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ENTECAVIR RESULTS IN CONTINUED VIROLOGIC AND BIOCHEMICAL IMPROVEMENT AND HBeAg SEROCONVERSION THROUGH 96 WEEKS OF TREATMENT IN LAMIVUDINE-REFRACTORY, HBeAg(+) CHRONIC HEPATITIS B PATIENTS (ETV-026)

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Background: In lamivudine (LVD)-refractory, HBeAg(+) chronic hepatitis B (CHB) patients, switching to entecavir (ETV) was superior to continued LVD at Week 48 for achieving histologic improvement, undetectable HBV DNA and ALT normalization. Long-term data for efficacy and safety through 96 weeks of treatment are reported here.

Methods: 286 HBeAg(+) CHB patients who were refractory to current LVD therapy were randomized 1:1 to ETV 1.0 mg (n=141) or continued LVD 100 mg (n=145). At Week 48, patients who achieved Virologic Response (HBV bDNA <0.7 MEq/mL but positive for HBeAg) could continue blinded therapy through Week 96. A patient was a responder for a cumulative endpoint if the patient had a confirmed response (two sequential measurements) for the endpoint at any time during treatment.

Results: 77 ETV-treated and 3 LVD-treated patients continued blinded therapy to a second year of therapy. In this cohort, the proportion of ETV-treated patients with HBV DNA <300 copies/mL increased from 21% at Week 48 to 40% at end of dosing, ALT normalization increased from 65% to 81% and mean HBV DNA reduction from baseline increased from 5.7 to 5.9 log10 copies/mL. In a cumulative analysis of all treated patients, viral rebound with ETV resistance mutations occurred in 9% of patients through Week 96. The cumulative analysis of efficacy endpoints for all treated patients through Week 96 is presented in the table below.

The Week 96 cumulative safety profile of ETV was comparable to that for LVD.

Conclusions: Through 96 weeks of treatment, ETV 1.0 mg results in continued clinical benefit in LVD-refractory HBeAg(+) patients as measured by the proportion of patients achieving an HBV DNA <300copies/mL, ALT normalization and HBeAg seroconversion. Patients treated for a second year experienced incremental benefit in viral load reduction and ALT normalization.

Cumulative Confirmed Virologic, Serologic, and Biochemical Endpoints through Week 96 (%)			
	ETV 1.0 mg n=141	LVD 100 mg n=145	p-value
HBV DNA <300 copies/mL	30	1	<0.0001
HBeAg seroconversion	16	4	0.0011
ALT ≤1 x ULN	85	29	<0.0001