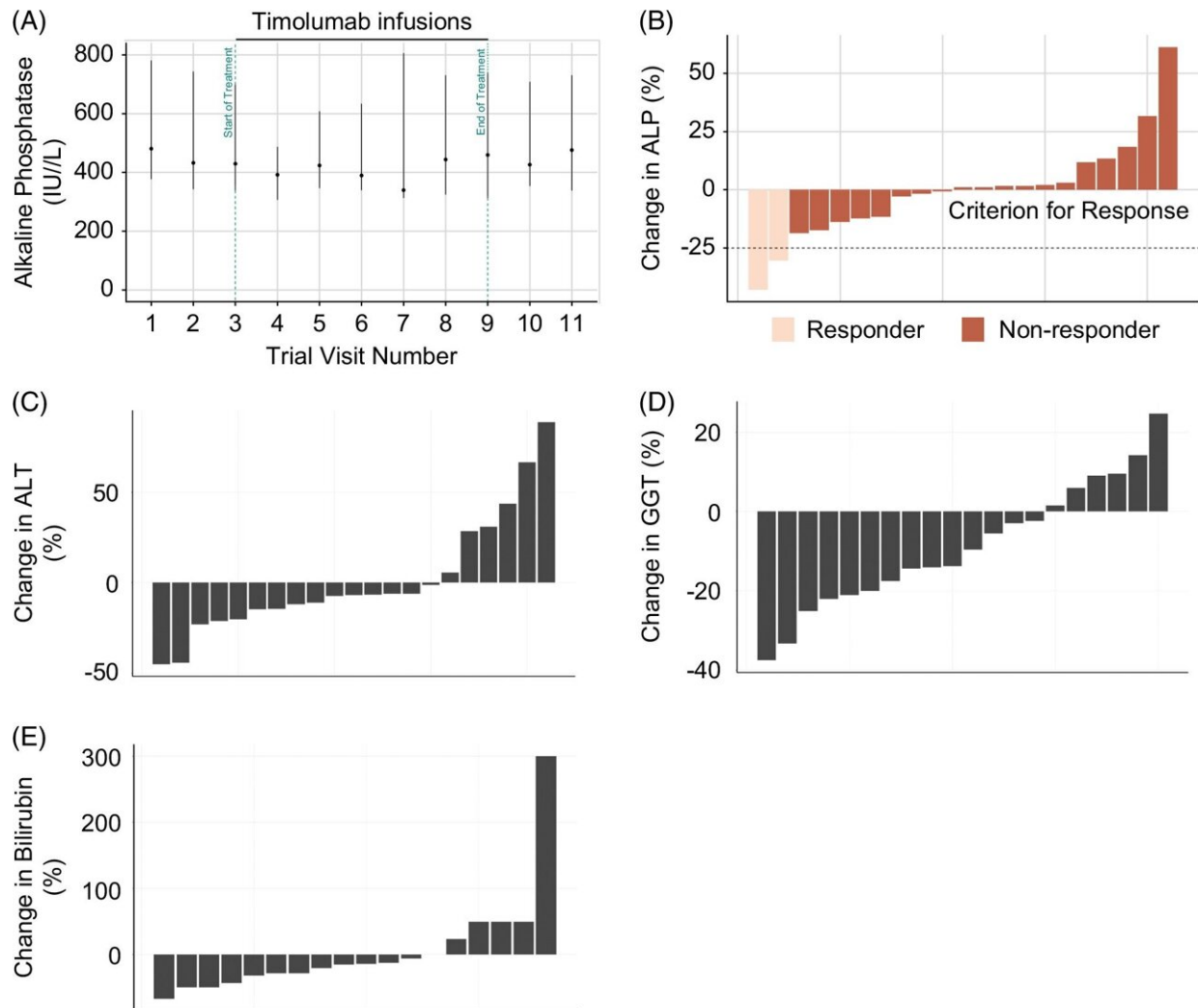


# Study explores potential target to treat liver disease

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Liver biochemistry pre-timolumab, during and post-timolumab treatment. (A) Median with IQRs of ALP (IU/L) in all evaluable patients during the BUTEO trial. Percentage change of ALP (B), ALT (C), GGT (D), and bilirubin (E) levels comparing pretreatment and posttreatment in all evaluable patients. Credit:

A clinical trial led by Birmingham researchers investigated targeting a molecule causing liver inflammation and fibrosis to treat patients with Primary sclerosing cholangitis (PSC)—a debilitating liver disease for which there is currently no treatment.

The findings, [published](#) in *Hepatology Communications*, highlight how the therapeutic agent timolumab was able to safely block the molecule of interest, a vascular adhesion protein called VAP-1, without causing significant adverse effects.

However, it did not produce significant change in the levels of alkaline phosphatase (ALP), an enzyme associated with liver disease, which meant the trial was stopped due to lack of treatment efficacy.

Nevertheless, researchers remain hopeful about the potential of VAP-1 as a target in [inflammatory diseases](#)—also thanks to the breadth of previous evidence gained in previous studies led by Professor David Adams at the University of Birmingham—and believe these findings may help guide future research focusing on this protein.

Dr. Chris Weston is Associate Professor at the University of Birmingham's Institute of Immunology and Immunotherapy, member of the NIHR Birmingham Biomedical Research Center's Inflammatory Liver Disease theme, and co-author of the study.

Weston said, "We believe that VAP-1 remains a viable target in inflammatory and fibrotic disease given the wealth of evidence in other preclinical models, and the use of small molecule inhibitors of VAP-1 that have been developed may provide an alternative means to target

VAP-1.

"Our findings may well help guide other studies using monotherapy or combined therapy with VAP-1, both in the liver and in other sites of inflammation and fibrosis."

Lead Clinical Investigator for the trial Professor Gideon Hirschfield, Chair in Autoimmune Liver Disease Research at the Toronto Center for Liver Disease and Honorary Professor at the University of Birmingham, added, "Primary sclerosing cholangitis can be a very debilitating chronic disease, which most often affects people of working age.

"It is key that we continue to investigate this condition, its causes and potential avenues for treatment, to find effective ways to improve the lives of patients in the U.K. and across the globe."

Primary sclerosing cholangitis (PSC) is a progressive inflammatory [liver disease](#) where the body's immune attacks its own liver. It affects people of all ages, frequently in association with [inflammatory bowel disease](#) (IBD).

**More information:** Gideon M. Hirschfield et al, Vascular adhesion protein-1 blockade in primary sclerosing cholangitis: Open-label, multicenter, single-arm, phase II trial, *Hepatology Communications* (2024). [DOI: 10.1097/HC9.0000000000000426](https://doi.org/10.1097/HC9.0000000000000426)

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