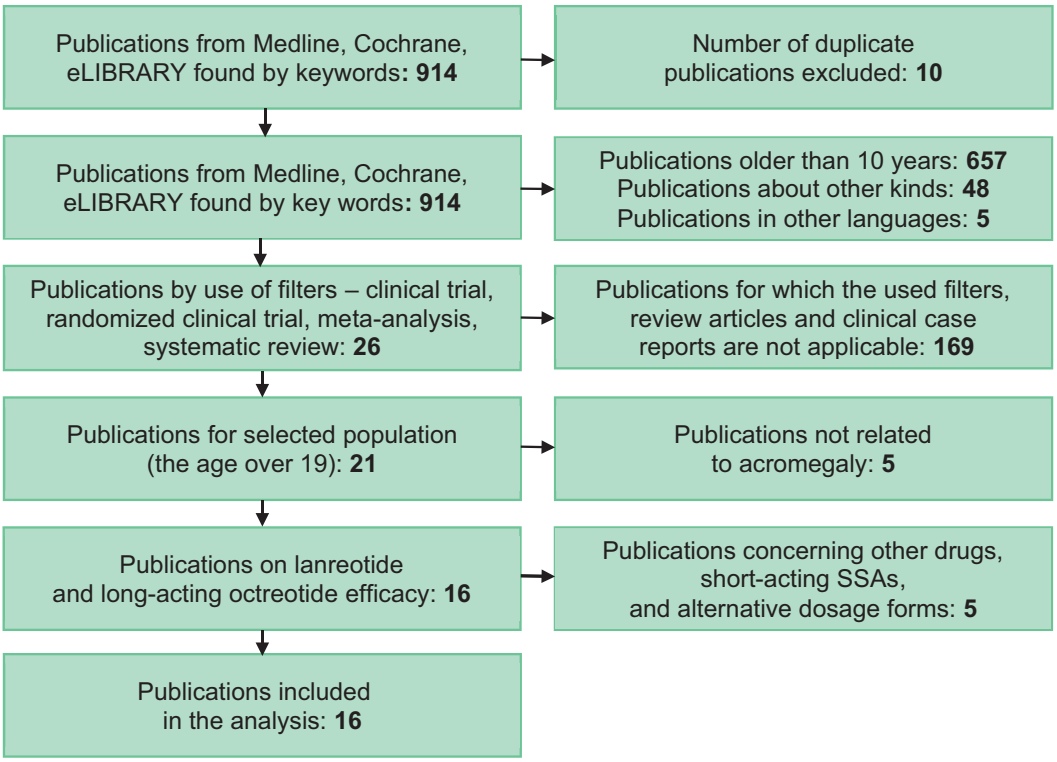

Figure 1 – Study selection scheme

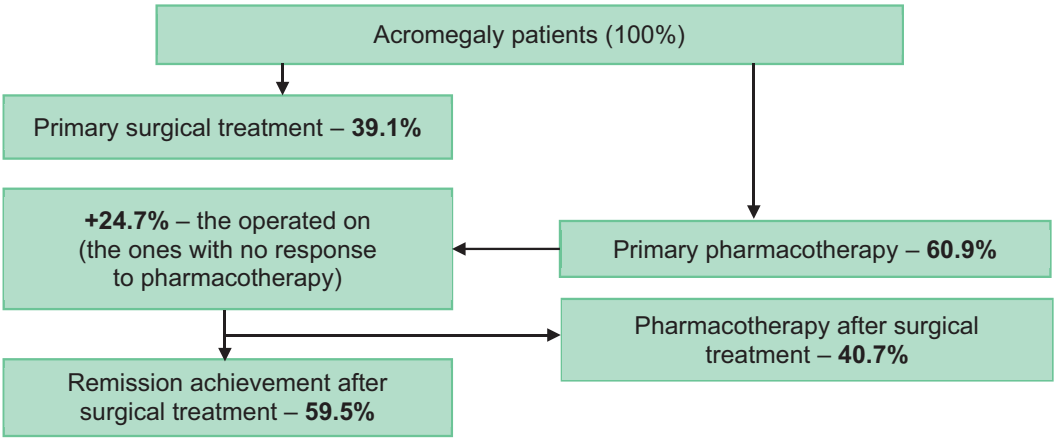

Figure 2 – Route of acromegaly patients according to Belaya Z.E. et al, 2020 [3]

Table 1 – Lanreotide titration scheme of long-acting gel for s/c administration in acromegaly patients in the first year of therapy according to Chanson P. et al., 2008 [26]

Therapy term	Dose	Frequency
Therapy start (1–3 mths)	90 mg – 100%	Once per 28 days
4–6 mths	60 mg – 17,4%; 90 mg – 12,8%;120 mg – 69,8%	Once per 28 days
7–12 mths	60 mg – 14,0%; 90 mg – 13,0%; 120 mg – 73,0%	Once per 28 days

Table 2 – Octreotide titration scheme in acromegaly patients in the first year of therapy according to Dreval A.V. et al., 2014 [5]

Therapy term	Dose	Frequency
Therapy start (1–3 mths)	20 mg – 100%	Once per 28 days
4–6 mths	10 mg – 5,6%; 20 mg – 58,22%; 30 mg – 53,16%	Once per 28 days
7–12 mths	10 mg – 5,1%; 20 mg – 41,8%; 30 mg – 13,9%; 40 mg – 39,2%	Once per 28 days

Table 3 – Median prices for different doses of long-acting somatostatin analogues

MP (INN)	Dose (mg)	Median price (rubles)	Median price +VAT+TM (rubles)	Median price +VAT+TM (USD)*
Lanreotide	60	30,830.85	37,931.04	523.1
Lanreotide	90	42,246.28	56,896.57	784.78
Lanreotide	120	61,661.70	75,862.08	1,046.37
Octreotide	10	7,949.95	9,780.78	134.9
Octreotide	20	15,899.91	19,561.58	269.81
Octreotide	30	23,849.85	29,342.35	404.72

Note: dollar exchange rate dated 05.10.21: 1 $ = 72.5 rubles.

Table 4 – Costs calculation of Somatulin® Autogel® annual course per one acromegaly patient (with prices in rubles, including VAT and TM)

Therapy term	Dosing regimen	Frequency of administration	Quantity of units	Cost per 1 unit	Cost per period
1–3 therapy mths.	90 mg, once per 28 days, s/c	1.00	3.0	56,896.57	170,689.70
4–6 therapy mths.	60 mg, once per 28 days, s/c	0.174	3.0	37,931.04	19,800.00
	90 mg, once per 28 days, s/c	0.128	3.0	56,896.57	21,848.28
	120 mg, once per 28 days, s/c	0.698	3.0	75862.08	158,855.20
7–12 therapy mths.	60 mg, once per 28 days, s/c	0.14	3.0	37,931.04	15,931.04
	90 mg, once per 28 days, s/c	0.13	3.0	56,896.57	22,189.66
	120 mg, once per 28 days, s/c	0.73	3.0	75,862.08	166,137.96
Cost per treatment course	575,451.84 rubles or 7,937.26 $				

Table 5 – Costs calculation of long-acting octreotide annual course per one acromegaly patient (with prices in rubles, including VAT and TM)

Therapy term	Dosing regimen	Frequency of administration	Quantity of units	Cost per 1 unit	Cost per period
1–3 therapy mths.	20 mg, once per 28 days, s/c	1.00	3.0	19,561.58	58684.73
4–6 therapy mths.	10 mg, once per 28 days, s/c	0.056	3.0	9,780.78	1643.17
	20 mg, once per 28 days, s/c	0.582	3.0	19,561.58	34154.51
	30 mg, once per 28 days, s/c	0.531	3.0	29,342.35	46742.36
7–12 therapy mths.	10 mg, once per 28 days, s/c	0.051	3.0	9,780.78	1496.45
	20 mg, once per 28 days, s/c	0.418	3.0	19,561.58	24530.22
	30 mg, once per 28 days, s/c	0.139	3.0	29,342.35	12235.76
	40 mg, once per 28 days, s/c	0.392	6.0	19,561.58	46008.83
Cost per treatment course	225,496.07 руб. or 3,110.29 $				

Table 6 – Cost-effectiveness ratios

Parameter	Long-acting lanreotide	Long-acting octreotide
Costs of pharmacotherapy for the first year (rubles/patient)	575,451.84	225,496.07
Costs of therapy for transsphenoidal adenomectomy (rubles)	240,358.0	240,358.0
Only need for surgery	15.7%	15.7%
Need for pharmacotherapy	36.2%	36.2%
Both surgery and pharmacotherapy	48,1%	48.1%
Remission rate*	0,51	0.24
Total costs per person per year, rubles	638,453.99	343,441.27
Cost-effectiveness ratio, rubles / case of achieved remission	1,251,870.56	1,431,005.31
Difference	179,134.74 rubles or 2,470.82 $	

Note: * – based on the data of the Russian Register [3]

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The study estimated direct medical costs for a one-year treatment course. The data on the medicines costs were taken from the register of marginal prices of the State Register of Medicines (SRMs)[1] as on September 2, 2021. The value added tax (VAT) of 10% and the weighted average trade margin (TM) of 11.845%[2] were also taken into account. To convert the price into US dollars, the current exchange rate as of 10/05/21[3] was used 1 $ = 72.5 rubles.

To calculate the therapy costs, the research data describing the routine use of the studied drugs in real clinical practice, were used [25].

In the study by Chanson P. et al. [26], conducted in Germany, an analysis of the dose titration of Somatulin® Autogel® in acromegaly patients, during a year of therapy (Table 1) is presented. Under the conditions of the Russian healthcare system, Dreval A.V. et al. [5] conducted a dose titration study of octreotide preparations in acromegaly patients (Table 2).

The analysis of direct medical costs [25] took into account the main pharmacotherapy and the cost of a surgical intervention (transsphenoidal adenomectomy) in case of a failure, to achieve remission within a year. The cost was calculated on the basis of the Decree of the Government of the Russian Federation dated December 28, 2020 No. 2299[4] "On the Program of State Guarantees of Free Medical Care for Citizens for 2021 and for the planning period of 2022 and 2023." According to this document, microsurgical and endoscopic interventions for pituitary adenomas belong to the class of high-tech medical care (HTMC) and, depending on the complexity of the operation, are estimated at 169,754 rubles. (HTMC 1), or – 310,961 rubles. (HTMC 2). The median cost was considered to amount to 240,358 rubles.

Based on the data of the Register [3], published in the article by Belaya Zh.E. et al., there are several route options in acromegaly patients (Fig. 2).

– Group 1. They undergo surgical treatment and achieve remission without pharmacotherapy prescription.

– Group 2. Acromegaly patients undergo surgical treatment, but require subsequent pharmacotherapy.

– Group 3. Pharmacotherapy is primarily prescribed, and then a patient undergoes surgical treatment.

– Group 4. Primarily pharmacotherapy is prescribed, against this background, there is either remission achieved and the patient remains on maintenance doses of drugs, or the dose of drugs is increased.

Based on the research hypothesis, the method of "cost-effectiveness" as a clinical and economic analysis was chosen [25]. This method implies the correlation of costs with the results obtained and the comparison of two or more alternative medical technologies by this indicator. At the same time, the results are presented in the form of "natural" indicators of clinical effectiveness, the number of the years of saved lives, or other objective criteria that are significant for a particular pathology[5]. In the case of the SSAs therapy for acromegaly, the percentage of patients who had achieved remission, was chosen as an efficiency criterion.

In this analysis, only direct costs were taken into account, so the final formula was as follows [25]:

$$CER = DC/Ef$$

where: CER (a cost-effectiveness ratio) shows the costs per unit of efficiency; DC denotes direct costs; Ef is the effectiveness of a medical technology application.

At the final stage of the study, a sensitivity analysis was performed, its purpose was to determine the model sensitivity to changes in the initial parameters – drug prices and changes in the model, taking into account the real clinical practice of using octreotide and lanreotide in acromegaly patients [25].

RESULTS

Efficacy and safety analysis

Octreotide, including a long-acting one, was registered for use in acromegaly patients long ago and has a large evidence base [4, 5]. Lanreotide is a more modern drug. Its prolonged form was registered only in 2014 (Somatulin® Autogel®), however, the effectiveness of its use was confirmed in a number of studies and meta-analyses [12-23

The PRIMARYS protocol [20] was an open-label, one-year CT of a long-acting lanreotide efficacy in the standard regimen (120 mg once per 28 days) for the control of acromegaly symptoms. The number of participants was 90 people with a newly diagnosed disease. A clinical presentation was assessed using the Acromegaly Symptom Assessment Questionnaire (PASQ) as a part of European Network for Patient Safety and Quality of Care: PaSQ; and a quality of life (QoL) was assessed using the AcroQoL questionnaire. Acromegaly symptoms and QoL improved significantly from weeks 12 to 48, with a weak correlation between the total PASQ score ($R= –0.55$, $p<0.0001$) and the total AcroQoL score, and a physical condition score ($R= –0.67$, $p<0.0001$) [20] during week 48.

Similar results on the Somatulin® Autogel® effectiveness are presented in the work by Antsiferov M.B. et al., which provides the data from the Moscow Register of Patients. A statistical analysis showed that the

[1] State register of maximum selling prices, 2021. Available from: https: //minzdrav.gov.ru/opendata/7707778246-gosreestrpredelnyhotpusknyhcen/visual. Russian

[2] Omelyanovsky VV, Avksentieva MV, Sura MV, Khachatryan GR, Gerasimova KV, Ivakhnenko OI, Dzanaeva AV. Guidelines for conducting a comparative clinical and economic evaluation of a medicinal product. Approved by order of the Center for Healthcare Quality Assessment and Control of the Ministry of Health of the Russian Federation dated December 29, 2018 No.242, Moscow, 2018. – 46 p. Russian

[3] Bank of Russia. Available from: https://www.cbr.ru/eng/about_br/irp/.

[4] Decree of the Government of the Russian Federation of December 28, 2020 N 2299 "On the Program of State Guarantees of Free Provision of Medical Care to Citizens for 2021 and for the Planning Period of 2022 and 2023" (with amendments and additions). Russian

[5] State register of maximum selling prices, 2021. Russian

hormones level after 12 weeks of treatment (GH <1.2 mcg / l and an insulin-like growth factor-1 (IGF-1), which corresponds to <110% of the upper age limit) is the effectiveness marker of a 12-month treatment course. A decrease in IGF-1 below 110 and 125% of the upper age norm, respectively, after 12 weeks, was a predictor of an adequate and stable hormonal control [24].

Clinical data on the use of long-acting lanreotide based on a multicenter SODA study are presented by Salvatori R et al., 2017 [12]. In this work, a two-year efficacy and safety of lanreotide, a long-acting s/c gel, was studied. The study included 241 acromegaly patients treated with lanreotide. IGF-1 levels below the upper reference value were achieved in 71.2% after 1 year of treatment and in 74.4% after 2 years. The most frequent adverse events (AEs) value ≤2.5 μg/l was recorded in 83.3% after 1 year and in 80.0% after 2 years; STH <1.0 μg/l – in 61.7% after 1 year and in 61.4% after 2 years. The most common adverse event (AE) was arthralgia (25.7%). 10 of 106 serious AEs reported by 42 patients, were treatment related [21].

In the recent network meta-analysis by Leonart L.P. et al. [12], a clinical efficacy of different drugs for the acromegaly treatment were compared. The study included 2059 articles. The results showed that pegvisomant and long-acting lanreotide were statistically superior to placebo: a relative risk (RR), a 95% confidence interval (CI) were 0.06 (0.00–0.55) and 0.09 (0.0-0. 88), respectively. No significant differences were found out; however, when comparing lanreotide and long-acting octreotide, there was a trend towards the advantage of the first one (RR 95%, CI was 0.74 (0.06–7.91). No serious side effects of treatment were notified.

Among the Russian publications, the Russian Registry of Pituitary-Hypothalamic tumors data should be notified, where a large sample demonstrated a clinical advantage of lanreotide in achieving remission of the disease – 51% vs 24% for long-acting octreotide. Thus, based on the analyzed data, the cost-effectiveness method was chosen for a further analysis, and the remission rates were included in the pharmacoeconomic model as an efficiency criterion [3].

Cost analysis and model developing

The prices for the drugs under study were included in the cost analysis. The price for each formulation of lanreotide (Somatulin® Autogel® 60 mg, 90 mg and 120 mg) was taken into account separately. According to the recommendations of the Federal State Budgetary Institution "Centre for Expertise and Quality Control in Health Care" (the Ministry of Health of Russia)[6], when calculating a price for long-acting octreotide preparations, a median price was considered (Table 3).

[6] Omelyanovsky VV, Avksentieva MV, Sura MV, Khachatryan GR, Gerasimova KV, Ivakhnenko OI, Dzanaeva AV. Guidelines for conducting a comparative clinical and economic evaluation of a medicinal product. Russian

Based on current clinical guidelines [1], works by Chanson P. et al. [26] and Dreval A.V. et al. [5], one patient's treatment models with lanreotide or long-acting octreotide in the first year of therapy were developed. The results of the cost analysis for a treatment course are presented in Tables 4 and 5.

The total costs for pharmacotherapy in adult patients with acromegaly during the first year using long-acting octreotide was significantly lower than the costs for lanreotide: 225,496.07 rubles vs 575,451.84 rubles ($3,110.29 vs. $7,937.26), but achieving remission was much less common.

Results of cost-effectiveness analysis

At the next stage of the study, a comparative CEA analysis of the lanreotide and long-acting octreotide use in acromegaly patients during the first year of therapy was carried out. The cost of transsphenoidal adenomectomy, as well as the need for different types of treatment in acromegaly patients in the first year of treatment, were taken into account: the frequency of surgery, the appointments of pharmacotherapy, and their combinations. The calculation results of the cost-effectiveness ratios are presented in Table 6.

Despite the fact that the drug costs analysis showed lower total costs for the annual therapy course with long-acting octreotide compared to lanreotide, when calculating the cost-effectiveness ratio for one achieved remission case, the advantage of using lanreotide over long-acting octreotide was revealed: 1,251,870.56 RUB vs 1,431,005.31 RUB ($17,267.18 vs. $19,738.0).

The use of lanreotide in acromegaly patients makes it possible to reduce the total costs during the year per 1 patient in remission by 179,134.74 rubles. ($2,470.82) compared to long-acting octreotide.

Sensitivity Analysis Results

A sensitivity analysis demonstrated the stability of the model to change: prices for lanreotide – up to +18%; prices for octreotide – up to –22%; prices for transsphenoidal adenomectomy – up to + 59%; a reduction in the remissions frequency when using lanreotide – up to –12%.

DISCUSSION

The data obtained have also been confirmed by the international studies by Marco N.F. et al. [14]; Marty R. et al. [27]; Neggers S.J. et al. [28]; Orlewska E. et al. [9].

Marco N.F. et al. calculated the annual treatment costs with long-acting somatostatin analogs. For the calculation, the average dose of lanreotide was taken – 103 mg / 4 weeks, and octreotide – 24 mg / 4 weeks. The median annual cost of octreotide was $43,526 and the median annual cost of lanreotide was $41,216. The costs of lifelong treatment with octreotide, lanreotide, pegvisomant, or SSAs + pegvisomant were $1,667,052; 1,578,567; 2620833; and $2,573,339, respectively [14].

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In the study by Marty R. et al., Somatulin® Autogel® (90 mg) and Sandostatin Lar® (20 mg) were chosen to calculate annual cost savings per patient. The results were as follows: 356.4 euros, 929.5 euros and 1457.5 euros for France, Germany and the UK, respectively. It was concluded that annual cost savings for the healthcare system could be as high as €948,236, €3,176,618 and €3,645,213 in France, Germany, and the UK, respectively [27].

Annual costs for lanreotide and octreotide were calculated by Neggers S.J. et al. to be $41,216 and $43,526, respectively. Somatulin® Autogel® was cheaper to use, with the same 60% efficacy for the both drugs. The authors calculated that on average, the disease is diagnosed in a patient aged 40 years and, if successfully treated, does not shorten the patient's life expectancy. Assuming a life expectancy in the US of 78.3 years, the median treatment time per patient was 38.3 years and the treatment cost with lanreotide was $1,578,567 and with octreotide – $1,667,052 [28].

Some studies have also estimated the total costs of treating acromegaly patients. In the publication by Knutzen R. et al., all costs for the treatment of one acromegaly patient are described. Orthopedic surgery and dental care were included. The total costs were approximately US$1 million per patient from the time of the diagnosis until 25 years later [29].

The data obtained in this study, made it possible to speak about the feasibility and effectiveness of using the drug lanreotide, a long-acting gel for the treatment of adult acromegaly patients, both in the form of preoperative therapy and in cases where remission had not been achieved after surgical treatment. Despite the significant cost of lanreotide (almost twice the cost of octreotide preparations), based on the clinical data and observational studies, a higher efficiency of lanreotide in achieving disease remissions is probable. That indicates its better clinical and economic efficiency.

The results of this work have shown that the use of Somatulin® Autogel® for the acromegaly treatment in patients over 18 years old is clinically effective and economically justified within the framework of the state drug benefit system of the Russian Federation.

CONCLUSION

The analysis of literature sources made it possible to conclude that Somatulin® Autogel® was more clinically effective and more convenient to use than long-acting octreotide preparations.

According to the Russian Register, the achievement of remission with the use of lanreotide, a long-acting s/c gel, in comparison with long-acting octreotide, is 51% vs 24% (with a comparable safety profile).

The total costs of pharmacotherapy for acromegaly patients during the first year when using long-acting octreotide was lower than when using lanreotide: 225,496.07 rubles vs 575,451.84 rubles ($3,110.29 vs $7,937.26).

According to the results of the cost-effectiveness analysis, for one achieved case of remission, the advantage of using lanreotide over long-acting octreotide was revealed: 1,251,870.56 rubles vs 1,431,005.31 rubles ($17,267.18 vs. $19,738.0). Thus, the total costs during the year per 1 patient with the achieved remission are reduced by 179,134.74 rubles ($2,470.82).

A sensitivity analysis showed that the treatment model for acromegaly patients was resistant to an increase in the price of lanreotide to +18%, a decrease in the price of octreotide to –22%, an increase in the price of transsphenoidal adenomectomy to +59%, and a decrease in the remission rate on lanreotide to –12%.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHORS' CONTRIBUTION

Ivan S. Krysanov – concept development and study design, carrying out calculations; Ekaterina V. Makarova – carrying out calculations, text writing; Victoria Yu. Ermakova – literature search, data analysis.

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