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Entecavir (ETV) Therapy in Chronic Hepatitis B Patients Previously Treated with Adefovir (ADV) with Incomplete Response On-Treatment or Relapse Off-Treatment

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Introduction

- The primary objective of antiviral treatment for chronic hepatitis B (CHB) is sustained suppression of viral replication and remission of liver disease[1]
- Many adefovir (ADV) treated patients fail to achieve full viral suppression and ADV resistance is observed more frequently in these patients[2,3]
- According to CHB treatment guidelines[1,4], entecavir (ETV) is recommended for the treatment of patients with ADV-resistant HBV
- Previously presented results of study ETV-079 (E.A.R.L.Y.) demonstrated the superiority of ETV over ADV in HBV DNA reduction as early as treatment day 10, which was maintained through 96 weeks of treatment[5, 6]
- Patients who did not achieve a response to therapy (HBe seroconversion and undetectable HBV DNA by PCR), or who relapsed during off-treatment observation were eligible for enrollment into the open-label ETV study AI463-901

Patients and Methods

Study population

- ETV-079 was a randomized, open-label study comparing the early antiviral efficacy, safety and viral kinetics of ETV (0.5 mg daily) with ADV (10 mg daily) in nucleoside-naïve HBeAg(+) patients with CHB
- Study ETV-901 is an open-label rollover study of continued ETV treatment for patients previously enrolled in Phase 2/3 ETV clinical studies. Patients were treated with ETV 1.0 mg daily
- Twenty-four patients treated with ADV 10 mg daily in ETV-079 enrolled in ETV-901
- This analysis consists of 18 of these 24 patients who at the time of entry into ETV-901 had detectable serum HBV DNA
  - 14/18 patients failed to achieve HBV DNA <300 copies/mL on ADV in ETV-079. The remaining four patients achieved HBV DNA <300 copies/mL entered post-dosing follow-up and experienced virological relapse (treatment gaps from last ADV dose in ETV-079 to first ETV dose in ETV-901: 128, 113, 105 and 98 days)

Study endpoints

- HBV DNA <300 copies/mL
- Serum ALT normalization (≤1 x ULN)
- HBe seroconversion

Efficacy assessments were based on available HBV DNA at Weeks 24 (n=16) and 48 (n=9) following switch to ETV in ETV-901 and genotypic resistance was not performed as part of this analysis

Results

Table 1: Baseline Characteristics of ADV Switch Cohort at ETV-901 Entry

	ADV switch cohort (n=18)
Mean age, years	33
Male, n (%)	13 (72)
Region:	
Asia-Pacific, n (%)	11 (61)
US, n (%)	7 (39)
Race:	
Asian, n (%)	17 (94)
Non-Asian, n (%)	1 (6)
Median HBV DNA, $\log_{10}$ copies/mL	6.17
Median ALT, U/L	45

Figure 1: ETV-079/901 Schematic: ADV Switch Cohort

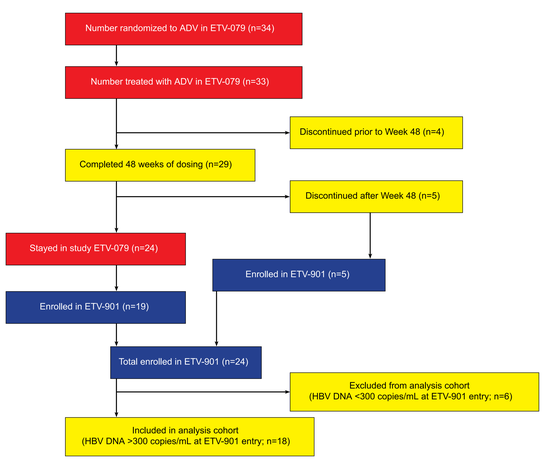

Figure 2: HBV DNA Profiles - All Patients

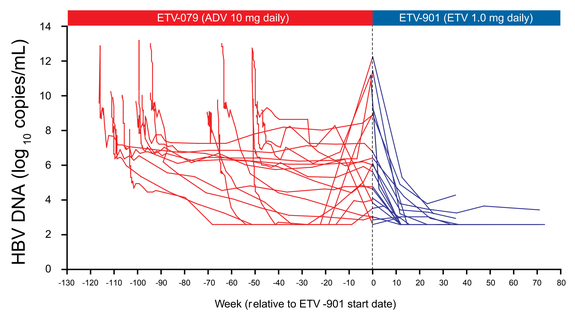

Table 2: Efficacy Endpoints for ADV Switch Cohort at Weeks 24 and 48 in ETV-901

	Week 24 n=16*	Week 48 n=9*
HBV DNA <300 copies/mL, n (%)	8 (50)	8 (89)
ALT ≤1 x ULN, n (%)	11 (69)	7 (78)
HBe seroconversion, n (%)	3 (19)	2 (22)

*2 of the 18 patients included in this analysis did not have Week 24 data, and 9 patients did not have Week 48 data at the time of database lock

HBV DNA

At 24 weeks:

- Mean reduction in HBV DNA was 4.54 $\log_{10}$ copies/mL and 8/16 patients achieved HBV DNA <300 copies/mL

At 48 weeks:

- 8/9 patients (89%) achieved HBV DNA <300 copies/mL
- No patients experienced virological rebound following switch from ADV to ETV in ETV-901

ALT

- At entry into ETV-901, 53% (8/15) of patients had normal ALT. Seven patients who achieved ALT normalization in ETV-079, lost this response by ETV-901 entry
- ALT normalization rates increased to 69% (11/16) and 78% (7/9) at Weeks 24 and 48 respectively in ETV-901

Safety

- The safety profile of ETV in ADV-treated patients remained consistent with previously reported experience[5]

Summary of Results

- Patients who were suboptimal responders to, or relapsed from ADV during study ETV-079 experienced rapid reductions in HBV DNA when switched to ETV 1.0 mg daily
- Mean change in HBV DNA levels were -4.54 $\log_{10}$ at Week 24, and –5.75 $\log_{10}$ at Week 48
- HBV DNA levels continued to decline to undetectable levels with extended ETV treatment
- No patients experienced virological rebound during ETV therapy in ETV-901

Conclusion

- CHB patients switched from ADV to ETV achieve rapid reductions in HBV DNA and increased rates of virological suppression with extended treatment

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Disclosures

Ching-Lung Lai – Global Advisory Board: Bristol-Myers Squibb; Consulting and Speaking: Bristol-Myers Squibb. Richard Elion – Grants: Bristol-Myers Squibb, Gilead, Tibotec, GlaxoSmithKline and Taimed; Advisory: Bristol Myers-Squibb, Gilead, Tibotec, GlaxoSmithKline and Taimed. Morris Sherman – Speaker/Advisor: Bristol-Myers Squibb and Gilead. Hie-Won Hann – Grant/Research Support: Bristol-Myers Squibb, Gilead and Novartis; Speakers Bureau: Bristol-Myers Squibb, Gilead, Novartis and GlaxoSmithKline. DJ Lorne Tyrrell – Research Support: GlaxoSmithKline. Kim Mencarini, Hui Zhang, Uchenna Iloeje and Bruce Kreter – Bristol-Myers Squibb employees. The following people have nothing to disclose: Nancy Leung, Chao Wei Hsu, Chee-Kiat Tan and Cheng-Yuan Peng.

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