
In the U.S., we recently had TWO MEETINGS in Washington, D.C. to address "Barriers to Biosimilars" in the U.S.

FDA/FTC Workshop on a Competitive Marketplace for Biosimilars- March 9, 2020

Theories advanced by the participants for lower biosimilar uptake in the U.S. included:

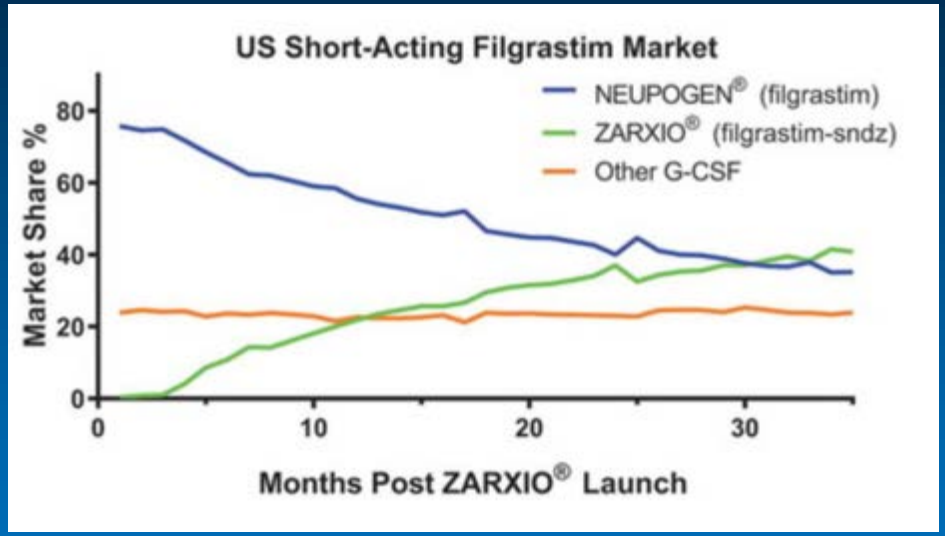
- Disinformation about biosimilars which undermine physician confidence in biosimilars.
- Need for patient/physician education on biosimilar safety
- Patent litigation and trade practices (e.g. pay-for-delay)

Pfizer/Hatch Foundation/ Biosimilars Forum Meeting- March 10, 2020

- Featured many of the same participants as the previous day's meeting.
- Reiterated many of the same points, arguing that access was being impeded by disinformation about biosimilars that led to low confidence in biosimilars among physicians and patients.

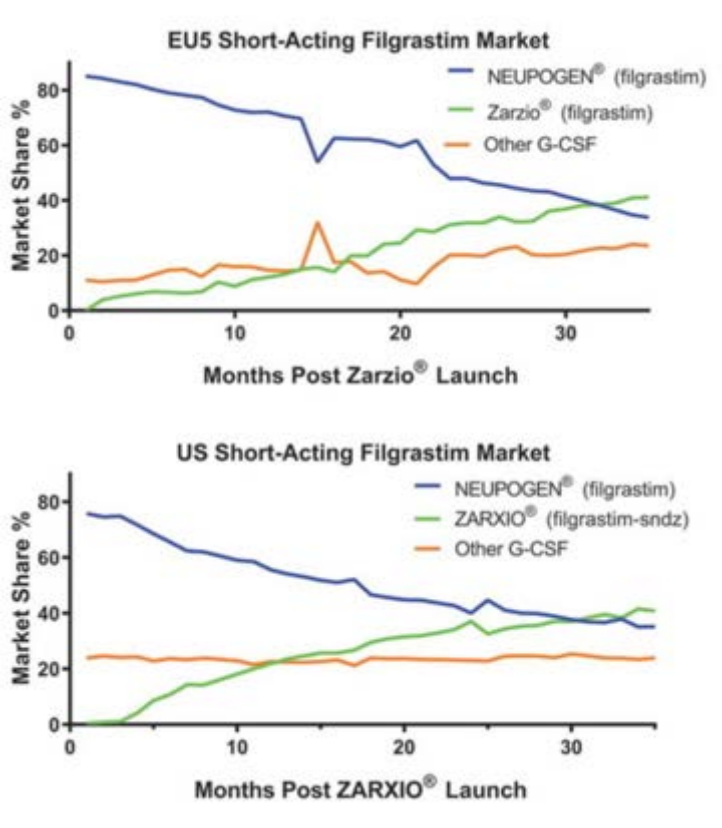
Biosimilar WITH Suffix Surpasses Market Share of NON-SUFFIX Reference product.

- The first U.S. biosimilar, filgrastim-sndz (Zarxio), launched at a 15% discount, gained 24% of the market share for filgrastim in the United States within the first year
- It surpassed its reference product in terms of market share [at roughly 30 months], ***even though the reference product does not have a suffix.***



In U.S., Distinct Naming is not affecting uptake/market share….

- *A 2019 study by Amgen showed the first U.S. biosimilar filgrastim had identical market share to its E.U. counterpart (~40%) 36 months after their respective launches.*



PRICE (Discount %) seems to be the main obstacle.

- *U.S. biosimilars have historically launched at lower discounts (10-15% range) than in Europe (30-50%).*
- *Yet this is changing.*
- *As 4 or 5 biosimilars become available, we are starting to see higher "European-size" discounts; with infliximab, pegfilgrastim, and rituximab biosimilars as well, launching in the 25-35% range.*
- ***In 2019, Zarxio (filgrastim-sndz) achieved a majority (55%) market share- after dropping from a 15% discount at launch- to a 38% discount.***

AND Physicians Do Not Have Low Confidence in Biosimilars…

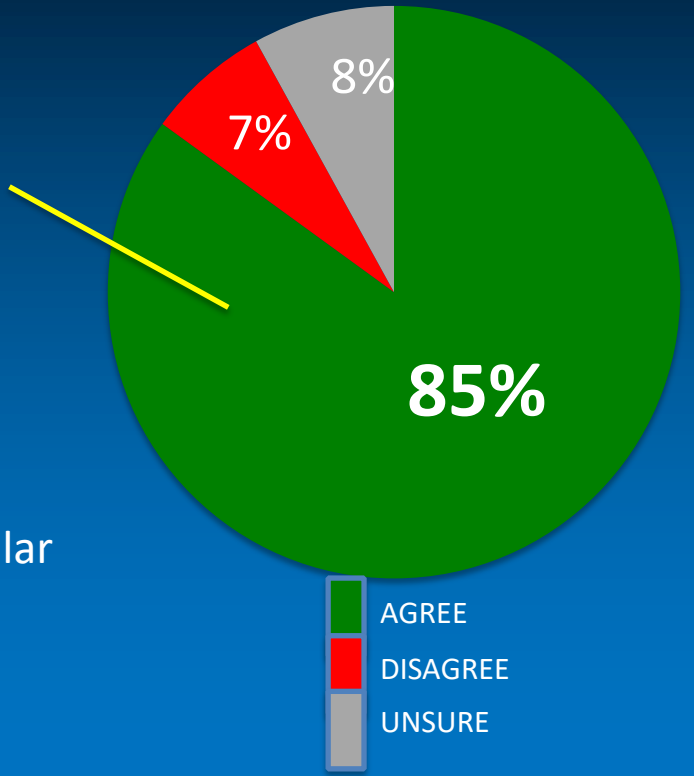
"Today I'd like to speak to some issues that occur in discussions about biosimilars. The first is that "misinformation" continues to be spread affecting the objectivity of prescribers and creating an anti-biosimilar bias among physicians, slowing the uptake of the biosimilar market. ***In a meeting I ran last week with rheumatologists from around the country, when asked if anyone felt that biosimilars were in anyway inferior to originators, not one person raised their hand."***

Madelaine Feldman, MD, FACR; ASBM Chair
FDA Meeting, 3/9/2020

U.S. Physicians Support for Distinct Naming is Strong.

A May 2019 Survey of 202 U.S. biologic prescribers conducted by ASBM revealed:

- **85% Support the FDA's distinct suffix system.**
- **71% Support FDA decision** not to rename previously-approved products with suffixes
- **69% Support FDA decision** not to rename biosimilar products approved prior to establishment of biosimilars pathway (biosimilar insulins, growth and reproductive hormones)



Physicians Worldwide Have Consistently Supported Distinct Naming…

68% *of Canadian physicians support Health Canada issuing distinct names. (2017)*

94% *of Latin American Physicians consider WHO's BQ Proposal to be "useful" in helping patients receive the correct medicine. (2015)*

85% *of US physicians support FDA issuing distinct names. (2019)*

76% *of Australian physicians support TGA issuing distinct names (2016)*

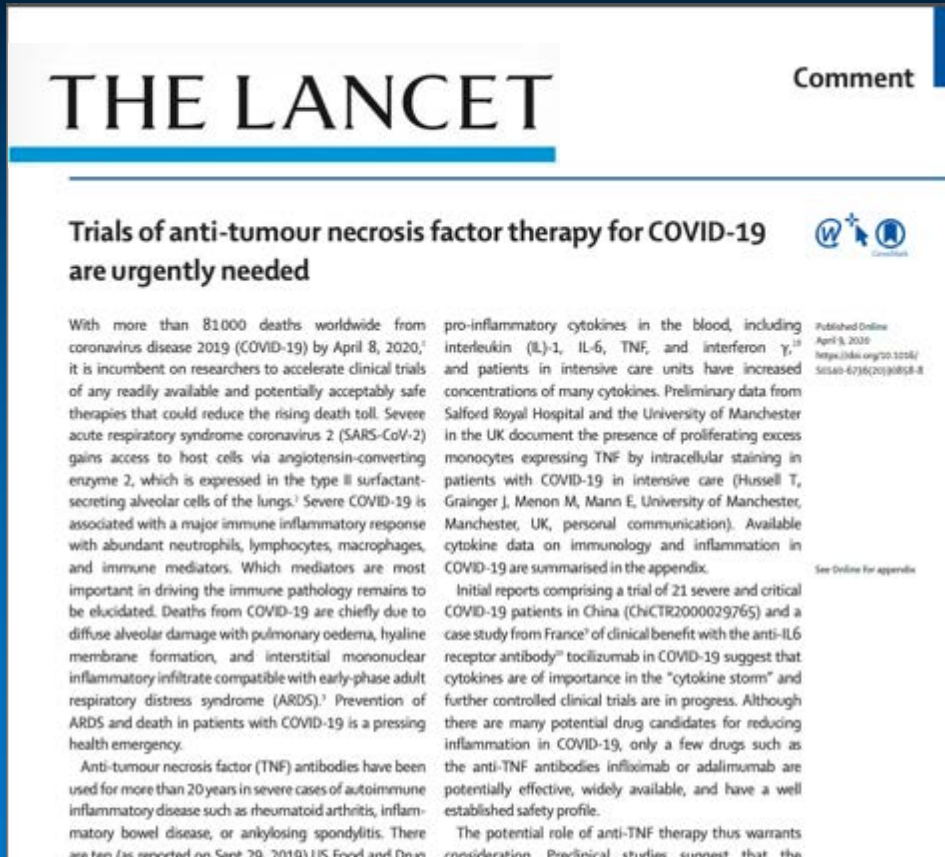
*As we learn more, we are seeing that distinct biologic naming is NOT a barrier to access, rather that it **builds confidence** in the safe use of biosimilars among physicians.*

As the number of biosimilars continue to increase, so does the VALUE of Distinct Naming as a pharmacovigilance tool.

Biologic Naming May Have Even Greater Relevance in Light of the COVID-19 Pandemic…

"Although there are many potential drug candidates for reducing inflammation in COVID-19, only a few drugs such as the anti-TNF antibodies infliximab or adalimumab are potentially effective, widely available, and have a well established safety profile."

(The U.S. has 11 approved biosimilars to these 2 reference products; Europe has 12. Each region also has 2 biosimilars for etanercept, another TNF inhibitor)



THE LANCET

Comment

Trials of anti-tumour necrosis factor therapy for COVID-19 are urgently needed

With more than 81 000 deaths worldwide from coronavirus disease 2019 (COVID-19) by April 8, 2020,[1] it is incumbent on researchers to accelerate clinical trials of any readily available and potentially acceptably safe therapies that could reduce the rising death toll. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) gains access to host cells via angiotensin-converting enzyme 2, which is expressed in the type II surfactant-secreting alveolar cells of the lungs.[2] Severe COVID-19 is associated with a major immune inflammatory response with abundant neutrophils, lymphocytes, macrophages, and immune mediators. Which mediators are most important in driving the immune pathology remains to be elucidated. Deaths from COVID-19 are chiefly due to diffuse alveolar damage with pulmonary oedema, hyaline membrane formation, and interstitial mononuclear inflammatory infiltrate compatible with early-phase adult respiratory distress syndrome (ARDS).[3] Prevention of ARDS and death in patients with COVID-19 is a pressing health emergency.

Anti-tumour necrosis factor (TNF) antibodies have been used for more than 20 years in severe cases of autoimmune inflammatory disease such as rheumatoid arthritis, inflammatory bowel disease, or ankylosing spondylitis. There

pro-inflammatory cytokines in the blood, including interleukin (IL)-1, IL-6, TNF, and interferon γ,[3,4] and patients in intensive care units have increased concentrations of many cytokines. Preliminary data from Salford Royal Hospital and the University of Manchester in the UK document the presence of proliferating excess monocytes expressing TNF by intracellular staining in patients with COVID-19 in intensive care (Hussell T, Grainger J, Menon M, Mann E, University of Manchester, Manchester, UK, personal communication). Available cytokine data on immunology and inflammation in COVID-19 are summarised in the appendix.

Initial reports comprising a trial of 21 severe and critical COVID-19 patients in China (ChiCTR2000029765) and a case study from France[5] of clinical benefit with the anti-IL6 receptor antibody[6] tocilizumab in COVID-19 suggest that cytokines are of importance in the "cytokine storm" and further controlled clinical trials are in progress. Although there are many potential drug candidates for reducing inflammation in COVID-19, only a few drugs such as the anti-TNF antibodies infliximab or adalimumab are potentially effective, widely available, and have a well established safety profile.

The potential role of anti-TNF therapy thus warrants

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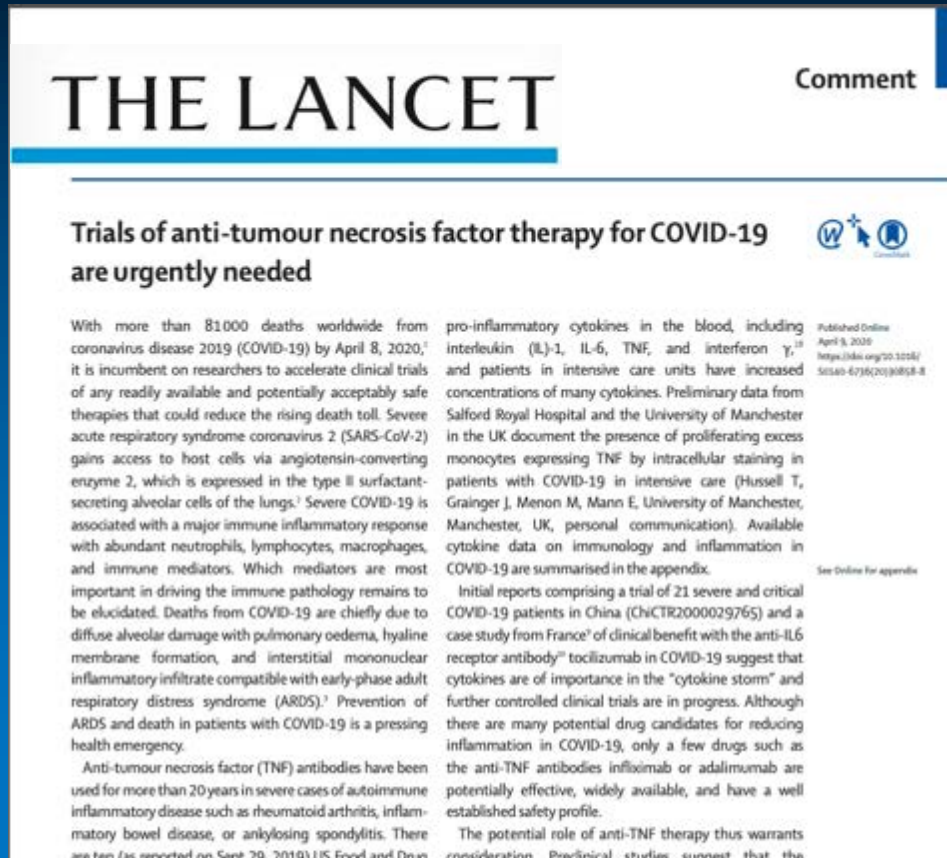
See Online for appendix

Benefits of Harmonized Naming in COVID-19 Fight

If trials of anti-TNF therapy prove successful in treating COVID-19, accurate identification of these products- and accurate attribution of any adverse events or reduced efficacy, will become even more critical.



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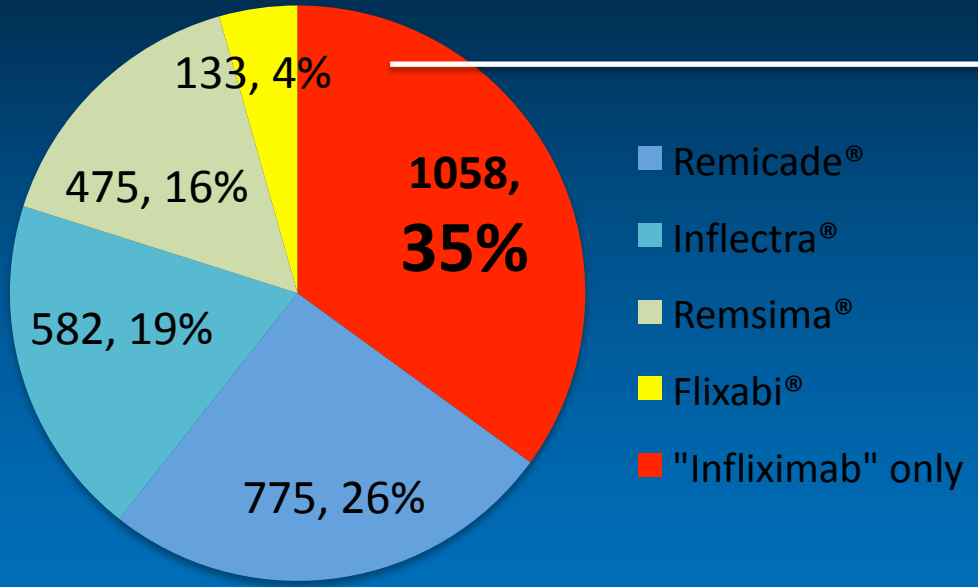
EU PV data shows that [Brand Name + INN] is not sufficient to accurately attribute adverse events.



35% of EU adverse event reports for infliximab in 2018 did not specify brand name.

Note that this is **despite the fact** that reporting by brand name has been **required by law** since 2012.

Source: EudraVigilance- European database of suspected adverse drug reaction reports. www.adrreports.eu ; accessed May 3, 2019.

Summary

- *We and NRAs have long called for WHO leadership on this issue.*
- *The recent COVID-19 Pandemic is a once-in-a-century example of why global leadership is so essential.*
- *Countries look to WHO and in the absence of action must develop siloed, non-inter-operable approaches to naming.*
- *As we increasingly see that distinct naming is NOT a barrier to access, its value increases as the number of biosimilars increases.*
- *Wealthy countries may have sufficient resources to deal with these problems on their own - but the WHO also exists to provide an international standard for countries that do not have these resources.*
- ***Unanimous agreement cannot be not a precondition for leadership, let alone the establishment of a voluntary standard- and should not preclude it.***

Petition/Letter

- *During our April 11, 2018 meeting with FDA and Health Canada, a Health Canada's Anthony Ridgway proposed **circulating a petition among national regulators** to gauge support for WHO action on distinct naming.*

- ***ASBM proposes to draft a petition or letter, to be approved by, and circulated to regulators the INN Expert Committee.***
- *We understand you can't provide an answer at this meeting, however we wanted to proposed for consideration by the Expert Group, and stand ready to respond.*

Health Canada Explicitly Cited Lack of WHO Standard

"In coming to this decision, Health Canada also took into consideration…**there is no internationally adopted naming scheme** to distinguish among biologics that, based on active ingredient, will be assigned the same International Nonproprietary Name (INN) by the World Health Organization"

Other Options or Factors to Consider:
Global naming approach:

Wait for a recommendation from the World Health Organization for international consistency

March 9, 2019 Meeting in Ottawa

Health Canada again reiterated that it would harmonize with an international standard if and when the WHO makes such a standard available.

Mr. Ridgway and Ms. Hardy emphasized that Health Canada would still be willing to put such a request in writing, as Mr. Ridgway had suggested in April 2018.

FDA's Lubna Merchant expressed similar willingness on part of the FDA.

SafeBiologics

ALLIANCE *for* SAFE BIOLOGIC MEDICINES

Thank You For Your Attention