A LONG WAR BEGINS: BIOSIMILARS VERSUS PATENTED BIOLOGICS
A RETROSPECTIVE ANALYSIS OF THE EU-5 AND JAPANESE ERYTHROPOETINS MARKETS

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Introduction

Patent expiries on leading biologics are creating new momentum in the market for biosimilars (copies of off-patent biologics) paving the way for their development. Unlike generics (copies of chemical molecules), as these are proteins produced by living organisms, biosimilars are complex and difficult to produce. In the context of financial crisis, biosimilars could represent an important potential savings for health systems. **However, little is known about the factors influencing the competition between biosimilars and their reference products (REF).** As of the end of 2012, three therapeutic classes have been 'biosimilarized' meeting strict European Medicines Agency (EMA) regulatory requirements or near-equivalents: human growth hormones (h-GHs), Granulocyte-Colony Stimulating Factors (G-CSFs) and erythropoetins (EPOs). Compared to the global growth hormone and G-CSF markets, the global EPO market is by far the biggest.

Objectives

- To analyze key global EPO markets and to categorize them by **dominant distribution models:** Retail market (R), Hospital market (H) or both (R+H).
- To **characterize the factors affecting biosimilar EPO (BIOSIM-EPO) uptakes**, particularly that of BIOSIM-EPO prices relative to reference EPOs (REF).
- To identify, if possible, **country profiles where BIOSIM-EPO have gained significant market shares.**

Methods

- **Selection of countries :**

Countries assessed for eligibility (n= 45): 27 EU countries, Argentina, Australia, Brazil, Canada, Cuba, India, Japan, Malaysia, Mexico, Peru, Saudi Arabia, Singapore, South Africa, South Korea, Taiwan, Turkey, the US and Venezuela

Countries excluded (n= 38): looser regulatory framework for biosimilars than in the EU; < 3 years of experience with BIOSIM-EPO in 2012; where pharmaceutical firms do always respect intellectual property and countries with a < US$ 2.5 billion biological market in 2010 (the EU-5 markets account for 75% of the global EU biologicals market and are treated as one market)

Countries selected (n= 7)
EU-5 countries (France, Germany, Italy, Spain and the UK), Japan and the US

Countries excluded (n= 1): no BIOSIM-EPO on their national market at the end of 2012

Countries analysed (n= 6)
EU-5 countries (France, Germany, Italy, Spain, the UK) and Japan

Fig. 1: Inclusion and exclusion criteria for countries in the study

- **Factors evaluated:** national EPO market sizes and EPO retail/ hospital distribution mixes; policy promoting BIOSIM-EPO prescriptions or the substitution; BIOSIM-EPO prices relative to reference EPO.
- **Data on medicine volumes, values and ex-manufacturer prices** for all EPOs were provided by IMS Health. Volumes were calculated in DDD (Defined Daily Doses) and prices in euros per DDD. Data were available from 2007 until 2012.

- **Selection of medicines :** all marketed EPOs

✧ 1st generation EPOs (1G)
- ✓ 1Gα = REF (INN: Epoetin alfa): unpatented « biosimilarized » EPO.
- ✓ **BIOSIM-EPO: Biosimilars of REF** (INN: Epoetin alfa, zeta, theta, kappa).
- ✓ 1Gβ (INN: Epoetin beta): patented EPO.
- ✓ Excluded from the analysis : 1Gδ (INN: Epoetin delta): patented EPO only marketed in the EU from 2007 to 2009 and very little consumed.

✧ 2nd generation EPOs (2G)
- ✓ 2Gα (INN: Darbepoetin alfa): patented EPO.
- ✓ 2Gβ (INN: Methoxy PEG beta): patented EPO.

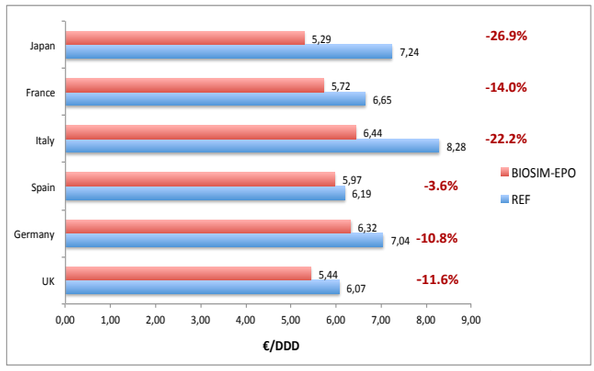

Fig. 2: BIOSIM-EPO prices discounts (€/DDD) vs. REF in 2012

Results

✧ **Japan:** the largest market, mixed distribution channels, no policy promoting the use of BIOSIM-EPO.

✧ **France:** large-sized market, dominant retail market distribution, no policy promoting the use of BIOSIM-EPO.

✧ **Italy and Spain:** medium-sized markets, dominant hospital distribution, no policy promoting the use of BIOSIM-EPO.

✧ **Germany:** small-sized market, dominant retail market distribution, policy promoting the prescription of BIOSIM-EPO (quotas) and to substitute patented for 'bioidenticals' EPO.

✧ **UK:** the smallest market, mixed distribution channels, no policy promoting the use of BIOSIM-EPO.

✧ The price differences between BIOSIM-EPO and their reference play no role at a global level (e.g. -10.8% in Germany and -26.9% in Japan).

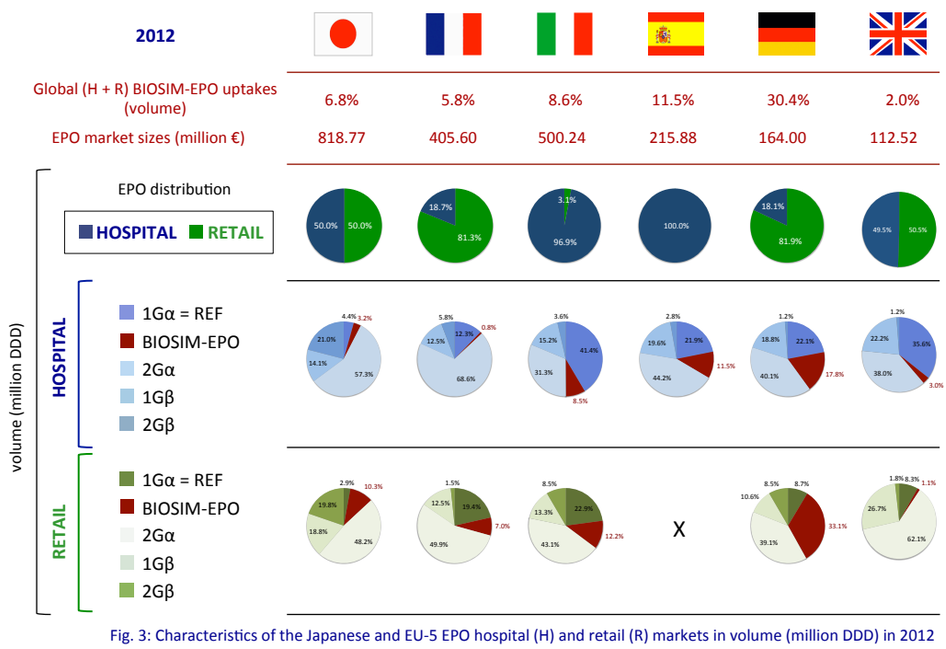

Fig. 3: Characteristics of the Japanese and EU-5 EPO hospital (H) and retail (R) markets in volume (million DDD) in 2012

Conclusion

The EPO markets prove to be highly country specific. National EPO market sizes, EPO retail/hospital distribution mixes and BIOSIM-EPO prices relative to reference EPO are not determining factors of BIOSIM-EPO uptakes. The particular situation in Germany, where the market share of biosimilars is higher than in other countries, is likely due to a deliberate policy of development of these products. No country profiles where BIOSIM-EPO takes particularly market shares have been identify, while such country profiles have been identified for biosimilar G-CSFs (see Bocquet et al. To What Extent Can Biosimilars Compete with Brand Name Biologics? A EU-5 Granulocyte-Colony Stimulating Factors Markets Analysis, Value in Health Volume 16, Issue 7, page A455, Nov. 2013).

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