Poster Number 485

Efficacy and Safety of Entecavir in Nucleos(t)ide Naïve Asians With HBeAg-Positive and -Negative Chronic Hepatitis B: Results from Studies ETV-022/027

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BACKGROUND

- Hepatitis B is endemic in China and other parts of Asia
- Entecavir (ETV) 0.5 mg demonstrated superior virologic, histologic and biochemical activity compared to lamivudine (LVD) 100 mg in nucleoside-naïve HBeAg(+) and HBeAg(-) chronic hepatitis B (CHB) patients (Phase III studies ETV-022/027)
- The safety profile of ETV was comparable to LVD in the two studies
- This analysis presents the efficacy and safety data of ETV among Asian patients with CHB participating in the two phase III studies (ETV-022/027) at Week 48

METHODS

Study Population and Design

- CHB patients from Phase III studies ETV-022/027 who:
 - Received ETV 0.5 mg or LVD 100 mg for a minimum of
 52 weeks
 - Self-identified as Asian

End Points

- Primary end point was histologic improvement (≥2-point reduction in the Knodell necroinflammatory score, without worsening of the Knodell fibrosis ccore) at Week 48
- Other key end points were virologic, biochemical, and serological response and safety at Week 48

Resistance and Safety Analyses

- Asian HBeAg(+) patients were part of the ETV resistance monitoring program
- Genotyping was performed on paired baseline and on-treatment samples from all patients with:
 - HBV DNA ≥ 300 copies/mL (50 IU/mL) through Week 48
 - Virologic breakthrough (confirmed $\geq 1 \log_{10}$ increase in HBV DNA from nadir) while on treatment
- Safety was assessed by the incidence of clinical adverse events (AEs) and laboratory abnormalities

STUDY RESULTS

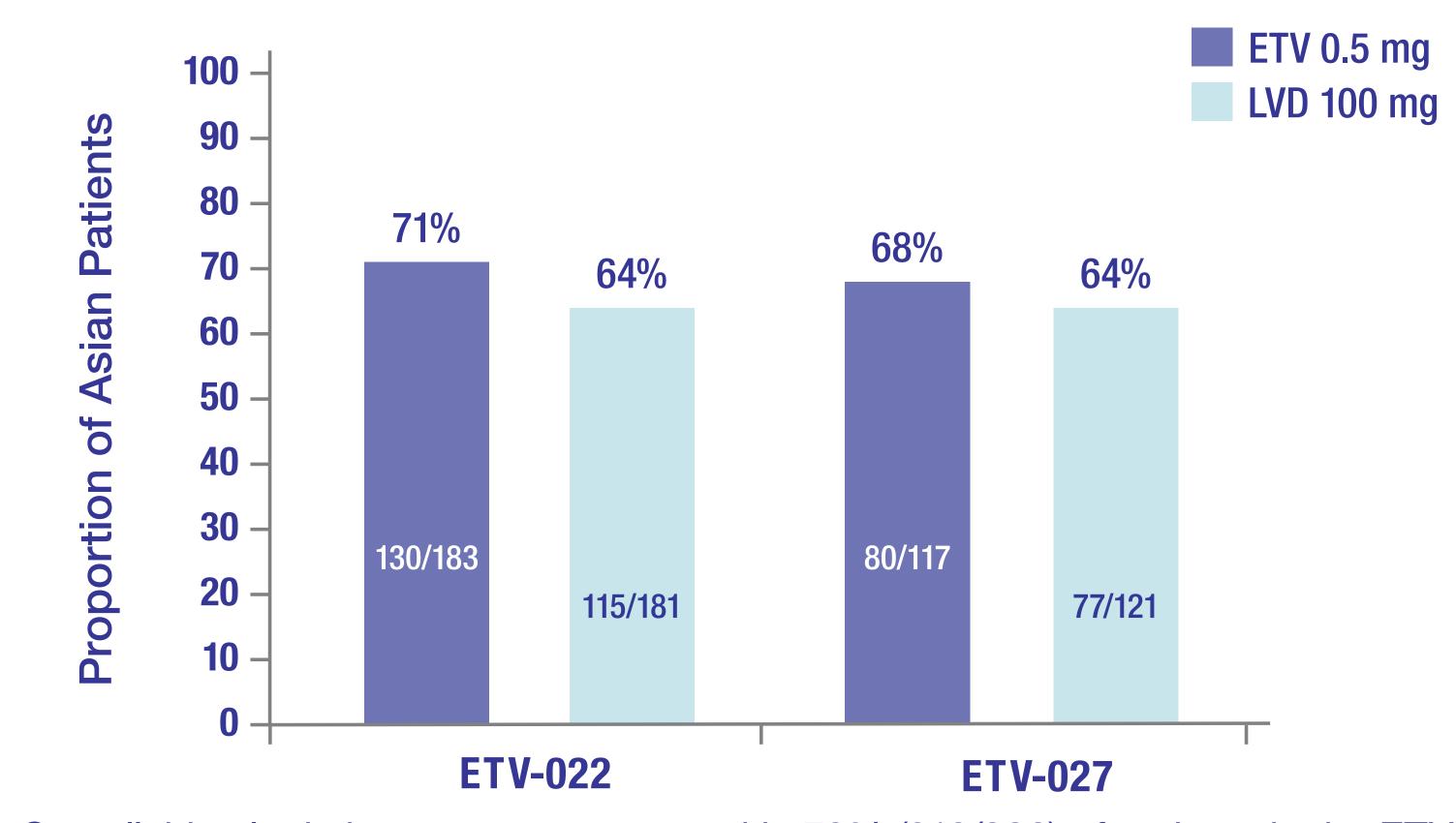
- Nearly half of all patients in ETV-022/027 were Asian:
 - 48% (326/679) on ETV
 - 50% (331/668) on LVD
- Among 657 Asian patients enrolled in the two studies:
 - 406 were HBeAg (+)
 - 251 were HBeAg (-)

Table 1 Demographics and Baseline Characteristics

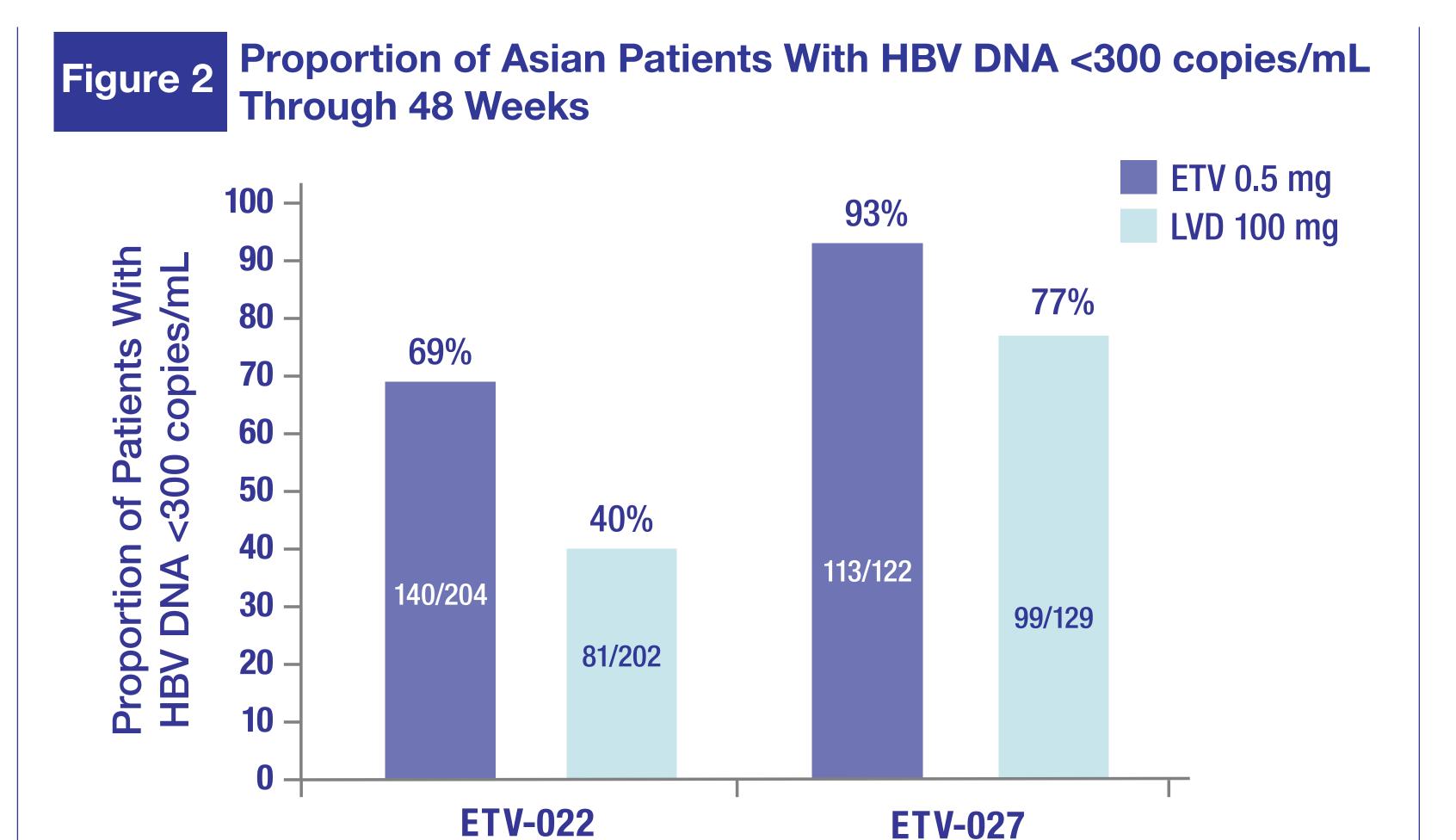
	ETV-022 (HBeAg[+])		ETV-027 (HBeAg[-])		
	ETV 0.5 mg (N=204)	LVD 100 mg (N=202)	ETV 0.5 mg (N=122)	LVD 100 mg (N=129)	
Age, mean (years)	32	32	44	44	
Male (%)	158 (77)	140 (69)	97 (80)	110 (85)	
HBV DNA by PCR, mean log ₁₀ copies/mL	9.64	9.69	7.64	7.35	
ALT, mean (U/L)	137	158	144	138	
Knodell necroinflammatory Score, mean	7.6	7.6	8.3	7.7	
Knodell fibrosis score, mean	1.6	1.5	1.8	1.8	
Ishak fibrosis score, mean	2.2	2.1	2.3	2.4	
HBV genotype: A B C D Other	25	22 31 121 157		24 87 88	



Figure 1 Histologic Improvement Through 48 Weeks

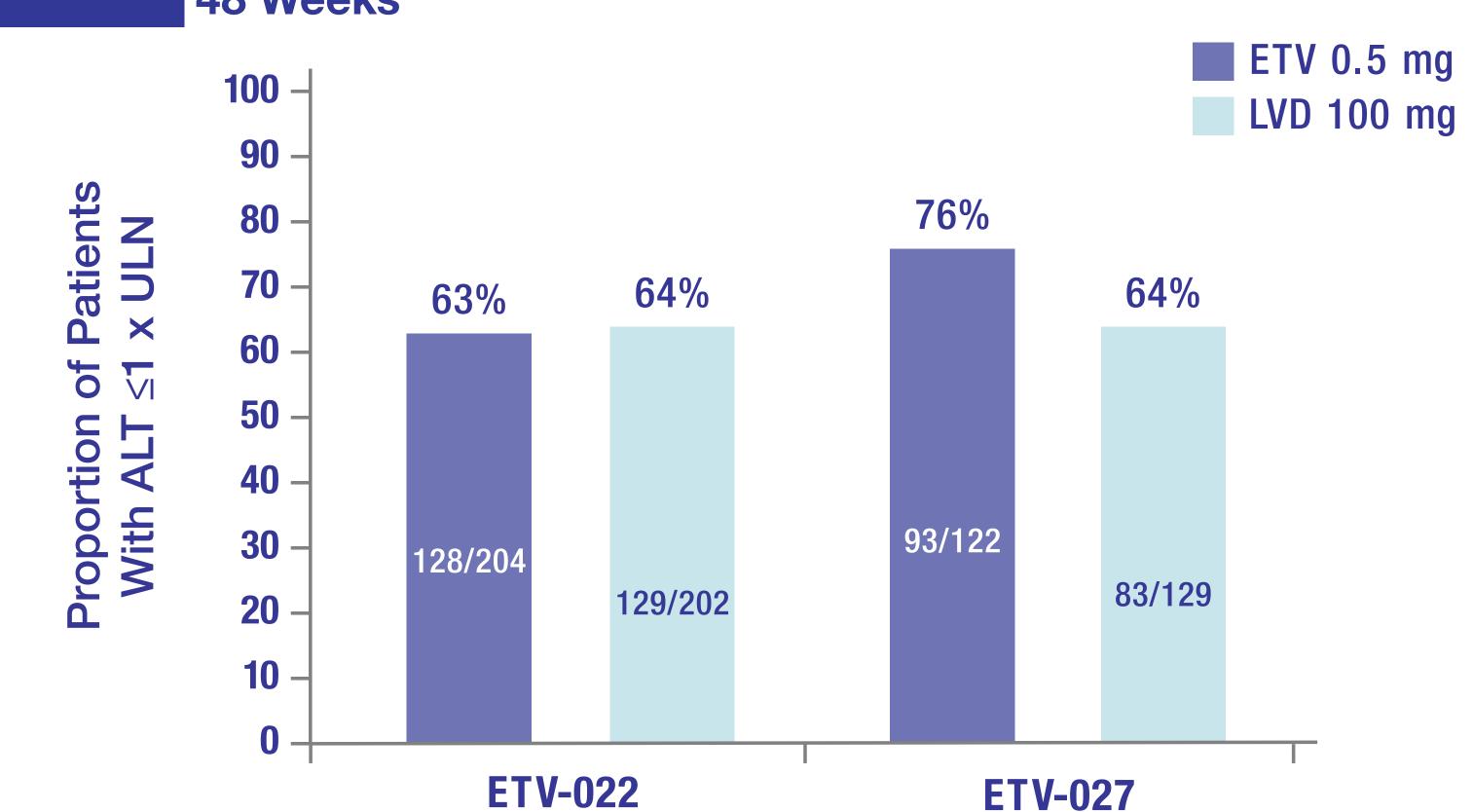


 Overall, histologic improvement occurred in 70% (210/300) of patients in the ETV group versus 64% (192/302) in the LVD group



• Overall, 78% (253/326) of patients in the ETV group and 54% (180/331) in the LVD group had HBV DNA levels <300 copies/mL

Figure 3 Proportion of Asian Patients With ALT ≤1 x ULN Through 48 Weeks



• Overall, 68% (221/326) in the ETV group and 64% (212/331) in the LVD group had ALT normalization

Serologic Response in HBeAg(+) Asian Patients Treated With ETV Through Week 48

- 16% (33/204) of patients had loss of HBeAg
- 16% (32/204) of patients had HBeAg seroconversion
- One (1) patient had HBsAg loss

Resistance in Both HBeAg(+) and HBeAg(-) Asian Patients Treated With ETV Through Week 48

No Asian patients developed ETV resistance

Table 2 Cumulative Safety of Asian Patients from ETV-022 and ETV-027

	ETV 0.5 mg (N=326) N (%)	LVD 100 mg (N=331) N (%)
Any adverse event	287 (88)	283 (85)
Grade 3-4 adverse events	31 (10)	34 (10)
Serious adverse events	18 (6)	21 (6)
Discontinuation due to adverse events	3 (<1)	7 (2)
All deaths	1* (<1)	0 (<1)
On-treatment ALT flare [†]	7 (2)	7 (2)

* There was one death in the ETV 0.5 mg arm in study ETV-027 on Day 314 due to liver cancer † ALT flare: ALT >2 x baseline and >10 x ULN by clinical laboratory evaluation

SUMMARY OF RESULTS

- In this subanalysis of Asian patients enrolled in studies ETV-022/027, ETV use at Week 48 demonstrated:
 - Histologic improvement in 70% of patients
 - HBV DNA <300 copies/mL in 78% of patients
 - ALT normalization in 68% of patients with HBeAg loss and seroconversion occurring in 16% of HBeAg(+) patients
- Resistance did not develop in any Asian patient in ETV-022/027
- Safety was comparable to previously reported data

CONCLUSIONS

- ETV 0.5 mg demonstrated significant histologic, virologic, and biochemical responses compared with LVD 100 mg in nucleosidenaïve Asian patients with HBeAg positive and negative chronic hepatitis B at Week 48
- Efficacy and safety profiles for ETV were similar and consistent with the findings in the overall studies

Disclosures

David Cohen and Hong Tang are employees of Bristol-Myers Squibb
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