# Letters to the Editors

## Reply to: Is Etanar a new biologic?

*M. Scheinberg*

## Why Etanar is a new biologic type rhTNFR:Fc

Sirs,

Expiration of patents for biological innovator products, including mAbs, has increased the development of similar versions of the original biopharmaceutical products, termed biosimilar, biocomparable, biocompetitor, etc, which can provide affordable biological treatment to patients (1).

With the aim to establish biosimilarity with the reference medicinal product, an extensive physicochemical characterisation of Etanar in relation to the reference medicinal product (RMP) was conducted by analysing several batches during the manufacturing process at different time points in order to gain as much insight into the originator product as possible.

By definition a "biosimilar" drug product must share the same amino acid sequence as its reference product (2). Thus, it is necessary to confirm the identity of their amino acid sequence. Extensive physicochemical and biological characterisation for Etanar and its reference product was conducted in order to demonstrate their highly similar properties. A series of state-of-the-art analyses showed that Etanar has: Identical primary as well as higher order structures as RMP; indistinguishable monomer and aggregate contents, overall comparable glycan types, and distributions; and comparable potencies and binding affinities as the RMP. In accordance with analytical procedures for Etanar, comparative analysis has been performed on three batches of Etanar (batch no.: 20100801, 20101007, 20110521) and three batches of RMP for critical quality attributes such as purity, charge, activity, structure characterisation, posttranslational modification and so on. The applied analytical methods include: SEC-HPLC, HIC-HPLC, SDS-PAGE, cIEF, L929 neutralisation killing test, TNF-α binding assay, LC-MS/MS peptide mapping, SEC-DLS, CD, DSC, N-glycan profiling and sialic acid content determination by HPLC-FLD method. Analytical tests have been performed on several critical quality attributes through the above methods, and the results show that Etanar and RMP are comparable.

Comparative analytical study was done for more than 20 items on five aspects including purity, charge, activity, structure characterisation and posttranslational modification between Etanar and RMP. It shows that the physical characteristic (purity, charge) and activity are highly similar; the primary structure is generally consistent and the secondary structure and spatial configuration are highly similar as well.

From the point of view of clinical results, we understand that to be an open clinical study (no control group) and when patients have the knowledge about what kind of drug they were receiving this necessarily introduces a range of bias that positively impacts the results. Obviously another factor that also impacts on results is desire of the physicians to achieve a substantial improvement in their patients.

Moreover, we believe that it could also affect results the fact that most of these patients were monitored and treated in rheumatology centres with models of integrated patient-centred care delivery (disease management) and we cannot estimate how much this impacts on results. On the other hand, patients were followed under strict treat-to-target strategy and it is well known that good results are achieved with this strategy. Finally, in our Biomab Arthritis Center we have shown in previous works at EULAR, ACR and Panlar remission or low activity rates of about 75-80% by using DAS28 (3, 4).

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