A MCDM Model Design for HER2+ Breast Cancer Treatment Technique Using AHP Method

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Abstract

Purpose - The aim of this paper is to present a multi-criteria decision-making model in order to apply Analytical Hierarchy Process (AHP) method for the selection of the best treatment technique for HER2+ breast cancer from two different treatment alternatives: Kadcyla and Lapatinib plus Capecitabine. The study analyzes the decision making process of oncologists when there are more than one alternative treatment techniques for them to choose.

Design/methodology/approach – Data are collected from oncologists by using an online survey after the literature review was carried out and interviews with a drug developer and oncologists were made. In order to analyze the decision making process of oncologists and the effectiveness of two drugs based on determined attributes, AHP method was used and the results were verified with TOPSIS and Weighted Product methods.

Findings – In this paper, it is proven that Kadcyla is better in AHP model when compared to Lapatinib plus Capecitabine in terms of meeting the expectations of the oncologists while fighting against HER2+ breast cancer.

Research limitations/implications - The biggest limitation of the research seems to be a halo effect that the oncologists might be experiencing because one of the alternative drug combinations in the research is more frequently prescribed than the other one which could affect the subjectivity of the answers.

Originality/Value - This paper gives an insight about the factors that are taken into account when choosing the best cancer treatment technique and their significance level. It presents a model for identifying the most effective targeted drug combination. It will be useful for academicians, oncologists and drug developers in terms of a better understanding of the needs in cancer treatment.

Keywords – multi criteria decision making, analytical hierarchy process, HER2+ breast cancer, treatment, targeted drug delivery

1. Introduction

Humankind has been suffered from diseases throughout the history. One of the most common diseases that people encountered is cancer. In cancer, there is an uncontrollable growth of abnormal cells which is against the normal cell division rules. Normal cells in the body are often controlled and managed by the signals. These signals give commands to the normal tissues whether to divide, alter into a different cell or die. However, the abnormal cells gain autonomy against the signals and do not comfort order coming from these signals in the body **[1]**. In order to improve the symptoms or cure or control cancer, which has also lots of types like lung, colon and rectal (colorectal), pancreatic, breast, liver, bladder, prostate and so on, several treatment techniques are developed by the scientists. The most commonly used techniques include surgery, radiation therapy, chemotherapy, and some combination of them **[2]**. However, the current standard treatments do not give the optimum treatment because of the lack of specificity, high toxicity of many anticancer agents, the high hydrophobic structure of cytotoxic chemotherapeutics, and the low efficacy. These types of reasons limit the treatment and can cause side effects, noncompliance, and patient inconvenience **[3]**.

The problems that are encountered in the current standard cancer treatment techniques encourage the scientists to work on the application of targeted drug delivery systems in cancer treatments. Targeted drug delivery is a method used for delivering medication to a patient in order to increase drug accumulation in the related parts of the body **[4]**. Before the developments in the targeted drug delivery systems, camptothecin, taxanes, platinating agents, doxorobucin, nucleoside and nucleotide analogs, which are the classical chemotherapeutic agents, have been consumed in chemotherapy against several tumor types for several decades **[5]**. However, as explained in the previous paragraph, high toxicity of these anticancer agents limits the application of chemotherapy and generally causes the multidrug resistance (MDR) in the body. MDR refers to the resistance of both tumor cells and normal cells to the used anticancer agent and also concurrent cross-resistance to other anticancer drugs in the chemotherapy **[6]**. MDR can cause several problems in the cancer treatment with chemotherapy and these problems decrease the clinical success rate of the cancer therapy proportionally. However, the structure of the drugs is changed in targeted drug delivery systems, which have high biocompatibility, high stability, drug release targeting with high precision, high drug accumulation or low drug elimination in the tumor tissue via active or passive targeting, in order to destroy the effects of MDR **[7]**. One of these drugs was introduced with the name of Kadcyla (T-DM1), which is used by the oncologists to treat HER2+ breast cancer after the prior treatment with trastuzumab and a taxane. This drug is a combination of trastuzumab (monoclonal antibody), MMC (stable linker), and DM1 (cytotoxic drug). It is generally given to the patient via intravenous infusion for 90 minutes in the first infusion and then followed with 30 minutes doses in each three week period **[8]**. The other commercial drug combination is Lapatinib plus Capecitabine, which is also used in the treatment of HER2+ breast cancer after the trastuzumab-based therapy, like Kadcyla. It includes Lapatinib (tyrosine kinase inhibitor) and Capecitabine (anticancer chemotherapy drug) and generally given to patient at 1250 mg per day continuously plus Capecitabine at a dose of 2000 mg per square meter of body-surface area on days 1 through 14 of a 21-day cycle **[9]**.

The drugs that were mentioned above is analyzed by using AHP method, which is a decision making tool used for pair-wise comparisons, considering attributes. These attributes can be mainly summarized as factors about patient, tumor, and drugs. They are evaluated after the survey in order to select the best drug combination and evaluate the choosing process of oncologists.

In the lights of all the things that were mentioned above, the main idea of this study is to design a multicriteria decision-making model by using Analytical Hierarchy Process (AHP) for the selection of the best treatment technique from the Kadcyla and Lapatinib plus Capecitabine for HER2+ breast cancer.

In this context, the literature research about cancer (especially HER2+ breast cancer), targeted drug delivery systems, methodology, analysis and results, and conclusion are presented at the following sections of this article.

2. Literature Research

Cancer which occurs when abnormal cells grow and spread through human body is the biggest disease of the current era. Those abnormal cells can appear in many parts of the body causing different types of cancer depending on the part where they appear. The most common cancer types include lung cancer, breast cancer, colorectal (colon and rectal) cancer etc. based on the data published by WCRF in 2012 **[10]**.

Millions of people are getting caught by cancer resulting in millions of deaths every year. It is estimated that more than 1,7 million of new cancer cases will be diagnosed whereas the number of deaths will be around 600.000 only in US in 2018 **[11]**. As more and more people are being diagnosed with cancer many techniques have been and are still being developed in order to fight against cancer while the efficacy and the adverse effects of the treatment being the key points as the number of different types of adverse effects which are found to be related to modern cancer treatment methods is no less than 500 **[12]**.

Breast cancer is the most common type of cancer among the women followed with lung and colorectal cancers **[13]**. In 2017, 255,180 new cases were estimated with 41,070 deaths in Unites States **[14]**. Therefore, 16 percent of people who had breast cancer died last year in United States. Breast cancer can start from several parts of the breast, which are ranged from ducts (breast channels which transfer milk to the nipple) to glands (the cell which makes milk) because of the DNA mutations, inheritage of genes, and the environment. In the public, breast cancer is generally assumed to start with a lump or mass. However, although many cancer types can cause a mass in the breast, it is not necessary for all types of breast cancers. In some types of breast cancers, cancer cells are only observed on screening mammograms, which detects the cancer in earliest stages. It is also significant to identify whether the tumor is benign (there is abnormal growth; but they do not spread out of breast) or malignant (both abnormal growth and tendency to spread outside of breast). In the malignant cancer, the cancer cells spread through the body via blood or lymph system **[15]**.

In terms of this research, HER2+ breast cancer name derived from the human epidermal growth factor receptor 2. These receptors located in the outside of breast cells and receive signals, which are coming from body. These signals give commands to the normal tissues whether to divide, alter into a different cell or die. However, the HER2 proteins can start to grow faster because of the DNA mutations, inheritage of genes, and environmental factors in randomly. This can cause breast cells to divide faster than their normal cell division rules, which creates the breast cancer **[16]**. HER2+ breast cancer can be seen in anybody who has

breast tissue. However, it is generally seen in women rather than men, especially in young women who are overweight and older women who gave birth **[16]**.

3. Targeted Drug Delivery Systems

Targeted drug delivery systems aim to leave anti-cancer drugs directly into cancer cells as these drugs contain toxic materials, which may cause the healthy cells to die as well. In this way the side effects of the therapy is expected to minimize while increasing the therapeutic efficacy.

In this part of the study, two alternative solutions to chemotherapy will be introduced: Kadcyla and Lapatinib plus Capecitabine. Additionally, the usage areas and characteristics of those drugs are presented.

Both of those drugs have been developed as a result of the studies on targeted drug delivery systems and they aim to find and destroy the cancer cells just like chemotherapy but the difference is that those drugs can easily recognize cancer cells from the receptors of these cells.

3.1 Kadcyla

Kadcyla (Trastuzumab Emtansine) is an antibody-drug conjugate, which consists of Trastuzumab (Herceptin), and Emtansine (DM1). In Kadcyla, those two agents –Trastuzumab and Emtansine- are attached to each other to form the combination. It is used to treat metastatic HER2+ breast cancer. The prerequisite for a patient to be able to use Kadcyla is that they should have already been treated with taxane and/or trastuzumab as a chemotherapy drug and the cancer should be metastatic which means that it spread to other parts of the body from the breast.

Trastuzumab and Emtansine have different responsibilities when fighting against the cancer cells. Emtansine is a very toxic medicine so it should directly go to cancer cells and that is why it is attached to Trastuzumab. Trastuzumab helps find HER2+ cells and attaches to them. After Trastuzumab finds cancer cells Kadcyla goes inside and destroys those cells. In this way, the damage to healthy cells is minimized with targeted therapy. In clinical studies, it is proved that Kadcyla helps women having HER2+ breast cancer live longer compared to some other treatment methods **[17]**.

Treatment with Kadcyla for a patient takes place every 3 weeks in the form of a 30-minute intravenous infusion.

3.2 Lapatinib Plus Capecitabine

The drug combination of Lapatinib and Capecitabine is another treatment alternative for HER2+ breast cancer. Lapatinib itself is a targeted anti-cancer drug. It is a dual tyrosine kinase inhibitor and used in combination therapy as it blocks the activity of two receptors which cause cells to grow: HER2 (Human Epidermal Growth Factor Receptor 2) and EGFR (Epidermal Growth Factor Receptor). As the cancer cells in the case of metastatic HER2+ breast cancer have many HER2 receptors on the cell surface, Lapatinib targets those cells to slow down or completely block the cell growth. Lapatinib can either be given with Capecitabine or used together with hormonal therapy **[18]**.

Capecitabine is basically a chemotherapy drug. It is usually used for fighting against colon cancer, rectal cancer and metastatic breast cancer. Capecitabine can be used as a monotherapy. However, the research shows that when used together with Lapatinib it almost doubles the median time to progression increasing it from 4.4 months to 8.4 months **[19]**.

4. Methodology

The study grew out of an idea of analyzing a decision making process of oncologists when there are more than one alternative treatment techniques which could be applied to HER2+ breast cancer patients who had previously been treated with trastuzumab plus taxane therapy in metastatic phase.

After reviewing the literature, it is found that there are alternative solutions to chemotherapy, which have already been, or currently being developed in order to increase the therapeutic efficacy. Hence, the study focuses on targeted drug delivery systems.

In order to have a more specific research problem, interviews have been made with a drug developer and two oncologists. Those interviews and literature reviews have led to the comparison of alternatives (drug combinations) which are T-DM1 (Kadcyla) and Lapatinib plus Capecitabine and the attributes, which could affect the decision of an oncologist when deciding on the treatment. These attributes are mainly classified as patient related factors, tumor related factors, and drug related factors. Patient related factors are comprised of age, general health condition, menopause condition, preference, and ethnicity of patients. Tumor related factors contain size, location, and stage of the tumor. In addition, drug related factors were determined as therapeutic index, structure, delivery, adverse effect grade, median survival time, recurrence probability, frequent usage, and maximum dosage of the drugs.

Based on the results of the interviews a comprehensive survey, which allows both using AHP method and carrying out some statistical analysis, were done. The online survey has been shared with oncologists who have already prescribed both of the drugs for their patients before. In order to apply AHP model to the research, sample size can be ranged from 3 to 9000. Therefore, appropriate sample size selection depends on the target of the research and representativeness of population. Because of this reason, the sample of the survey includes 9 oncologists who are aged between 34 and 59. Moreover, the participants' experience level ranges from 2 years to 33 years while their targeted drug prescribing varied from 10 to 500 in a week. It is important to have such diversity in order to include different attitudes and views among the oncologists in the analysis. As it can be understood from the previous sentences, the number of participants is enough for applying AHP technique.

The participants were asked to answer a total of 67 questions in the survey which includes five demographic questions while the remaining 62 are related to the pair-wise comparisons of attributes and alternatives.

The analysis were carried out using software programs such as SPSS and Microsoft Excel. The validity of the results was also double checked by using TOPSIS and Weighted Product methods and similar results were observed in these methods.

5. Results and Discussion

In the first part of the survey, the participants have compared each of the main criteria with each other, which means that they have answered three pair-wise comparison questions.

One of those three questions is given as an example in Figure 1.

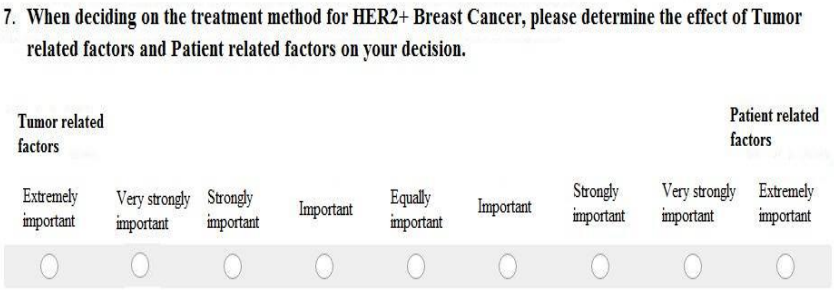

Figure 1: A sample question used in the survey

The overall result of the nine oncologists' answers to those three questions is as follows:

Table 1: The weight of main criteria

Attributes	Weight	Normalized
Patient Related Factors	0,13	15%
Tumor Related Factors	0,56	64%
Drug Related Factors	0,19	22%

Table 1 shows the relative weight of the three main criteria. It can easily be seen that tumor related factors have by far the highest importance while weight of patient related and drug related factors are close to each other.

It should also be noted that the view of the participants on patient related and drug related factors differ from each other, significantly.

The next step is to determine the weight of the sub-criteria. The procedure is the same and the question format in the survey does not change.

Table 2: Sub-criteria of patient related factors

Attributes	Weight	Normalized
Age	0,15	16%
General Health Condition	0,44	49%
Manopause	0,09	10%
Preference	0,17	20%
Ethnicity	0,04	5%

In terms of the attributes related to the patient, the most important factor is the general health condition of the patient, which has a relative importance of almost 50%. Its importance level is 2.5 times of the second important factor: patient's treatment preference.

An interesting point here is that based on the answers given by a participant who is from a different culture, the importance level of ethnicity of the patient in terms of treatment method decision is 37% for him despite the overall importance level is only 5% among all participants. This could be counted as a proof for the thought that oncologists having different cultures and/or backgrounds may have different opinions on such issues.

Table 3: Sub-criteria of tumor related factors

Attributes	Weight	Normalized
Size	0,16	17%
Location	0,09	9%
Stage	0,68	74%

Tumor stage is very dominant when compared to other tumor related factors as almost all –except one- of the respondents defined it as the most important one. Size of the tumor comes second and its significance level is almost twice of the one for tumor location.

Table 4: Sub-criteria of drug related factors

Attributes	Weight	Normalized
Therapeutic Index	0,05	6%
Structure	0,03	3%
Delivery	0,04	4%
Adverse Effect Grade	0,11	13%
Median Survival Time	0,26	30%
Recurrence Probability	0,25	29%
Frequent Usage	0,07	8%
Maximum Dosage	0,05	6%

The median survival time after starting the treatment and decreasing the recurrence probability of the disease are the most important attitudes among the drug characteristics based on the survey results. Adverse effect grade of the drugs is also important as it may be expected considering the effect of adverse effects of conventional techniques on the patients.

At the final step, the participants were asked to evaluate the performance/effectiveness of the alternatives in terms of each attribute. The answers were again recorded on the 9-point scale.

Table 5 shows the result of the each pair-wise comparison between Kadcyla and Lapatinib plus Capecitabine with regards to the attributes.

The pair-wise comparison was carried out for 16 attributes in total. Kadcyla have been found to be better in 11 attributes while Lapatinib Capecitabine is better in 4 and they came out equal for one of the attributes.

Table 5 only shows the comparison of drugs in terms of different criteria. It reflects the perception of the oncologists. It is important especially for the criteria, which are more likely to be evaluated subjectively. For example, in the case of “patient preference” criterion the evaluation of the oncologist is possibly highly affected by their previous experiences meaning that may change from person to person. However, for some other criteria the results of previous clinical tests are already available and the answers of the oncologists match with this scientific data.

Table 5: Pair-wise comparisons of the alternative drugs

	Attributes	Alternatives	Effectiveness	Normalized
Patient Related Factors	Age	Kadcyla	0,50	50%
		Lapatinib Capecitabine	0,50	50%
	General Health	Kadcyla	0,80	83%
		Lapatinib Capecitabine	0,16	17%
	Menopause	Kadcyla	0,70	76%
		Lapatinib Capecitabine	0,23	24%
	Preference	Kadcyla	0,15	15%
		Lapatinib Capecitabine	0,83	85%
	Ethnicity	Kadcyla	0,69	76%
		Lapatinib Capecitabine	0,22	24%
Tumor Related Factors	Size	Kadcyla	0,75	80%
		Lapatinib Capecitabine	0,19	20%
	Location	Kadcyla	0,68	74%
		Lapatinib Capecitabine	0,23	26%
	Stage	Kadcyla	0,86	87%
		Lapatinib Capecitabine	0,13	13%
Drug Related Factors	Therapeutic Index	Kadcyla	0,84	85%
		Lapatinib Capecitabine	0,14	15%
	Structure	Kadcyla	0,19	20%
		Lapatinib Capecitabine	0,73	80%
	Delivery	Kadcyla	0,80	83%
		Lapatinib Capecitabine	0,16	17%
	AE Grade	Kadcyla	0,79	82%
		Lapatinib Capecitabine	0,17	18%
	Median Survival	Kadcyla	0,84	85%
		Lapatinib Capecitabine	0,14	15%
	Recurrence Probability	Kadcyla	0,76	81%
		Lapatinib Capecitabine	0,18	19%
	Frequent Usage	Kadcyla	0,18	19%
		Lapatinib Capecitabine	0,76	81%
	Maximum Dosage	Kadcyla	0,26	28%
		Lapatinib Capecitabine	0,66	72%

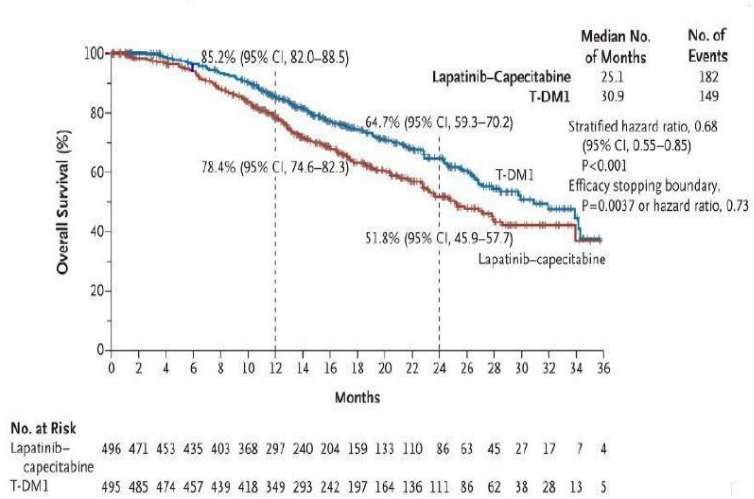

Figure 2: Comparison of overall survival rates **[20]**

Figure 2 has been shared so that the evaluation for median survival time can be validated. The graph shows that overall survival rate is usually higher when Kadcyla is used which is approved by the oncologists as well based on the survey results.

This is also the case for "frequent usage" and "maximum dosage" criteria. The details of how frequently and how much those drugs are taken were given in **[21].**

However, it is not possible to come up with the result just by using this comparison table. Since it does not consider the weights of the criteria it is difficult to make a comment on the result of the decision process just by using this table. For example, Lapatinib Capecitabine may happen to come out as a better solution if the significance level of the criteria in which Lapatinib Capecitabine is superior is much higher than the other criteria's. However, the result of this survey is determined after the final calculations, which simply multiplies the weight of the criteria with the relative effectiveness values of the drugs.

Table 6: Drugs' overall effectiveness in terms of patient related factors

Weight	0,16	0,49	0,10	0,20	0,05	
Targeted Drugs	Age	Gen. Health	Menopause	Preference	Ethnicity	Aggregation
Kadcyla	0,50	0,83	0,76	0,15	0,76	63%
LC	0,50	0,17	0,24	0,85	0,24	37%

Table 7: Drugs' overall effectiveness in terms of tumor related factors

Weight	0,17	0,09	0,74	
Targeted Drugs	Size	Location	Stage	Aggregation
Kadcyla	0,80	0,74	0,87	84%
LC	0,20	0,26	0,13	16%

Table 8: Drugs' overall effectiveness in terms of drug related factors

Weight	0,06	0,03	0,04	0,13	0,30	0,29	0,08	0,06	
Targeted Drugs	Therapeutic Index	Structure	Delivery	AE Grade	Median Sur.	Recurrence P.	Frequent Usage	Max Dosage	Aggregation
Kadcyla	0,85	0,20	0,83	0,82	0,85	0,81	0,19	0,28	72%
LC	0,15	0,80	0,17	0,18	0,15	0,19	0,81	0,72	28%

Previously, the drugs had been compared for each sub-criterion. At this step they are compared for the main criteria. Table 6 to Table 8 show those drugs' effectiveness considering the main criteria.

Since Kadcyla is better in each aspect it is now obvious that it should be the choice unless the priorities of the oncologists change. However, in order to show the overall result one final calculation has been carried out even though it became obsolete due to the fact that Kadcyla is superior to Lapatinib Capecitabine in general.

Table 9: Final result of the analysis

Weight	0,15	0,64	0,22		AHP
Targeted Drugs	Patient	Tumor	Drug	Aggregation	Rank
Kadcyla	0,63	0,84	0,72	79%	1
LC	0,37	0,16	0,28	21%	2

The biggest reason for obtaining such a result is that tumor related factors for which the gap between Kadcyla and Lapatinib Capecitabine is the highest has the highest importance level as well.

As it can be seen from the AHP, Multi-criteria Decision Making (MCDM) models aim to select best alternative among a finite set of decision alternatives. Like AHP, TOPSIS is another important method of Multiple Criteria Decision Making. In this model, it is assumed that the ratings and weights of alternatives are numerical data. In addition to that, TOPSIS method can be applied for both single decision maker and group decision making. As explained before, the survey in this paper was filled with 9 specialists. Because of this reason, TOPSIS method for group decision making is used to evaluate and rank alternatives, which are Kadcyla and Lapatinib plus Capecitabine. According to this method, there are several steps for the evaluation of the effectiveness of drug combinations. In the first step, the decision matrix with weights, which was found at the beginning of AHP model, was taken.

Table 10: Decision matrix of the research in terms of patient related factors

Weight	0,16	0,49	0,10	0,20	0,05
Targeted Drugs	Age	Gen. Health	Menopause	Preference	Ethnicity
Kadcyla	0,50	0,83	0,76	0,15	0,76
LC	0,50	0,17	0,24	0,85	0,24

In the second step, vector normalized decision matrix for patient related factors was calculated by taking squares of each cell and can be seen from Table 11.

Table 11: Vector normalized decision matrix for patient related factors

Weight	0,16	0,49	0,10	0,20	0,05
Targeted Drugs	Age	Gen. Health	Menopause	Preference	Ethnicity
Kadcyla	0,25	0,69	0,57	0,02	0,57
LC	0,25	0,03	0,06	0,72	0,06
Sum of Squares	0,50	0,72	0,63	0,74	0,63
Root of SoS	0,71	0,85	0,79	0,86	0,79

In the third step of TOPSIS, the weighted normalized decision matrix was calculated by dividing each cell of Kadcyla and LC to the root of sum of squares of each column and then multiplying weights of each column.

Table 12: Weighted normalized decision matrix for patient related factors

Targeted Drugs	Age	Gen. Health	Menopause	Preference	Ethnicity
Kadcyla	0,12	0,48	0,10	0,03	0,05
LC	0,12	0,10	0,03	0,19	0,01

In the next step, positive ideal and negative ideal solutions was calculated and shown in Table 13.

Table 13: Positive and negative ideal solutions for patient related factors

Pos. Ideal	0,12	0,48	0,10	0,19	0,05
Neg. Ideal	0,12	0,10	0,03	0,03	0,01

At the final step of the analysis, the separation measures from the positive and negative ideal solutions and relative closeness to the ideal solutions were calculated. In similar to the AHP model, effectiveness of Kadcyla in terms of patient related factors was found as the best one when compared to LC in TOPSIS method.

Table 14: Separation measures and relative closeness for patient related factors

	S*	S-	C*	Rank
Kadcyla	0,16	0,39	0,71	1
LC	0,39	0,16	0,29	2

As it can be explained in the previous part, same calculations were done for the tumor related factors and below Table 15 was obtained. According to this table, because of the good effectiveness of Kadcyla in all sub-criteria of tumor related factors, positive ideal solution was obtained as Kadcyla. Therefore, relative closeness of the Kadcyla was found 1 and dominates this field of research.

Table 15: Separation measures and relative closeness for tumor related factors

	S*	S-	C*	Rank
Kadcyla	0,00	0,63	1,00	1
LC	0,63	0,00	0,00	2

The same calculations were also repeated for the drug related factors of the research and Kadcyla again has high effectiveness when compared to LC.

Table 16: Separation measures and relative closeness for drug related factors

	S*	S-	C*	Rank
Kadcyla	0,07	0,35	0,82	1
LC	0,35	0,07	0,18	2

In order to provide validity, another method, which is Weighted Product, is also used in the analysis part. According to this method, the decision matrix with weights, which was found at the beginning of AHP model, was taken, again. Then, the values in each cell for each attributes to the each column's weight power were taken and multiplied through the row. According to Table 17 to Table 20, the calculations show similarity to the AHP and TOPSIS model.

Table 17: Weighted Product model for patient related factors

Weight	0,16	0,49	0,10	0,20	0,05		
Targeted Drugs	Age	Gen. Health	Menopause	Preference	Ethnicity	v(aj)	Rank
Kadcyla	0,50	0,83	0,76	0,15	0,76	0,54	1
LC	0,50	0,17	0,24	0,85	0,24	0,29	2

Table 18: Weighted Product model for tumor related factors

Weight	0,17	0,09	0,74		
Targeted Drugs	Size	Location	Stage	v(aj)	Rank
Kadcyla	0,80	0,74	0,87	0,84	1
LC	0,20	0,26	0,13	0,15	2

Table 19: Weighted Product model for drug related factors

Weight	0,06	0,03	0,04	0,13	0,30	0,29	0,08	0,06		
Targeted Drugs	Therapeutic Index	Structure	Delivery	AE Grade	Median Sur.	Recurrence P.	Frequent Usage	Max Dosage	v(aj)	Rank
Kadcyla	0,85	0,20	0,83	0,82	0,85	0,81	0,19	0,28	0,66	1
LC	0,15	0,80	0,17	0,18	0,15	0,19	0,81	0,72	0,22	2

Table 20: Weighted Product model for the general research

Weight	0,15	0,64	0,22		
Targeted Drugs	Patient	Tumor	Drug	v(aj)	Rank
Kadcyla	0,54	0,84	0,66	0,75	1
LC	0,29	0,15	0,22	0,18	2

6. Conclusions

The survey, which was completed with the participation of nine oncologists, has proved that Kadcyla is better at meeting the expectations of the oncologists when fighting against HER2+ breast cancer.

Although the expectation of the authors was to obtain a result such that the alternatives would have aggregate values which are a bit closer to each other, it turned out that there is a significant difference. It might be due to a bias because of the fact that the oncologists are more used to prescribing Kadcyla and this may have affected their choices.

On the other hand, in some parts of the survey the results match with the expectations perfectly. Those attributes are mainly the drugs' ability to increase the median survival time, the drugs' allowance of more frequent usage and higher dosage to be taken per treatment.

The validity of AHP analysis has been double-checked by using other methods like TOPSIS and Weighted Product. All methods gave similar results which menans that the developed model works fine and it can be applied for solving problems that are even more complex.

The authors strongly believe that the model is applicable to different cases. However, it would be more helpful when there are more alternatives and/or characteristics of the alternatives or the relative importance of criteria is similar.

The model could form a basis for automated decision-making applications, which might be a subject for future researches.

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