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Researchers identify gene variants linked to hepatitis C treatment-related anemia

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In two recent studies, researchers have identified two functional variants in the inosine triphosphatase (ITPA) gene that protect patients with hepatitis C virus (HCV) against anemia brought on by antiviral treatment. The ability to identify those patients protected against treatment-induced anemia will ensure completion of antiviral therapy and successful elimination of the virus. Full findings of these studies appear in the February issue of *Hepatology*, a journal published by Wiley-Blackwell on behalf of the American Association for the Study of Liver Diseases.

Chronic HCV affects up to 170 million individuals worldwide and is a leading cause of end-stage liver disease. While HCV is curable with treatment of pegylated interferon (pegIFN) and ribavirin (RBV), many patients have difficulty tolerating these antiviral drugs. Prior studies have shown that 9% to 22% of patients enrolled in phase III trials of pegIFN plus RBV require modification of their dose due to hemolytic anemia brought on by the drugs. A reduction in RBV limits treatment efficacy, thus impacting the viral clearance success rate.

Alessandra Mangia, M.D., from Casa Sollievo della Sofferenza Hospital in Italy, and colleagues evaluated the association between ITPA variants and anemia in a cohort of 238 Caucasian patients treated with variable pegIFN and weight-based doses of RBV. The research team found that the ITPA variants were strongly and independently associated with protection from anemia, but did not provide an increase in sustained virological response.

"When anemia develops only four weeks after the start of treatment, physicians are required to immediately reduce ribavirin dosages. This early reduction will affect the overall duration of treatment which, with the combination of pegIFN and RBV, lasts 24 weeks for patients infected with HCV genotypes two and 3 (G2/3) and 48 weeks for patients with HCV genotype one (G1) infection. Currently, only the use of the drug erythropoietin (EPO)—an expensive drug that due to its high cost cannot be reimbursed in several countries—might prevent unsuccessful antiviral treatment in these cases," explained Dr. Mangia.

"Our findings demonstrated that ITPA variants are strongly associated with protection from week four anemia and help us in selecting in advance who will need early ribavirin dose reduction and possibly supportive EPO treatment. This may lead to a more rational use of economical resources and to an individualized use of supportive EPO treatment," concluded Dr. Mangia. "Patients with a genetic profile that included the two ITPA variants may be safely administered higher doses of RBV, increasing the likelihood of HCV elimination after treatment—an important finding given that to achieve viral clearance high dosages of RBV need to be used in the early phases of treatment."

A related study led by Fumitaka Suzuki, M.D., from Toranomon Hospital in Japan found similar results in its cohort of 61 Japanese patients with HCV. Patients in this study received a triple therapy of pegINF, RBV and the protease inhibitor, telaprevir. Dr. Suzuki and colleagues found that ITPA variants impacted blood levels; however a sustained virological response could be achieved with careful monitoring of anemia and prompt adjustment of RBV dose. The authors suggest that future investigation of the influence of ITPA gene variants on RBV-induced anemia are needed on larger scales and on patients of various ethnicities.

More information: Article: "ITPA Genetic Variants are Protective

Against Anemia During Antiviral Therapy for G2/3 HCV, but Do Not Decrease the Need for RBV Dose Reduction or Increase SVR." Alexander J. Thompson, Rosanna Santoro, Valeria Piazzolla, Paul J. Clark, Susanna Naggie, Hans L. Tillmann, Keyur Patel, Andrew J. Muir, Kevin V. Shianna, Leonardo Mottola, Daniela Petruzzellis, Mario Romano, Fernando Sogari, Domenico Facciorusso, David B. Goldstein, John G. McHutchison, Alessandra Mangia. Hepatology; Published Online: January 10, 2010 (DOI: 10.1002/hep.24068); Print Issue Date: February 2011. onlinelibrary.wiley.com/doi/10 … 2/hep.24068/abstract

Article:"Influence of ITPA Polymorphism on Decreases of Hemoglobin during Treatment with Pegylated IFN, Ribavirin and Telaprevir." Fumitaka Suzuki, Yoshiyuki Suzuki, Norio Akuta, Hitomi Sezaki, Miharu Hirakawa, Yusuke Kawamura, Tetsuya Hosaka, Masahiro Kobayashi, Satoshi Saito, Yasuji Arase, Kenji Ikeda, Mariko Kobayashi, Kazuaki Chayama, Naoyuki Kamatani, Yusuke Nakamura, Yuzo Miyakawa and Hiromitsu Kumada. Hepatology; Published Online: January 18, 2010 (DOI: 10.1002/hep.24058); Print Issue Date: February 2011. onlinelibrary.wiley.com/doi/10 … 2/hep.24058/abstract

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