

Entecavir for the Treatment of Chronic Hepatitis B Infection

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Entecavir (ETV) is approved or has applied for approval worldwide to treat chronic hepatitis B infection. Entecavir is a potent and selective inhibitor of the HBV DNA polymerase, affecting DNA priming, DNA synthesis, and reverse transcription.

Trials in the woodchuck hepatitis model demonstrated that treatment with entecavir for 14-36 months resulted in significantly reduced rates of hepatocellular carcinoma compared to historical controls.¹

Pivotal clinical trials demonstrated the superiority of entecavir (ETV) to lamivudine (LVD) for multiple endpoints across three major patient groups: nucleoside-naïve patients infected with HBeAg(+)² or HBeAg(-)³ viruses, and patients infected with LVD-refractory virus.⁴ The following table summarizes the major efficacy results from these trials:

Entecavir Efficacy in Phase III Trials After 48 Weeks									
	Nucleoside-Naive			Nucleoside-Naive			LVD-Refractory		
	HBeAg(+)			HBeAg(-)			HBeAg(+)		
	ETV	LVD	p-value	ETV	LVD	p-value	ETV	LVD	p-value
	N=354	N=355		N=325	N=313		N=141	N=145	
Histological Improvement	72%	62%	0.009	70%	61%	0.014	55%	28%	0.001
Undetectable HBV DNA (<300 copies/ml, <57 IU/ml)	67%	36%	<0.0001	90%	72%	<0.0001	19%	1%	<0.001
Mean Change Baseline HBV DNA (copies-IU/ml)	-6.9 -1.31	-5.4 -1.02	<0.0001	-5.0 -0.95	-4.5 -0.85	<0.001	-5.11 -0.97	-0.48 -0.09	<0.001
ALT ≤ 1.0 x ULN	68%	60%	0.02	78%	71%	0.045	61%	15%	0.001
HBeAg Seroconversion	21%	18%	NS	NA	NA	NA	8%	3%	0.06
HBeAg Loss	22%	20%	NS	NA	NA	NA	10%	3%	0.028
HBsAg Loss	2%	1%	NS	<1%	<1%	NS	0%	0%	NS

In nucleoside-naïve patients continued on treatment for 2 years with entecavir, 81% of HBeAg(+) patients⁵ and 96% of HBeAg(-) patients⁶ achieved undetectable levels of HBV DNA, and among LVD-refractory patients,⁷ 40% of patients reached undetectable levels HBV DNA.

Nucleoside-naïve patients with compensated cirrhosis have also been evaluated from within the pivotal trials.⁸ Results were consistent with those of the total HBeAg(+) and HBeAg(-) populations.

At 2 years of treatment in nucleoside-naïve patients, no genotypic or phenotypic resistance to entecavir occurred. At 1 year of treatment in LVD-refractory patients, HBV with genotypic resistance to entecavir was detected in 7% of patients; viral rebound due to resistance was detected in 1% of patients. During the second year of treatment, viral rebound due to entecavir resistance occurred in 9% of patients.⁹

Entecavir has been similarly well tolerated as lamivudine in comparative studies. The potent clinical activity and low or absent resistance rates support entecavir as primary antiviral therapy for patients with chronic hepatitis B infection.

References

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