№2 Том4 2016

Фармакоэкономика
теория и практика

www.pharmacoeconom.com

Pharmacoeconomics
theory and practice

№2 Volume4 2016

- МЕТОДОЛОГИЯ АНАЛИЗА ЗАТРАТ
- ОРИГИНАЛЬНЫЕ РОССИЙСКИЕ ФАРМАКОЭКОНОМИЧЕСКИЕ ИССЛЕДОВАНИЯ
- РЕПОРТАЖ С X НАЦИОНАЛЬНОГО КОНГРЕССА С МЕЖДУНАРОДНЫМ УЧАСТИЕМ "РАЗВИТИЕ ФАРМАКОЭКОНОМИКИ И ФАРМАКОЭПИДЕМИОЛОГИИ В РОССИЙСКОЙ ФЕДЕРАЦИИ" 4-5 апреля 2016 года В НИЖНЕМ НОВГОРОДЕ

www.pharmacoeconom.com

PHARMACOECONOMIC ANALYSIS OF TELAVANCIN USE IN RUSSIAN HEALTHCARE SYSTEM FOR TREATMENT OF PATIENTS WITH COMPLICATED SKIN AND SOFT TISSUE INFECTIONS

Kolbin A.S.[1,2], Vilyum I.A.[1,3], Proscurin M.A.[2], Balikina Yu.Ye.[2]

[1] First State Medical University of St. Petersburg named after academic I.P. Pavlov
[2] Saint Petersburg University
[3] Federal State Budgetary Institution «Saint-Petersburg multidisciplinary center» of the Ministry of Health Russian Federation

Abstract
It is the first time a comparative pharmacoeconomic analysis of telavancin (Vibativ®) use for treatment of patients suffering from nosocomial infections caused by resistant bacterial flora using the example of patients with complicated skin and soft tissue infections was held. The study was carried out using mathematical modelling with a one-month horizon. Cost-benefit analysis, budget-impact analysis, and sensitivity analysis were used. The study found that telavancin use showed high clinical efficacy and one of the best safety profiles among other medical treatment technologies for such groups of patients. Telavancin use makes more economic sense in terms of cost-efficacy ratio than daptomycin, tigecycline and linezolid. Telavancin use is more advantageous in terms of budget impact analysis as compared to linezolid and daptomycin use: saving up to 32,705,178 rubles from the budget, which enables to treat up to 126 more patients.

Key words: *complicated skin and soft tissue infections, pharmacoeconomics, telavancin*

Rationale

About thirty thousand cases of nosocomial infections (NI) are reported in the Russian Federation (RF) annually [1-3]. Bacteria of the *Staphylococcus genus* (*S.aureus*) still remain one of the most common causative agents of NI [4]. The epidemiological situation is complicated by wide spreading of bacteria resistant to oxacillin and methicillin (oxacillin-resistant *Staphylococcus aureus* (ORSA) and methicillin-resistant *Staphylococcus aureus* (MRSA) in hospitals. In Russia, the rate of isolation of S.aureus in hospitals is 75.0% of all gram-positive pathogens, and more than half of them are methicillin-resistant [5]. Complicated skin and soft tissue infections (CSSTI) are among the most common infections that are treated in the inpatient setting [6]. Telavancin is the first representative of the new generation of glycopeptide antibiotics, semi-synthetic lipoglycopeptides [7;8,9;10;11]. Clinical studies have demonstrated the effectiveness of telavancin in CSSTI patients [12-14]. Foreign pharmacoeconomic studies conducted have demonstrated that telavancin use is reasonable [15].

Objective

To determine the pharmacoeconomic sense of telavancin use for treatment of patients with complicated skin and soft tissue infections from the standpoint of the state healthcare system and the standpoint of a patient in Russia.

Methods

The methodology of clinical and economic analysis utilized industry-specific standards "Clinical and Economic Study" used in the RF and expert guidelines [16-20]: cost-effectiveness analysis (CEA) with calculation of the corresponding coefficient (cost-effectiveness ratio, CER); incremental analysis with calculation of the corresponding coefficient (incremental cost-effectiveness ratios, ICERs). Additionally, a budget-impact analysis (BIA) with a one-year and three-year horizon was performed [21].

Characterization of costs and effectiveness indicators. Costs. Direct costs (DC) were listed: underlying disease (NP) treatment cost—cost of antibacterial medicinal products (MP); cost of treatment aimed at correction of adverse events (AE) caused by MP for the treatment of the underlying disease; cost of laboratory and instrumental investigations, and inpatient and outpatient treatment; treatment cost when therapy with MP of the strategies under consideration is ineffective. Indirect costs (IC) were listed as well: patient's lost earnings owing to temporary disability; outlay of the Social Insurance Fund on temporary disability benefits; lost profits determined as lost gross regional product (GRP). Costs were estimated on the basis of public data [22-25].

Treatment effectiveness. The effectiveness criterion used was efficacy, assessed from the results of randomized clinical studies (RCS) and meta-analyses. Effectiveness criteria included: clinical recovery rate—resolution of clinical symptoms of the infection, %; microbiological response rate—clearing of an infectious nidus from the pathogen; multiple negative bacterial flora tests of biosubstrates, %.

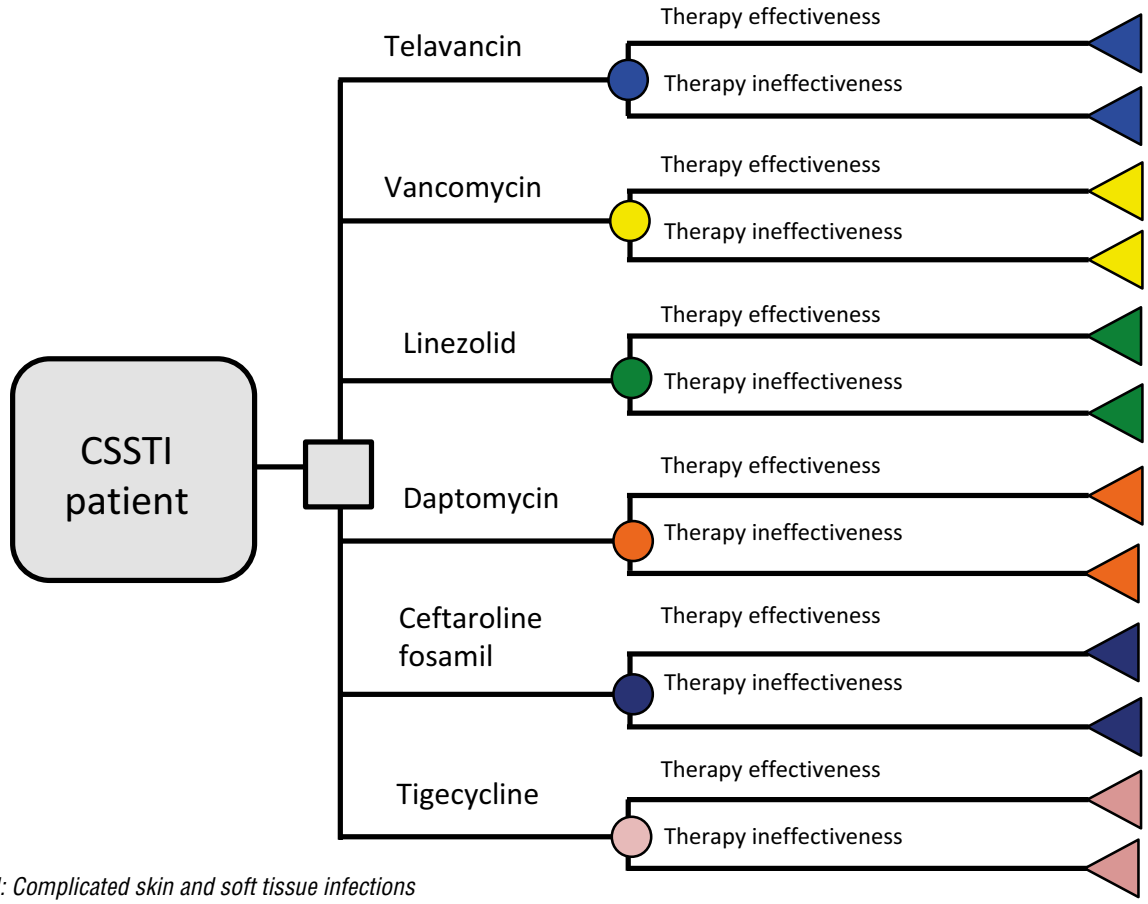
Treatment efficacy was evaluated among the strategies use of drugs shown during CSSTI caused by multi-resistant gram-positive flora: telanvacin, vancomycin, linezolid, daptomycin, ceftaroline fosamil, tigecycline. Studies with simultaneous inclusion of all six formulations we observed was not due to this indirect comparison of the data was performed according to the selected performance criteria based on RCTs with comparable populations of patients for demographic, somatic status and CSSTI type [12, 19, 26 - 29].

Model structure. A model of rendering aid to a CSSTI patient was made [12; 26-29].

Model of decision analysis for evaluation of pharmacoeconomic effectiveness of the medical aid strategies under consideration in complicated skin and soft tissue infections. Modeling started with the choice of an MP for CSSTI therapy: telavancin 10 mg/kg/day; vancomycin 2 g/day; linezolid 1,200 mg/day; ceftaroline fosamil 1,200 mg/day; daptomycin 4 mg/kg/day;

Kolbin A.S. - tel.: 8 921 759 04 49, e-mail: alex.kolbin@mail.ru

tigecycline 100 mg/day. An antibiotic therapy course was changed only when one of the strategies was reported to be ineffective. The duration of modeling was 30 days (1 month). In the case of therapy ineffectiveness, it was assumed that a patient would develop a septicemic condition that requires further treatment in an intensive care unit (ICU), initiation of a different antibacterial therapy, and a surgical intervention owing to aggravation of the infectious process. A schematic representation of a decision tree model for a CSSTI patient model is given in Fig.1.



CSSTI: Complicated skin and soft tissue infections

Fig.1. Model of decision analysis for evaluation of pharmacoeconomic effectiveness of CSSTI therapy with medicinal products of the strategies under consideration.

Data sources for mathematical modeling

An estimation model determined the cost of disease, probability of development of various events in different strategies of therapy for CSSTI patients—effective and ineffective treatment rates, and complication rates. Table 1 summarizes indicators of therapy effectiveness in patients with disorders under consideration.

Table 1. Effectiveness indicators of the strategies under consideration [26-29]

Effectiveness indicators	Telavancin	Vancomycin	Linezolid	Ceftaroline fosamil	Daptomycin	Tigecycline
CSSTI						
Clinical recovery rate, %	92,0 [19] 93,0	86,9 [29]	75,3 [26]	91,4 [28]	75,0 [27]	86,4 [29]
Microbiological response rate, %	84,0 [12]	83,9 [29]	71,0 [26]	86,6 [28]	-	80,2 [29]

CSSTI: Complicated skin and soft tissue infections

Calculation of medical aid cost in different strategies. The calculations are based on the data from standards of financial outlay per medical aid volume unit [23] and the General Tariff Agreement (GTA) for 2016 [24]. Calculation of MP cost in the strategies under comparison is given in Table 2.

Table 2. Cost of therapy with medicinal products of the strategies under consideration

Therapy strategy	Medicinal products (INN)	Trade names	Presentation	Price/ package (RUB)	Course cost
CSSTI					
Telavancin, 10 mg/kg/day, 14 days	Telavancin	Vibativ®	lyophilisate for solution for infusion, 750 mg, vial (1)	11 000,00	143 733,33
Vancomycin, 2 g/day, 14 days	Vancomycin	Edicin®	lyophilisate for solution for infusion 1.0 g, vials (1)	618,35	17 313,80
Linezolid, 1,200 mg/day, 14 days	Linezolid	Zyvox®	solution for infusion 2 mg/ml, 300 ml, single-use infusion bags (10)	21 906,80	61 339,04
Ceftaroline fosamil, 1,200 mg/day, 14 days	Ceftaroline fosamil	Zinforo®	powder for concentrate for solution for infusion, 600 mg, vials (10)	28 081,33	78 627,92
Daptomycin, 4 mg/kg/day, 14 days	Daptomycin	Cubicin®	lyophilisate for solution for infusion, 500 mg, vials (1)	5 919,25	46 406,92
Tigecycline, initial dose 100 mg, then 50 mg every 12 h, 14 days	Tigecycline	Tygacil®	lyophilisate for solution for infusion, 50 mg, vials (10)	28 923,80	83 879,02

INN: International nonproprietary name; CSSTI: Complicated skin and soft tissue infections

Cost of medical aid strategies for CSSTI patients. The cost of treatment of the underlying disease (CSSTI) includes outlay on the therapy with MP of the strategies under consideration and outlay on other medical and diagnosis measures, provided for as part of in-hospital stay in accordance with the corresponding diagnosis-related group (DRG) tariff ("Gangrene, phlegmon", cost: RUB 64,098.00).

Table 3. Total cost of CSSTI treatment with the strategies under consideration

Outlay list	Telavancin	Vancomycin	Linezolid	Ceftaroline fosamil	Daptomycin	Tigecycline
Outlay on pharmacotherapy per month, RUB	143 733,33	17 313,80	61 339,04	78 627,92	46 406,92	83 879,02
Outlay on hospital aid, RUB	64 098,00					
Total, RUB, 30 days of therapy	207 831,33	81 411,80	125 437,04	142 725,92	110 504,92	147 977,02

Cost of ineffective therapy. Cost of ineffective therapy with medical aid strategies for CSSTI patients. In the case when any of the CSSTI therapy strategies under consideration proved ineffective, it was assumed that a patient would develop a septicemic condition that requires further therapy in an ICU and initiation of a combination antibacterial therapy against gram-positive and gram-negative bacteria. It was also assumed that a patient would undergo a surgical intervention under general anesthesia (GA) for the purpose of clearing an infectious nidus. Considering the fact that more than half of the patients had a clinical form of CSSTI, an abscess, the cost of surgical intervention was assessed according to the GTA on the DRG "Phlegmon, abscess drainage with necrectomy", which is equal to RUB 37,517.80, and GA cost is determined according the tariff "General combination anesthesia with invasive artificial respiration without fluorinated anesthetics (FA -) in surgeries lasting 1 to 3 hours at Anesthesiology and Resuscitation Department I – II". Thus, the cost of ineffective therapy consists of the cost of medical aid under the corresponding DRG, stay in an intensive care unit, cost of antibacterial therapy, and cost of a surgery and GA. Outlay on antibiotic therapy was calculated as the average cost of medicines against resistant gram-positive flora and a course of broad-spectrum MP, including anaerobic, carbapenems.

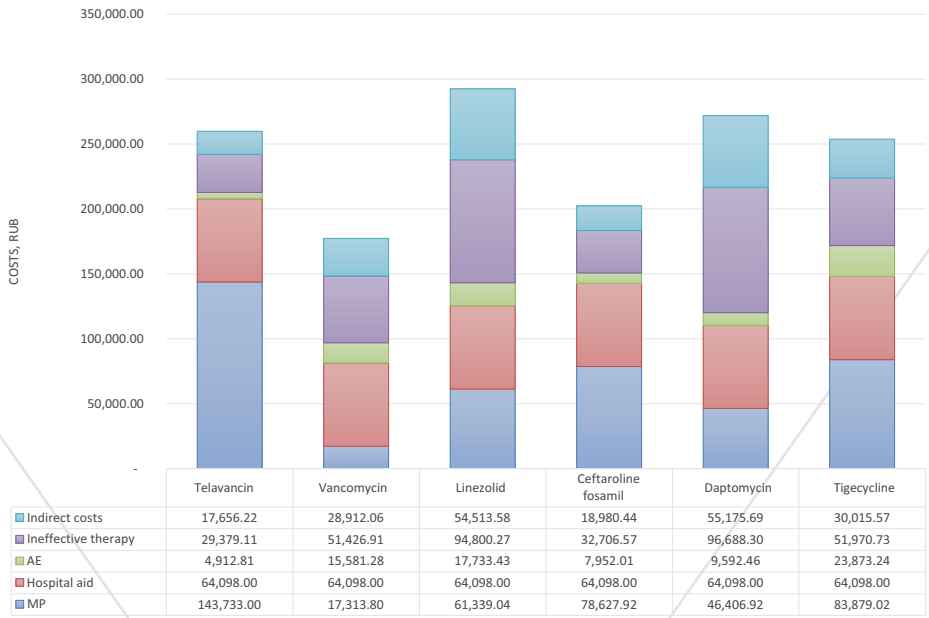
Indirect costs. Indirect costs were calculated only for the patients in whom the use of the strategies under consideration proved ineffective and required prolongation of in-hospital stay, and indirect costs covered the entire number of days of disability [30;31].

Cost of medical aid in the case of AE development. Cost of therapy aimed at correction of AE associated with MP used for the treatment of disorders under consideration consisted of the cost of medical and diagnosis measures that are provided for in the case various complications of pharmacotherapy develop, as established in the GTA [24] under the corresponding nosology or clinical condition.

Results

Use of the medical aid strategies under consideration in complicated skin and soft tissue infections.

The main scenario assessed the cost of each of the treatment strategies for patients of the target group. All strategies under comparison were modeled over a one-month time horizon. The results obtained are presented in Fig. 2.



	Telavancin	Vancomycin	Linezolid	Ceftaroline fosamil	Daptomycin	Tigecycline
Indirect costs	17,656.22	28,912.06	54,513.58	18,980.44	55,175.69	30,015.57
Ineffective therapy	29,379.11	51,426.91	94,800.27	32,706.57	96,688.30	51,970.73
AE	4,912.81	15,581.28	17,733.43	7,952.01	9,592.46	23,873.24
Hospital aid	64,098.00	64,098.00	64,098.00	64,098.00	64,098.00	64,098.00
MP	143,733.00	17,313.80	61,339.04	78,627.92	46,406.92	83,879.02

Fig.2. Total DC of treatment with the strategies under comparison calculated per patient, one-month modeling horizon.

As demonstrated by the data given in Fig. 2, the highest cost over a one-month modeling horizon was in linezolid strategy: RUB 292,484. The total costs of telavancin use were 11.2% lower and constituted RUB 259,779 per patient. The lowest cost was that of vancomycin strategy, which totaled to RUB 177,332. At the same time, the greatest difference was primarily explained by difference in the cost of pharmacotherapy and outlay on ineffective therapy. For example, MP costs component in telavancin group was equal to RUB 143,733, while the same costs constituted RUB 17,313 in vancomycin group, which is 8.3 times lower. MP costs in ceftaroline fosamil and tigecycline strategies were similar (RUB 78,627 and RUB 83,879, respectively). At the same time, telavancin strategy demonstrated the lowest costs of AE management, RUB 4,912 on average per patient. The same component in vancomycin group constituted RUB 15,581 (3.2 times higher), and the highest outlay on AE equal to RUB 23,873 was in tigecycline group. In general consideration of the strategies, the percentages of therapy components in DC differed between the groups of MP under consideration. For example, the MP itself was the main component of DC in telavancin (55.3%), ceftaroline fosamil (38.8%), and tigecycline (33%) groups. In vancomycin group, the largest outlay was on hospital aid (36%), while only 9.8% of the total costs accounted for the MP itself. In linezolid and daptomycin groups, the largest outlay was on ineffective therapy (32% and 35%, respectively). Telavancin group demonstrated the lowest outlay on AE management and ineffective therapy (2% and 11.3%, respectively). The incidence of various AE was assessed in the treatment groups over the observation period. Such AE as paresthesia, dyspnea, and psychiatric disorders were more common in telavancin group. At the same time, daptomycin strategy was associated with the highest number of AE, some of which occurred only in the group that received this product (altered renal function, fungal infection, hypotension, urinary tract infections, extremity pain, hypertension, and arthralgia). In terms of clinical recovery rate, telavancin strategy possessed a higher effectiveness compared to other treatment strategies: the corresponding value was 92%. This value was somewhat lower, 91.4% for ceftaroline fosamil strategy. The lowest effectiveness was demonstrated by linezolid (75.3%) and daptomycin (75%) strategies. Also, it should be noted that telavancin group had the smallest share of patients with prolonged in-hospital stay compared to other treatment strategies.

The results of ICER calculation are given in Table 4.

Table 4. ICER calculation for the strategies under comparison (clinical recovery rate).

Strategy	DC, RUB	DC increment, RUB	Effect	Effectiveness increment	ICER
Telavancin	259,779.14	82,447.09	92.00%	5.10%	1,616,609.59
Vancomycin	177,332.05		86.90%		
Telavancin	259,779.14	-32,705.18	92.00%	16.70%	Dominates
Linezolid	292,484.32		75.30%		
Telavancin	259,779.14	57,414.20	92.00%	0.60%	9,569,033.95
Ceftaroline fosamil	202,364.93		91.40%		
Telavancin	259,779.14	-12,182.22	92.00%	17.00%	Dominates
Daptomycin	271,961.36		75.00%		
Telavancin	259,779.14	5,942.57	92.00%	5.60%	106,117.33
Tigecycline	253,836.57		86.40%		

As demonstrated by the data given in Table 4, telavancin strategy dominated (was more effective and less expensive) over linezolid and daptomycin strategies for the treatment of CSSTI patients. Compared to tigecycline strategy, ICER for telavancin strategy was equal to RUB 106,117, which is 12 times lower than the society's willingness-to-pay threshold of RUB 1,341,308 (telavancin makes pharmacoeconomic sense). Compared to vancomycin strategy, ICER for telavancin strategy was equal to RUB 1,616,609, which is 20% higher than the society's willingness-to-pay threshold of RUB 1,341,308 (telavancin makes pharmacoeconomic sense as second-line therapy). Compared to ceftaroline fosamil strategy, ICER for telavancin strategy was equal to RUB 9,569,033.95, which is 7 times higher than the society's willingness-to-pay threshold of RUB 1,341,308 (ceftaroline fosamil makes pharmacoeconomic sense). Sensitivity analysis was performed for the purpose of testing the analysis results if the input parameters are changed.

Probabilistic sensitivity analysis. In simultaneous multiple changes of such parameters as effectiveness and MP costs, the results of the sensitivity analysis confirm the conclusions obtained in the main scenario.

Budget-impact analysis. Total costs of use of telavancin, vancomycin, linezolid, ceftaroline fosamil, daptomycin, and tigecycline for treatment of patients with complicated skin and soft tissue infections were calculated. The calculation included direct costs linked to the use of the strategies under comparison and indirect costs. The calculation took into account the effectiveness of each of the strategies. The difference in total direct costs was defined as a saving associated with the use of this or that strategy. The number of patients the saved amount could be spent on was calculated as well. The outlay per patient is RUB 259,779 for telavancin and RUB 177,332 for vancomycin. The costs are equal to RUB 292,484 for linezolid, RUB 202,365 ceftaroline fosamil, RUB 271,961 for daptomycin, and RUB 253,837 for tigecycline. Table 5 gives the results of comparison of total DC of the treatment strategies under comparison. The outlay on treatment of 1,000 patients with different strategies was calculated, and three variants were considered where 100%, 60%, and 30% of patients receive the product under consideration.

As demonstrated by Table 5, telavancin use is more preferable than linezolid strategy from the viewpoint of budget-impact analysis: telavancin strategy makes it possible to save a considerable amount in the budget, and the saved amount makes it possible to treat a significant additional number of patients with this strategy. The amount saved equals up to RUB 32,705,178, and the additional number of patients treated can be as high as 126. Similar data were obtained from comparison with daptomycin: telavancin use makes it possible to save up to RUB 12,182,218 and treat up to 47 more patients. Transition to telavancin strategy from tigecycline, vancomycin, and ceftaroline fosamil strategies will require additional investments from the budget within reasonable limits.

Discussion

It is the first time a comparative pharmacoeconomic analysis of telavancin (Vibativ®) use for treatment of patients suffering from NI caused by resistant bacterial flora using the example of patients with complicated skin and soft tissue infections was performed in Russia. Six medical technologies of CSSTI treatment were evaluated as part of a pharmacoeconomic model. The highest DC over a one-month modeling horizon were in linezolid strategy. The total costs of telavancin use were 11.2% lower. The lowest costs were those of vancomycin strategy. The greatest difference was primarily explained by difference in the cost of pharmacotherapy and outlay on ineffective therapy. The lowest indirect costs were observed in telavancin group. Telavancin strategy was also more effective compared to the other strategies under comparison: the clinical recovery rate was 92%. The lowest effectiveness was demonstrated by linezolid (75.3%) and daptomycin (75%) strategies. Also, it should be noted that telavancin group had the smallest share of patients with prolonged in-hospital stay compared to other treatment strategies. The cost-effectiveness analysis of CSSTI therapy demonstrated that telavancin strategy was more effective compared to other treatment strategies in terms of clinical response rate, at its total costs were lower than those in linezolid and daptomycin use. Thus, telavancin strategy dominated over those strategies. Compared to vancomycin, tigecycline, and ceftaroline fosamil strategies, telavancin strategy was a more effective but also

www.pharmacoeconom.com

Table 5. Comparison of total costs of therapy of patients with complicated skin and soft tissue infections.

Therapy under consideration	100% of patients receive the therapy	60% of patients receive the therapy	30% of patients receive the therapy
	Total costs in RUB		
Telavancin	259,779,138	155,867,483	77,933,741
Vancomycin	177,332,049	106,399,229	53,199,615
Linezolid	292,484,316	175,490,590	87,745,295
Ceftaroline fosamil	202,364,934	121,418,961	60,709,480
Daptomycin	271,961,356	163,176,813	81,588,407
Tigecycline	253,836,568	152,301,941	76,150,970
Saving in Telavancin use compared to:			
Vancomycin	-82,447,089	-49,468,253	-24,734,127
Linezolid	32,705,178	19,623,107	9,811,553
Ceftaroline fosamil	-57,414,204	-34,448,522	-17,224,261
Daptomycin	12,182,218	7,309,331	3,654,665
Tigecycline	-5,942,571	-3,565,542	-1,782,771
Additional number of patients treated with telavancin if the budget is equal to telavancin use			
Vancomycin	-	-	-
Linezolid	126	76	38
Ceftaroline fosamil	-	-	-
Daptomycin	47	28	14
Tigecycline	-	-	-

a more expensive alternative. ICER was calculated. Comparison of telavancin strategy against linezolid and daptomycin strategies for treatment of patients with complicated skin and soft tissue infections showed that telavancin strategy was less expensive but more effective; thus, it is possible to conclude that telavancin use makes absolute economic sense in terms of cost-effectiveness ratio when compared to those strategies for treatment of patients with skin and soft tissue infections. Compared to vancomycin, ceftaroline fosamil, and tigecycline strategies, telavancin strategy for treatment of patients with complicated skin and soft tissue infections was more expensive, but the effectiveness increased as well. ICER for telavancin strategy compared to tigecycline was RUB 106,117, which is 12 times lower than the society's willingness-to-pay threshold of RUB 1,341,308; thus it is possible to make a conclusion that telavancin use makes economic sense in this case. The same values in comparison to vancomycin and ceftaroline fosamil strategies reached RUB 1,616,609 and 7,445,540, with the former being 20% higher than the society's willingness-to-pay threshold, and the latter being 7 times higher than this threshold. In this case, vancomycin and ceftaroline fosamil strategies make more pharmacoeconomic sense.

The probabilistic sensitivity analysis was performed by simultaneous multiple changes of such parameters as effectiveness and MP cost. The results of the sensitivity analysis confirm the conclusions obtained in the main scenario. Additionally, total Russian healthcare budget outlay on telavancin, vancomycin, linezolid, ceftaroline fosamil, daptomycin, and tigecycline use for treatment of patients with complicated skin and soft tissue infections were calculated. The calculation included direct costs linked to the use of the strategies under comparison and indirect costs. The calculation took into account the effectiveness of each strategy. Telavancin use is more preferable than linezolid strategy from the viewpoint of budget-impact analysis: telavancin strategy makes it possible to save a considerable amount in the budget, up to RUB 32,705,178, and the saved amount makes it possible to treat a significant additional number of patients (up to 126) with this strategy. Similar data were obtained from comparison with daptomycin: telavancin use makes it possible to save up to RUB 12,182,218 and treat up to 47 more patients. Analysis of the results of budget impact, for wide use estimated strategy requires an additional investment of 2 to 45% when compared with the strategies of use tigecycline, vancomycin and ceftaroline fosamil.

Conclusions

1. Telavancin use as therapy for CSSTI demonstrates high clinical effectiveness and one of the best safety profiles among other medical technologies for the treatment of this group of patients.

2. Telavancin use in therapy of CSSTI is economically dominant in terms of cost-effectiveness ratio compared to daptomycin, tigecycline, and linezolid.

3. Telavancin use for CSSTI treatment is more preferable than linezolid and daptomycin strategies from the viewpoint of budget-impact analysis: its use makes it possible to save a considerable amount in the budget, up to RUB 32,705,178, and to treat up to 126 more patients with this strategy.

Study limitations

This pharmacoeconomic analysis has the following peculiarities related to study limitation parameters. Firstly, safety and efficacy data used for effectiveness indicators and obtained in RCS differ from the conditions of actual practice and the conditions provided for in the model. Secondly, direct costs of aid for various nosologies were calculated with reference to the standards of care registered in the RF, while the description of the patient population and effectiveness indicators were taken from foreign studies.

References

1. Kozlov R.S. Nosocomial infections: epidemiology, pathogenesis, prevention, control. / R.S. Kozlov // Clinical Microbiology and Antimicrobial Chemotherapy. No. 1. – Vol.2. - 2000. -P.16-30.
2. Hospital-acquired infections: Prevention and Control of Nosocomial Infections / edited by Richard P. Vencel. – 2nd ed, revised and expanded. - Moscow: Medicine, 2004. - 840 p. 616.9 B-607 Reference room.
3. Hospital-acquired infections: new horizons of prevention / V.I. Pokrovsky, V.G. Akimkin, N.I. Briko, E.B. Brussina, L.P. Zueva, O.V. Kovalishena, V.L. Stassenko, A.V. Tutelyan, I.V. Feldblyum, V.V. Shkarin // Epidemiology and infectious diseases. - 2011. – No. 1. - P. 4-7.
4. Vincent J.L., et al. The prevalence of nosocomial infection in intensive care units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC) Study. EPIC International Advisory Committee. JAMA 1995; 274(8): 639-44.
5. Scientific report on the results of antibiotic resistance study of bacterial pathogens of nosocomial infections in departments with intensive use of antibiotics in Russian hospitals (ReVANSH). Research Institute of Antimicrobial Chemotherapy. Smolensk, 2009
6. Garau J., Ostermann H., et al., on behalf of REACH Research Team Current management of patients hospitalized with complicated skin and soft tissue infections across Europe (2010-2011): assessment of clinical practice patterns and real-life effectiveness of antibiotics from the REACH study. Clinical microbiology and infection, 2013.
7. Dekhnich A.V. et al. / Telavancin: Clinical and microbiological aspects. // Clinical Microbiology and Antimicrobial Chemotherapy. - 2015. - Vol.17. – No. 2. - P.84-126.
8. EUCAST data. Antimicrobial wild type distributions of microorganisms. http://mic.eucast.org/Eucast2/
9. Higgis D.L., et al. Telavancin, a multifunctional lipoglycopeptide, disrupts both cell wall synthesis and cell membrane integrity in methicillin-resistant Staphylococcus aureus. Antimicrob Agents Chemother. 2005; 49 (3): 1127 – 34.
10. Lunde C.S., et al. Telavancin disrupts the functional integrity of the bacterial membrane through targeted interaction with the cell wall precursor lipid II. Antimicrob Agents Chemother. 2009; 53(8): 3375 – 83.
11. Attwood R.J., et al. Telavancin: a novel lipoglycopeptide antimicrobial agent. Am J Health Syst Pharm. 2007; 64 (22): 2335-48.
12. Stryjewski M.E., O'Riordan W.D., Lau W.K., et al. Telavancin versus standard therapy for treatment of complicated skin and soft-tissue infections due to grampositive bacteria. Clin Infect Dis 2005; 40:1601-7.
13. Stryjewski M.E., Chu V.H., O'Riordan W.D., et al. Telavancin versus standard therapy for treatment of complicated skin and skin structure infections caused by gram-positive bacteria: FAST 2 study. Antimicrob Agents Chemother 2006; 50:862-7.
14. Stryjewski M.E., Graham D.R., Wilson S.E., et al. Telavancin versus vancomycin for the treatment of complicated skin and skin-structure infections caused by gram-positive organisms. Clin Infect Dis 2008; 46:1683-93.
15. Laohavaleeson S., et al. Cost-effectiveness of telavancin versus vancomycin for treatment of complicated skin and skin structure infections. Pharmacotherapy. 2008; 28(12):1471-82.
16. On adoption of the industry-specific standard "Clinical and economic studies. General provisions": Order of the Ministry of Healthcare of the Russian Federation No. 163 as of May 27, 2011.
17. Avksentieva M.A., Gerassimov B.V., Sura M.V. Clinical and economic analysis (evaluation, choice of medical technologies, and quality management of medical aid) / edited by Vorobiev P.A. – Moscow: Newdiamed, 2004. – 404 p.
18. Beloussov Y.B. Planning and conducting clinical studies of medicines. – Moscow: Society of clinical investigators, 2000. – 579 p.
19. Basic notions in evaluation of medical technologies: Guidance manual. Edited by Kolbin A.S., Zyryanov S.K., Beloussov D.Y. Moscow: OKI Publishing House, 2013. - 42 p. : il.
20. Walley T., Haycox A., Boland A. Pharmacoeconomics. Elsevier Health Sciences, 2004. – 216 c.
21. Josephine A. Mauskopf., et al Principles of Good Practice for Budget Impact Analysis: Report of the ISPOR Task Force on Good Research Practices — Budget Impact Analysis. Value in Health. 2007;10(5);336-347.
22. Website of the State Register of Medicines. http://grls.rosminzdrav.ru.
23. Decree of the Government of the Russian Federation as of December 19, 2015 N 1382 "On the Program of State Guarantees of Free Medical Aid for Citizens in 2016 and over the Planned Period of 2017 and 2018"
24. Information portal for Mandatory Medical Insurance in Saint Petersburg.
25. http://zakupki.gov.ru/epz/main/public/home.html
26. Weigelt J., et al. Linezolid versus Vancomycin in Treatment of Complicated Skin and Soft Tissue Infections. Antimicrob. Agents Chemother. 2005;49:2260 – 2266.
27. Arbeit R.D., et al. The safety and efficacy of daptomycin for the treatment of complicated skin and skin-structure infections. CID 2004:38; 1673 – 1681.
28. Wilcox M.H., et al. CANVAS 2: the second Phase III, randomized, double-blind study evaluating ceftaroline fosamil for the treatment of patients with complicated skin and skin structure infections. J Antimicrob Chemother 2010; 65 Suppl 4: iv53–65.
29. Florescu I., et al. Efficacy and safety of tigecycline compared with vancomycin or linezolid for treatment of serious infections with methicillin-resistant Staphylococcus aureus or vancomycin-resistant enterococci: a Phase 3, multicentre, double-blind, randomized study
30. Federal Law as of December 29, 2006 N 255-FZ (amended on December 3, 2011) "On Mandatory Social Insurance of Temporary Disability and Maternity"
31. Territorial body of the Federal State Statistics Service in Saint Petersburg and Leningrad Oblast, official website, http://petrostat.gks.ru/

www.pharmacoeconomics.com