Biosimilars in Supportive Care

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What are biosimilars and why should we use them?

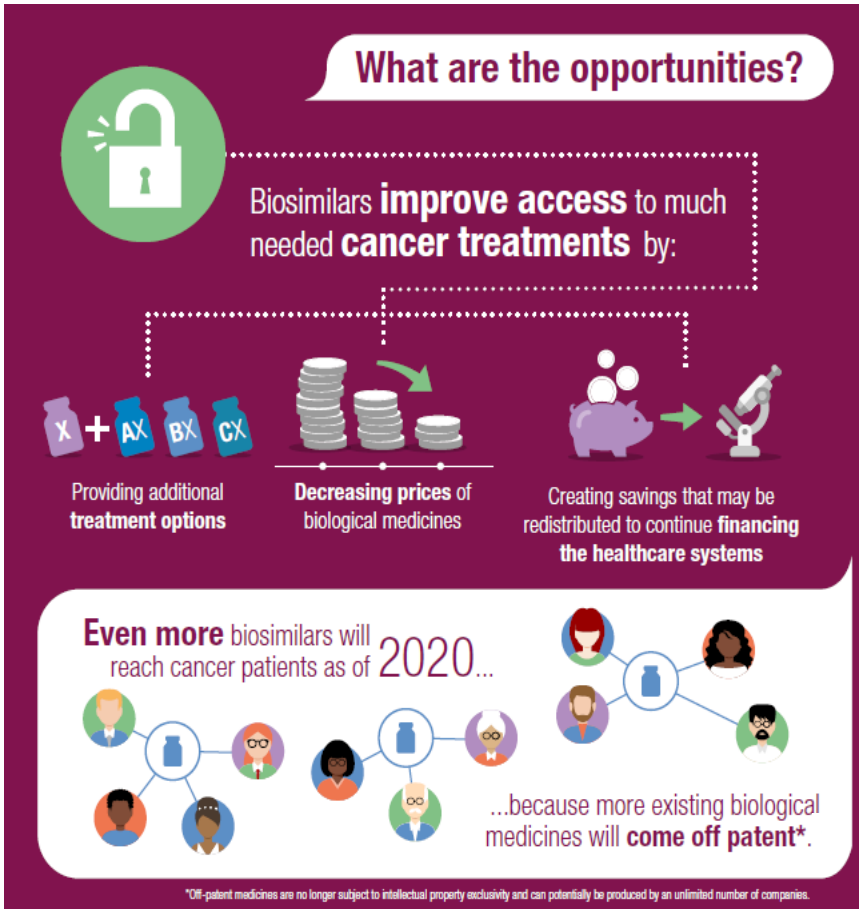
EMA[1]

"A biosimilar is a biological medicinal product that contains a version of the **active substance** of an already authorised original biological medicinal product."

"**Similarity** to the reference medicinal product **in terms of quality characteristics, biological activity, safety and efficacy** based on a comprehensive comparability exercise needs to be established."

1. EMA. Guideline on similar biological medicinal products, 2014; 2. FDA. Scientific considerations in demonstrating biosimilarity to a reference product. Guidance for Industry, 2015

Value proposition of biosimilars in the EU



Reduce budget impact to allow for reallocation of funds, in order to:

- Improve healthcare services
- Acquire new technologies
- Pay for innovative medicines
- Support earlier initiation of therapies

Foster innovation

- Original reference products may be improved (e.g. new formulation) by anticipated biosimilar competition
- Biosimilar life cycle may prompt novel products (e.g. development of subcutaneous infliximab)

Increase patient access

Potentially mitigate risk of shortages

ESMO. Infographic Understanding Biosimilars for Cancer Patients. Available at: https://www.esmo.org/content/download/158275/2892910/file/ESMO-Understanding-Biosimilars-for-Cancer-Patients.pdf. Accessed October 2019;
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Biosimilars in supportive care

- Epoetin
  - Available in Europe since 2007, US since 2018
- **Filgrastim**
  - Available in Europe since 2008, US since 2015
- **Infliximab**
  - Available in Europe since 2014, US since 2016

Filgrastim – UK implementation

- First supportive care biosimilar
- Very careful and cautious – reviewed all the literature before implementation
- Encouraged by national commissioning bodies
- Regional tendering process
- Drug & Therapeutics Committee, local chemotherapy group
- Training and education for staff and patients

Impact of biosimilar filgrastim

- The introduction of biosimilar medicines has been shown to increase access to treatment[1]
- Following the introduction of biosimilar filgrastim in the UK, usage in London increased by 40%[2]
- At the same time, it delivered budget savings (despite increased use) for reinvestment - £1million/yr in London alone[1]
- This effect was replicated across Europe - all countries saw a jump in the use of filgrastim following EMA approval (a 5-fold increase in Sweden) with estimated cost savings of 85 million Euros/yr[1]

Filgrastim in the UK – present day practice

- Switch freely between brands depending on **regional procurement contract** (based on best value for money)
- Cost savings £££
- Prescribed generically, pharmacy supply current preferred brand
- Pockets of practice where innovator is still used
  - Paediatrics
  - Stem cell mobilisation for transplant

Filgrastim – safety & efficacy

- Real world data from NEXT (n=2,012) and MONITOR-GCSF (n=1,447) demonstrate that rates of neutropenia, febrile neutropenia, dose delay or reduction as well as incidence of adverse effects were consistent with those reported for the originator products[3,4]
- Stem cell mobilisation: A pooled analysis of 12 autologous and five allogeneic healthy donor biosimilar cell mobilisation studies showed no significant differences between biosimilar vs originator G-CSF in the median number of CD34+ cells mobilised or in the number of G-CSF injections and leukaphoresis procedures required to harvest the target CD34+ cell dose[5]
- Larger 10 year follow up study in progress of 242 healthy volunteer donors - to date no concerns with efficacy or safety[6]
- No sign of induced immunity in any of these studies

Filgrastim – switching brands

- In the Pioneer study, 258 breast cancer patients receiving TAC chemotherapy were randomised to one for four arms (double-blind):
  - Biosimilar
  - Alternate cycles Neupogen/biosimilar
  - Alternate cycles biosimilar/Neupogen
  - Neupogen
- Repeated switching had no effect on efficacy, safety or immunogenicity[7]

Lipegfilgrastim – a biobetter??

- Glycopegylated filgrastim
  - glycopegylation thought to be better than traditional pegylation as polymer chains added distant to the active site, prevention variation in activity and increasing structural homogeneity
- Trials
  - Phase 3 trial demonstrated non-inferiority compared to pegfilgrastim[8]
- NOT a biosimilar pegfilgrastim!!

Infliximab – UK experience

- Initial evidence from PLANETRA and PLANETAS demonstrated efficacy in rheumatoid arthritis and ankylosing spondylitis[9,10]. Fears over extrapolation of indications allayed by NOR-SWITCH trial[11]
- NHSE/NICE issues guidelines for implementation
- BGS guidelines – advocate use in IBD but brand prescribing and no automatic substitution[12]
- Off label use for treatment of checkpoint inhibitor related colitis followed
- NHS saved £99 million in the year 2017/18 through use of biosimilar infliximab (all use – rheumatology and IBD)[13]

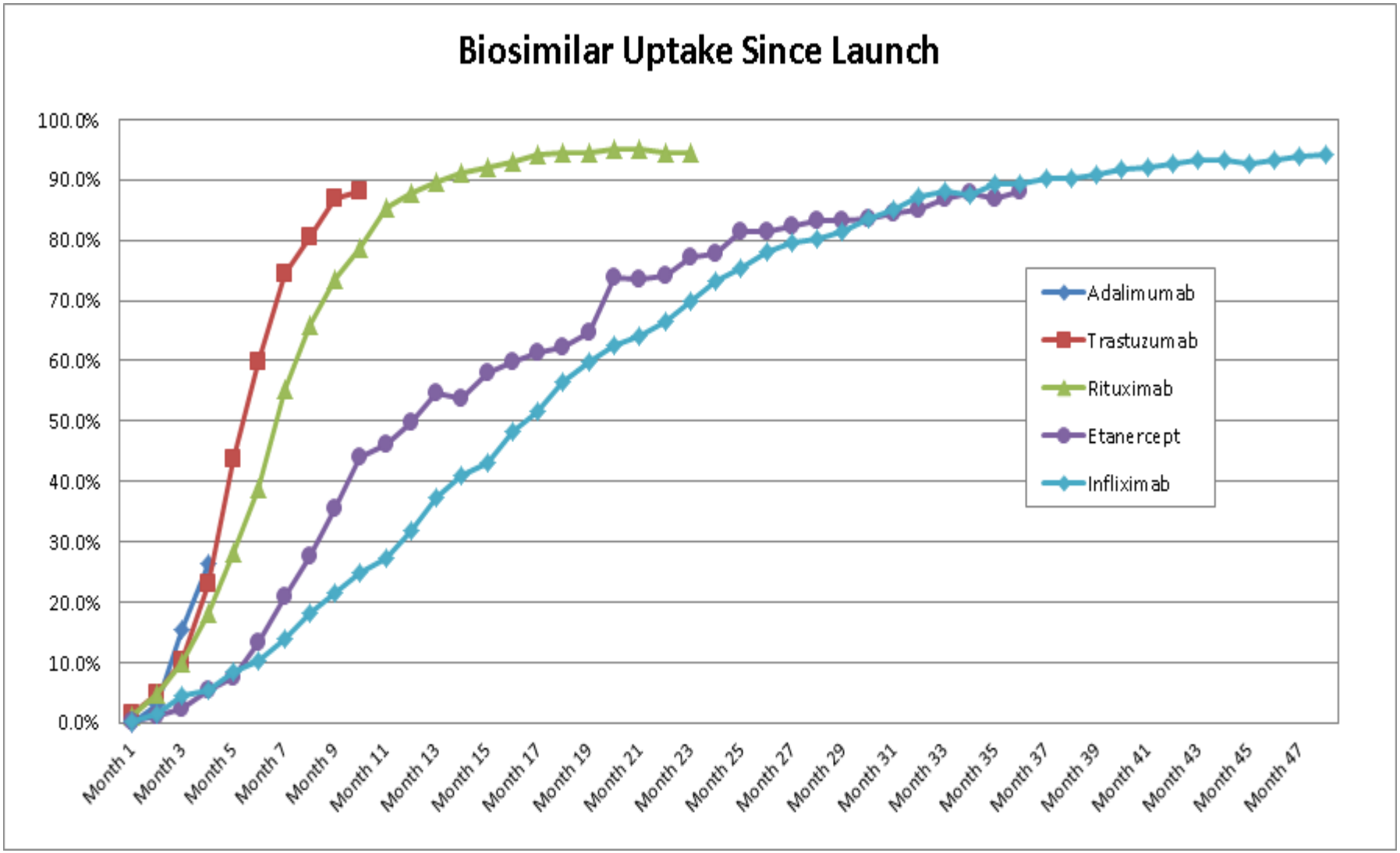
Infliximab – safety, efficacy and switching

NOR-SWITCH:

- 482 patients previously stable on Remicade for at least 6 months were randomised to continue on originator or switch to biosimilar (double-blind)
- After 52 weeks follow up the biosimilar demonstrated non-inferiority in terms of worsening of disease and frequency of adverse events
- Included 93 patients with ulcerative colitis and 155 with Crohn's disease

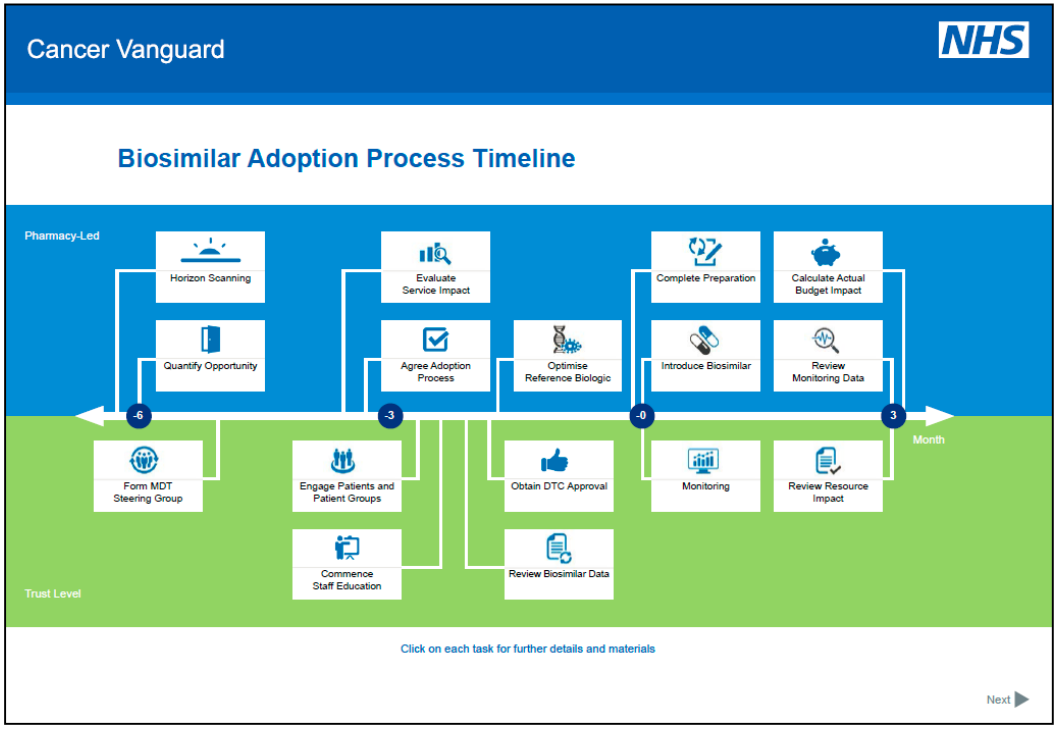
National uptake of Biosimilars in NHS in England

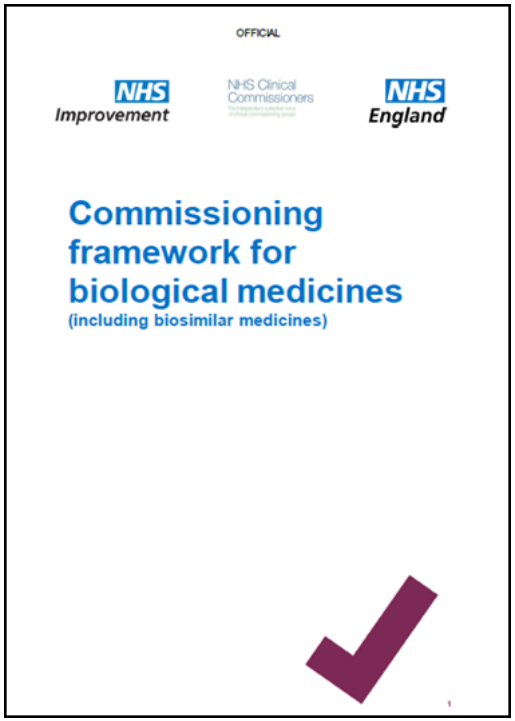
(data from NHS London Procurement Partnership)



Full year national savings at 98% = £100m

UK Landscape is positive for Biosimilars





Medicines Optimisation CQUIN is driving the uptake of Biosimilars:

- 90% of new patients will be prescribed the best value biological medicine within 3 months of launch of a biosimilar medicine
- and at least 80% of existing patients within 12 months

NHSE commissioning framework for biological medicines, 2017…

Many biological medicines are coming off patent and "biosimilars" are becoming available. These medicines are highly similar to other biological medicines already licensed for use but are typically much cheaper than the originator products. This competition provides the NHS with an opportunity to save hundreds of millions of pounds, whilst also increasing access to these important medicines. There is the potential to realise savings of at least £200-300m per year by 2020/21 if the NHS embraces the use of best value biological medicines in a proactive, systematic, and safe way. Our aim is that at least 90% of new patients will be prescribed the best value biological medicine within 3 months of launch of a biosimilar medicine, and at least 80% of existing patients within 12 months, or sooner if possible. This guidance is designed to support the NHS to achieve this.

And 2019…

As original biological medicines lose their patent protection, biosimilar medicines are becoming available across different therapeutic areas. There are currently 15 'reference' (or 'originator') biological medicines that have biosimilars approved for use in the UK, as well as many in development. As the biosimilar market develops, increased competition between biological medicines has the potential to deliver significant savings to the NHS of at least **£400m to £500m per year by 2020/21** through increased uptake of the best value biologic medicines, including biosimilars.[1]

The five ‘winnings’ of biosimilars in Europe

Cost–benefit
Biosimilars offer higher value compared with the originator, as they offer lower cost for equal quality[1]

Supporting a sustainable, competitive market
Biosimilars induce competition, with subsequent lower innovator prices (and also for a whole therapeutic group)[2]

Potential for earlier patient access
Patients may be able to access costly advanced medicines earlier,[3] with a resultant health gain[4]

Availability of budget for treatment of more patients
More patients can be treated for the same level of budget[1]

Availability of budget for other treatments
Biosimilars create headroom in the budget for new (costly) medicines[1]

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3. Acknowledgement: Dr Gunar Stemer

Global Barriers to implementation of biosimilars
(from ISOPP biosimilars implementation survey 2019)

- A reluctance to swap established patients to biosimilars
- Reluctance of prescribers to use biosimilars
- Insurance adaption/ payer preferences
- Lack of regulatory pathways (Kenya)
- Sourcing and Quality (Ghana)

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