Real-World Evidence of Biosimilar Utilisation and Pharmacoeconomics in People Living with Breast or Lung Cancer

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Abstract

As the medical community continues to explore and harness the potential of biosimilars, it is imperative to accumulate robust real-world evidence (RWE) to guide informed decision-making, and enhance patient outcomes in cancer treatment. This article reviews the current understanding and utilisation of biosimilars in the treatment of breast and lung cancers by reviewing existing RWE. A literature search of PubMed, MEDLINE, and Scopus was performed to analyse observational studies pertaining to the adoption of biosimilars in people living with breast or lung cancer, with publications considered since 2019. The review summarises the current RWE relating to biosimilar use for its approved indications across breast and lung cancer. Despite the scarcity of evidence addressing the cost-effectiveness of biosimilars in breast and lung cancer treatment, biosimilars may offer a dual benefit by enhancing patient outcomes, while ensuring cost-effectiveness, thereby increasing access to oncology therapies globally. The increased access to biosimilars within community oncology practices, hospitals, and national healthcare systems, promises substantial cost savings. This review highlights the evolving landscape of biosimilar utilisation in oncology, revealing their potential as a more affordable and inclusive approach to cancer care, while also indicating areas for further research.

Key Points

1. The pharmacoeconomic evaluation of biosimilars in breast and lung cancer therapy has indicated the potential to reduce treatment costs.

2. The utilisation rates of biosimilars, as reported in real-world evidence, vary considerably, depending on geographical location and treatment stage.

3. Community-based oncology practices, hospitals, and national healthcare systems can achieve substantial cost savings through the widespread utilisation of biosimilars. The adoption of biosimilars in a large oncology network is not only feasible, but also has the potential for noteworthy economic gains.

EXPLORING THE USE OF BIOSIMILARS IN ONCOLOGY TREATMENT

In recent years, biosimilars have emerged as a revolutionary approach to oncology treatment. The development of biosimilars follows a globally consistent framework, with slight variations in guideline wording between countries. Biosimilars are highly similar to already approved biological reference product (RP), evaluated through comprehensive comparability studies with their RPs, demonstrating no clinically meaningful differences in terms of efficacy, safety, and immunogenicity.[1] This is supported by a robust regulatory framework, and licensed by esteemed regulatory bodies, such as the UK's Medicines and Healthcare Products Regulatory Agency (MHRA), the European Medicines Agency (EMA), and the U.S. Food and Drugs Administration (FDA). Of note, it is important to recognise that in certain parts of the world, many non-approved biologic copies are available, which cannot be considered as biosimilars. Biosimilars have the potential to improve patient outcomes and mitigate healthcare expenditures, by offering a more affordable alternative for biologics.[2] Consequently, biosimilars contribute to expanding access to advanced oncology therapies within the global patient population.[3]

Healthcare professionals have shown increased interest in biosimilars due to their safety, efficacy, and cost-effectiveness.[4] The ability to offer high-quality treatment options that match the efficacy of biologics at a reduced cost signifies a pivotal transformation within the field of oncology.[2,4] It plays a crucial role in payer coverage decisions and physician adoption of biosimilars,[4] all while upholding patient outcomes.[5] However it remains pertinent to consider whether RWE substantiates this assertion.

The Call for Real-World Evidence to Advance Oncology Care Through Biosimilars

Despite the growing interest, hesitancy still surrounds the utilisation of biosimilars, highlighting the need for RWE to emphasise their value and impact adoption.[6,7] The availability of data that underscores the worth and impact of biosimilars is paramount. This entails evidence that supports the efficacy, safety, and cost-effectiveness of different therapeutic options, and determines the factors that influence treatment decisions, ultimately leading to better patient outcomes.

RWE is derived from real-world data (RWD) and observations made within routine healthcare settings, establishing the practical use, safety, and efficacy of treatments.[8] The pivotal advantage of RWE lies in its ability to garner increased acceptance among various stakeholders regarding the benefits of biosimilar utilisation. This expansion goes beyond the confines of clinical trials and epidemiological studies, effectively bridging the gap between research and real-world application.[8,9] The RWE not only validates the outcomes observed in such controlled trials,[10] but also enhances understanding of treatment delivery, efficacy, and systemic outcomes in routine care. Such insights are key in driving forward patient utilisation, and establishing the true health economic benefit.[11]

Of significance, the economic burden of cancer treatment has escalated in recent years across European countries, driven by an increase in the number of people living with cancer and the associated healthcare costs.[12] As such, conducting budget impact analyses has become a prerequisite for payers' application dossiers.[12]

Globally, cancer stands as one of the leading causes of death, contributing to nearly 10 million deaths in 2020.[13] The most common cancers are breast cancer (2.26 million cases) and lung cancer (2.21 million cases).[13] Biosimilars, such as monoclonal antibodies that target specific markers within malignant cells and tumour micro-environments, are increasingly used as an anticancer therapy.

The following article provides a comprehensive review of current RWE concerning the adoption of biosimilars across their approved indications in lung and breast cancer, and the associated pharmacoeconomic impact. The literature conveys tangible real-world outcomes concerning biosimilar use within oncology care. The article adopts a scoping review approach, involving a search of peer-reviewed literature within PubMed, MEDLINE, and Scopus, along with grey literature, such as abstract proceedings, consultancy reports, and policy documents. These sources were analysed for instances of RWE or RWD stemming from observational studies focused on biosimilar use, and their associated cost-effectiveness in people living with breast cancer or lung cancer, published from 2019 onwards. The search employed keywords including: "real-world" OR "observational" AND "biosimilar" AND "cancer" OR "oncology" AND "breast" OR "lung" AND "cost-effectiveness" OR "economic". Eligibility was restricted to studies written in English, which were subsequently retrieved and assessed for relevance.

CURRENT STATUS OF BIOSIMILARS IN THE REAL-WORLD ONCOLOGY SETTING

Currently, the integration of biosimilars in oncology practice is in a state of evolution, especially as numerous patents for biologic drugs expire. To date, there are a number of EMA- and FDA-approved biosimilars for cancer treatment, including monoclonal antibodies, such as rituximab, bevacizumab, and trastuzumab, alongside supportive care agents for cancer care, including pertuzumab, filgrastim, pegfilgrastim, and epoetin-α.[2,4,14]

There are a number of oncology-approved biosimilars that marked a significant milestone in the treatment of cancer, which have been approved in both the USA and Europe since 2017.[14,15] One such type are trastuzumab biosimilars, monoclonal antibodies used to treat early and metastatic human epidermal growth factor receptor-2 (HER2)-positive(+) breast cancer.[14,16,17] Another type of oncology-approved biosimilar in both the USA and Europe are bevacizumab biosimilars, targeted monoclonal antibodies used to treat various cancers, including unresectable advanced, recurrent, or metastatic non-squamous non–small cell lung cancer (NSCLC).[14,18-23]

Recognising the adverse health implications and years of life lost due to inadequate treatment access, the World Health Organization (WHO) has formally included bevacizumab and trastuzumab in its list of essential medications.[24] Previously, trastuzumab access was hindered in lower-income countries due to the high cost.[25] Consequently, the introduction of more cost-effective alternatives, such as biosimilars of bevacizumab and trastuzumab, could increase treatment accessibility by fostering price competition.[26-28] A national survey conducted among Brazilian oncologists (N=144) identified that 73% had concerns about treatment accessibility influenced by therapy cost, which in turn impacted their decision-making and prescription choices.[29]

Therefore, increased utilisation of RWE plays a crucial role in substantiating the adoption of biosimilars for the treatment of breast and lung cancer. RWE that reinforces the safety, efficacy, and immunogenicity of biosimilars is important to enhance physician confidence, and foster increased adoption of biosimilars.[30] This, in turn, can improve broader access to effective therapies, leading to cost reductions and positive implications for health economics.[30]

Since the market availability of biosimilars for breast and lung cancers, a comprehensive review of the real-world impact is pivotal in understanding their influence and optimal utilisation. This evaluation is essential to demonstrate potential savings achievable through switching to, for example, bevacizumab and trastuzumab biosimilars.[12]

Real-World Evidence of Bevacizumab Biosimilars Utilisation in Oncology Practice

Only a handful of RWE studies have analysed the utilisation of bevacizumab biosimilars within oncology practice.[31-34] One of the first retrospective, observational studies evaluating the implementation of a bevacizumab biosimilar used structured patient-level data sourced from the USA nationwide Flatiron Health electronic health records-derived database (2019–2020).[31] The study identified uptake of the bevacizumab biosimilar across all approved indications; 14% of its use was in the treatment of NSCLC.[31] Based on these findings, the authors concluded that physicians are comfortable in initiating or transitioning patients to bevacizumab biosimilars.[31]

Another retrospective cohort analysis of RWE in the USA (2019–2020) examined medical and pharmacy claims concerning bevacizumab biosimilar use.[32] The study included patients with NSCLC (n=18) who were treated with a bevacizumab biosimilar, representing 8.7% of the full cohort of people living with cancer (N=206).[32] However, notably the analysis was performed on a small sample size, therefore limiting the analysis outcomes.[32]

The real-world use of bevacizumab biosimilar was also assessed through a retrospective, observational study across all approved indications within the first 12 months (2020–2021) following its introduction to the National Cancer Centre of China.[33] Among the included cohort, a substantial proportion of cases (n=186 out of 259) pertained to NSCLC, with 48.8% receiving a bevacizumab biosimilar as a first-line therapy.[33] Of note, the majority of those pre-exposed were switched from a RP or other biosimilars to the bevacizumab biosimilar in question within a 28-day span.[33] In another retrospective study including patients with locally advanced or metastatic NSCLC (N=946) treated at a single centre in China, the efficacy and safety of the bevacizumab biosimilar was compared with the RP, providing insights for those patients who would be typically excluded from clinical trials data.[34]

Real-World Evidence of Trastuzumab Biosimilars Utilisation in Oncology Practice

In 2022, a literature review identified a number of studies exploring the real-world effectiveness of trastuzumab biosimilars beyond clinical trials.[35] A retrospective evaluation identified neoadjuvant patients with HER2+ early breast cancer (EBC) to establish the real-world clinical data of the trastuzumab biosimilar in comparison with the RP, and drawing comparisons with outcomes from Phase III trials.[35]

In addition, a retrospective analysis conducted in India, a resource-constrained low- to middle-income country, identified patients with non-metastatic HER2+ breast cancer (n=87 out of 135).[36] In this setting, patients receiving a neoadjuvant trastuzumab biosimilar in combination with chemotherapy were compared with the RP to identify the patterns of use, and associated clinical outcomes. Of those included, 67% (n=70) received the trastuzumab biosimilar compared with 33% (n=34) who received the RP.[36] Of note, 23% (n=31) were treated with chemotherapy alone due to financial constraints that limited their access to trastuzumab.[36]

Additional studies concerning the RWE of trastuzumab biosimilars have since emerged. In a study in HER2+ EBC (N=44), the utilisation of a neoadjuvant trastuzumab biosimilar in combination with pertuzumab and chemotherapy (n=20) in a single centre in Spain, to determine the real-life preclinical and clinical data compared with the RP (n=24).[37] Likewise, RWE from Germany analysed data from a large university breast cancer centre to compare the efficacy and safety outcomes of those patients with HER2+ EBC (N=124), for which 31% (n=46 out of 124) received trastuzumab biosimilar, compared with 63% who received the RP (n=77 out of 124).[38]

In Denmark, a retrospective nationwide study encompassing those with HER2+ metastatic breast cancer (N=117) assessed first-line treatment with a trastuzumab biosimilar in combination with pertuzumab.[39] The study used data from the Danish Breast Cancer Group (DBCG) registry, that included 117 patients who had received the trastuzumab biosimilar in combination with pertuzumab.[39]

In addition, RWE was also reported from Türkiye, with retrospective analysis of medical records comparing the trastuzumab biosimilar with neoadjuvant chemotherapy for patients with HER2+ EBC (n=159), or metastatic breast cancer (n=53), in terms of safety and efficacy compared to the RP.[40] In neoadjuvant therapy, 64% (n=59) received the trastuzumab biosimilar, whereas 36% (n=33) received the RP. In adjuvant therapy, 40% (n=27) received the trastuzumab biosimilar compared with 60% (n=40) who received the RP.[40]

Finally, a prospective observational study conducted in a single Portuguese oncology hospital tracked the treatment of cancer patients, and identified 59 patients receiving a trastuzumab biosimilar to assess the RWE safety profile.[41]

THE REAL-WORLD COST-EFFECTIVENESS OF ONCOLOGY BIOSIMILARS

Godman[42] identified that there is a rising cost of medicines for various diseases, including cancer, and Safdar et al.[43] highlighted a substantial increase in healthcare expenditure associated with cancer treatments. Oncology biologics stand as some of the most expensive pharmaceuticals available on the market today, imposing a growing financial burden on both patients and healthcare systems.[44]

Godman[42] expressed concerns regarding the affordability of drugs such as trastuzumab, and emphasised the potential of lower-cost biosimilars that could help address this burden. Sadfar et al.[43] advocate the need for innovative strategies to alleviate the financial burden on healthcare systems, suggesting biosimilars as one potential option. Initiatives aimed at reducing biosimilar prices and enhancing their utilisation have been suggested as options to achieve substantial savings, and provide an alternative that is more accessible.[42] Miller et al.[15] estimated a 20–30% cost-saving benefit from trastuzumab biosimilars, attributing this benefit to increased competition in the USA markets. However, to date, limited pharmacoeconomic analyses of biosimilar use exists.

The introduction of biosimilars in oncology care offers the prospect of broader access to therapies, particularly for patients with limited financial means, such as lower ability to pay, and healthcare systems of low- and middle-income countries.[25] Biosimilar competition has also contributed to reductions in list prices, leading to an overall decline in pharmaceutical spending by as much as 5% across Europe.[45] In the field of oncology, depending on the system and product, price reductions of up to 12% have been observed.[45]

Pharmacoeconomic Evaluation of Biosimilars in Breast and Lung Cancer Therapy

Pharmacoeconomic evaluation plays an important role in evaluating breast and lung cancer treatments, given their high costs.[42,43] Consequently, the pharmacoeconomic evaluation of biosimilar utilisation within this context holds significant importance.

Despite only a few studies having delved into the RWE regarding the cost-effectiveness of biosimilars in breast and lung cancer, promising outcomes have been documented. Notably, a review analysis of average sales price data from the USA's Centers for Medicare & Medicaid Services identified a 15% lower entry price for biosimilars compared with their RPs in 2019.[46] This shift was also accompanied by a decrease in RP price, ultimately resulting in a 45,659 USD reduction in combined treatment costs for the trastuzumab biosimilar and RP in 2022, as compared with 2018.[46] This data shows that biosimilars may effectively decrease cancer treatment costs, and cut healthcare expenses.[46]

Other RWE examples of successful implementation of biosimilars have emerged from various medical centres. For instance, a medical centre in California, USA, saved over 4 million USD in 2 years, by implementing an organisational-wide switching to a standardised brand for bevacizumab and trastuzumab biosimilars, and reduced average costs by 23%.[47,48] Corresponding with this, a community-based oncology practice in Wisconsin, USA, experienced net savings of 285,252 USD and 274,360 USD by switching to bevacizumab and trastuzumab biosimilars, respectively.[49]

On a larger scale, a national network of over 100 clinics in Tennessee, USA, found that switching to bevacizumab and trastuzumab biosimilars

saved 4.4 million USD compared with RPs.[50] Such RWD demonstrates that it is possible to adopt biosimilars across a large oncology network, and achieve significant cost savings.[50] A budget impact analysis of the USA Medicare payer system estimated potential savings of 25 million USD over 5 years, with the switching of an RP to a bevacizumab biosimilar.[51]

The National Institute for Health and Care Excellence (NICE) in the UK identified that the weighted discount of biosimilar trastuzumab combined with pertuzumab for the adjuvant treatment of HER2+ EBC fell below the 20,000 GBP per quality-adjusted life-year threshold value.[52]

In a single centre in Spain, the adoption of a trastuzumab biosimilar for HER2+ EBC led to a reduction of 1,474 EUR per patient in treatment costs.[37] Similar findings were reported at the National Cancer Institute of Naples in Italy for trastuzumab biosimilars introduced for breast cancer, which resulted in a cost-saving of over 800,000 EUR within the first 2 years, and projected further savings over time.[53]

The cost-effectiveness of a trastuzumab biosimilar combined with pertuzumab was evaluated in a partitioned survival analysis by Cheng et al.,[54] carried out in the Singapore healthcare system in patients with HER2+ metastatic breast cancer. It identified an incremental cost-effectiveness ratio of 272,244 USD per quality-adjusted life-year gained.[54] Notably, the incremental cost-effectiveness ratio was still considered high and cost-effective, but the authors noted that the price reductions for pertuzumab would improve the overall cost-effectiveness.[54]

Similarly, the Spanish National Health System (SNS) demonstrated cost-effectiveness through a 3-year budget impact analysis with the introduction of bevacizumab biosimilars for cancer treatment.[55] This approach projected 52,361,778 EUR in savings by the third year, with an 80% share and a 13.6% cost reduction.[55] These findings extended to the specific indications of metastatic breast cancer and metastatic NSCLC, with per-treated patient-year differences of 6,624 EUR and 9,740 EUR, respectively.[55] The authors also concluded that the lower price of biosimilars has the greatest impact in indications such as metastatic NSCLC, where higher doses are required.[54] Further supporting these observations, economic modelling by McBride et al.[55] indicated the cost-effectiveness of trastuzumab biosimilars in metastatic breast cancer as both monotherapy and combination therapy with pertuzumab, compared to RPs.[56]

Chai et al.[57] provided a budget impact analysis from a Chinese healthcare payer perspective, estimating a saving of over 46 million USD over 5 years through the adoption of a trastuzumab biosimilar for patients with HER2+ breast cancer. Luo et al.[58] also assessed the cost-effectiveness of a bevacizumab biosimilar for first-line treatment combined with chemotherapy, in the Chinese healthcare system, for patients with advanced or recurrent non-squamous NSCLC.[58] The study identified a cost-effective strategy based on adjusted real-world dosages, and the incremental cost-effectiveness ratio of cost per quality-adjusted life-years.[58] Similarly, Leung et al.[59] demonstrated cost-effectiveness with combination regimens with trastuzumab biosimilars in Taiwan.[59]

The pharmacoeconomic evaluation and adoption of biosimilars in breast and lung cancer therapy hold considerable potential for cost savings, and expanded access to effective treatments. Despite residual uncertainties, and considerations surrounding biosimilar utilisation, a growing body of RWE underscores their substantial impact on healthcare economics and patient outcomes.

SOCIOECONOMIC IMPLICATIONS OF BIOSIMILARS AND THE ROLE IN ONCOLOGY CARE

Simoens and Vulto[60] argue that the introduction of biosimilars to the market, coupled with competitive pricing against alternative treatments, holds substantial promise in curtailing the costs associated with oncology care by offering a more economical option, and thus broadening treatment options for patients.[60] This potential for cost-effectiveness should play a pivotal role in influencing the reimbursement decisions and policy-making strategies of countries.[60]

This article reviewed the RWE of the application of biosimilars in the oncology field, specifically

focusing on breast and lung cancer. The recent evidence considered herein demonstrates that the cost of approved biosimilars compared with RPs indicates a favourable economic advantage, particularly in neoadjuvant breast cancer.[1] Notably, these studies suggest that biosimilars can be up to approximately 40% less expensive than their RPs. The identified data demonstrating cost reduction, alongside maintained safety and efficacy, can potentially free up resources for enhancing patient care. Furthermore, biosimilars can help broaden treatment options, ultimately improving options for both patients and prescribers.

It is important to note the global variability in economic factors and substitution policies, and incentives impacting the adoption and switching to biosimilars. The significance of pricing might differ across regions, with financial incentives that have driven biosimilar uptake in Europe, potentially also being effective in countries like China, as more biosimilars become available.[61] For example, a study of the National Community Oncology Network in China highlighted that a substantial cost saving was achieved through a pharmacist-driven biosimilar substitution programme, with significant cost savings noted for payers, patients, and providers.[62] However, non-medical switching requirements posed notable barriers to switching.[62]

However, Simoens and Vulto[60] outline several factors that impact the post-biologic patent expiry cost-effectiveness landscape, such as residual uncertainties surrounding biosimilars, switching and substitution practices, the potential nocebo effect, differences in administration forms, and value-added services.[60] At the forefront of biosimilar utilisation, many practitioners bear the responsibility of instilling confidence in other healthcare practitioners and their patients, who may be unfamiliar with the biosimilar concept. Addressing scepticism and facilitating an understanding of their integration as a viable treatment option is paramount. Healthcare practitioners should equip themselves with the knowledge and understanding of the steps required for their implementation.

Despite the growing utilisation of RWE, and the existence of data-rich clinical databases and registries, data heterogeneity exists among countries. The evidence is still small, and thus, ongoing comprehensive understanding of biosimilar uptake, switching trends, and economic implications is still of importance to accurately establishing the impact of biosimilars.[1] Discrepancies observed in real-world outcomes could potentially be attributed to non-pharmacological variables, such as patient demographics, timing, administration methodologies, and clinical settings.[11] This highlights the need for a harmonised approach globally. Looking forward, economic evaluations of oncology biosimilars are still in their early stages, with available evidence limited primarily to a handful of developed countries. The current RWE corroborates the cost-effectiveness, efficacy, and affordability of oncology biosimilars, such as bevacizumab and trastuzumab biosimilars, from the payer's perspective, while dependent on factors such as uptake rate and price discounts.[63] Efforts should continue to focus on expanding the evidence base to encompass more diverse datasets across the world, and also to consider the long-term cost-effectiveness of oncology biosimilars.[63] However, the potential for cost savings still remains substantial, subject to effective pricing regulation, and well-defined procurement policies for biosimilars.[57,60]

CONCLUSION

The integration of biosimilars into oncology care is a key strategy to mitigate the financial burden endured by both patients and healthcare systems. Supported by the RWE, cost-effective alternatives with biosimilars holds the potential for noteworthy savings, and improved accessibility across both breast and lung cancer treatments.

This review indicates the limited RWE concerning the cost-effectiveness of biosimilars with regards to breast and lung cancer treatment, emphasising the necessity for further coverage in various settings and geographical locations, to fully grasp the impact biosimilars have on the healthcare landscape. The majority of RWD studies exhibit relatively modest sample sizes, thereby underscoring the importance of further data encompassing larger cohorts and extended periods of analysis. Therefore, further pharmacoeconomic evaluation of biosimilars within breast and lung cancer is warranted.

In summary, pharmacoeconomics offers a pivotal perspective for steering the stakeholder's decision-making process surrounding the implementation of biosimilars. Biosimilars can enhance value, affordability, and patient access to oncology care, thereby inducing a shift within the broader market dynamics.[64] In the broader perspective, the transition towards utilising lower cost biosimilars can result in a notable reduction in the total cost of care, whilst maintaining the quality of care for those living with cancer.

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