

(36% versus 4%; $P=0.001$) were also greater in the patients who relapsed. Normal laboratory indices before termination of treatment reduced the relative risk (RR) of relapse by 3- to 9-fold compared to patients who had not achieved these results (normal AST: RR 0.33, CI 95% 0.13-0.85, $P=0.01$; normal γ -globulin: RR 0.14, CI 95% 0.02-0.96, $P=0.02$; normal IgG: RR 0.11, CI 95% 0.02-0.78, $P=0.005$; normal AST + γ -globulin + IgG: RR 0.17, CI 95% 0.06-0.56, $P=0.001$). **Conclusions:** Patients with type 1 autoimmune hepatitis who are treated to normal serum AST, γ -globulin and IgG levels have a lower frequency of relapse after corticosteroid withdrawal than patients treated to near-normal levels despite histological remission. The conventional laboratory indices of liver inflammation complement the histological findings in defining the optimal treatment end point, and their normalization should be the goal of therapy prior to drug withdrawal.

Disclosures:

The following people have nothing to disclose: Aldo J. Montano-Loza, Herschel A. Carpenter, Albert J. Czaja

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MOLECULAR MIMICRY BETWEEN TARGET ANTIGEN OF ANCA AND MICROBIAL PROTEIN FTSZ IN AUTOIMMUNE LIVER DISORDERS Birgit Terjung¹, Jennifer Soehne¹, Howard J. Worman², Tilman Sauerbruch¹, Ulrich Spengler¹; ¹Department of Internal Medicine, University of Bonn, Bonn, Germany; ²Department of Medicine and of Anatomy and Cell Biology, Division of Digestive Diseases, College of Physicians and Surgeons, Columbia University, New York, NY

Background: Recently, we identified tubulin-beta isotype 5 (TBB-5) as target antigen of perinuclear antineutrophil cytoplasmic antibodies (atypical p-ANCA) in autoimmune liver disorders such as primary sclerosing cholangitis (PSC) and autoimmune hepatitis (AIH) (Hepatology 2006;4(Suppl.1):229A). TBB-5 shares high structural homology with the microbial cell division protein FtsZ which is present in almost all bacteria of the intestinal microflora and represents an evolutionary precursor protein of tubulin-beta. Here, we investigated whether atypical p-ANCA also react with FtsZ. **Methods:** Extracts of recombinant FtsZ were resolved by two-dimensional gel electrophoresis and reactive proteins were detected by immunoblotting using atypical p-ANCA positive sera from patients with autoimmune liver disorders ($n=15$). Sera from IL-10 $-/-$ mice ($n=20$), which had been grown either under specific pathogen free conditions (SPF) or in individually-ventilated cages and which developed evidence of an ulcerative colitis-like syndrome, were investigated for reactivity on immunoblots with tubulin extracts from HL-60 cells and recombinant FtsZ. Moreover, the murine sera were tested by immunofluorescence microscopy for the presence of atypical p-ANCA on ethanol-fixed human neutrophils. **Results:** In 85% of the sera from patients with atypical p-ANCA and autoimmune liver disorders, reactive protein spots of approximately 42 kD molecular weight and isoelectric points of 4.8 and 4.9 were detected. MALDI-TOF MS analysis confirmed FtsZ in both reactive spots. Pre-absorbing ANCA-positive sera with recombinant FtsZ abolished the characteristic staining pattern of atypical p-ANCA. Of note, sera from IL-10 $-/-$ mice raised under SPF conditions did not show any atypical p-ANCA staining on neutrophils and no reactivity on immunoblots with tubulin extracts or recombinant FtsZ was found. In contrast, atypical p-ANCA staining as well as reactivity with tubulin extracts and recombinant FtsZ were detected in 80% of the sera from mice whose intestines were colonized by the intestinal microflora in individually ventilated cages. **Conclusions:** Our findings suggest an essential role of the intestinal microflora in the pathogenesis of autoimmune liver disorders: the high structural homology between FtsZ and TBB-5 apparently leads to molecular mimicry between the microbial antigen FtsZ and the TBB-5 autoantigen. Thus, antibodies generated in susceptible individuals exhibit dual reactivity with both FtsZ and TBB-5 and give rise to the characteristic fluorescence pattern of atypical p-ANCA when sera are tested on ethanol-fixed neutrophils by immunofluorescence microscopy.

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ENTECAVIR MAINTAINED VIROLOGIC SUPPRESSION THROUGH 3 YEARS OF TREATMENT IN ANTIVIRAL-NAÏVE HBEAG(+) PATIENTS (ETV 022/901) Ting-Tsung Chang¹, You-Chen Chao², Sabahattin Kaymakoglu³, Hugo Cheinquer⁴, Mario Pessoa⁵, Robert Gish⁶, Fred Poordad⁷, Joanna Yang⁸, Helena Brett-Smith⁷, Robert Hindes⁸; ¹National Cheng Kung University Medical College, Tainan, Taiwan; ²Tri-Service General Hospital, Taipei, Taiwan; ³Department of Gastrohepatology, Istanbul Medical Faculty, Istanbul, Turkey; ⁴Universidade Federal Do Rio Grande Do Sul, Porto Alegre, Brazil; ⁵Instituto De Infectologia Emilio Ribas, Hospital Dia Av. Dr. Arnaldo, Sao Paulo, Brazil; ⁶California Pacific Medical Center, San Francisco, CA; ⁷Department of Hepatology and Liver Transplantation, Cedars-Sinai Medical Center, Los Angeles, CA; ⁸Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, CT

Background: Entecavir (ETV) demonstrated superior virologic suppression compared to lamivudine (LVD) after 96 weeks in antiviral-naïve HBeAg(+) chronic hepatitis B (CHB) patients (study ETV-022). Patients achieving a Virologic Response (VR) defined as HBV DNA < 0.7 MEq/mL and HBeAg(+) during the 2nd year of therapy could roll-over to study ETV-901, where they received open-label ETV 1 mg QD. Preliminary efficacy results of ETV after 3 years of treatment in patients with a VR are presented here. **Methods:** 198 of 243 patients who entered the 2nd year of therapy in ETV-022 achieved a VR through Week 96. 151 patients then entered study ETV-901, and 122 received open-label entecavir for at least 1 additional year. The proportions of patients with HBV DNA < 300 copies/mL by PCR assay, HBeAg loss or seroconversion, and ALT normalization were evaluated. **Results:** Efficacy parameters through 3 years of ETV therapy are presented in the table below. **Conclusions:** HBeAg(+) CHB patients who achieved VR after 2 years of entecavir therapy in ETV-022 maintained virologic suppression and ALT normalization during the third year of therapy in ETV-901, with continued HBeAg loss and seroconversion.

	Wk 144(%) N=122*
HBV DNA <300 copies/mL	87%
ALT \leq 1xULN	85%
HBeAg loss during 3rd year of treatment†	31%
HBeAg seroconversion during 3rd year of treatment†	16%

Disclosures:

Ting-Tsung Chang - Investigator: BMS
 You-Chen Chao - Investigator: BMS
 Sabahattin Kaymakoglu - Investigator: BMS
 Hugo Cheinquer - Investigator: BMS, GSK, Novartis, Roche; Consultant: BMS, Roche
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 Robert Gish - Consultant and Speakers Bureau: Bayer, BMS, Eximius F.Hoffmann-LaRoche, Gilead; Consultant and Speakers Bureau: GSK, InterMune, Orthobiotech, Schering-Plough; Consultant and Speakers Bureau: Valeant; Consultant: Amgen, Anadys, Chiron, Corixa, ; Consultant: Human Genome Sciences, Metabasis Therapeutics; Consultant: SciClone, United Therapeutics, Pharmasset, Idenix; Consultant: Hepa-hope, Nucleonics, Innogenetics, XTL; Consultant: Zymogenics
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ASSESSMENT AT THREE YEARS SHOWS HIGH BARRIER TO RESISTANCE IS MAINTAINED IN ENTECAVIR-TREATED NUCLEOSIDE NAÏVE PATIENTS WHILE RESISTANCE EMERGENCE INCREASES OVER TIME IN LAMIVUDINE REFRACTORY PATIENTS Richard J. Colonna, Ronald E. Rose, Kevin Pokornowski, Carl J. Baldick, Kenneth Klecszewski, Daniel Tenney; Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, CT

Background: Entecavir (ETV) is a potent inhibitor of hepatitis B virus (HBV) with proven clinical efficacy. ETV resistance (ETVr) requires pre-existing lamivudine resistance (LVDr) substitutions and an additional change at RT residues T184, S202 or M250. ETVr substitutions are observed following LVD therapy, but only in the presence of LVDr substitutions. **Methods:** Patients exhibiting vi-