

## Durability of HBeAg Seroconversion Following Adefovir Dipivoxil Treatment for Chronic Hepatitis B

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### Background

- HBeAg seroconversion (HBeAg loss with development of anti-HBe) has been considered an important therapeutic marker in the treatment of chronic hepatitis B (CHB) in HBeAg+ patients
- Study 481 evaluated the durability of seroconversion following adefovir dipivoxil (ADV) treatment

### Primary Purpose

- To investigate the durability of HBeAg seroconversion in patients with CHB who have seroconverted while participating in a previous Gilead-sponsored study of ADV

### Methods

- This presentation is of data from patients (n=45) who had confirmed seroconversion to anti-HBe during treatment with ADV 10 mg QD, the approved dose for the treatment of CHB
    - Patients seroconverting on placebo<sup>a</sup> or ADV 30 mg QD also participated in Study 481 but are not included in this presentation
    - The study of origin was 437 for all seroconverters on ADV 10 mg QD
  - Study 481 enrolled CHB patients with compensated liver function
  - Entry criteria required HBV DNA < 10<sup>5</sup> copies/mL by Roche Amplicor PCR assay in conjunction with confirmed seroconversion on ADV
  - Patients were followed off treatment with serologic assessments at least every 24 weeks
  - Data cutoff for this presentation was 29 September 2005 (Study 481 is ongoing)
- a. All maintained seroconversion at last follow-up in Study 481.

### Results

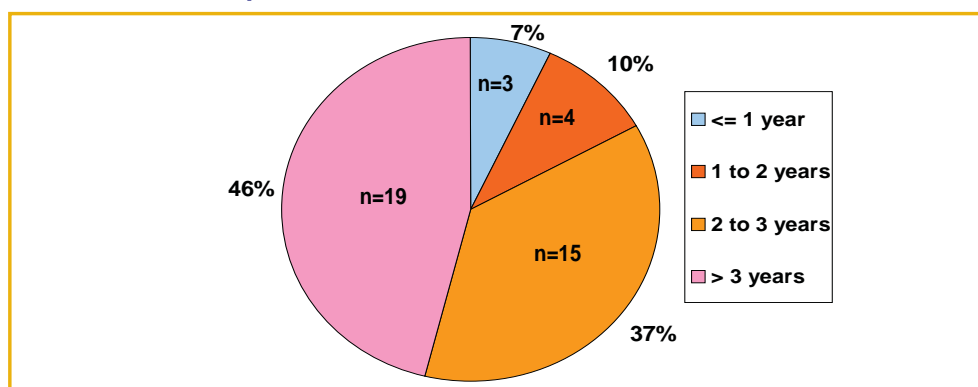
**Table 1. Characteristics of Patients with Confirmed HBeAg Seroconversion on ADV 10 mg QD at Last Time Point on ADV**

Characteristic	N=45
Age (median years)	34
Male	64%
Asian	73%
Caucasian	27%
ALT (median IU/L)	25 (range 9-110)
HBV DNA (median log <sub>10</sub> copies/mL)	3.0 (range 2.6-3.2)
HBV DNA < 1000 copies/mL	93%
Genotype	
A	10 (22%)
B	9 (20%)
C	21 (47%)
D	4 (9%)
G	1 (2%)

#### Durable Seroconversion in Majority Off Drug

- The majority of patients 41/45 (91%) maintained durable seroconversion at the last 2 assessments
  - Median follow-up off drug was 144 weeks
  - Interquartile range (IQR) 122-194 weeks; range 13-245 weeks
- Four patients (9%) lost seroconversion and reverted to HBeAg+
  - n=3 at follow-up week 12
  - n=1 at follow-up week 16
  - Median follow-up off drug 18 weeks
  - At the time of seroreversion patients had ALT 84-222 IU/L and all had HBV DNA > 10<sup>5</sup> copies/mL

**Figure 1. Patients With Durable Seroconversion Off Drug Had Substantial Follow-up**

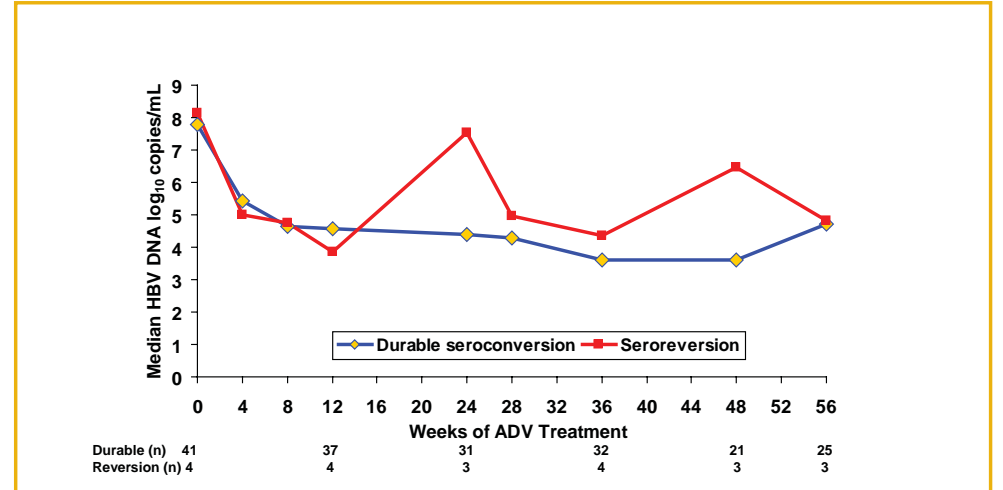


**Table 2. Characteristics at Last Time Point on ADV Were Similar for Those Maintaining Seroconversion or Seroreverting in 481**

Parameter	Durable Seroconversion (n=41)	Seroreversion (n=4)
Age (median years)	34	39
Male	26 (63%)	3
Asian	29 (71%)	4
ALT (median IU/L)	25	26
HBV DNA (median log <sub>10</sub> copies/mL)	3.0	3.0
HBV DNA < 1000 copies/mL	38 (93%)	4
Genotype C (n=21) <sup>a</sup>	17/21 (81%)	4/21 (19%)

a. Statistical testing of durability of seroconversion off treatment across genotypes (A, B, C, D, G) showed no significant difference (p=0.32).

**Figure 2. Dynamics of HBV DNA in First Year of ADV Treatment for Patients With Durable Seroconversion and Seroreversion in Study 481**



**Table 3. Duration of ADV Treatment After Seroconversion Was Longer For Durable Seroconverters**

Duration of:	Durable Seroconversion (n=41)	Seroreversion (n=4)
	Time (weeks)	Time Interval for Each Patient <sup>b</sup>
ADV Treatment After Seroconversion	Median 41 weeks <sup>a</sup> (IQR 28-73; range 9-144)	20 weeks 21 weeks 24 weeks 32 weeks
ADV Treatment Before Seroconversion	Median 48 weeks <sup>a</sup> (IQR 24-68; range 4-213)	107 weeks 130 weeks 72 weeks 108 weeks

a. Median weeks were calculated from the time of 1<sup>st</sup> documented seroconversion.

b. Patients are presented in the same order.

**Table 4. Study 481 Final Assessments Off Drug**

Parameter	N=45
Median follow-up off drug (weeks)	143 (IQR 110-193) range 13-245
ALT (median IU/L) at last assessment	28 (IQR 21-41)
HBV DNA (median log <sub>10</sub> copies/mL) at the last assessment	3.0 (IQR 3.0-4.2) range 3.0-7.6
HBV DNA < 1000 copies/mL at last assessment	44%

### Conclusions

- Among patients who seroconverted to anti-HBe on ADV 10 mg QD, seroconversion was maintained in 91% over a median off-treatment follow-up of 3 years
- Four patients (9%) seroreverted to HBeAg+ within 16 weeks off drug
  - Patients who seroreverted had a shorter duration of ADV treatment after seroconversion than those with durable seroconversion