Egyptian Drug Authority
Pharmaceutical care Sector
Hospital Pharmacy General Administration

OncoCare
Biosimilars

WHAT ARE BIOSIMILARS?

A ***Biosimilar*** is defined by the USA Food and Drug Administration (**FDA**) as a biological product that is highly similar to and has no clinically meaningful differences in terms of safety, purity and potency from an existing FDA -approved product which is called ***Reference Product.***

Biosimilars Overview:

Biologics have been used increasingly in the treatment and supportive care of cancer; however, their high cost places a significant burden on healthcare systems.

- The expiration of patents for biologics has led to the development of biosimilars, with the aim of reducing cost and increasing accessibility to novel treatments, which are affordable for a greater number of patients.
- There are many types of biological products approved for use in the United States, including therapeutic proteins (such as ***Filgrastim***), monoclonal antibodies (such as ***Adalimumab***), and vaccines (such as those for **influenza and tetanus**).

Newsletter, August 2020
Volume 1, Issue 2

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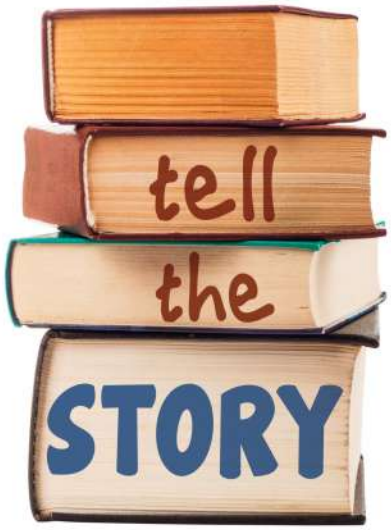
REFERENCE BIOLOGICS VS BIOSIMILARS



HISTORY OF BIOSIMILARS

- The European Union established a legal framework for the approval of biosimilars in 2003.
- In 2005, the European Medicines Agency (EMA) guidelines came into force and the first biosimilar, **Omnitrope® (Sandoz, Kundl, Austria)** was approved in Europe in 2006.
- In the United States, the first biosimilar was approved in 2015

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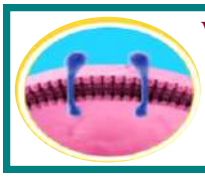
هيئة الدواء المصرية
قطاع الرعاية الصيدلية
الإدارة العامة لصيدلة المستشفيات

BIOSIMILARS & GENERICS

Item	Biosimilar	Generic
Source	Living organisms	Chemical synthesis
Size	Large molecule	Small molecule
Structure	Complex, Heterogeneous	Well defined
Manufacturing process	Difficult	Relatively Simple
Stability	Unstable, Sensitive to external conditions	Stable
Immunogenicity	Immunogenic	Non Immunogenic
Bio-equivalence	Similar	Bioequivalent
Interchangeable with reference product	No	yes
Time for marketing approval	7-8 years	2-3 years
Preclinical studies	Required	Not required, only bioequivalence
Cost	High	Low

BIOSIMILARS IN PRACTICE

TRASTUZUMAB



WHAT IS TRASTUZUMAB?

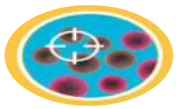
Is a humanized monoclonal antibody that targets the HER2 protein.

PRIOR TO TRASTUZUMAB

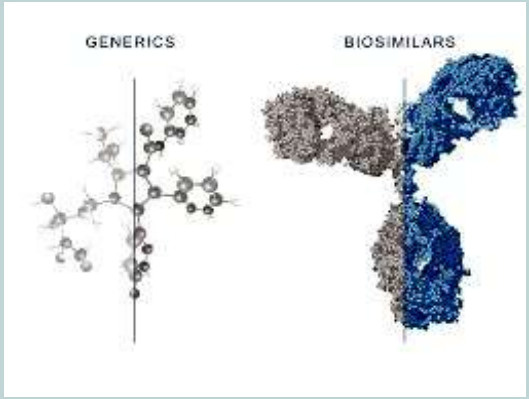
Women with HER2-positive breast cancer had few treatment options and progressed rapidly.

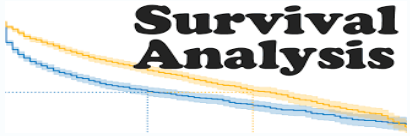
HOW DOES TRASTUZUMAB WORK?

Trastuzumab blocks the activity of HER2, which plays an important role in the control of cell growth



By targeting only cancereous cells, Trastuzumab avoids harming healthy cells.





The introduction of trastuzumab in previously untreated patients with meta-static disease resulted in a **4.8** -month increase in median overall survival (OS)

December 2017
Ogivri

December 2018
Herzuma

January 2019
Ontruzant

March 2019
Trazimera

2020 (Egypt)
Hertaz

ECONOMIC EFFECT

The introduction of trastuzumab biosimilars will be accompanied by the expectation of cost savings, although, with a projected discount of approximately 20% to 30%.

- The discovery of the HER2 proto-oncogene and the development of the HER2-targeted antibody trastuzumab (Herceptin, Genentech) more than two decades ago represent landmark achievements in the treatment of breast cancer.
- Between 15% and 20% of patients with breast cancer have HER2-positive (HER2þ) disease

RECONSTITUTION, STORAGE AND STABILITY

Reconstitution	♦ Reconstitute each 420 mg vial (multidose vial) with 20 mL of bacteriostatic sterile water for injection (SWFI may be used if a patient has a known hypersensitivity to benzyl alcohol). ♦ Direct the stream of diluent into the lyophilized powder (which has a cake-like appearance). The reconstituted solutions (in the vial) will have a concentration of 21 mg/mL Swirl vial gently to mix; do not shake. Slight foaming may occur during reconstitution. ♦ Allow vial to rest undisturbed for ~5 minutes. Prior to administration, further dilute the appropriate volume for the trastuzumab dose in polyvinylchloride or polyethylene bags containing 250 mL NS; do not use D5W. Gently invert bag to mix; do not shake. Do not mix trastuzumab products with other medications.
Storage & Stability	♦ A vial of Trastuzumab reconstituted with BWFI, as supplied, is stable for 28 days after reconstitution when stored refrigerated at 2–8°C . ♦ Discard any remaining multi-dose reconstituted solution after 28 days. ♦ The solution of Trastuzumab for infusion diluted with 0.9% Sodium Chloride solution, should be stored at 2–8°C for no more than 24 hours prior to use.

ADMINISTRATION: IV

- Administered by IV infusion;
  - √ Loading doses are infused over 90 minutes;
  - √ Maintenance doses may be infused over 30 minutes if tolerated.
  - √ Do not administer with D5W. Do not administer IV push or by rapid bolus. Do not mix with any other medications.
- Observe patients closely during the infusion for fever, chills, or other infusion-related symptoms.
- Treatment with acetaminophen, diphenhydramine, and/or meperidine is usually effective for managing infusion-related events.

INFUSION-RELATED EVENTS

Infusion-related Event	Management
Mild-moderate infusion reactions	Decrease infusion rate
Dyspnea or clinically significant hypotension	Interrupt infusion
Severe or life-threatening infusion reactions:	Discontinue trastuzumab

BASELINE RISK FACTORS FOR TRASTUZUMAB-INDUCED CARDIOTOXICITY

Age > 65 years

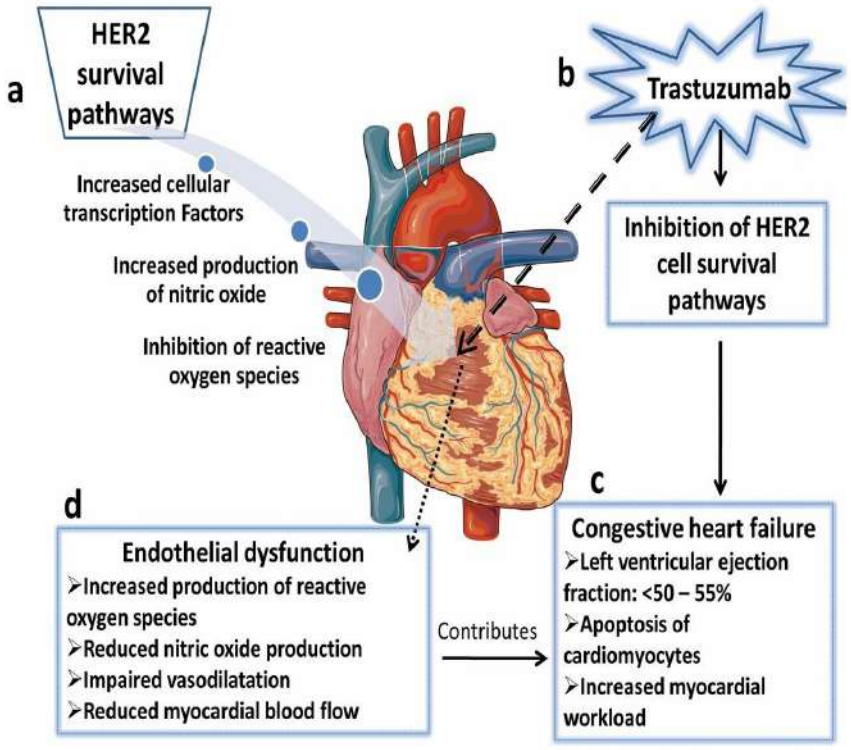
BMI > 30 Kg/m^2

Hypertension

Previous or concomitant anthracy-cline use

Previous left ventricle dysfunction

Previous radiation therapy



PATIENT COUNSELING TIPS: TRASTUZUMAB

1-Check Heart & Lung Conditions.

-Assessment of left ventricular ejection fraction prior to initiation and at regular intervals during treatment must be carried out.

- Ask patient if already had finished or still taking a regimen of ***anthracycline drugs***.

- Monitor for signs/symptoms of interstitial lung disease/pneumonitis.

The Tip:

" Undergo heart functions tests while you are taking it"

2-Fetal Infusion Reactions:

- Most reactions occur during or within 24 hours of the first infusion

"Stop infusion at once if anaphylaxis or hypotension occur".

3- For female patients:

" Pregnancy tests must be carried out before starting using it"

" Use birth control while taking it and continue until seven months after stopping the drug"

- Can result in embryo-fetal harm i.e.: pulmonary hypoplasia, skeletal malformations, and neonatal death.

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10. Winning with biosimilars Opportunities in global markets.