and 50% of them have achieved the closest to cure outcome of HBsAg loss.
2. Early post-treatment increases in ALT activity and/or re-detectability of serum HBV DNA are usually short-lived and should be first followed for spontaneous resolution rather than retreated immediately.

19 ANTIVIRAL EFFECT OF ENTECAVIR: RESULTS FROM 160 CHRONIC HEPATITIS B PATIENTS IN AN INTERNATIONAL MULTICENTER COHORT STUDY

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Background and Aims: Entecavir (ETV) is a potent inhibitor of viral replication in chronic hepatitis B (CHB) patients. We investigated the efficacy and safety of ETV in CHB patients in clinical practice.
Methods: In this investigator-initiated project within the European network of excellence (VIRGIL) we studied all HBV monoinfected patients treated with ETV monotherapy from 7 large European referral centers. HBV DNA and ALT levels were measured every 3 months. Virologic response (VR) was defined as serum HBV DNA levels <80 IU/mL. Screening for resistance was performed at baseline in treatment-experienced patients or in case of virologic breakthrough by direct sequencing.
Results: A total of 160 patients (68 (43%) HBeAg+) were analyzed, of whom 57 (36%) patients were treatment experienced (14 LAM; 14 ADV; 20 sequential LAM and ADV, 5 LAM with ADV add-on; 3 sequential LAM, ADV, TDF; 1 LdT). 119 patients were treated with 0.5 mg and 41 patients with 1 mg, all of whom were treatment-experienced. Virologic and biochemical endpoints at the end of follow-up are summarized in the table. Multivariate analysis demonstrated that independent baseline predictors of VR were low HBV DNA levels (HR 0.69; 95% CI 0.60–0.81; $p < 0.001$), HBeAg negativity (HR 2.59; 95% CI 1.49–4.52; $p = 0.001$), high ALT levels (HR 1.08; 95% CI 1.04–1.11; $p < 0.001$), and presence of LAM-resistant mutations (HR 0.17; 95% CI 0.04–0.67; $p = 0.01$. No important side effects associated with ETV were noted.
Conclusion: ETV is effective and well tolerated, but its potency is mainly compromised by presence of LAM-resistant mutations at baseline.

	ETV 0.5 mg (n = 119)	ETV 1 mg (n = 41)	Total group (n = 160)
Baseline HBV DNA (IU/mL)	6.3±1.7	6.1±1.7	6.3±1.7
Median follow-up (mth)	10 [3–23]	13 [3–31]	11 [3–31]
HBV DNA decline (IU/mL)	4.2±1.7	3.3±2.0	4.0±1.8
HBV DNA <80 IU/mL	89/119 (75%)	23/41 (56%)	112/160 (70%)
Virologic breakthrough	2/119 (2%)	6/41 (15%)	8/160 (5%)
Genotypic resistance	0/119 (0%)	4/41 (10%)	4/160 (3%)
ALT normalization	68/93 (73%)	15/26 (58%)	83/119 (70%)
HBeAg loss	5/38 (13%)	2/30 (7%)	7/68 (10%)
HBsAg loss	0/119 (0%)	0/41 (0%)	0/160 (0%)

20 ENTECAVIR MAINTAINS A HIGH GENETIC BARRIER TO HBV RESISTANCE THROUGH 6 YEARS IN NAIVE PATIENTS

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Background and Aims: Entecavir (ETV) provides both potent viral suppression and a high genetic barrier to resistance. As a result, in nucleoside-naive patients, ETV resistance (ETVr) was rare through 5 years. The barrier to resistance in lamivudine (LVD)-refractory patients is reduced.
Methods: All patients receiving continuous therapy in registrational trials were monitored for resistance through year 6. Sequencing was performed on serum samples with detectable HBV DNA (⩾300 copies/mL) at each cross-sectional end-of-year analysis, or with viral breakthrough at anytime, or at discontinuation from study with detectable HBV DNA. Cumulative probabilities of resistance were determined through year 6.
Results: In years 1 through 6, respectively, 663, 278, 149, 120, 108 and 99 nucleoside-naive patients were treated and monitored, with 94% in year 6 having HBV DNA <300 copies/mL. No patient in year 6 showed emerging ETVr at T184, S202 or M250 ± LVD resistance (LVDr) M204I/V±L180M. The cumulative probability of genotypic ETVr in nucleoside-naive patients remained at 1.2% through 6 years. Among LVD-refractory patients treated with ETV, 187, 146, 80, 52, 33 and 29 were monitored in years 1 through 6, respectively. The cumulative probabilities of genotypic ETVr at years 1 through 6 were 6%, 15%, 36%, 47%, 51%, and 57% respectively, and of virological breakthrough with ETVr was 50% through year 6. Among the 74 LVD-refractory patients who achieved undetectable HBV DNA on ETV, 5 subsequently developed ETVr.
Conclusions: ETVr remains rare (1.2%) in nucleoside-naive patients through 6 years. *LVDr HBV* has a reduced resistance barrier to ETV, and patients with *LVDr HBV* may benefit from add-on or combination therapy.

21 TWO YEARS SAFETY AND EFFICACY OF TENOFOVIR DISOPROXIL FUMARATE (TDF) IN PATIENTS WITH HBV-INDUCED CIRRHOSIS

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Background and Aims: Tenofovir disoproxil fumarate (TDF) has activity against hepatitis B virus (HBV) and was recently approved for the treatment of chronic HBV (CHB). An efficacy and safety analysis was performed of the subset of cirrhotic patients receiving TDF for 96 weeks in two Phase 3 CHB registration trials, GS-174–0102 and GS-174–0103.
Methods: In study 0102 (HBeAg- CHB) and 0103 (HBeAg+ CHB) patients were randomized 2:1 to double-blind TDF 300 mg or adefovir dipivoxil (ADV) 10 mg once daily for 48 weeks; if Week (W) 48 biopsy was performed patients were eligible to receive open-label TDF for 7 additional years with the option to initiate combination emtricitabine