Biosimilars: Myth or Fact?

RT Whiteman, PharmD
Pharmacy Practice Resident
St. Luke's Boise Medical Center

Objectives

By the end of the presentation, the audience will be able to:

- Explain the differences in complexity for biologic and non-biologic medications
- State length of market exclusivity granted to biologic medications
- Explain the criteria for a biologic medication to be granted approval to be marketed as a biosimilar

Do we answer these questions the same way?

- A physician calls the pharmacist, saying "I heard there is a 'generic' version of Cymbalta® being released. Is it going to be the same thing as the brand product?"
- A physician calls the pharmacist, saying "I heard there is a 'generic' version of Remicade® being released. Is it going to be the same thing as the brand product?"

The Scene for Debate

- Brand vs. Generic Drugs
  - Hatch-Waxman Act
    - Small molecule drugs only
- Biologic Drugs
  - Different problems
  - Development
  - Production

Synonym Bank

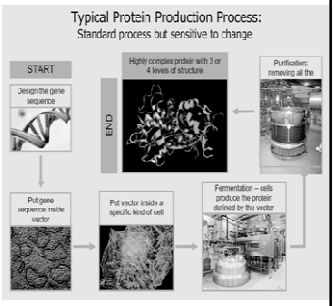
- Biosimilars
- Follow-on biologics
- Subsequent entry biologics (Can)
- Similar biological medicinal products
- Biogenerics
- Generic biopharmaceuticals
- Comparable biologics

Biopharmaceuticals

- In general
  - Proteins
  - Derived from living organisms
    - Bacteria, yeast, mammalian cells
    - Complex manufacturing process
  - Usually given IV or subcutaneously
  - Treat complex conditions

Biopharmaceutical

- Genetic material integrated into organism
- Organism makes protein from DNA
- Protein folded / modified
- Protein extracted by manufacturer
- Many copies are made
- Copies sealed in vials
- Drug sold for minimal fee



AMGEN

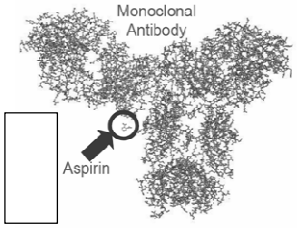
- AMGEN Biopharmaceutical Development

Biotechnology

- Advantages
  - Targeted therapy
    - Possibly alter disease course
      - Cancer therapeutics
      - Immune conditions
  - Efficacy
    - May be more effective than many non-biologic

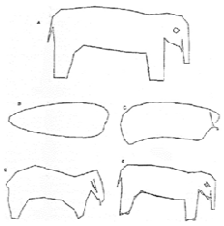
Size Matters

- Proteins vs. Chemicals
  - Proteins larger, more complex
- Molecular Weights
  - Aspirin 180 D
  - Enoxaparin 4500 D
  - Rituximab 145 kD



Challenges for Biosimilars

- Limitations to what can be studied
  - Ethics
  - Innovation



Challenges for Biosimilars

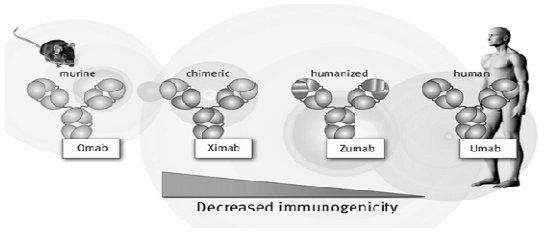
- Product Variability
  - Within reference products
  - Among biosimilars
- Bio-identical?
  - Key point in debate

Challenges for Biosimlars

Immunogenicity

- Immune recognition of biologics
  - Drug deactivation
    - Treatment failure
  - Immune response
- Causes of immunogenicity
  - Multi-factorial
    - Product variability
    - Medication aggregation
    - Immune suppression

Immunogenicity



Bexxar (Tositumomab) Remicade (infliximab) Avastin (Bevacizumab) Simponi (golimumab)

Challenges for Biosimilars

- Cost Savings
  - Development
    - $2-3 million vs. $75-250 million
  - Manufacturing
    - Much more expensive
  - Competition
    - Need competitors
  - How much can we save?

Legislative Background

- Hatch – Waxman Act
  - Generic drug approval
    - Abbreviated New Drug Application (ANDA)
    - Period of exclusivity

"Do a double-blind test. Give the new drug to rich patients and a placebo to the poor. No sense getting their hopes up. They couldn't afford it even if it works."

Legislative Background

- 505(b)(2)
  - Amendment to Hatch-Waxman
  - Hybrid between ANDA and NDA
    - Small changes in parent product
  - Safety / efficacy in humans
  - Examples:
    - Follistem®, Glucagen®, Omnitrope™

The European Way

- European Medicines Agency
  - Biosimilar pathway approved in 2005
  - Addressed biosimilars specifically
  - Approved products
    - 14 drugs based on 3 reference products
    - 1 product rejected by EMA
    - 3 products company withdrawn
    - Quite limited!

Affordable Care Act

Biologics Price Competition and Innovation Act (BPCI)

- Biosimilars may enter market
  - Competition / Innovation?
    - No "tracing" the elephant
  - 12 years of *exclusivity* for reference product
    - Several important drugs to lose patent in the next few years
      - Lantus®, Humalog®, Humira®, Neupogen®

BPCI

- Requirements to demonstrate biosimlarity:
  - Work the same
  - Already approved for a condition
  - Same strength, route, dosage form
  - Chemically the same
    - Minor differences allowed

BCPI

- To demonstrate biosimilarity
  - Analyzed in a laboratory
  - Assessed in animals
  - At least one study in humans
    - Approved condition
    - Shows physiologic similarity, lack of immunogenicity
  - FDA has discretion to determine how necessary these elements are

Interchangeability

- Per BCPI
  - May substitute **without** authorizing provider
  - Somewhat controversial
- Colorado State Law
  - Requiring Rph to notify prescriber of substitution
    - Made an international splash

Biosimilars - Conclusion

- Large, complex, protein medications based on a reference product
  - Complex and expensive production / manufacturing process
- May enter market after reference product has 12 years of exclusivity
- Designed to be interchangeable with reference product
  - May be less expensive

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