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Extended Research Article

# The clinical utility and safety of biomarker-guided immunosuppression withdrawal in liver transplantation: the LIFT prospective RCT

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## Plain language summary

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# Plain language summary

After liver transplantation, the body's immune system may reject the transplanted organ. In order to prevent rejection, the immune system has to be weakened or suppressed by administering anti-rejection medications. The majority of liver transplant patients need to take the anti-rejection drugs for life, which can be problematic due to their many side effects. However, years after transplantation, a small group of patients can stop their anti-rejection drugs without undergoing rejection. This phenomenon is known as transplantation tolerance. In a study completed in 2012, it was possible to identify liver transplant patients who had developed tolerance with high precision by conducting a genetic test in a liver biopsy.

The objective of the current clinical trial was to validate this test of tolerance. This was done by enrolling patients more than 3 years after transplantation and allocating them at random to two groups. All the patients in group A had their anti-rejection medication gradually discontinued, while in group B only those patients who had a positive test result had their anti-rejection medication weaned. The expectation was that more patients would be able to stop their anti-rejection medication in group B than in group A.

One hundred and twenty-two patients were enrolled in the trial, out of whom 80 patients attempted to discontinue the anti-rejection drugs, while 34 patients maintained their normal medications. Among patients who attempted to stop anti-rejection drugs, 67.5% developed rejection, 27.5% completely stopped the anti-rejection drugs, but 16% were considered as truly tolerant after having had a liver biopsy. Overall, drug discontinuation was successful in a much lower proportion of patients than originally predicted. Furthermore, the test of tolerance was not accurate enough to identify tolerant patients before initiating anti-rejection drug discontinuation. As a result of the diagnostic test not performing as expected, the trial had to be terminated prematurely.

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