



MTX, methotrexate; ASAS20, assessments in ankylosing spondylitis, 20% improvement; ADA, antidrug antibody; PK, pharmacokinetics

FIGURE 12.2 ADA sampling times in Remsima study CT-P13 1.1. Study CT-P13 1.1 was a randomized, double-blind, parallel group study performed in ankylosing spondylitis patients who were not receiving concomitant methotrexate. Patients received multiple iv infusions of 5 mg/kg of Remsima or Remicade during a 54-week period. The primary objective was to demonstrate comparable PK at steady state (between Weeks 22 and 30); samples for ADA testing were collected at the indicated time-points.

8-week time-point and equivalent therapeutic efficacy to Enbrel was demonstrated, the Agency judged that the transient difference did not compromise biosimilarity.

12.23 CHOICE OF SENSITIVE STUDY POPULATION IN RELATION TO EXTRAPOLATION

The FDA recommends that if a sponsor is seeking to extrapolate immunogenicity findings for one condition of use to other conditions of use, the sponsor should consider using a study population and treatment regimen that are adequately sensitive for predicting a difference in immune responses between the proposed product and the reference product across the different conditions of use (FDA, 2015). The FDA guidance goes on to explain that, usually, this will be the population and regimen for the reference product for which development of immune responses with *adverse outcomes* is most likely to occur.

Extrapolation of immunogenicity data across therapeutic indications has been permitted for most biosimilar products approved to date in the EU, namely, somatropin, filgrastim, follitropin-alfa, insulin glargine, infliximab, and etanercept. The single exception to date was for a different route of administration for epoetin alfa, based on prior evidence of an incremental risk of immunogenicity for the subcutaneous route for treatment of renal anemia patients with the reference product (Casadevall, 2005). Additional comparative clinical efficacy, safety, and immunogenicity data were considered necessary to support approval of biosimilar versions for