

Six month maintenance therapy with 10 mg Clevudine maintains the viral suppression and biochemical improvement achieved with six months therapy with 30 mg

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ABSTRACTS

BACKGROUND : In the pivotal phase III clinical trials, Clevudine 30 mg once daily for 6 months showed potent antiviral activity along with a marked post-treatment antiviral effect. E-max modeling has shown that the 30 mg dose achieved >90% of maximum predicted effect compared to approximately 77% at the 10 mg dose.

OBJECTIVE : To evaluate the effect of 6 months maintenance therapy with 10 mg Clevudine once daily in treatment-naïve patients following 6 months therapy at 30 mg once daily.

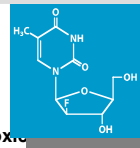
METHODS : Safety, antiviral activity, biochemical improvement and serologic response were monitored in patients receiving Clevudine 30 mg for 24 weeks followed by Clevudine 10 mg for an additional 24 weeks as a maintenance therapy with a 12-week follow-up period. Preliminary results from the 54 naïve patients (39 HBeAg(+), 15 HBeAg(-)) who have completed the study are presented here.

RESULTS : The median baseline HBV DNA was 7.47 log₁₀ copies/mL. At week 24, 66% of patients (53% HBeAg(+), 100% HBeAg(-)) and at week 48, 76% of patients (68% HBeAg(+), 100% HBeAg(-)) were HBV DNA negative by PCR (<300 copies/mL). 77% of patients (82% HBeAg(+), 67% HBeAg(-)) at week 24 and 92% (89% HBeAg(+), 100% HBeAg(-)) at week 48 had normal serum ALT. HBeAg loss occurred in 8% and 16% at week 24 and 48, respectively.

CONCLUSION : Clevudine 30 mg once daily therapy was well tolerated and demonstrated significant viral suppression and biochemical improvement. While a maintenance dose of 10 mg once daily is not recommended due to the potential for resistance selection, it was able to sustain the antiviral and biochemical responses achieved with 30 mg.

Clevudine (L-FMAU)

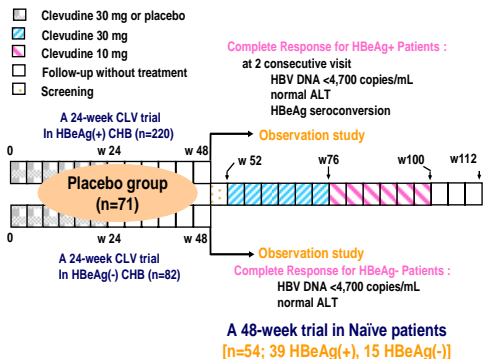
- Thymidine analog
- A potent inhibitor against HBV
- Preclinical results



- Potent *in vitro* activity against HBV (EC₅₀ = 0.1 μM in HepG 2.2.15 cells)
- Little or no cytotoxicity and no bone marrow toxicity
- No mitochondrial toxicity at concentrations up to 1,000 μM
- CLV-TP is not an inhibitor or substrate for cellular DNA polymerases
- Uniquely not incorporated into cellular DNA

- In Phase III clinical trials
- Clevudine showed potent and durable antiviral activities

STUDY DESIGN



Inclusion and Exclusion Criteria of 24-week Clevudine Therapy

Inclusion Criteria

- HBV DNA levels ≥10⁶ copies/mL for HBeAg+ patients
- HBV DNA levels ≥10⁵ copies/mL for HBeAg- patients
- Serum ALT level : 1.2 to 15 times of ULN

Exclusion Criteria

- HIV or HCV seropositivity
- Hepatocellular carcinoma or decompensated LC
- Other significant associated diseases in other organs
- Breastfeeding and pregnant women
- Previous treatment with any nucleoside analogue

METHODS

1. Measurement of serum HBV-DNA

- Digene Ultra-sensitive Hybrid Capture II HBV DNA test ; From baseline to the end of the study. ; **Limit of Detection (LOD):** 4,700 copies/mL
- COBAS AmpliCor HBV monitor test ; When HBV DNA levels reduced to <4,700 copies/mL ; **Limit of Detection (LOD):** 300 copies/mL

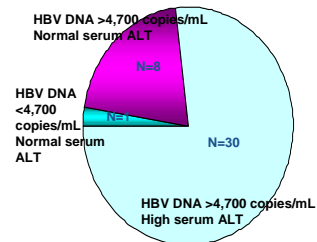
2. Determination of HBeAg and Anti-HBe

- Radioimmunoassay (Abbott Laboratories, North Chicago, IL)

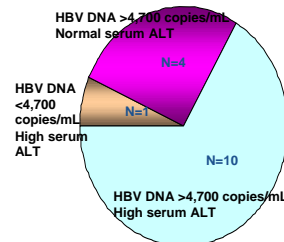
3. Serum ALT level

RESULTS

Baseline Characteristics of HBeAg(+) CHB Patients Treated with Clevudine for 48 weeks (N=39)



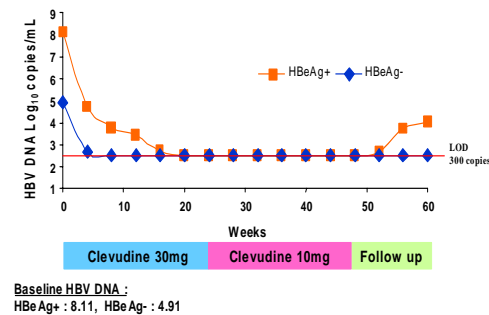
Baseline Characteristics of HBeAg(-) CHB Patients Treated with Clevudine for 48 weeks (N=15)



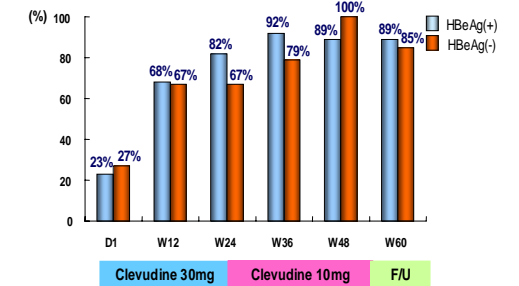
Subject Characteristics at Baseline

Median Age (years)	37
Gender (n, %)	
Male	39 (72%)
Female	15 (28%)
Median Serum HBV DNA (log ₁₀ copies/mL)	7.47
HBeAg positivity	39 (72%)
Median serum ALT (IU/L)	67
Serum ALT category	
normal	13 (24%)
1<, <2 x ULN	19 (35%)
2=<, <5 x ULN	15 (28%)
>=5 x ULN	7 (13%)
HBV DNA <4,700 copies/mL	2 (4%)

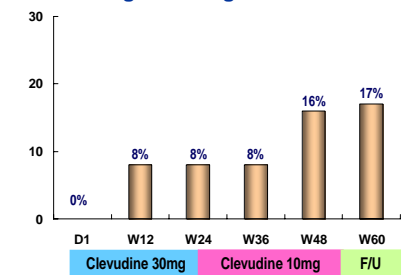
Median Serum HBV DNA Level over Time (log₁₀ copies/mL)



Proportion of Patients with Normal Serum ALT Level



Loss of Serum HBeAg following 48-week Clevudine therapy



Clinical Adverse Events during 48-week Clevudine Therapy (N=54)

Adverse Events*	Number
Myalgia	5
Diarrhea	4
Abdominal Pain	4
Anorexia/Nausea	3
Pruritus	2
Rash	2

* All the adverse events were mild and transient (None were serious)

SUMMARY and CONCLUSIONS

- Clevudine once daily dosing was well tolerated.
- A 48-week Clevudine therapy produced highly potent antiviral activity and biochemical improvement with a sustained effect in naïve chronic hepatitis B patients when used as mono-therapy.
- Six month maintenance therapy with 10 mg Clevudine maintains the viral suppression and biochemical improvement achieved with six months therapy with 30 mg Clevudine.
- Clevudine showed sustained antiviral effects after the cessation of the therapy.

Proportion of Patients with HBV DNA <300 copies/mL (Detection limit of AmpliCor PCR)

