Management of patients with past or present history of liver disorder

Evidence-based Medicine | Official Recommendations | Expert opinion

Steps to be taken before abatacept initiation in patients with a history of liver disease

Abatacept, in combination with methotrexate, can be associated with liver transaminase elevation. No studies have specifically addressed the impact of liver failure on the pharmacokinetic of abatacept or the effects of abatacept in patients with liver failure.

Consequently, the Summary of Product Characteristics indicates that no recommendations can be made about the optimal dosage.

Cases of hepatitis B reactivation have been reported in patients receiving antirheumatic drugs such as abatacept (5).

Patients should therefore be screened for hepatitis B and C before abatacept therapy is started.

What are the alarm symptoms of liver disease?

No clinical signs of hepatitis or liver failure have been reported during abatacept therapy. Reported liver disorders were usually detected only by routine laboratory tests performed to monitor the treatment.

When and how should the transaminase levels be monitored and what is the best course of action in case of transaminase elevation?

- **Monitoring the transaminase levels**

  During the clinical studies, transient or intermittent mild-to-moderate elevations in the liver transaminase levels with no clinical evidence of liver disease were reported in abatacept-treated patients.

  The Summary of Product Characteristics gives no recommendations about monitoring the transaminase, bilirubin, or γGT levels during abatacept treatment. However, in the European label abatacept should be given in combination with methotrexate, which requires transaminase monitoring.

- **Course of action in the event of transaminase elevation**

  In practice, the first step is to look for another cause of transaminase elevation and to adjust the methotrexate dosage if appropriate.

Additional information on the risk of liver disorders during abatacept treatment

- **Hepatotoxicity of drugs in general**

  All drugs are potentially hepatotoxic. However, drug-induced hepatotoxicity is rare, with rates ranging from 1% to 1/100 000 depending on the drug and mechanism involved (direct toxicity or immunoallergic response). Pre-existing liver disease must be diagnosed before treatment initiation and can increase the risk of hepatotoxicity via synergistic or additive effects. Therefore, monitoring should be reinforced in this situation. Thus, except for severe cirrhosis of the liver, no liver disorders are considered to be absolute contraindications to the use of hepatotoxic compounds, if appropriate monitoring is done.

- **Viral hepatitis and abatacept**

  A case of hepatitis E was reported during the clinical trials. Screening tests for hepatitis B and C should be performed before starting abatacept treatment.

- **Transaminase elevation during the therapeutic trials**

  The Summary of Product Characteristics indicates that, during the placebo-controlled clinical trials, 1955 patients received abatacept, in combination with methotrexate in 81.9% of cases. In these clinical trials in adults, liver test abnormalities (including transaminase elevation) were more common with abatacept than with the placebo (difference >0.2%). The rate of liver test abnormalities was estimated between 0.1% to 1%. No data are available on the proportions of patients with transaminase elevation.

  Combination of potentially hepatotoxic drugs (methotrexate, NSAIDs, glucocorticoids, sulfasalazine, or leflunomide) to abatacept was not associated with an increased incidence of hepatic cytolysis.

- **Data on liver function during long-term abatacept therapy**

  No data on the long term hepatic safety of abatacept treatment have been published. No case study has been reported

- **Liver abnormalities reported to registries**

  No liver safety data from registries have been published to date.

- **Liver abnormalities in the French pharmacovigilance database**

  Only two cases of liver abnormalities have been reported to the French pharmacovigilance database. The first case reported a Cholestasis (alkaline phosphatase at 4N and γGT at 20N) with moderate liver cytolysis in a RA patient. The liver function tests returned to normal after abatacept discontinuation. The second patient was a woman with Still's disease who presented with hepatic cytolysis (ASAT 5ULN and ALAT 3ULN) developed after a first abatacept infusion.

In conclusion

In sum, abatacept has no known hepatotoxic effects except for transaminase elevation in 0.1% to 1% of patients. There is no hepatic contraindication to abatacept treatment except severe liver failure, which limits the use of all drugs and requires pharmacokinetic and pharmacodynamic studies to define the modalities of abatacept use, if any.

Finally, as with all immunosuppressant agents, abatacept treatment requires screening tests for hepatitis B and C.