Subcutaneous Abatacept

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The subcutaneous form of abatacept has not yet been licensed for use in Europe but was approved by the FDA in August 2011 for patients with moderate-to-severe RA.

Practical administration modalities

Subcutaneous abatacept is used in the fixed dose of 125 mg/week starting 7 days after a single abatacept infusion in a dose of 10 mg/kg. The dose does not need to be adjusted for body weight.

Pharmacokinetics

A weekly subcutaneous dose produces therapeutic concentrations with a lower total dose than with intravenous administration. The therapeutic range is achieved regardless of patient weight and, consequently, a single weekly 125-mg dose can be used in patients with rheumatoid arthritis (122). The pharmacokinetic data suggest that an IV loading dose may not always be necessary before starting subcutaneous abatacept: thus, the desired therapeutic concentration is achieved starting at the second subcutaneous injection in most patients (123).

Efficacy

Subcutaneous abatacept is similar in efficacy to intravenous abatacept, as shown by a randomized controlled noninferiority trial of intravenous abatacept (10 mg/kg) versus subcutaneous abatacept (125 mg/week after an IV dose of 10 mg/kg on day 1) in 1457 patients with RA and an inadequate response to methotrexate. After 6 months, the ACR20 response rate was 76% with subcutaneous abatacept and 75.8% with intravenous abatacept. The response profiles were similar in terms of ACR response rates, disease activity, and functional improvements (122). After 6 months, all the study patients were given subcutaneous abatacept. Efficacy was sustained over 24 months (124). In an open-label study in 123 patients, switching to the subcutaneous route after 5 years on the intravenous route had no significant impact on efficacy (125).

Safety

The safety profile with the subcutaneous route was good and similar to that reported with the intravenous route. In the non-inferiority trial, the 6-month adverse event and serious adverse event rates were 67% and 4.2%, respectively, with subcutaneous abatacept versus 65.2% and 4.9%, respectively, with intravenous abatacept. Furthermore, rates were similar for severe infections, malignancies, and autoimmune events. Injection-site reactions were usually moderate in intensity and occurred in 2.6% of patients treated subcutaneously and 2.5% of those treated intravenously. Immunogenicity was also comparable with the two routes: the rate of abatacept antibody detection was 1.1% with subcutaneous administration and 2.3% with intravenous administration (122). In another study, switching to the subcutaneous route after 5 years of intravenous treatment had no effect on the safety profile (125). Finally, the overall immunogenicity of subcutaneous abatacept is low, similar to that of intravenous abatacept, and is not affected by re-starting abatacept therapy after a 3-month interruption. Withdrawal-reintroduction was well tolerated and had no adverse effect on efficacy (126).