Biosimilar mAbs

Outlook

EMEA Workshop

on Biosimilar Monoclonal Antibodies

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No answers yet!

- **Should the biosimilar framework** *(or better: its "philosophy"?)* **be "opened" for differences in the amino acid sequence?**

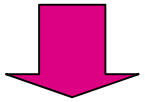
- **Could some concepts be applicable to 2nd generation products?**

How far does „similarity“ need to go?

- *„The active substance of a similar biological medicinal product must be similar, in molecular and biological terms, to the active substance of the reference medicinal product.“*

  Guideline CPMP/BWP/437/04

- *„For example, a medicinal product containing interferon alfa-2a manufactured by Company X claiming to be similar to another biological medicinal product should refer to a reference medicinal product containing as its active substance interferon alfa-2a.* ***Therefore, a medicinal product containing interferon alfa-2b could not be considered as the reference medicinal product.****“*

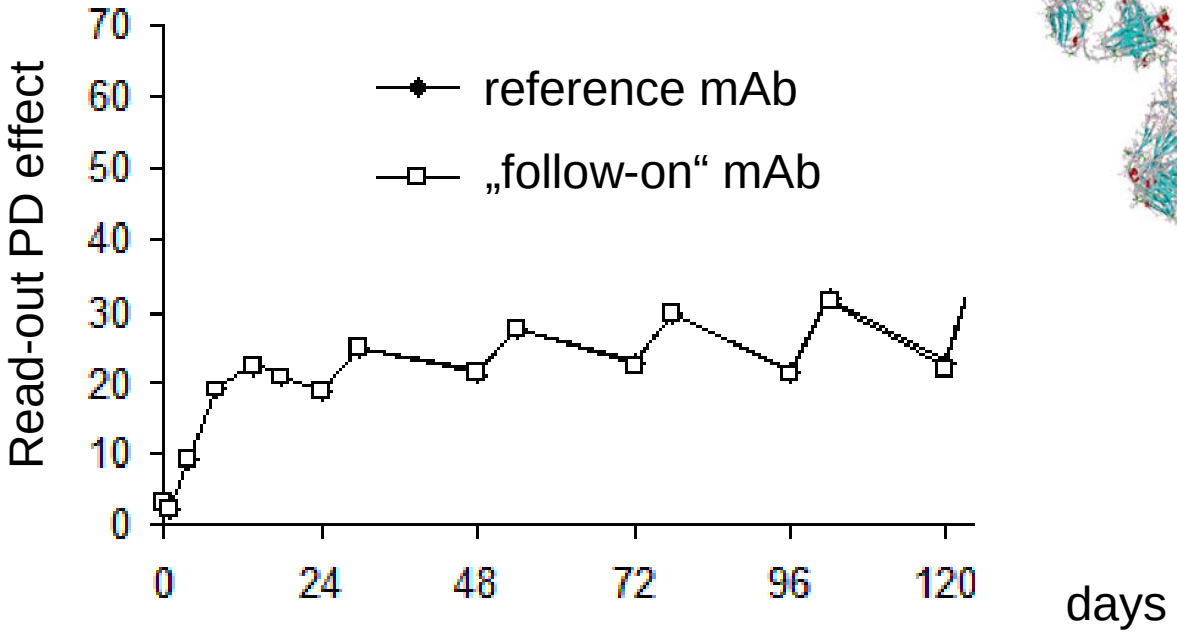


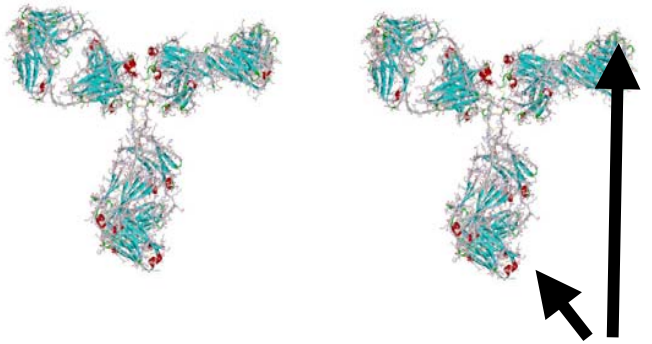
Guideline CPMP/BWP/437/04

Difference is only 1 aa => current understanding is that a biosimilar must be ***identical on the amino acid level***

Outlook: Open questions for discussion

- **What about products which are similar on a non-clinical level (e.g. potency, in-vitro/in-vivo behaviour), but structurally different?**
  (e.g. mAbs that differ in the backbone of the protein but share the same fine specificity?)





(Constructed) Example:
1 aa difference in CDR3 region
or
different IgG1 allotype used in cloning of the gene

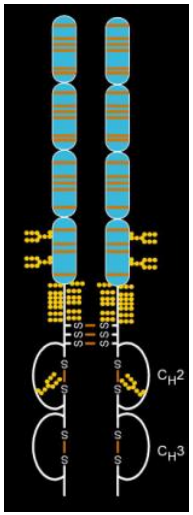
(invented example)

Outlook: Open questions for discussion

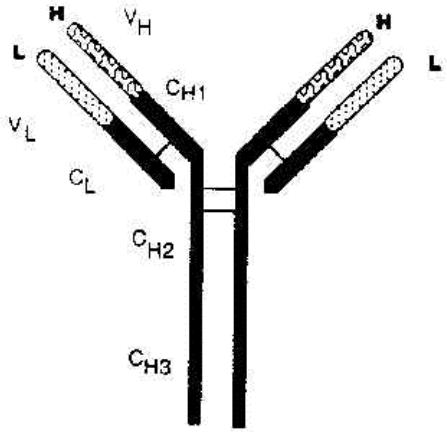
- **What about „true“ 2nd generation proteins (the „real“ „follow-on“ biologicals?)**
  - » Examples:
    - – Fully human anti-TNFalpha mAbs
    - – Engineered first generation mAbs
  - » Full development programme?
  - » Only one indication, rest PD markers?

- **To what extent is risk-assessment relevant as regards structural differences?**

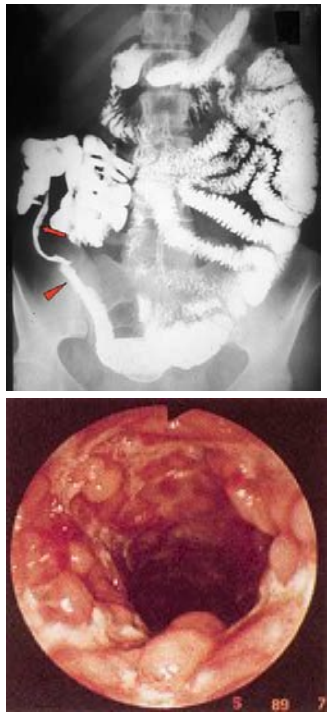
„mAb is more than FAb“



Enbrel®
Etanercept



Remicade®
Infliximab



- **Infliximab is efficacious in Crohn‘s disease[1)], but etanercept is not[2)]**

1) European Medicines Agency (EMEA). European Public Assessment Report for Remicade, http://www.emea.europa.eu/humandocs/Humans/EPAR/remicade/remicade.htm (2007).

2) Sandborn, W.J. et al: Etanercept for active Crohn's disease: a randomized, double-blind, placebo-controlled trial. Gastroenterology 121(5):1088-94 (2001).

The floor is yours!