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Calculation of the cost-effectiveness of subcutaneous administration of trastuzumab

Rational selection of medicines with an assessment of their pharmacoeconomic effectiveness is the most effective way to ensure safe and efficient treatment and economical use of budget funds allocated for drug therapy, as well as to reduce the time of hospitalization and treatment of patients.

The purpose of the research was to evaluate the pharmacoeconomic effectiveness of using the subcutaneous and intravenous forms of drug Trastuzumab.

Research tasks:

1. Estimate costs when using subcutaneous trastuzumab in an outpatient chemotherapy room (OCR).
2. Estimate costs when using intravenous trastuzumab in a day patient department (DPD).
3. Estimate costs when using intravenous trastuzumab in a round-the-clock hospital.

Results: The paper presents the pharmacoeconomic analysis of targeted therapy with trastuzumab in two forms for intravenous administration (IV) and trastuzumab emtansine for subcutaneous administration (SC) in breast cancer by cost minimization method.

The costs of used drugs are according to the price-list of the unified national distributor SK Pharmacia as of January 1, 2018.

At comparable efficacy and toxicity, the estimated cost-effectiveness of trastuzumab per 100 patients per year is KZT 16,939,600 (\$ 50,972) for SC administration in OCR and IV administration in DPD vs. KZT 41,783,200 (\$ 125,728) for SC administration in OCR and IV administration in a round-the-clock hospital.

Conclusions: Based on the above, the subcutaneous form is economically feasible for conducting targeted therapy with trastuzumab.

Keywords: breast cancer, subcutaneous form (SC), intravenous form (IV), pharmacoeconomic analysis, cost minimization.

Relevance: Problems associated with the rational use of medicines make an integral part of efficient health care. Studies on the use of medicines shall include analysis and assessment of many factors that influence the use of drugs. Data on the efficacy, safety, consumption, and use of medicines are essential components that determine public policy regarding medicines.

Rational selection of medicines with an assessment of their pharmacoeconomic effectiveness is the most effective way to ensure safe and efficient treatment and economical use of budget funds allocated for drug therapy, as well as to reduce the time of hospitalization and treatment of patients [1-4].

This substantiates the need for a pharmacoeconomic evaluation of the effectiveness of targeted therapy with two forms of trastuzumab and trastuzumab emtansine.

Both medicines are included in the current version of the drug formulary of the Republic of Kazakhstan and the drug formulary of our institution. They have the same mechanism of action and are both indicated for targeted therapy of breast cancer (BC).

The purpose of the research was to evaluate the pharmacoeconomic effectiveness of using the subcutaneous and intravenous forms of drug Trastuzumab.

Research tasks:

1. Estimate costs when using subcutaneous trastuzumab in an outpatient chemotherapy room (OCR).
2. Estimate costs when using intravenous trastuzumab in a day patient department (DPD).

3. Estimate costs when using intravenous trastuzumab in a round-the-clock hospital.

Materials and Methods: The study was based on the results of the treatment of 120 breast cancer patients who received Trastuzumab.

Results and Discussion: We applied the cost minimization method to analyze the costs of using Trastuzumab (brand name Herceptin) for intravenous administration (IV) and trastuzumab emtansine for subcutaneous administration (SC) produced by Roche [5].

The analysis covered direct medical costs: the cost of drugs, the cost of per dosage and per course of targeted therapy (18 dosages), the average cost of hospital stay (3 bed days per 1 IV dosage, installation of IV port), a visit to a chemotherapist in the outpatient department of Karaganda Regional Cancer Dispensary.

Final analysis of phase 3 of HannaH (2019) clinical trials in patients with HER2new-positive BC revealed no significant differences in the efficacy, as well as frequency and severity of side effects [6]. Therefore, the cost of therapy for side effects was not considered.

The prices of used drugs were according to the price-list of the unified national distributor SK Pharmacia as of January 1, 2018 (the price per vial of Trastuzumab 600 mg SC form was KZT 398,465.00, per vial of trastuzumab 440 mg IV form was KZT 404,939.58).

One dosage per patient of trastuzumab emtansine SC is 600 mg, regardless of body weight. In total, one patient receives 18 dosages a year (10800 mg), that is, 18vial s of trastuzumab SC.

The first dosage of trastuzumab IV per patient is 8 mg/kg (at an average body weight of 70 kg; the consumption is 560 mg per patient). During the remaining 17 sessions, the patient receives 6 mg/kg per each intravenous administra-

tion, i.e., 420 mg, or 7700 mg in a year, i.e., 17,5 vials per year.

Direct costs for the purchase of drugs are presented in table 1.

Table 1 – Direct costs of targeted therapy with trastuzumab and trastuzumab emtansine

Name of the drug	Units	Unit cost (KZT)	The amount of drug per treatment	Direct costs of treatment per patient per year
Trastuzumab SC	1 vial 600 mg	398,465.00	10800 mg (18 vials)	KZT 7,172,370.00 (\$ 21,582.6)
Trastuzumab IV	1 vial 440 mg	404,939.58	7700mg (17.5 vials)	KZT 7,086,442.65 (\$ 21,323.5)

Note: *\$1 = KZT 332.33 at the rate of the National Bank of Kazakhstan as of January 1, 2018

One course of targeted therapy includes:

- OCR (visits to a chemotherapist at the outpatient department):

- Per cycle – 2 visits to the outpatient department;

- Per course (18 cycles) – 36 visits (18x2=36) to the outpatient department.

- Day patient department (visits to a chemotherapist at the outpatient department and staying at the day patient department):

- Per cycle – 1 visit to the outpatient department and

- 3 bed days at the day patient department;

- Per course (18 cycles) – 18 visits to the outpatient department and 54 (18x3=54) bed days at the day patient department;

- Additionally, installation of IV port before the first drug administration.

- Round-the-clock hospital (visits to a chemotherapist at the outpatient department and staying at the round-the-clock hospital):

- Per cycle – 1 visit to the outpatient department and 3 bed days at the round-the-clock hospital;

- Per course (18 cycles) – 18 visits to the outpatient department and 54 (18x3=54) bed days at the round-the-clock hospital;

- Additionally, installation of IV port before the first drug administration.

Table 2 offers indirect costs of targeted therapy with trastuzumab in hospital and outpatient settings.

Table 2 – Indirect costs of targeted therapy

Structural unit	OCR	Day patient department	Round-the-clock hospital
Cost per visits to a chemotherapist (KZT)	KZT 3,418.00	KZT 3,418.00	KZT 3,418.00
Cost per 3 bed days (KZT)	0	KZT 6,590.00	KZT 20,392.00
Installation of IV port	0	KZT 112,300.00	KZT 112,300.00
Indirect costs per cycle	KZT 6,836.00	KZT 10,008.00*	KZT 23,810.00*
Indirect costs per 1 course (18 cycles)	KZT 123,048.00** (\$ 370.26)	KZT 292,444.00** (\$ 913.86)	KZT 540,880.00** (\$ 1,627.53)

Notes:

*The costs do not include installation of an IV port

** \$1 = KZT 332.33 at the rate of the National Bank of Kazakhstan as of January 1, 2018

Thus, total costs per course of targeted therapy with trastuzumab per patient consist of direct and indirect costs.

Table 3 shows the total cost of targeted therapy with trastuzumab per patient in hospital and outpatient settings.

Table 3 – Total costs per course of targeted therapy with trastuzumab in hospital and outpatient settings

Name of the drug	Direct costs	Indirect costs	Total costs
Trastuzumab SC*	KZT 7,172,550.00 (\$ 21,582.6)	KZT 123,048.00 (\$ 370.26)	KZT 7,295,598.00 (\$ 21,954.86)
Trastuzumab IV*	KZT 7,172,550.00 (\$ 21,582.6)	KZT 292,444.00 (\$ 913.86)	KZT 7,464,994.00 (\$ 22,496.46)
Day patient department			
Trastuzumab IV*	KZT 7,172,550.00 (\$ 21,582.6)	KZT 540,880.00 (\$ 1,627.53)	KZT 7,713,430.00 (\$ 23,210.13)
Round-the-clock hospital			

Note: \$1 = KZT 332.33 at the rate of the National Bank of Kazakhstan as of January 1, 2018

The difference in costs CMA is calculated by the formula:

$$CMA1 = DS1 - DS2,$$

$$CMA2 = DS1 - DS3,$$

where DS is the cost of each compared drug;

CMA was the difference in costs associated with the compared forms of the drug.

Thus, CMA was equal to:

CMA1 (SC form administered in OCR and IV form administered in DPD) – KZT 169,396 (\$ 509.72) per year;

CMA2 (SC form administered in OCR and IV form administered at the round-the-clock hospital) – KZT 417,832 (\$ 1257.28) per year.

At comparable efficacy and toxicity, the estimated cost-effectiveness of trastuzumab per 100 patients per year is:

KZT 16,939,600 (\$50,972) for SC administration in OCR and IV administration in DPD vs.

KZT 41,783,200 (\$125,728) for SC administration in OCR and IV administration in a round-the-clock hospital.

It is worth mentioning that Trastuzumab SC is funded through the outpatient Republican budget, while IV form is funded through the global budget of the Regional Cancer Dispensary. In 2018, the amount of KZT 222,741,935.00 was released from the global budget (the cost of 559 vials of trastuzumab SC at KZT 398,465.00 vial) and spent to buy other drugs for the treatment of cancer patients.

The social efficiency of subcutaneous trastuzumab is due to a significant "deontological" advantage of outpatient therapy. Most of the time, the patient stays at home in a familiar, comfortable environment, surrounded by loved ones. It allows improving the quality of life of patients and increasing satisfaction with the provided medical care.

Conclusions: Based on the above, the subcutaneous form is economically feasible for conducting targeted therapy with trastuzumab.

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