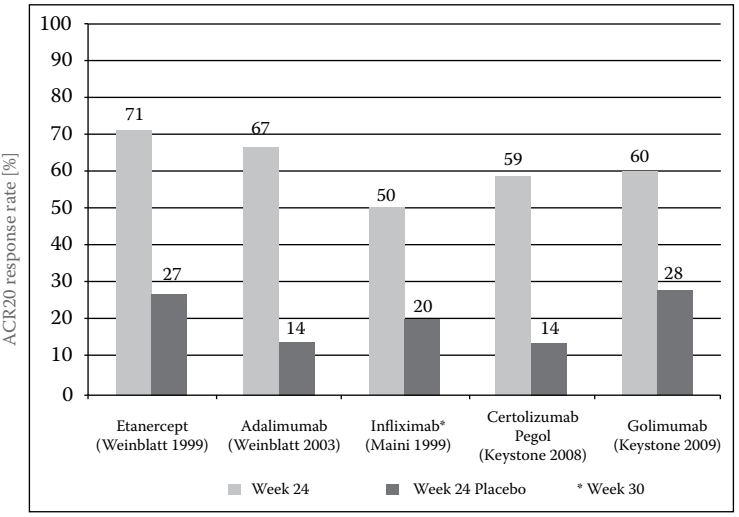

› Response rates of anti-TNFs vary depending on study protocols

FIGURE 7.2 **(See color insert.)** The clinical ACR 20 responses to Etanercept, Adalimumab, Infliximab, Certolizumab, and Golimumab at 24 weeks are clinically comparable.

designed to complement all other analytical data and to provide confirmation that the biosimilar is essentially the same as the reference product. Without this paradigm shift of understanding, physicians will often consider biosimilar clinical trials to be inadequate. This issue will be addressed more specifically in Section 7.4.

7.3 IMMUNOGENICITY

As with the development of any biologic, including the original reference product used to create the biosimilar, it is difficult to predict human immunogenicity using preclinical models. Therefore, although the analytical data on the molecular attributes of the biosimilar can be evaluated for similarity to its reference product, it is challenging to predict overall immunogenicity. A clinical trial can evaluate if there are major signals of differential immune responses. Since the reference product has been used for many years (sometimes multiple decades), there is a substantial database regarding the types of immunogenicity that would be expected from these products. Therefore, the biosimilar sponsor can look specifically for these types of immune responses. It is less complicated to evaluate immunogenicity for a biosimilar than to evaluate a completely new biologic that has not been exposed to humans previously.

Unfortunately, some have erroneously used the experiences of pure red cell aplasia (PRCA) caused by erythropoietic agents in Europe to suggest that there is an increased risk of immunogenicity for biosimilars. The Eprex/Erypo (epoetin alfa) immunogenicity problem was due to a formulation change in the originator product (Casadevall, 2002; Macdougall, 2005), well before the existence of any biosimilars and prior to Eprex/Erypo subsequently being used as a reference product for