

History of HBV drug trials and current treatment Prospect for the road to a cure

February 18, 2021

Hie-Won Hann, MD, FAASLD
Professor of Medicine
Director, Liver Disease Prevention Center
Thomas Jefferson University Hospital
Philadelphia, PA

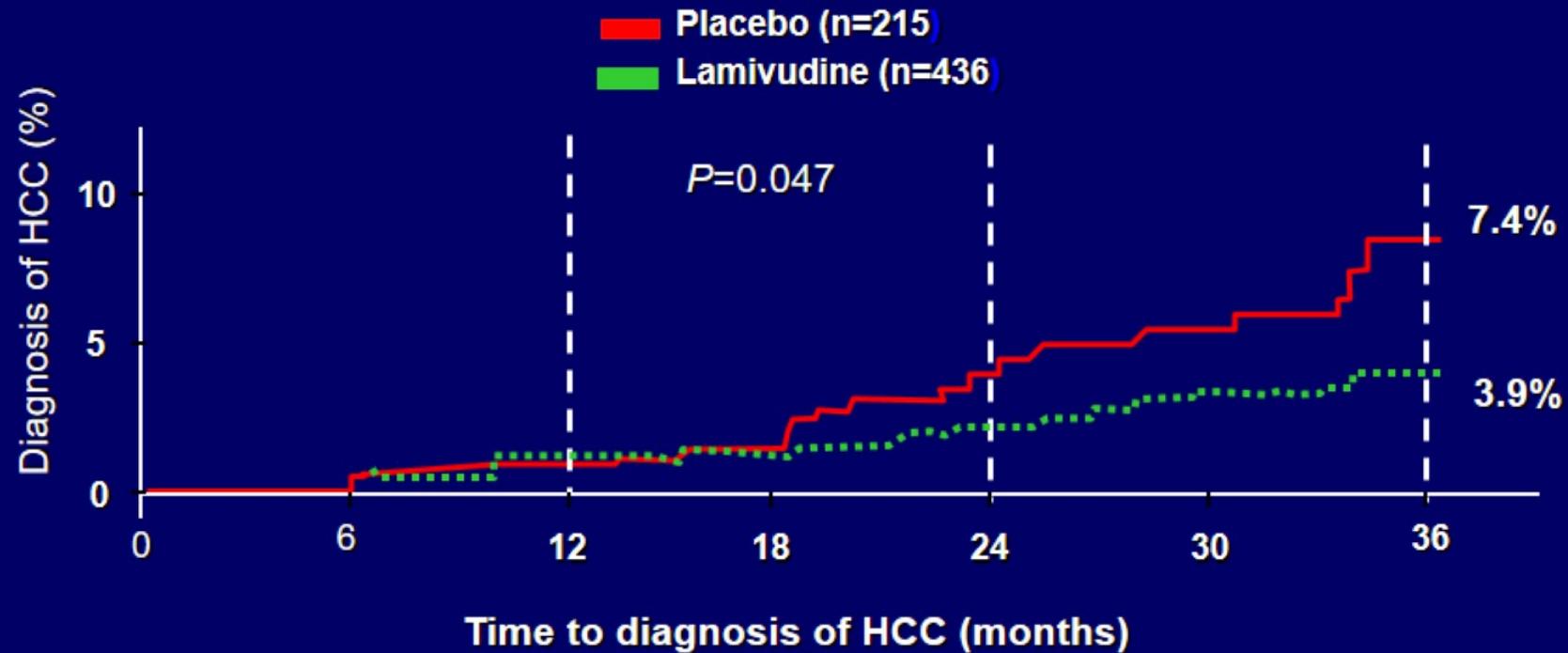
Clinical Trials

- Phase 1. Safety, safety dosage, Side Effects. 20-80 (subjects)
- Phase 2. Effectiveness, dosage trial. 100-200
- Phase 3. Effectiveness, Side Effects, Compare with other products. 300-3000
- FDA approval
- Phase 4. Further observation of effectiveness, Side Effects, Safety etc 1000 +

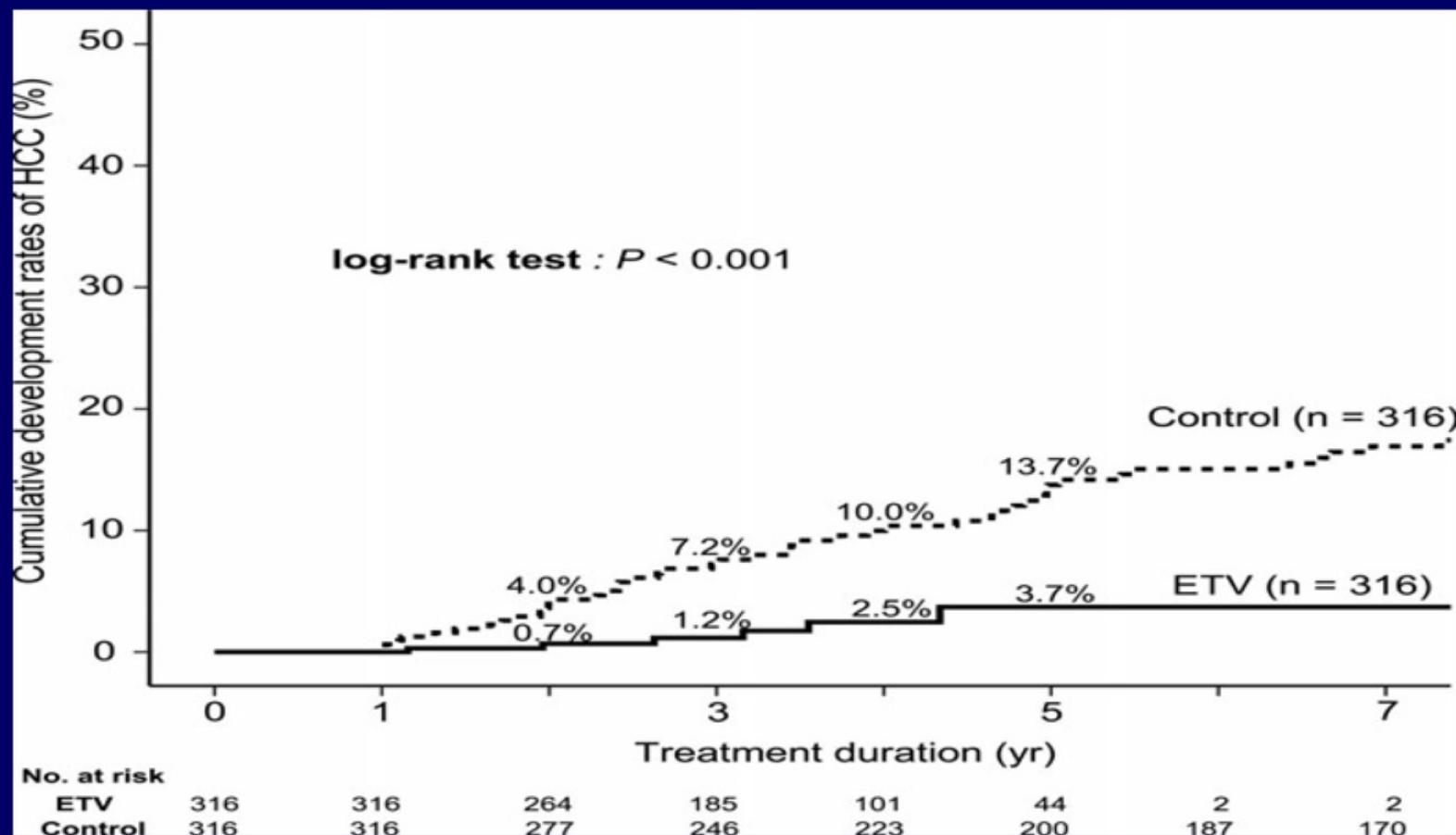
Clinical Trials of the currently available anti-HBV drugs we have conducted at Jefferson 1996-present

- Lamivudine (Epivir-HBV) 8 trials 1998 (FDA approved)
- Lobucavir 3 trials halted
- Adefovir (Hepsera) 4 trials 2002 (FDA approved)
- Entecavir (Baraclude) 4 trials 2005 (FDA approved)
- Telbivudine (Tyzeka) 3 trials 2006 (FDA approved)
- Tenofovir Disoproxil
Fumarate (Viread) 3 trials 2008 (FDA approved)
- Tenofovir Alafenamide
(Vemlidy) 3 trials 2016 (FDA approved)
- ABI (HBV Cure drug?)

Antiviral Therapy Suppresses Development of Hepatocellular Carcinoma in Chronic Hepatitis B (Lamivudine)



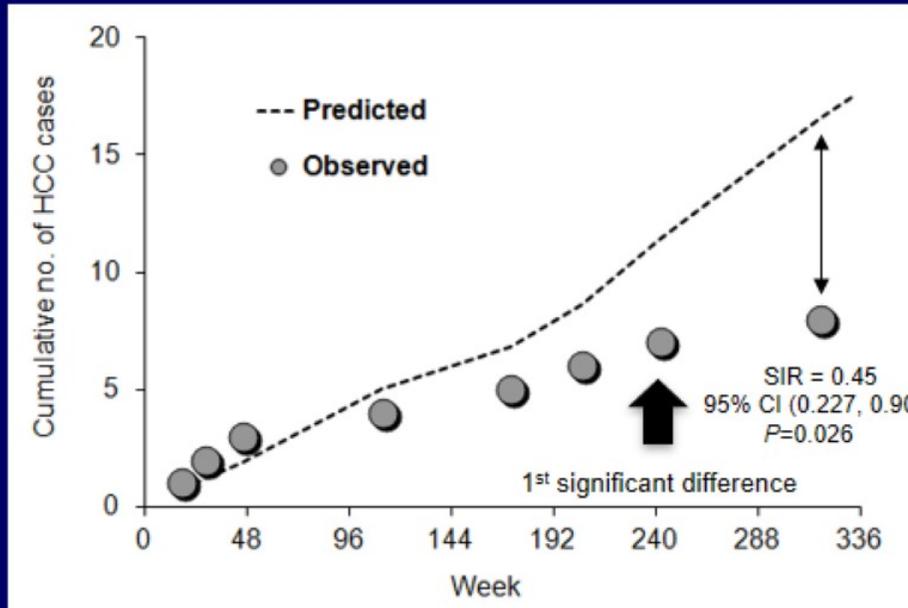
HCC cumulative incidence rates at 5 years between Entecavir-treated and the control group



Observed vs. Predicted HCC Cases

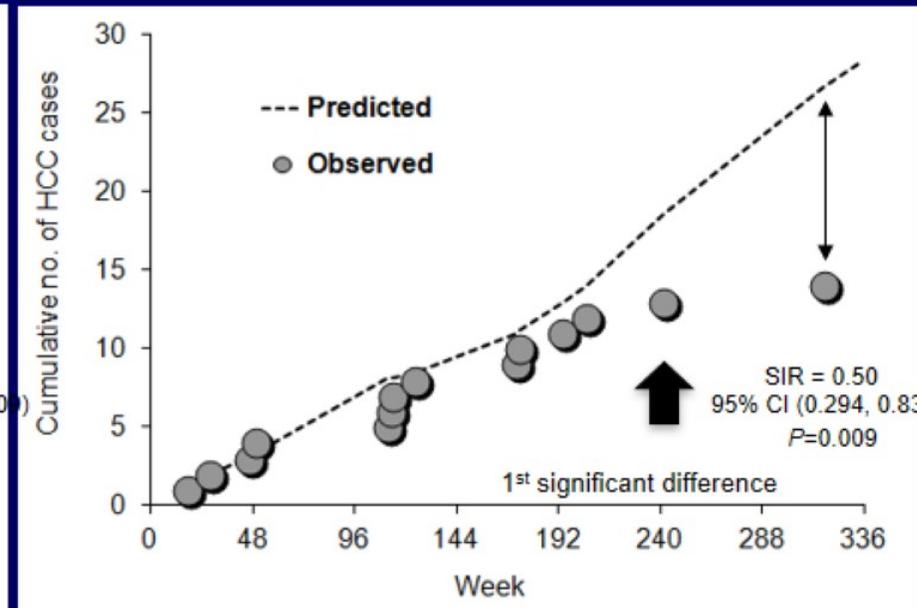
Non-cirrhotics

n=482



All Patients

n=634



- ◆ Incidence of HCC in patients on **TDF** in Studies 102/103 was lower than predicted by the REACH-B model
- ◆ In non-cirrhotic patients, the effect of **TDF** becomes noticeable between 2–3 years of therapy, became statistically significant at 5 years and remained statistically significant at 6 years of therapy (55% reduction)

REACH-B is a risk calculator developed in non-cirrhotic patients so it may underestimate the risk in cirrhotics



Worldwide HCC

Etiology	1985	2000	2016
HBV	80-85%	60%	50%
HCV	The rest	25%	25%
ALD NASH		Increasing	Increasing

Perz JF et al. *J Hepatol.* 2006 Oct;45(4):529-38.

Jemal A et al *CA: a Cancer Journal for Clinicians.* 2011;61

El-Serag HB. *Gastroenterology.* 2004;127(5, Supplement 1):S27-S34

Ha et al. *Cancer* 2016;122:2512-23 (used SEER Data)