EXTENDING THE USE OF BIOSIMILAR DRUGS: ARE WE WILLING TO ACCEPT THE UNCERTAINTY RELATED TO SWITCHING IN ORDER TO IMPROVE PATIENT ACCESS TO MODERN MEDICINES?

Perspective of a researcher

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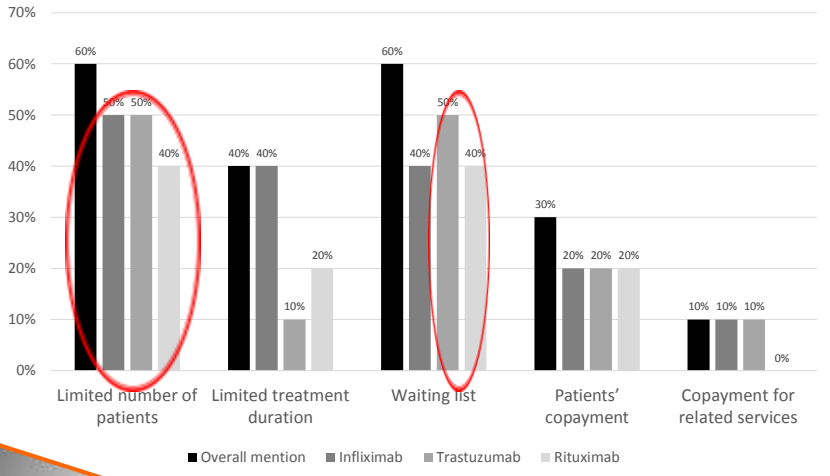
Environment

- Many of modern treatments are biological medicines, whose patent are about to expire in the near future
- Price of modern biologic medicines are adjusted to high income countries
- Cost of health services are adjusted to local purchasing power and salaries -> limited cost saving potential for pharmaceuticals in CEE
- Even a drug is cost effective in high income countries, it may not be cost effective in CEE
- Higher unmet medical need and more limited healthcare resources
- Still, many of these drugs are reimbursed in CEE (political reasons?)
- To maintain financial sustainability, various types of access limits have been introduced in CEE countries

Access limits in 10 CEE countries: waiting list, limited number of treated patients

**result of a policy survey in 10 CEE countries*

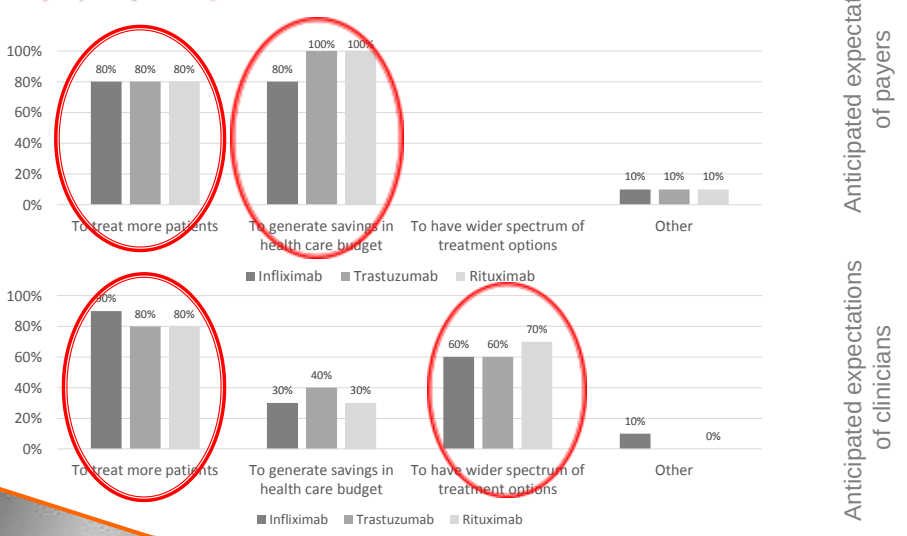


TODAY'S RESEARCH FOR TOMORROW'S HEALTH

Reference: Inotai et al. Mapping of the biosimilar drug policy in 10 CEE countries. Abstract accepted for ISPOR Vienna 2016

Anticipated Expectations of using biosimilars in 10 CEE countries: treat more patients

**result of a policy survey in 10 CEE countries*



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Why extended use of biosimilars is not an obvious solution for policy-makers?

- Biosimilars offer therapeutic alternative with original biologics at reduced drug price for *de novo* patients
- In maintenance care, as opposed to generic drugs, biosimilars are not identical to their originators
- Switch/substituting from original to biosimilar is thus not an obvious option for clinicians and decision makers, mainly due to fear of
  - adverse events
  - reduced therapeutic effect
- Concern is based on very few number of highly cited studies
  - immunogenicity - PRCA among erythropoietin users in early 2000s (Bennett 2004) (modification of the manufacturing process)
  - reduced therapeutic effect – Haemophilia, Factor VIII in late 90s (Bacon 2011)

Trade-off: use or not to use biosimilars?

- **Societal loss from unrealized cost-savings**
  - biosimilars must be cheaper than original biological drugs
  - price erosion through reference pricing system
- **Fear from limited information on therapeutic equivalence**
  - different efficacy: EMA mandates confirmatory evidence in one indication
  - frequent switch may reduce therapeutic effect (see haemophilia: Factor VIII) and induce non-adherence / non-persistence
  - Increased risk of adverse events: immunogenicity

Certainty	**Uncertainty**
Key stakeholders: payers (generic manufacturers)	Key stakeholders: innovative manufacturers; clinical KOLs; pharmacologists; regulators

Biosimilar switch - Trade off?

- If savings generated from switching from original biological drugs to biosimilar offset the risk, even it is conservatively overestimated, from societal perspective, switch is the appropriate decision
- However, automatic substitution among biosimilars cannot be justified
- Potential negative consequences should be monitored by surveillance system.

How to handle uncertainty related to switching?

How to handle uncertainty I: evidence from systematic review

- Systematic literature review on consequences of switching (153+68+9 hits) included papers: 58
- Non-empirical evidence (41) (no original clinical data reported)
  - 32 mentioned hypothetical risk for switching to biosimilars, but mainly without any empirical justification
- Systematic literature reviews (5)
  - None of the reviews opposed switching to biosimilars
  - Three systematic reviews argued explicitly that switching to biosimilars was not associated with increased risk, while efficacy was maintained
- Empirical evidence (12) (original clinical trials)
  - Covering a total of 1096 switcher patients
  - 2 trials reported explicitly that there were no adverse events or loss of efficacy
  - 10 trials concluded that overall there was no increased risk while efficacy was maintained

Reference: Inotai et al. Real concern or just a hype? – evidence on negative clinical consequences of switching from original to biosimilar based on a systematic literature review. Abstract accepted for ISPOR Vienna 2016

Potential benefit of biosimilars

(by assuming therapeutical equivalence of biosimilar and original)

	biological drug is reimbursed without volume cap	biological drug is reimbursed with volume cap or with high copayment	biological drug is not reimbursed
new patients	• savings in drug budget	• Improved patient access → health gain	• health gain (vs. older treatment) with cost increase
patients on maintenance drug therapy	• savings in drug budget • potential immunogenicity risk of switch	• patients with no access: Improved patient access → health gain • patient with access: cost-savings & potential immunogenicity risk of switch	• health gain (vs. older treatment) with cost increase

Potential benefit of biosimilars

(by assuming therapeutical equivalence of biosimilar and original)

- Cost minimisation (CMA): compares 2 alternatives only in terms of cost, as their outcomes are found identical

	biological drug is reimbursed without volume cap	biological drug is reimbursed with volume cap or with high copayment	biological drug is not reimbursed
new patients	• savings in drug budget **CMA**	• Improved patient access → health gain ~~CMA~~	• health gain (vs. older treatment) with cost increase ~~CMA~~
patients on maintenance drug therapy	• savings in drug budget **CMA** • potential immunogenicity risk of switch ~~CMA~~	• patients with no access: Improved patient access → health gain ~~CMA~~ • patient with access: cost-savings & potential immunogenicity risk of switch ~~CMA~~	• health gain (vs. older treatment) with cost increase ~~CMA~~

How to handle uncertainty II: economic modelling

- Cost utility analysis and economic modelling (e.g. Markov model) is required
  - With conservative overestimation of negative consequences (if any)
  - Handling uncertainty in sensitivity analyses
  - Models can be populated with more accurate data gained from registries or payers' database
  - Decisions may be reconsidered based on future data

How to handle uncertainty of switching to biosimilars?

Technique	Policy level	INN level
Systematic analysis of available evidence in the scientific literature	✓	✓
Awaiting results of larger ongoing clinical studies on consequences of switching to biosimilars • PLANETAS, • PLANETRA, • NOR-SWITCH etc.	(✓)	✓
Ex post: analysing available real world data • drug utilisation data in payers' dispensing database, • registries	✓	✓
Ex ante: health economic models • overestimating potential risks • applying sensitivity analyses/scenario analyses		✓

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Conclusion

- Timely access and volume cap of expensive biological drugs is an issue in lower income European countries
- There is no hard clinical evidence against switching based on systematic literature review
- Prevention of switching patients currently on biological treatment to biosimilars due to hypothetical risk seems to be DISPROPORTIONAL compared the expected social benefit
- For maintenance patients one switch from original to biosimilar under medical supervision should be considered
- Available real world evidence (payers' database and registries) should not be wasted without analysis on consequence of switching
- Consequences of switch should be evaluated in health economic models

Thank you for your attention

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