ISSN NO: 2770-0003
Date of Publication: 15-04-2022

# Biosimilar in Oncology

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**Abstract:** Biosimilar medicines are biologic treatments that are clinically equivalent to a previously approved reference biological product in terms of quality, efficacy, safety, and immunogenicity, and have the potential to lower biologic costs. Given the growing number of oncology biosimilars, it is critical to quantify the economic impact of biosimilars in oncology, using trastuzumab and rituximab as examples, which have the highest budgetary impact in Oncology Units, respectively. Biologics are important in cancer treatment not only because of their therapeutic effects and ability to improve outcomes, but also because they are supportive care agents. These are more difficult to make and take longer to get to market. Because biologics are much more expensive than small-molecule medications, their usage has put a growing economic strain on healthcare systems around the world. Biosimilars are intended to be substantially similar to existing branded biologics, but because biologics cannot be precisely duplicated, they should not be referred to as generic, exact copies of the originator biologic. As patent protection for some of the most extensively used biologics begins to expire, biosimilars have the potential to enhance access and give lower-cost options for cancer treatment.

## Introduction:

Biologics have become a critical component of cancer treatment.[1] As a result, biologics are currently included in the therapy regimens suggested by major oncology guidance publications. When compared to chemotherapy alone, monoclonal antibodies like bevacizumab and trastuzumab have proven to enhance critical outcomes including progression-free survival (PFS) and overall survival (OS).[2] Unlike cytotoxic chemotherapeutics, biologics have enabled for more precise and targeted cancer treatment. Bevacizumab, for example, is designed to block the human epidermal growth factor 2 (HER2) receptor while trastuzumab is designed to target vascular endothelial growth factor.[3,4] Recombinant biologic agents are proteins or peptides generated from DNA that are typically identical to endogenous hormones, cytokines, or antibodies.[5] Biosimilars are biological medications that contain a highly similar version of an already approved biologic's active component, often known as the reference product.[6]

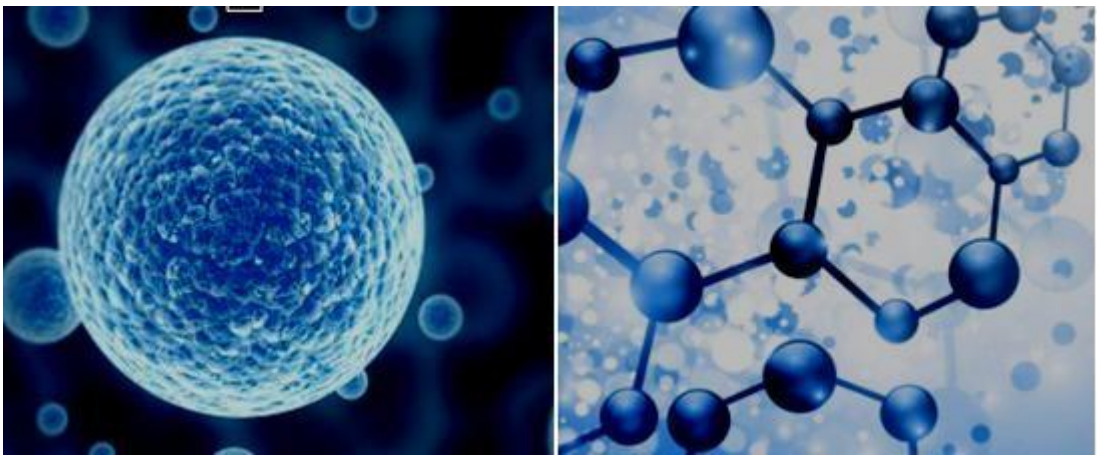

Fig ;1 Oncology biosimilars and biosimilar development

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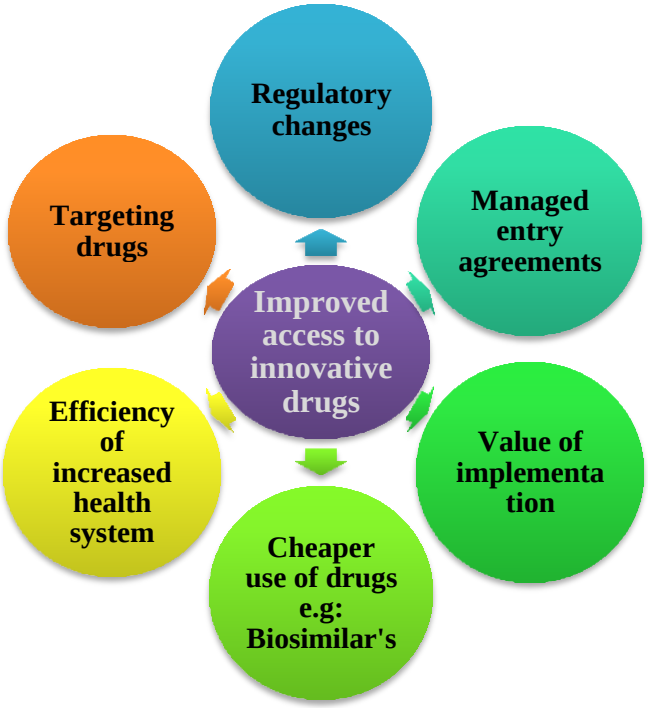
**The Evolving Regulatory Framework GuidingPrinciples for Biosimilarity:**

The European Medicines Agency (EMA) was the first to establish broad recommendations for biosimilar development and licencing, and the World Health Organization (WHO) has created a regulatory framework that can be tailored to meet the needs of other nations. The general ideas indicated in these guidance materials, as well as current draught FDA guidelines, will very certainly impact the development of regulatory paths for biosimilar development and approval in the United States and elsewhere. President Barack Obama signed the Patient Protection and Affordable Care Act into law on March 23, 2010, amending the Public Health Service (PHS) Act to create a separate, expedited licensure process for biological products that are "biosimilar" to or "interchangeable" with an FDA-licensed biological product.[7,8] The overall goal of biosimilar development should be to demonstrate adequate enough similarity in chemical composition, biologic activity, and pharmacokinetics so that existing efficacy and safety data for the reference biologic can be used, rather than to replicate the existing efficacy and safety data package for a reference biologic, which would be a huge waste of patient and public resources.[9] Because of these qualities, when a manufacturing method is changed, the producer must demonstrate that themodification does not result in clinically substantial changes in the product's efficacy or safety.




Fig;2 potential source to sustain cancer

**Oncology Practise Using Biosimilars:**

Previous research on biosimilars identified a number of concerns about their use in clinical practise. Because biosimilar agents have now been licenced in the EU, these issues can be examined more thoroughly using publicly available data and regulatory documentation. Other articles have looked at the issues surrounding the launch of the first biosimilar ESAs. We'd liketo focus on biosimilars in oncology, where they're used as supportive therapy for immunosuppressed patients receiving multiple cycles of cytotoxic therapy, or for healthy stem cell donors who don't receive any direct therapeutic benefit from treatment. Oncologists shouldbe aware that the words "biosimilar," "similar biotherapeutic product," "subsequent entry biologic," and "follow-on biologic product" all refer to the same product. Extrapolation, substitution, labelling, traceability, safety, and immunogenicity are all essential properties of these items. We'll go through these critical points for each biosimilar product in detail in the sections that follow. [10]

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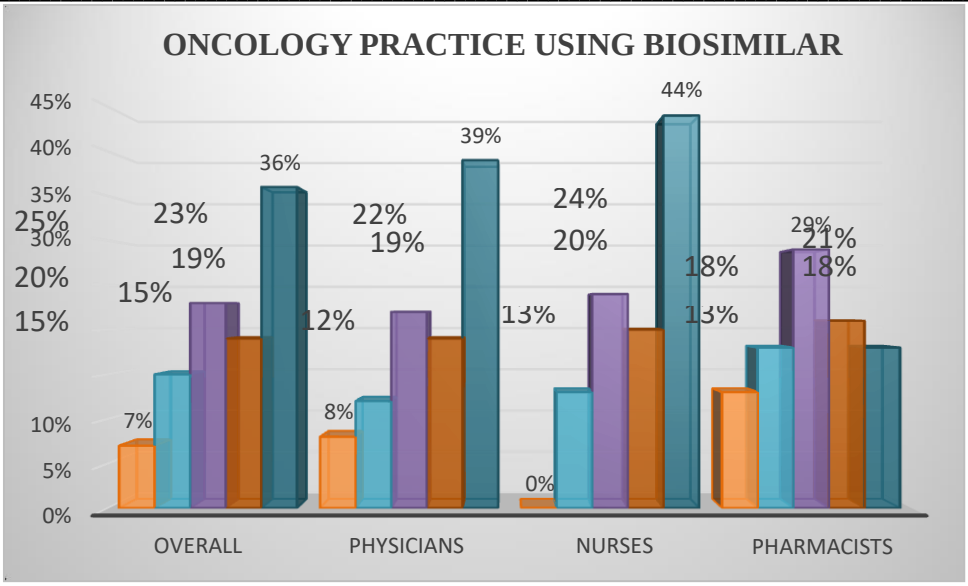


Fig; 3 oncology practice using biosimilar

## Immunogenicity And Safety:

Immunogenicity is the most severe safety concern with in all monoclonal antibodies. Many, but not all, potential immunogenic reactions are detected by analytical tests and clinical trials,therefore postmarketing obligations and pharmacovigilance are essential.( 11)Biosimilar ESAs in oncology include extra postmarketing studies in their risk-management strategy to address safety issues such as pure red cell aplasia, thrombotic vascular events, and tumour development potential, as well as to monitor possible off-label subcutaneous use in renal anaemia patients.(12) Because a potential higher risk of immunogenicity in individuals treated with PLD108 cannot be ruled out (a small number of patients treated with PLD108 had G-CSF antibodies), the proposed risk-management strategy includes plans for targeted questionnaire follow-up of potential immunogenicity in addition to routine pharmacovigilance.(13)

## What is the Significance of Biosimilars in Oncology?

**Biosimilars' potential advantages:**

Biologics have become key components of the standard of treatment for cancer patients because they can be very effective, potentially life-saving therapies for a variety of illnesses.(14) Cancer is a significant financial burden for patients and health-care systems, costing countries billions of dollars annually.(15) Biologics have a higher price tag than small-molecule medicines, which can contribute significantly to the escalating expense of cancer treatment.Biologics may be rationed,withheld until later stages of sickness, or discontinued due to their high cost and restricted availability.Only the most serious situations are considered, limiting patient access to the best possible care.(16) Biosimilars have the potential to reduce cancer treatment costs while also expanding patient access to biologic medicines.When compared to their reference biologics, biosimilars have reduced development and production costs. As a result, biosimilars might cost up to 30% less than the reference biologic . Biosimilars have the ability to also lower biologics costs by increasing pricing competition into the market Lowering prices could help you save money boost patient access to biologics and reduce the financial burden of cancer on both patients and health-care systems therapies. This has been proved in the EU, where payers and providers have benefited from the availability of biosimilars.Restrictions on the use of biologic therapy are being eased by health-care officials .(17)

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**Biosimilar in the treatment of cancer:**

The first biosimilars to hit the market were oncology supportive care treatments, which were approved in the EU over a decade ago. Filgrastim (NeupogenR; Amgen Inc, CA, USA) is a physiologically active version of the cytokine granulocyte colony-stimulating factor that has been licenced for the treatment of febrile neutropenia in at-risk chemotherapy patients[18].The EMA approved the first filgrastim biosimilars (TevagrastimR; TEVA GmbH, Ulm, Germany and RatiograstimR; Ratiopharm GmbH, Ulm, Germany) in 2008, and by 2014, seven biosimilars of filgrastim were available in the EU after comparative clinical trials confirmed their efficacy and safety profiles were similar to the originator filgrastim . Filgrastim biosimilars accounted for the vast bulk of filgrastim use in the European Union by 2015 Biosimilars for the long-acting version of filgrastim, pegfilgrastim (NeulastaR; Amgen Inc), are also available, and as of February 2020, 13 filgrastim or pegfilgrastim biosimilars have been approved in the EU and/or the US.[19] Filgrastim biosimilars have offered evidence of the biosimilar development and approval process's reliability due to their comparatively long tenure on the market. In the real world, several postmarketing trials have shown that filgrastim biosimilars have the same efficacy as the original filgrastim in treating febrile neutropenia during chemotherapy. Furthermore, the availability of these biosimilars has reduced the cost of granulocyte colony-stimulating factor therapy and enhanced patient access to it[20] . Biosimilars accounted for more than 80% of filgrastim use in Sweden by 2013, and daily filgrastim use climbed up to fivefold compared to before biosimilars were available.

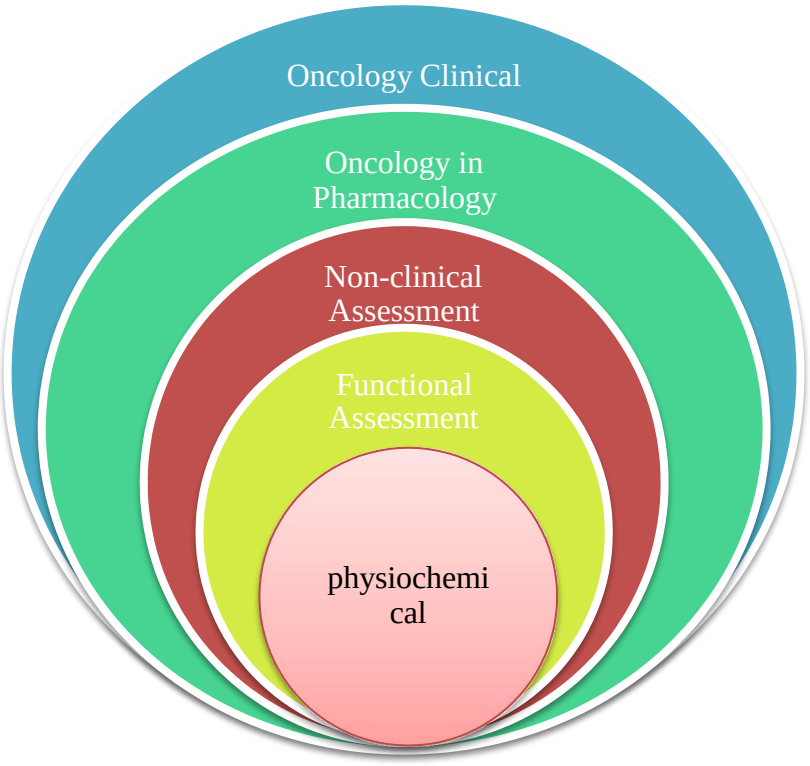


Fig.4. Assessment of Biosimilarity in a Step-by-Step Manner

**Biosimilars Report on Oncology:**

Because of the high cost of pharmaceuticals in the United States, particularly biologic medicines, biosimilar treatments have been developed to give market competition and, if widely adopted, cost savings. Biosimilars may make it easier for patients to have access to effective biologic medicines. However, there are numerous impediments to biosimilar adoption, including physician awareness, perceptions, and preferences, as well as commercial payer awareness, perceptions, and preferences.[21]) The American Society of Clinical Oncology (ASCO) recognises the importance of biosimilars in oncology therapy and applauds efforts to

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hasten their safe and widespread adoption. ASCO also understands the obstacles that must be overcome in order to reduce the cost of biologic medications, which is one of the fastest-growing categories of pharma spending.[22]

**In Biosimilar Development, Regulatory Considerations:Endpoint of the Comparability Trial:**

When it comes to evaluating new cancer medicines, os has long been regarded the "goldstandard," especially by regulatory agencies. When it comes to comparability, survival endpoints may not be sensitive enough (such as in the case of biosimilar agents). It's also possible that the sample size needed for proper statistical inference would be unreasonably high.[23]) In 2015, Jackisch et al. assessed the sensitivity of outcomes for both mbca and ebc in trastuzumab and biosimilar agent similarity studies. They used or and pfs data from a meta-analysis of data from trastuzumab clinical trials for mbca and total pcr, as well as event-free survival (efs) in the neoadjuvant setting. They discovered that utilising the shorter-term endpoint of orr to determine equivalency could lead to significant disparities in long-term pfs, despite previous studies suggesting tumour response as a potential proxy for pfs in mbca.[24]

**Pharmacovigilance And Safety Surveillance:**

Clinical testing prior to biosimilar approval may not reveal all probable related side events, as it does with most biologics. Clinical safety assessment for as a result, biosimilars should be continued once marketing begins. All biologics manufacturers, including those who make biosimilars, are required to file pharmacovigilance reports.As part of the marketing permission application, you must submit plans.[25] A pharmacovigilance plan's purpose is to discover and analyse the frequency and nature of product-related adverse events that may not have been noticed during clinical testing, as well as to offer a structure for reporting and managing such incidents quickly,Because the entire spectrum of trastuzumab's mechanisms of action is yet unclear, post-authorization immunogenicity testing is critical for trastuzumab biosimilars' pharmacovigilance plan.[26] The ema has taken a different approach, advising biosimilars to extract the summary of product features for the label from the reference product, just as generic pharmaceuticals.

**Conclusion:**

Biosimilar medicines are biologic treatments that are clinically equivalent to a previously approved reference biological product in terms of quality, efficacy, safety, and immunogenicity, and have the potential to lower biologic costs. Given the growing number of oncology biosimilars, it is critical to quantify the economic impact of biosimilars in oncology, using trastuzumab and rituximab as examples, which have the highest budgetary impact in Oncology Units, respectively. Because certain biosimilar agents have already been assigned the same INN as their reference product, the first step is to accurately name the product class and, in particular, the individual product. In addition, especially in mobilisation procedures, extrapolation of indications leading to authorization plays a significant role. The product given (innovator or biosimilar) should then be defined and utilised during the entire treatment, which typically entails numerous cycles of therapy. Biosimilars in cancer and haematology Niederwieser and Schmitz 284 2011 John Wiley & Sons A/S.

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