Rituximab is not effective for the treatment of fatigue in primary biliary cholangitis

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Results from the RITPBC trial demonstrated that rituximab was not effective for treatment of fatigue in unselected patients with primary biliary cholangitis (PBC). The study, presented at The International Liver Congress 2017 in Amsterdam, The Netherlands, showed that rituximab was well tolerated and improved the anaerobic threshold, the level of exercise intensity at which lactic acid builds up in the body faster than it can be cleared away.

PBC is a chronic autoimmune disease that can damage and eventually destroy bile ducts.1 It is a chronic, inflammatory condition which can lead to cirrhosis, liver failure and cancer.1 A large proportion of patients respond to the administration of ursodeoxycholic acid (UDCA), which can significantly improve liver function tests, and slow the destruction of bile ducts as well as disease progression.2,3 However, more than 30% of patients do not respond adequately to UDCA treatment, and thus remain at high risk of disease progression which may require a liver transplant, as well as reduced survival rates.4 PBC affects mostly middle aged women and is a disease which may progresses silently for years; over time, symptoms such as fatigue and itching (pruritus) emerge, often resulting in poor quality of life for patients.1 In about 25% of patients, fatigue is severe enough to result in loss of capacity to work and to lead a normal social life.5 Fatigue is not related to the severity of liver disease.6 PBC-associated fatigue does not respond to UDCA therapy however, and there are no licensed treatments available.7,8 A pilot study in patients with PBC refractory to UDCA found that rituximab treatment produced a clinically significant reduction in fatigue.9

"This is the first randomised controlled trial of a treatment for fatigue in patients with PBC," said Dr Amardeep Khanna, Newcastle University, UK, and study author. "Rituximab was not found to be effective for the treatment of PBC-associated fatigue in this study, but we feel that future studies should target more specific types of fatigue, which may produce more favourable results."

The RITPBC study was a Phase 2, randomised, controlled, double-blind trial conducted in a single UK centre.7 The aims of the study were to assess whether rituximab improved fatigue in patients with PBC, safety and tolerability of rituximab in PBC and the sustainability of any beneficial actions of the drug.7 The primary outcome was improvement in fatigue domain score of the PBC-40 at 12 weeks, which is a disease-specific quality of life questionnaire. Fifty-seven patients with PBC and moderate to severe fatigue were randomised to receive two infusions of rituximab or placebo on days 1 and 15, and were followed for up to 12 months.

At 12 weeks, there was no statistically significant difference in fatigue score between rituximab and placebo. However, both treatment groups did experience an improvement in fatigue from the start of the study. Rituximab significantly improved the anaerobic threshold compared with placebo. There were four serious adverse events in the trial - one patient died before they had received the drug and the other three were in patients receiving placebo.

"This study is very important as it addresses fatigue, a major symptom experienced by patients with PBC. The fact that the results were non-significant from a clinical perspective should not undermine the relevance of the findings. Any new study results, positive or negative, in a rare disease such as PBC, adds to the body of evidence and will be crucial in informing the direction of future clinical studies. The current trial shows that although rituximab was not effective in reducing fatigue,

there is nevertheless still a connection between the symptom and the immunopathological process. Therefore, further characterisation of the type of fatigue experienced by PBC patients may be crucial in helping identify optimal treatment," said Prof Marco Marzioni, Professor of Gastroenterology, Università Politecnica delle Marche - "Ospedali Riuniti" University Hospital of Ancona, Italy and EASL Scientific Committee Member.

More information: Abstract: B-cell depleting therapy (rituximab) as a treatment for fatigue in primary biliary cholangitis: a randomised controlled trial (RITPBC) (LBP-506), The International Liver Congress 2017.

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