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Overcoming the Nocebo Effect in Biosimilar Use

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Background

- Biologics are class of drugs derived from living cells that are widely used in oncology, dermatology, rheumatology and gastroenterology
- Biosimilars are FDA-approved drugs that have no clinically significant differences when compared with reference biologics
- Despite large trials demonstrating no differences in safety, purity or potency, some patients and providers are skeptical about using biosimilars
- The 'nocebo effect' occurs when negative expectations lead to negative consequences following medical treatment
- Education about the nocebo effect can lead to increased biosimilar uptake among patients and providers

The Nocebo Effect: A Review

- A systematic review of double-blinded versus open-label studies of patients with inflammatory diseases found that infliximab biosimilar discontinuation rates were 14.7% versus 6.95% in open-label versus double-blinded studies [1].
- A systematic switch study of infliximab to an infliximab biosimilar found discontinuation in 59/260 patients (23%) by the third infusion, though no clinical or biological factors were independently associated with biosimilar discontinuation; 80% of discontinuations were related to patient's experienced inefficacy [2].
- NOR-SWITCH: A 52-week, randomized, non-inferiority, double-blind, multicenter, phase 4 study followed by a 26-week open trial where all patients received biosimilar CT-P13: First avoided the nocebo effect due to the double-blind design, but when looking at the overall patients' and physicians' global assessment of disease activity, an upward drift observed in the patients' assessment in both study arms, indicating a nocebo effect" [3].

Future Directions

- The nocebo effect for biosimilars is a major obstacle for their more widespread use and should be an area of focus in provider-targeted educational interventions.
- We plan to develop an educational intervention aimed at all stakeholders (physicians and other prescribers, nurses, pharmacists, psychologists).
- The intervention focus will include:
  - Education about biosimilar drugs for providers and patients
  - Communication "dos and don'ts"
  - Clear switch guidelines and workflows
- Our ultimate goal is to disseminate education materials and an optimal biosimilar ordering workflow throughout the entire CU Medicine and UCHealth systems

Why Biosimilars Matter

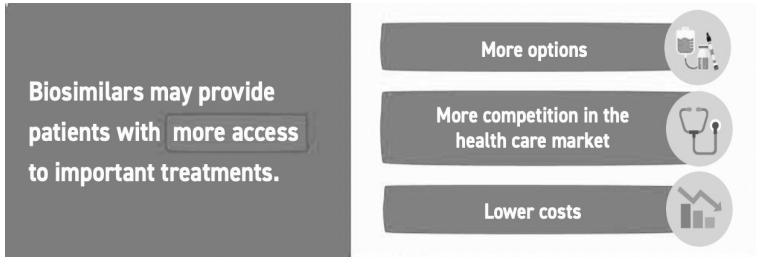

Fig. 1 Adapted from the 'Biosimilar Basics' handout on the FDA.gov website

Consequences of the Nocebo Effect

- Non-adherence
- Financial burden
- Disease relapse
- Symptom burden
- Additional medications to manage side effects
- Loss of patient trust
- Discontinuation rates in clinical trials or registries affecting interpretation of results, and evaluation and development of novel therapies [4]

Citations

[1] Odinet JS, Day CE, Cruz JL, Heindel GA. The Biosimilar Nocebo Effect? A Systematic Review of Double-Blinded Versus Open-Label Studies. J Manag Care Spec Pharm. 2018 Oct;24(10):952-959.

[2] Avouac J, Moltó A, Abitbol V, et al. Systematic switch from innovator infliximab to biosimilar infliximab in inflammatory chronic diseases in daily clinical practice: The experience of Cochin University Hospital, Paris, France. Semin Arthritis Rheum. 2018 Apr;47(5):741-748.

[3] Jørgensen KK, Goll GL, Sexton J, et al. Efficacy and Safety of CT-P13 in Inflammatory Bowel Disease after Switching from Originator Infliximab: Exploratory Analyses from the NOR-SWITCH Main and Extension Trials. BioDrugs. 2020 Oct;34(5):681-694.

[4] Kristensen LE, Alten R, Puig L, et al. Non-pharmacological Effects in Switching Medication: The Nocebo Effect in Switching from Originator to Biosimilar Agent. BioDrugs. 2018 Oct;32(5):397-404.