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Economic value of subcutaneous versus intravenous trastuzumab administration in the treatment of HER2-positive breast cancer: A systematic review

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ABSTRACT

Introduction: Trastuzumab is the standard therapy for HER-positive breast cancer, traditionally administered intravenously (T-IV). The subcutaneous trastuzumab (T-SC), introduced in 2013, may may offer cost savings compared to T-IV. While previous studies have examined the economic value of T-SC, no quality assessment of these studies or a currency-standardized comparison across countries has been conducted. This study aimed to address these gaps by systematically reviewing and assessing the quality of economic evaluations comparing T-SC and T-IV. Methods: A systematic review of publications until May 31, 2021, was performed using databases like MEDLINE, Cochrane, and ScienceDirect, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) statement. The quality of studies was assessed using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist. All costs were adjusted to 2019 Euro using World Bank's consumer price index (CPI). Results: There were 14 out of 368 studies included in this systematic review. Most studies were conducted from a hospital perspective, showing cost savings of T-SC ranging from €52.6 to €29,617.3 per patient annually. Quality assessments based on the CHEERS checklist revealed that the number of compliant sections or items in the studies ranged from 11 to 19 out of 24. Conclusion: This systematic review demonstrated that T-SC might offer cost savings compared to T-IV in treating HER2-positive breast cancer. However, the limited number of studies and their methodological heterogeneity highlight the need for further comprehensive research to inform decision-makers on trastuzumab use.

Keywords: *breast cancer, trastuzumab IV, SC, health economic, economic value*

1. INTRODUCTION

Breast cancer is the most common type of cancer with approximately 2.09 million new cases worldwide in 2018 that accounts for 24.2% of all new cases in women [1]. Breast cancer is the leading cause of cancer death in women with 15% of all cancer cases [1]. The rising incidence of breast cancer poses a significant burden to the healthcare systems. HER2 is one of genes that play an important role in the development of breast cancer [2]. 15-30% of breast cancer overexpresses HER2 [3]. Trastuzumab is recombinant humanized monoclonal antibody used as monotherapy or in combination with chemotherapy for HER2-positive breast cancer patients. Thanks to its efficacy and safety [4-6], trastuzumab is a standard therapy for HER2-positive breast cancer.

Trastuzumab was administered intravenously but since 2013 a subcutaneous formulation of trastuzumab was introduced. Subcutaneous trastuzumab (T-SC) was comparable to trastuzumab IV (T-IV) regarding to the pharmacokinetic effect, safety and therapeutic efficacy [7], [8]. However, T-SC improved patient

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convenience, increased patient compliance, reduced preparation time, and optimized medical resources. Therefore, there is an increased interest in evaluating the economic value of T-SC to assess the feasibility of this new formulation from a cost-effective perspective. Many studies reported the cost comparison of T-SC with T-IV in HER2-positive breast cancer. Currently, Inotai et al. (2018) published a systematic review of advantages and disadvantages of T-SC and T-IV in which monetary benefits of T-SC were evaluated [9]. However, the quality of the included studies in this review was not assessed [9]. Inotai et al. (2018) summarized results of each study, however, no comparison of economic value in the same currency between different countries was performed [9]. To address this gap in the literature, our objective was to conduct a systematic review of economic evaluations comparing the cost-effectiveness of T-SC and T-IV, while also assessing the quality of the included studies.

2. METHODS

This systematic review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocols (PRISMA-P) statement. The quality assessment was performed using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement checklists.

2.1. Searching and selection strategy

A systematic, electronic search of MEDLINE, Cochrane, Embase and ScienceDirect was performed for articles published until April 2020 with following keywords: economic value, trastuzumab, breast cancer, HER2-positive, intravenous, subcutaneous. The search was performed using Medical Subject Headings (MeSH) and the operators "OR" and "AND". Studies were selected based on the inclusion and exclusion criteria.

Inclusion criteria include studies that evaluate the economic value of subcutaneous versus intravenous trastuzumab in the treatment of HER2-positive breast cancer. Additionally, the studies must provide detailed results of cost components, be available in full-text, and be written in English.

Exclusion criteria include studies not conducted in a specific country, as well as review articles, letters, and reports.

2.2. Data extraction

Two reviewers independently assessed the studies. Any disagreements were discussed with the third author to reach a consensus. Two reviewers independently extracted the data. Data were extracted from relevant studies using a predefined data extraction form, comprising specific details about studying characteristics (author, nation, year, method, sample size, point of view, types of cost) and results (currency and index year, costs). All costs were converted into 2019 Euro by using Consumer Price Index (CPI) and exchange rate from database of World Bank in 2019[10].

2.3. Quality assessment using the CHEERS statement checklists

Quality assessment of included studies was performed by two reviewers using the consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist [11]. The CHEERS checklist consists of 24 items which are divided into 6 groups including title and abstract, introduction, methods, results, discussion, and other [11], [12]. Two reviewers had to determine which situation was “Yes” and which was “No”. In particular, we assumed that studies containing over a half of contents in each item would be assessed as “Yes”, or, conversely, the result was “No”[13].

3. RESULTS AND DISCUSSIONS

3.1. Results of systematic literature research and selection

The systematic literature research yielded 368 articles including 190 from MEDLINE, 80 from Cochrane, 67 from Embase and 31 articles from ScienceDirect. After removing 59 duplicated articles, 309 studies were included. We screened abstracts of 309 studies and excluded 291 articles which did not evaluate economic value of trastuzumab SC and IV (264 studies) and were not available in full-text (27 studies). After reviewing the full-text studies, we excluded 4 review articles and included 14 studies (Figure 1).

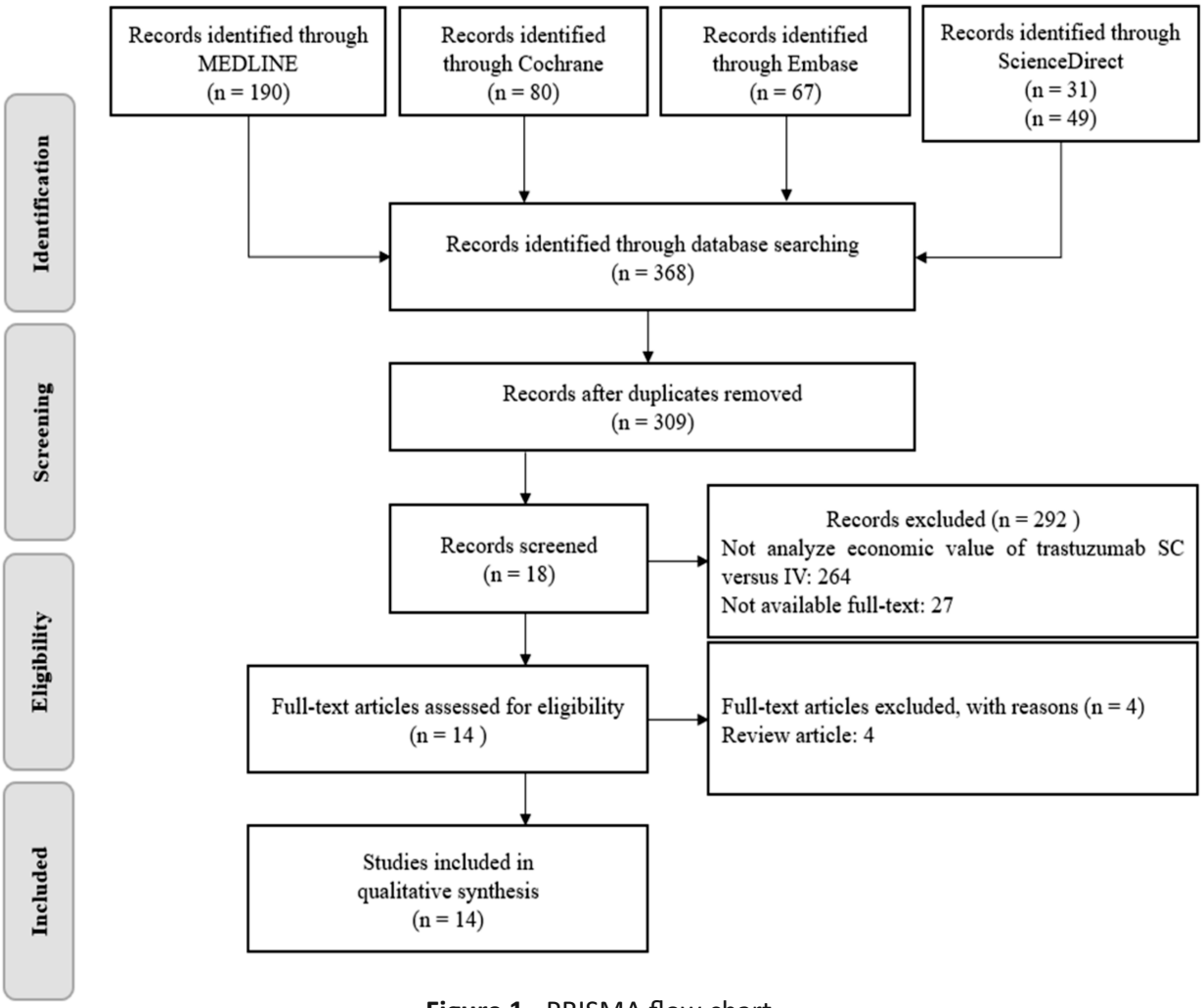

Figure 1. PRISMA flow chart

3.1.1. Study characteristics

Characteristics of the included studies are summarized in Table 1. This table aggregates information and sorts in chronological order.

The 14 studies were conducted between 2013 and 2018. Twelve out of fourteen studies were conducted in Europe including United Kingdom [15], Italy [16], [17], Sweden [18], [19] , Spain [20], [22], Belgium [21], Denmark [23], Ireland [25], Netherlands [26], and France [27]. One study was conducted in Chile [24] while the remaining study was in New Zealand [14]. In terms of study design, prospective study (11 studies) was the most popular. The three remaining studies are retrospective study [16], descriptive study [14] and cross- sectional study [22]. Two analytical methods were used, including cost minimization analysis in 4 studies [14], [20], [24], [25] and costs analysis in 10 studies.

There was a total of 4 ways in collecting data, with Franken et al. (2018) having the most diverse methods of collecting data, including observation, questionnaire, and database access. Hedayati et al. (2015) combined two methods including interviewing and accessing database [18]. Among the four methods, the most common way was observation, by which the data of six research were collected [14], [15], [20], [21], [25], [26]. Questionnaire was the second popular, which was used in five studies [17], [19], [22], [26], [27]. There were three studies collected data by accessing to database [16], [18], [26], which is the only way of collecting data in the study of Farolfi et al. (2014) [16]. The method of having interview was also used in three studies [18], [23], [24]. Only 3 studies with more than one objects. Among them, there are 2 studies analyzed costs saving on first patients (Hedayati et al. and Olofsson et al.) [18], [19]. Hedayati et al. (2015) analyzed on first patients with total of 2,769 SC administrations since not all the new diagnosed patients received 17 cycles of treatment during the given calendar year [18]. Meanwhile, Olofsson et al. (2015) studied on first and subsequent patients separately [19]. The

remaining study recorded 1st, 2nd, 3rd and subsequent cycle separately to resulted total treatment [20]. Four studies were performed from 2 different perspectives including hospital and patient perspectives [17], [23], hospital and societal perspectives [25], [26]. The remained 10 studies were reported from 1 perspective in which 6 studies were from hospital perspective [14], [15], [18], [21], [22], [27] and 4 studies were from societal perspective [16], [19], [20], [24]. All the14 studies estimated direct costs in which 7 studies further reported indirect costs [16], [19], [20], [23-25].

Table 1. Study characteristics

No	Author (Year)	Country	Year	Study design	Data collection methods	Analytical methods	Sample size	Perspective	Type of cost
1	North et al. (2013) [14]	New Zealand	2013	Descriptive study	Observation	Cost minimization analysis	18 patients 6 SC, 12 IV	Hospital	Direct costs (HCP time, consumables)
2	Burcombe et al. (2013) [15]	United Kingdom	2013	Prospective study	Observation	Cost analysis	24 patients 12 SC, 12 IV	Hospital	Direct costs (HCP time, consumables)
3	Farolfi et al. (2014) [16]	Italy	2014	Retrospective study	Access database (Log80)	Cost analysis	Not available	Societal	Direct costs (drug cost, drug wastage) and indirect costs.
4	Ponzetti et al. (2014) [17]	Italy	2015	Prospective study	Questionnaire	Cost analysis	Not available	Hospital and patient	Direct costs (drug wastage)
5	Hedayati et al. (2015) [18]	Sweden	2015	Prospective study	Interview and access database	Cost analysis	178 first patients	Hospital	Direct costs (consumables, pharmacy fees (HCP time)
6	Olofsson et al. (2015) [19]	Sweden	2015	Prospective study	Questionnaire	Cost analysis	195 patients (number of first and subsequent patients)101 (4-97) IV94 (16-78) SC	Societal	Direct medical costs (drug cost, consumables, HCP time), direct non-medical costs (transportation) and indirect costs (production loss, lost leisure time)
7	Lopez-Vivanco et al. (2016) [20]	Spain	2016	Prospective study	Observation	Cost minimization analysis	307 patients 159 IV, 148 SC	Societal	Direct costs (drug costs, HCP time, consumables). Indirect costs (lost productivity)
8	Tjalma et al. (2016) [21]	Belgium	2016	Prospective study	Observation	Cost analysis	130 patients 65 IV, 65 SC	Hospital	Direct costs (HCP time, consumables and drug wastage)

No	Author (Year)	Country	Year	Study design	Data collection methods	Analytical methods	Sample size	Perspective	Type of cost
9	Lazaro et al. (2016) [22]	Spain	2016	Cross-sectional study	Questionnaire	Cost analysis	76 patients	Hospital	Direct costs (drug cost, consumables, HCP time)
10	Jens Olsen et al. (2017) [23]	Denmark	2017	Prospective study	Interview	Cost analysis	Not available	Hospital and patient	Direct costs (HCP time, room time). Indirect cost (cost of patient's time)
11	Luis Rojas et al. (2017) [24]	Chile	2017	Prospective study	Interview	Cost minimization analysis	100 patients	Societal	Direct costs (drugs cost, HCP time, consumables, room time and ADR treatment). Indirect costs (lost productivity)
12	O'Brien et al. (2018) [25]	Ireland	2018	Prospective study	Observation	Cost minimization analysis	Not available	Hospital and societal	Direct costs (costs of HCP time, consumables, and drugs). Indirect costs (lost productivity)
13	Franken et al. (2018) [26]	Nether-lands	2018	Prospective study	Observation, questionnaire, and access database	Cost analysis	82 patients 45 SC, 37 IV	Hospital and societal	Direct costs (drugs, healthcare professional labor, consumables, traveling expenses). Indirect cost (productivity losses)
14	Blein et al. (2018) [27]	France	2018	Prospective study	Questionnaire	Cost analysis	Not available	Hospital	Direct costs (Consumables)

3.1.2. Study results

Table 2 summarizes the results of 14 included studies that analyzed economic value between subcu-taneous and intravenous trastuzumab in the treatment of HER2-positive breast cancer. All studies were presented in cost savings per patient/year (either 17 or 18 treatment cycles per years).

All the 14 included studies remarked that T-SC offered cost savings compared to T-IV, ranging from €52.6 to €29,617.3. In terms of direct costs, 13 out of 14 studies showed that T-SC was lower than T-IV. In contrast, in Farolfi et al. (2014), direct cost of T-SC was slightly more expensive than T-IV. However, T-SC reduced indirect costs compared to T-IV that resulted to total cost

savings of €52.6 (€50.4 in 2014). Among all 7 studies that investigate indirect costs, T-SC were found to save indirect costs relative to T-IV in 6 research [16], [19], [20], [23-26].

Table 2. Study characteristics

No	Author (Year)	Country	Object	IV		SC		Original Year Cost Savings			Updated Cost Savings in 2019		
				Direct cost	Indirect cost	Direct cost	Indirect cost	Direct cost	Indirect cost	Total cost	Direct cost	Indirect cost	Total cost
1	North et al. (2013) [14]	New Zealand	-	971.5	-	188.7	-	782.8	-	**782.8**	820.1	-	**820.1**
2	Burcombe et al. (2013) [15]	United Kingdom	(18 episodes)	3,135.6	-	716.4	-	2419.2	-	**2419.2**	2534.5	-	**2534.5**
3	Farolfi et al. (2014) [16]	Italy	-	13,655.0	668.4	14,154.0	119.0	-499.0	549.4	**50.4**	-520.6	573.2	**52.6**
4	Ponzettiet al. (2014) [17]	Italy	-	28,399.0	-	0.0	-	28,399.0	-	**28,399.0**	29,617.3	-	**29,617.3**
5	Hedayati et al. (2015)	Sweden	First patient	2,782.0	-	428.0	-	2,354.0	-	**2,354.0**	2,455.0	-	**2,455.0**
6			1 SC adm*	67.3	-	0.7	-	66.6	-	**66.6**	69.5	-	69.5
7	Olofsson et al. (2015)	Sweden	First patient	2,695.0	281.0	1,938.0	141.0	757.0	140.0	**897.0**	789.5	146.0	**935.5**
8			Sub-patient**	2,034.0	66.0	1,933.0	50.0	101.0	16.0	**117.0**	105.3	16.7	**122.0**
9	Lopez-Vivanco et al. (2016)	Spain	-	29,431.8	348.1	28,452.1	195.3	979.6	152.8	**1,132.5**	1,019.2	159.0	**1,178.2**
10	Tjalma et al. (2016)	Belgium	-	4,023.5	-	190.8	-	3,832.7	-	**3,832.7**	3,987.5	-	**3,987.5**
11	Lazaro et al. (2016) [22]	Spain	-	12,629.4	-	12,164.5	-	464.9	-	**464.9**	483.7	-	**483.7**
12	Jens Olsen et al. (2017)	Denmark	1st cycle	170.5	119.1	59.6	93.7	110.9	25.4	**136.3**	113.6	26.0	139.6
			2nd cycle	119.6	28.9	53.7	26.7	65.9	2.2	**68.1**	67.5	2.3	69.8
			3rd cycle	119.6	27.7	53.1	19.8	66.5	7.9	**74.4**	68.1	8.1	76.2
			Sub-cycle**	103.4	8.9	51.6	3.3	51.8	5.6	**57.4**	53.1	5.7	58.8
			Total treatment	1,857.3	300.3	888.8	186.4	968.5	113.9	**1,082.4**	992.3	116.7	**1,109.0**
13	Luis Rojas et al. (2017) [24]	Chile	-	70,665.7	147.4	65,404.1	103.3	5,261.6	44.1	**5,306.7**	5,391.3	45.2	**5,436.5**
14	O'Brien et al. (2018) [28]	Ireland	-	36,619.5	243.7	35,009.6	67.2	1,610.0	176.6	**1,786.6**	1,622.6	178.0	**1,800.6**
15	Franken et al. (2018) [26]	Nether-lands	(18 cycles)	31,554.0	180.0	30,907.8	88.2	646.2	91.8	**738.0**	651.3	92.5	**743.8**
16	Cécile Blein et al. (2018) [27]	France	(18 sessions)	223.2	-	23.4	-	199.8	-	**199.8**	201.4	-	**201.4**

*Note. *adm = administration, **sub = subsequent*

The highest and the least cost savings were both recorded in Italy. As being mentioned earlier, Farolfi et al. (2014) reported the least costs saving of €52.6 (€50.4 in 2014) because direct cost (drug cost, drug wastage) of T-SC was more expensive than T-IV and the analysis was in societal perspective[16]. Otherwise, the study of Ponzetti et al. (2014) estimated cost saving by assessing cost of drug wastage and recorded the cost saving per patient per total treatment was €29,617.3 (€28,399.0 in 2014) [17]. However, both studies did not describe in detail the methodology for the measurement of drug wastage.

Overall, cost savings of T-SC across studies in Europe ranged from €52.6 to €3,987.5 except for study by Ponzetti et al. (2014) with €29,617.3 [17]. Estimate of cost savings in New Zealand was also in this range while cost savings of T-SC in Chile was higher than that (€5,436.5) [14], [24]. The wide heterogeneity in cost savings of T-SC was due to the variations of treatment course, methods of data collection, and cost components, which are discussed below. A research conducted by Burcombe et al. (2013) [15] analyzed direct costs (HCP time and consumables), of T-SC versus T-IV in UK were €716.4 (£597.6 in 2013) and €3,135.6 (£2610.0 in 2013) respectively, resulting in the cost saving of €2,534.5 (£1,893.6 in 2013). North et al. (2013) analyzed the same components of direct costs of T-SC versus T-IV in New Zealand. T-SC was found to be associated with cost savings of €820.1 (NZD 1,304.6 in 2013) [14]. This result was similar to Olofsson et al. (2015) in Sweden (€820.1 vs €935.5). Olofsson et al. (2015) noted cost savings for direct costs was €789.5 (€757.0 in 2015) and for indirect costs was €146.0 (€140.0 in 2015), resulting in total cost savings of €935.5 (€897.0 in 2015) in first patients. Meanwhile, in subsequent patients, this study noted direct cost savings was €105.3 (€101.0 in 2015) and indirect cost savings was €16.7 (€16.0 in 2015), led to a total cost savings of €122.0 (€117.0 in 2015) per patient per total treatment. Olofsson et al. (2015) showed that cost savings in first patients were 8 times higher than subsequent patients (€935.5 vs €122.0). In addition to HCP time and consumables as reported in North et al. (2013), Olofsson et al. (2015) also estimated direct non-medical cost (transportation). This cost component was also studied by Franken et al. (2018) with the cost spent for travelling being €20.4 (€20.2 in 2018) and €7.6 (€7.5 in 2018) for T-IV and T-SC group, respectively. However, no difference in cost of transportation between the two groups was found in both research[19],[26].

Another analysis in Sweden was Hedayati et al. (2015) which estimated the economic value of T-SC by assessing the monetary benefits of changing actual T-SC process at a single Swedish healthcare institution. Hedayati et al. (2015) reported cost savings of €2,455.0 (€2,354.0 in 2015) per newly diagnosed patient (first patient) from avoiding port-a-cath surgery and €69.5 (€66.6 in 2015) associated with each SC administration. Hence, for first patient who received full of 17 cycles, the costs saving per patient would be €3,636.5. It should be noted that there was no reference group using T-IV. The authors reported cost savings of using T-SC instead of T-IV in newly diagnosed patients[18].

Beside Olofsson et al. (2015), study of Lopez-Vivanco et al. (2016), Lazaro et al. (2016), O'Brien et al. (2018), and also investigated direct cost savings by assessing drug cost, consumables and HCP time. Lopez-Vivanco et al. (2016) estimated direct cost savings at €1,019.2 (€979.6 in 2016) [20] which was similar to O'Brien et al. (2018) (€1,622.6)[25]. However, Lazaro et al. (2016) and reported at lower value of €483.7 [22]. Lopez-Vivanco et al. (2016) and Lazaro et al. (2016) were both conducted in Spain in 2016. Nevertheless, cost savings estimated by Lopez-Vivanco et al. (2016) were twice higher than that by Lazaro et al. (2016) (€1,01 9.2 versus €483.7) [20], [22]. This can be explained by differences in study design, perspective, analytical methods and data collection methods.

Both Lopez-Vivanco et al. (2016) and O'Brien et al. (2018) analyzed indirect costs which were similar to each other (€159.0 vs €178.0, respectively). As a result, a comparable cost savings was found between these two studies

(€1,178.2 vs €1,800.6, respectively)[20],[25].

Tjama et al. (2016) estimated direct cost on consumables, HCP time and drug wastage in Belgium. Thus, this study recorded the total cost savings per patient per full treatment at €3,987.5 (€3,832.7 in 2016) [21]. Jens Olsen et al. (2017) estimated costs saving in 1st, 2nd, 3rd, and subsequent cycles in Denmark. Consequently, cost savings of €1,109.0 (€1,082.4 in 2017) over a full treatment course of T- IV and T-SC were estimated. Notably, cost savings in the first cycle was the highest followed by the remained cycles (€139.6 vs €69.8, €76.2, €58.8)[23].

Luis Rojas et al. (2017) in Chile was the first study performed in Latin America (Chile) with diverse cost components estimated. Particularly, this study reported adverse drug reactions-associated costs (€1,371.2 ($1,574.3 in 2017)) that did not take noted in pre-study published in 2017. T-SC led to savings of €5,391.3 ($6,190.1 in 2017) for direct cost, and €45.2 ($51.8 in 2017) for indirect costs, resulting in €5,436.5 ($6,138.3 in 2017) for total savings in treatment costs[24].

A Dutch research conducted in 2018 reported comprehensive costs associated with one session of trastuzumab administration showed that the total cost for one cycle (including drug costs) via IV and SC route was (€1855.96 in 2018) and (€1763.36 in 2018) with €1,766.7 (€1,753.0 in 2018) and €1,730.6 (€1,717.1 in 2018) being direct cost respectively [26]. At the same year, a multi-center study was conducted by Blein et al. within 9 healthcare facilities in France, resulted that the costs of consumables for a T-SC pathway is significantly lower (€1.4 (€1.4 in 2018) per SC formulation versus €12.5 (€12.4 in 2018) per IV counterpart)[27].

There are 7 out of 14 studies investigated indirect costs. Most of the studies manifested savings of indirect cost, accounting for about 10% to 16% of total cost savings, except for the research of Franken at el. (2018). This can be explained by the assessed expenditure of lost productivity being the cost of unpaid work only.

This systematic review evaluated the contribution of different cost components in assessing cost savings to estimate the economic value of T-SC versus T-IV that led to distinct results. Hence, it is suggested that future studies to comprehensively evaluate all cost components are needed to achieve the most accurate estimates.

3.1.3. Quality assessment

There has been no checklist available to optimize reporting cost analyses. Therefore, CHEERS checklist is the best available until now. However, for such cost studies it will only achieve a maximum of 21 items. An independent assessment of articles based on CHEERS checklist showed the number of sections or items of the studies achieving ranged from 11 (Lazaro et al. [22]) to 19 (Luis Rojas et al. [24]) out of 24 items. Only 2/11 studies used discount rates for costs and results.

Most studies were funded by Hoffmann - La Roche. In addition, all studies were no conflicts of interest of contributors. The majority of the studies lacked items such as setting and location, discount rate, choice of health outcome, measurement of effectiveness, measurement and valuation of preference-based outcomes.

3.2. Discussion

This is the first systematic review comparing the economic value of T-SC with T-IV in the treatment of HER2-positive breast cancer using a consistent currency across studies from different countries. T-SC was found to save costs compared to T-IV (ranging from €52.6 to €29,617.3), that was in agreement with findings by Inotai et al (2018)[9]. However, Inotai et al (2018) did not discuss the quality of include studies. Our independent assessment of articles based on CHEERS checklist showed that the number of sections or items of the studies achieving ranged from 11 to 19 out of 24 items.

In addition, during our search we discovered another systematic review which was of Papadmitriou et al. (2015) [26]. However, this review was conducted quite early (2015) compared to the time of T-SC's first introduction (2013). Thus, only 2 studies were identified focusing in the use of healthcare resources in relation to SC or IV administration of trastuzumab: a time & motion study and one trial with no results yet published in a peer reviewed

journal. Papadmitriou et al. (2015) suggested to further validate the potential financial impact of T-SC compared to T-IV but did not conclude economic value of T-SC versus T-IV due to limited data at that moment.

In studies that analyzed both direct and indirect cost, the majority of costs saving came from direct cost savings, accounting for more than 85% of total cost savings. Across studies analyzing the drug costs, drug costs accounted for the majority of direct costs (over 90%).

Our study has some strengths. First, our systematic review provided the most updated evidence on economic value of T-SC by including more articles than Inotai et al. (2018) [9] (11 versus 9 articles). Second, direct comparisons across included articles were performed by exchanging all costs to Euro in 2019 per patient per total treatment. Third, this systematic review summarized and compared cost of each component. Forth, our study performed a formal quality assessment of the identified publications to enable more consistent and transparent reporting.We acknowledged several limitations. The CHEERS checklist is the best recommended scale for health economic research. Nevertheless, this scale was designed mostly for cost-effectiveness analysis studies. Although the CHEERS checklist may not be the most suitable scale for cost analyses, it is the best available until now. Moreover, despite the broad search of different libraries, the inclusion of studies written in English may lead to missing some relevant studies in other languages. Further searching for publications in other language and database might result in a larger number of included studies.

4. CONCLUSION

Our systematic review demonstrated that T-SC might offer cost savings compared to T-IV in the treatment of HER2-positive breast cancer. However, there is a small number of studies with the large heterogeneity in study design, cost components and perspectives. Future comprehensive studies are needed to better inform decision-makers with respective to the use of trastuzumab in breast cancer treatment.

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Giá trị kinh tế của trastuzumab tiêm dưới da so với đường tĩnh mạch trong điều trị ung thư vú HER2 dương tính: Nghiên cứu tổng quan hệ thống

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TÓM TẮT

Giới thiệu: Trastuzumab là liệu pháp tiêu chuẩn cho ung thư vú dương tính với HER2, được sử dụng qua đường tĩnh mạch (T-IV). Sự ra đời của trastuzumab dạng tiêm dưới da (T-SC) từ năm 2013 có thể mang lại lợi ích về chi phí so với T-IV. Mặc dù, các nghiên cứu trước đã đánh giá giá trị kinh tế của T-SC, chưa có đánh giá chất lượng nào của các nghiên cứu này hoặc so sánh tiêu chuẩn hóa tiền tệ giữa các quốc gia. Nghiên cứu này nhằm khắc phục những thiếu sót trên thông qua việc tổng quan hệ thống và đánh giá chất lượng các nghiên cứu kinh tế so sánh T-SC và T-IV. Phương pháp: Tổng quan hệ thống các công bố đến ngày 31 tháng 5 năm 2021 được thực hiện trên các cơ sở dữ liệu như MEDLINE, Cochrane, và ScienceDirect, tuân theo hướng dẫn PRISMA-P. Chất lượng nghiên cứu được đánh giá bằng bảng kiểm Consolidated Health Economic Evaluation Reporting Standards (CHEERS). Tất cả chi phí được quy đổi về Euro năm 2019 dựa trên chỉ số giá tiêu dùng (CPI) của Ngân hàng Thế giới. Kết quả: Có 14 trong số 368 nghiên cứu được đưa vào tổng quan hệ thống này. Hầu hết các nghiên cứu được thực hiện từ quan điểm bệnh viện, cho thấy T-SC giúp tiết kiệm chi phí từ €52.6 đến €29,617.3 mỗi bệnh nhân mỗi năm. Đánh giá chất lượng theo bảng kiểm CHEERS cho thấy số mục tuân thủ của các nghiên cứu dao động từ 11 đến 19 trên tổng số 24 mục. Kết luận: Tổng quan hệ thống này cho thấy T-SC có thể mang lại lợi ích tiết kiệm chi phí so với T-IV trong điều trị ung thư vú HER2 dương tính. Tuy nhiên, số lượng nghiên cứu còn

hạn chế và sự đa dạng trong phương pháp luận cho thấy cần có thêm các nghiên cứu toàn diện hơn để hỗ trợ nhà hoạch định chính sách về việc sử dụng trastuzumab.

Từ khóa: *ung thư vú, trastuzumab tĩnh mạch, tiêm dưới da, kinh tế y tế, giá trị kinh tế*

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