Vaccination with the recombinant preS-based hepatitis B virus vaccine VVX001: Results from a phase II clinical trial

I. Tulaeva[1,2,3], P. Munda[4], C. Cornelius-Nikl[1], P. Gattinger[1], R. Stauber[5], F. Lehmann[6], N. Goldmann[7], D. Glebe[7], R. Henning[8], P. Ferenci[4], M. Trauner[4], U. Wiedermann[9], R. Valenta[1,2,3,10]

[1]Medical University of Vienna, Center for Pathophysiology, Infectiology and Immunology, Institute of Pathophysiology and Allergy research, Vienna, Austria, [2]I M Sechenov First Moscow State Medical University (Sechenov University), Department of Clinical Immunology and Allergology, Moscow, Russian Federation, [3]Life Improvement by Future Technologies (LIFT) Center, Moscow, Russian Federation, [4]Medical University of Vienna, Department of Internal Medicine III, Division of Gastroenterology and Hepatology, Vienna, Austria, [5]Medical University of Graz, Department of Internal Medicine, Division of Gastroenterology and Hepatology, Graz, Austria, [6]Charité - Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Institute of Virology, Berlin, Germany, [7]Justus Liebig University, German Center for Infection Research, Institute of Medical Virology, Giessen, Germany, [8]Viravaxx AG, Vienna, Austria, [9]Medical University of Vienna, Center for Pathophysiology, Infectiology and Immunology, Institute of Specific Prophylaxis and Tropical Medicine, Vienna, Austria, [10]Karl Landsteiner University of Health Sciences, Center for Molecular Allergology, Krems, Austria

Type selection

Choose your preferred presentation format: Oral presentation

General data

Track: Clinical Immunology

Topic: Infectious diseases

Abstract text

Text: Hepatitis B virus (HBV) is a major public health threat; more than 250 million live with chronic hepatitis B (CHB). Conventional HBsAg-based vaccines have 10-20% non-response rate. VVX001 is based on HBV preS antigen and hypoallergenic peptides of major timothy grass pollen allergen Phl p 5. We have previously shown that allergic patients immunized with VVX001 developed antibodies capable of neutralizing HBV *in vitro*. The aim of this trial was to evaluate safety and immunological effects of VVX001 in target populations. Four cohorts were randomized 3/1 to 20µg of Alum-adsorbed VVX001/placebo: (1) vaccination naïve subjects, n=12; (2) non- and low-responders to conventional vaccination, n=20; (3) inactive HBV carriers, n=12; and (4) CHB patients on long-term NUC treatment, n=20. PreS-specific antibodies were detected by ELISA, T-cell responses were measured by CFSE staining. HBV-neutralizing capacity was determined using cultured HBV-susceptible NTCP-HepG2 cells. Blood chemistry and virology parameters were determined by the routine diagnostic laboratory.

Vaccination with VVX001 was well tolerated. NUCs were safely stopped in chronically infected patients after three VVX001 injections. A significant elicitation of preS-specific IgG was achieved in all cohorts ($p<0.001$). HBV-neutralizing antibodies could be induced even in non-responders to HBsAg-based vaccination and CHB patients. More than a half of the chronically infected patients had a >50% reduction of serum HBsAg at 8 months after the end of treatment.

In conclusion, VVX001 is safe to use and able to overcome immunological tolerance to HBV in HBsAg vaccine non-responders and even in chronically infected patients. Virus neutralization capacity of the preS-based vaccination was demonstrated. Further studies are needed to assess the potential of achieving a functional cure with higher doses of VVX001 and to implement VVX001 for HBV vaccination in HBsAg-based vaccine non-responders.

This research was supported by Viravaxx AG and DARC Program funded by the Country of Lower Austria.

Conflict of Interest statement

Do you have any conflict of interest to declare?: Yes

Conflict of Interest statement: Rudolf Valenta has received research grants from HVD Life-Sciences, Vienna, Austria, WORG Pharmaceuticals, Hangzhou, China, and from Viravaxx AG, Vienna, Austria. He served as a consultant for Viravaxx AG. Dieter Glebe has received research grants from Viravaxx AG and served as a consultant for Viravaxx AG. Rainer Henning was an employee of Viravaxx AG. Rudolf Valenta, Carolin Cornelius-Nikl and Inna Tulaeva are authors of patent applications regarding the vaccine. The other authors have no conflicts of interest to declare. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

Affirmation

1. Consent to participate and present onsite: Yes

2. Consent to publication publication: Yes

3. Consent on treatment of contact details saved in this system: Yes