Editorial

How do biosimilars sustain value, affordability and access to oncology care?

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1. Introduction

In order to sustain oncology care, biosimilars have been proposed as a cost-effective treatment option that may serve to improve affordability and access to therapy [1]. The particular interest in biosimilars derives from their reduced prices as a result of lower research and development costs and their potential to induce price competition with other products. In the area of oncology care, the European Medicines Agency has granted marketing authorisation to biosimilars that prevent or treat chemotherapy-associated adverse effects (i.e. five epoetin products, seven filgrastim products and seven pegfilgrastim products) or that treat different types of cancer (i.e. five trastuzumab products, six rituximab products and two bevacizumab products) by Spring 2020 [2]. This Editorial aims to discuss health economic aspects of each class of oncology biosimilars by means of a narrative overview of the current literature. The extent to which the economic benefits of oncology biosimilars will be captured in real-life practice depends on a plethora of factors, including regulatory procedures, government policies and incentives, and health care professional attitudes [3, 4].

2. Epoetin

Focusing on affordability and access to oncology care, a study calculated how the savings generated by supportive care biosimilars in oncology free up resources which

in turn can support access to therapeutic cancer treatments. When 100,000 cancer patients suffering from chemotherapy-associated anaemia were switched from reference to biosimilar erythropoiesis-stimulating agent in France, Germany, Italy, Spain and the United Kingdom, savings of €146 million allowed to treat an additional 12,913 patients suffering from diffuse large B-cell non-Hodgkin's lymphoma with rituximab; or 5,171 patients suffering from metastatic colorectal cancer with bevacizumab; or 4,908 patients suffering from metastatic HER2-positive breast cancer with trastuzumab [5].

3. Granulocyte colony-stimulating factor

When a biosimilar enters the market, there is a need to re-evaluate the value of therapy. Based on a literature review of economic evaluations of filgrastim, Cornes and Krendyukov argued that the value of filgrastim improved over its lifecycle as a result of more recent evidence supporting a significant increase in life expectancy with filgrastim and price reductions arising from biosimilar filgrastim market entry [6]. According to the authors, this improvement in value justified the addition of filgrastim to the World Health Organisation Model List of Essential Medicines.

4. Bevacizumab

There is evidence demonstrating that savings from introducing biosimilar bevacizumab can be substantial. An Italian comparison of drug costs found that the use of biosimilar versus reference bevacizumab would save €5,797 per patient suffering from metastatic colorectal cancer and €11,595 per patient suffering from advanced or metastatic renal

cell cancer [7]. However, this analysis did not consider discounts on reference bevacizumab and assumed that the price reduction of biosimilar versus reference bevacizumab would be limited to 20%.

5. Rituximab

Several studies quantified how biosimilar rituximab can contribute to affordability of and access to oncology care, considering its use in registered indications and off-label use. A budget impact analysis simulated the savings in drug costs from the third-party payer perspective generated by the market entry of biosimilar rituximab in the 28 countries of the European Union [8]. If biosimilar rituximab would be 30% less expensive than reference rituximab and if market uptake of biosimilar rituximab would be 30% and 50% respectively, one-year savings of €90-€150 million could be achieved, allowing an additional 7,531 patients (+6.4%) – 12,551 patients (+10.7%) to be treated with rituximab. Another study conducted a real-world budget impact analysis of switching 420 patients in a large Canadian university teaching hospital from reference to biosimilar rituximab [9]. Rituximab expenditure made up 7.7% of the hospital's annual pharmaceutical expenditure, 0.8% of which could be saved by switching patients to a biosimilar rituximab that is 10% cheaper than the reference product.

How are savings from biosimilar rituximab used? One approach is to implement a gainsharing arrangement and share biosimilar savings among stakeholders. This approach was followed by the Greater Manchester Medicines Management Group in the United Kingdom, which distributed savings equally between the clinical

commissioning groups and the hospital trusts [10]. Trusts can use those savings, for example, to employ additional staff who are involved in switching patients from the reference product to a biosimilar.

6. Trastuzumab

Biosimilar market entry improves the value of oncology care as exemplified by a literature review focusing on the use of intravenous trastuzumab as first-line treatment in metastatic breast cancer [11]. The authors identified four relevant economic evaluations and re-calculated the incremental cost-effectiveness ratios under the assumption that biosimilar trastuzumab would enter the market at a 30% price discount. As a result, the use of trastuzumab in metastatic breast cancer became more valuable and the authors argued that biosimilar trastuzumab would turn out to be cost-effective in the one of the four economic evaluations which found reference trastuzumab not to be cost-effective.

When focusing on intravenous trastuzumab, the 28 countries of the European Union can attain significant savings from introducing a biosimilar in the treatment of breast cancer and gastric cancer. Based on a number of assumptions (biosimilar trastuzumab is 30% less expensive than reference trastuzumab, switch rate from reference to biosimilar trastuzumab is 20% and increases by 5% in each following year), a budget impact analysis found that total savings over a five-year period amounted to €910-€1,134 million [12]. These savings could serve to increase access to biosimilar trastuzumab treatment by 55,082-58,104 patients.

In contrast to other budget impact analyses that draw on official drug prices, a Greek analysis accounted for rebates and clawbacks [13]. This study calculated the budget impact of three biosimilar trastuzumab products for new patients eligible for biologic therapy over a five-year time horizon. When applying official drug prices (net of a mandatory discount of the hospital price by 5%), mean annual savings arising from the use of biosimilar trastuzumab amounted to 5.18% of the budget associated with a market where only reference trastuzumab is available. When considering rebates and clawbacks, mean annual savings increased to 9.01%.

Such budget impact analyses focusing on intravenous trastuzumab do not consider all market dynamics, given that intravenous biosimilar trastuzumab is introduced in the presence of intravenous and subcutaneous formulations of reference trastuzumab. Therefore, an Italian cost comparison considered not only drug costs, but also administration costs and costs related to consumables and pharmacist time over a 17-cycle period from the hospital perspective [14]. Overall costs amounted to €8,499 per patient with intravenous biosimilar trastuzumab and €17,929 with subcutaneous reference trastuzumab. This cost difference largely originated from the difference in drug costs. Hence, this specific study suggests that if the price reduction of biosimilar as compared to reference trastuzumab is large enough, it may compensate for the higher costs related to consumables and pharmacist time of the intravenous as compared to the subcutaneous formulation.

Other variables that need to be taken into account are the vial size and drug wastage, and the dosing regimen (i.e. body-weight adjusted dose for the intravenous formulation and fixed dose for the subcutaneous formulation). For instance, an Italian cost

comparison indicated that the savings per patient from using intravenous biosimilar trastuzumab instead of subcutaneous reference trastuzumab increased when vial sharing was allowed [15]. Intravenous biosimilar trastuzumab was the cheapest therapy in patients with a weight below a certain threshold.

Finally, a study carried out a budget impact analysis from the National Health Service perspective of introducing intravenous biosimilars in the UK market where the reference product is available as an intravenous and a subcutaneous formulation [16]. The analysis focused specifically on rituximab and trastuzumab. The use of intravenous biosimilars as compared to subcutaneous reference products was associated with higher administration costs but lower drug costs, resulting in overall savings. Also, from a hospital perspective, the increased reimbursement associated with intravenous formulations exceeded higher administration costs.

7. Expert opinion

The above examples of cost comparisons, budget impact analyses and economic evaluations have shown that biosimilars can contribute to value, affordability and patient access to oncology care. Although the first oncology biosimilar received marketing authorisation from the European Medicines Agency in 2007 (i.e. biosimilar epoetin), the health economic evidence related to oncology biosimilars today is still limited and consists of a few peer-reviewed papers and conference abstracts. As a result, details of the methodologies used in these studies are scarce.

This editorial concludes with setting out a research agenda of the key health economic aspects of oncology biosimilars that require further investigation. First, future budget impact analyses need to draw on real-world data in general and need to consider reference product and biosimilar rebates in particular, with a view to provide a valid estimate of the budget impact of introducing oncology biosimilars. Second, in the presence of intravenous and subcutaneous formulations of some reference biologics, it is imperative that health economic studies assess all relevant market dynamics. Existing studies have attempted to weigh up the lower drug costs of intravenous biosimilars against the lower administration costs of subcutaneous reference products. However, this body of evidence fails to capture all cost implications of intravenous vs subcutaneous formulations (e.g. costs of nurse time, use in treatment regimen including intravenous chemotherapy, transport costs and productivity loss associated with administration in hospital or at home). Also, patient preferences and possible impact on quality of life are not accounted for. Third, there is a need to analyse the design and impact of gainsharing arrangements as a tool to deliver the benefits of oncology biosimilars.

In conclusion, although biosimilars represent a promising avenue to sustain oncology care, much more health economic research needs to be carried out to fully assess their potential.

Declaration of interest

SS is one of the founders of the KU Leuven Fund on Market Analysis of Biologics and Biosimilars following Loss of Exclusivity (MABEL). SS was involved in a stakeholder roundtable on biologics and biosimilars sponsored by Amgen, Pfizer and MSD; he has participated in advisory board meetings for Pfizer and Amgen; he has contributed to studies on biologics and biosimilars for Hospira, Celltrion, Mundipharma and Pfizer; and he had speaking engagements for Amgen, Celltrion and Sandoz. SS is a member of the leadership team of the ISPOR Special Interest Group on Biosimilars.

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