Management of patients with a past or present history of infusion reactions: acute or periinfusional reactions

Evidence-based Medicine | Official Recommendations | Expert opinion

Abatacept infusions may induce reactions, of which intensity is usually moderate. Infusion-related reactions occurred in 6.3% of abatacept treated patients compared to 2% of placebo treated patients (5).

Description of acute infusion- reactions

Acute infusion- reactions are defined as reactions that start within 1 hour after the initiation of the infusion. In the Phase II, III, and IV studies (phase II, AIM, ATTAIN, ATTEST), acute infusion reactions (within 1 h after infusion initiation) were more common in the abatacept arms than in the placebo arms (9.8% and 6.7%, respectively) (20).
The events most often reported with abatacept (1 to 2%) were as follows:

- Dizziness
- Headaches
- Hypertension

Acute infusion-related events reported in >0.1% and ≤1% of abatacept-treated patients included cardiopulmonary symptoms such as:

- Hypotension
- Dyspnea

The other symptoms included:

- Nausea
- Skin erythema, urticaria, pruritus, and rash
- Hypersensitivity
- Cough and wheezing

The intensity of these reactions was usually mild to moderate. Hypersensitivity reactions were rare.

Anaphylactic reactions were rare in the double-blind and long-term open-label phases. Treatment discontinuation because of an acute infusion-related reaction occurred in 0.4% of abatacept-treated patients and 0.2% of placebo-treated patients (20).
Severe hypersensitivity reactions requiring discontinuation of abatacept therapy are exceedingly rare (0.4% of abatacept-treated patients and 0.2% of placebo-treated patients) (47). In patients who discontinued abatacept then resumed the drug later on, no infusion-related reactions were recorded upon treatment restart (44).

Monitoring abatacept infusions

Although infusion-related reactions are usually non-serious with abatacept, their possible occurrence requires medical monitoring of patients during the infusions. However, no premedication is needed.

- Heart rate and blood pressure measurements before starting the infusion
- Abatacept infusion (100 mL in 30 minutes)
- Heart rate and blood pressure measurements at the end of the infusion then 30 minutes later

Management of a patient with an acute infusion reaction during abatacept infusion

The management depends on the nature and severity of the reaction. Decreasing the infusion rate may suffice to ensure resolution of the reaction. Therefore, the following sequence can be recommended.

Mild-to-moderate reactions

- 50% decrease in the infusion rate (e.g., decrease from 50 mL/h to 25 mL/h)
- If needed, IV administration of an antipyretic agent (acetaminophen) or antihistamine
- Discontinuation of the infusion if the symptoms persist despite the slower infusion rate
- Resumption of the infusion at a slower rate after complete resolution of the symptoms

Severe reactions (shock, anaphylactic reaction, bronchospasm)

- Immediate permanent discontinuation of the infusion with disconnection of the tubing from the abatacept pouch
- Appropriate resuscitation measures
- Adrenalin, antihistamines, and glucocorticoids in patients with anaphylaxis
- Call and seek advice from an intensivist
- Symptomatic treatment (e.g., inhaled beta2 adrenergic agonist)
- Appropriate patient monitoring, in the ICU if needed
- Contraindication of abatacept

Periinfusional reactions

Reactions potentially related to drug hypersensitivity may occur after the patient leaves the hospital, within the 24 hours following the infusion. Symptoms may include hypotension, urticaria, and dyspnea. These delayed reactions are uncommon.

No delayed reactions resembling serum sickness have been reported to date, probably because abatacept is an entirely human fusion protein with low immunogenicity. Antibodies to abatacept were assessed in 3985 RA patients who had been treated with abatacept for up to 8 years. Of 3877 patients, 187 (4.8%) developed anti-abatacept antibodies during the treatment. When binding to the CTLA-4 component of abatacept was confirmed, a test for neutralizing antibodies was performed. This test was positive in 22 of the 48 assessed patients. However, the clinical relevance of neutralizing antibodies is unknown. Overall, antibody development showed no correlation with the loss of efficacy or the occurrence of adverse events (20). These antibodies are not assayed in daily practice.