4 Year Efficacy of Tenofovir Disoproxil Fumarate (TDF) in Chronic Hepatitis B Patients with High Viral Load (HBV DNA ≥ 9 $\log_{10}$ copies/mL)

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AND

My presentation does include discussion of off-label or investigational use

FTC/TDF for the treatment of HBV

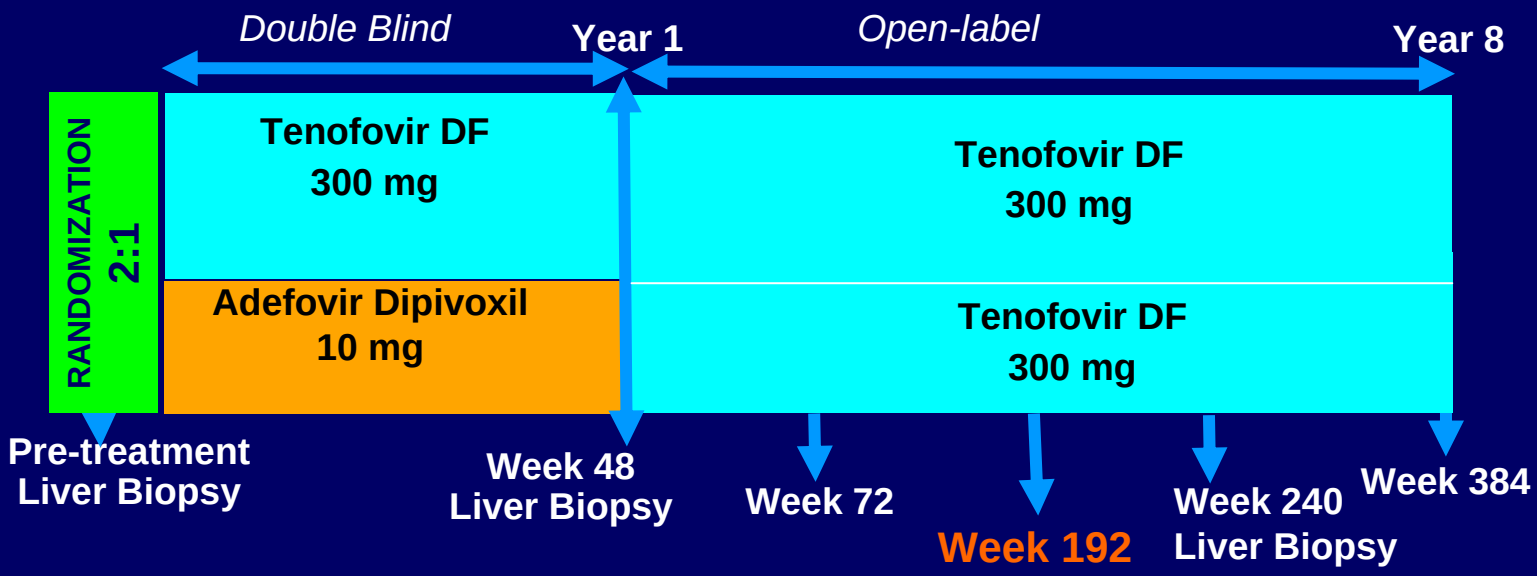
Introduction

- **Tenofovir DF (TDF) approved for HIV-1 in 2001 and chronic hepatitis B (CHB) in 2008 (~3 million patient years exposure)**
- **Week 48 data showed significantly greater antiviral activity of TDF compared to adefovir dipivoxil (ADV)**
- **HBV patients with exceedingly high levels of baseline viremia (HVL) represent a clinical challenge**

Objective

- **Evaluate the efficacy of up to 4 years of TDF therapy in patients with HVL, i.e., HBV DNA ≥ 9 $\log_{10}$copies/mL (or ≥ 8.24 $\log_{10}$IU/mL)**
- **HBeAg-positive and HBeAg-negative**

Study Design of Phase 3 Pivotal Studies 102 (HBeAg−) and 103 (HBeAg+)



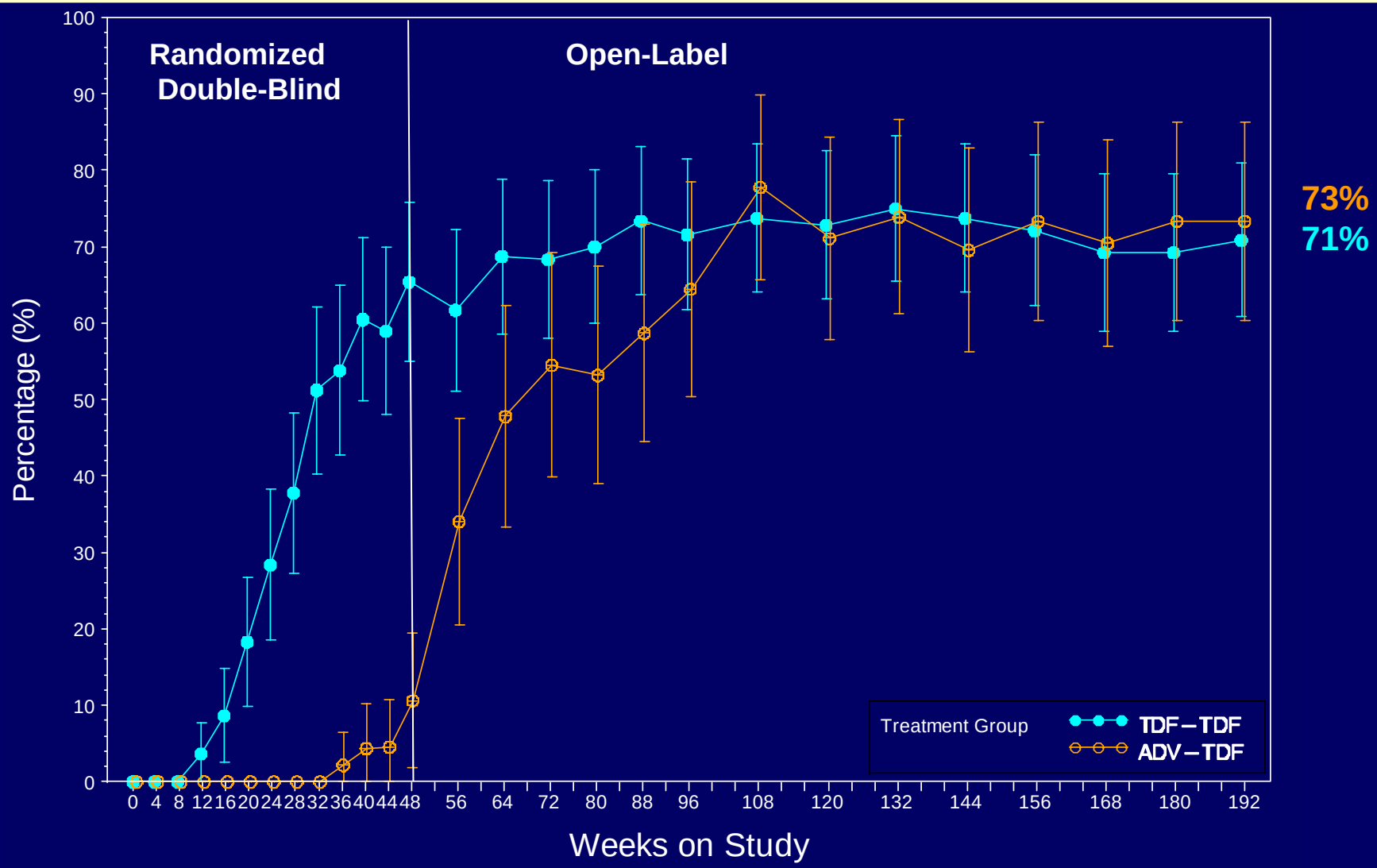
- 129/641 patients enrolled across the two studies had HVL at baseline
- On or after week 72 patients with a confirmed HBV DNA ≥400 copies/mL were eligible to add FTC; overall across both studies, 51 patients were eligible to add FTC (38 added and 13 did not); 35/51 had HVL

Patient Retention at Year 4: 84% (102) and 74% (103)

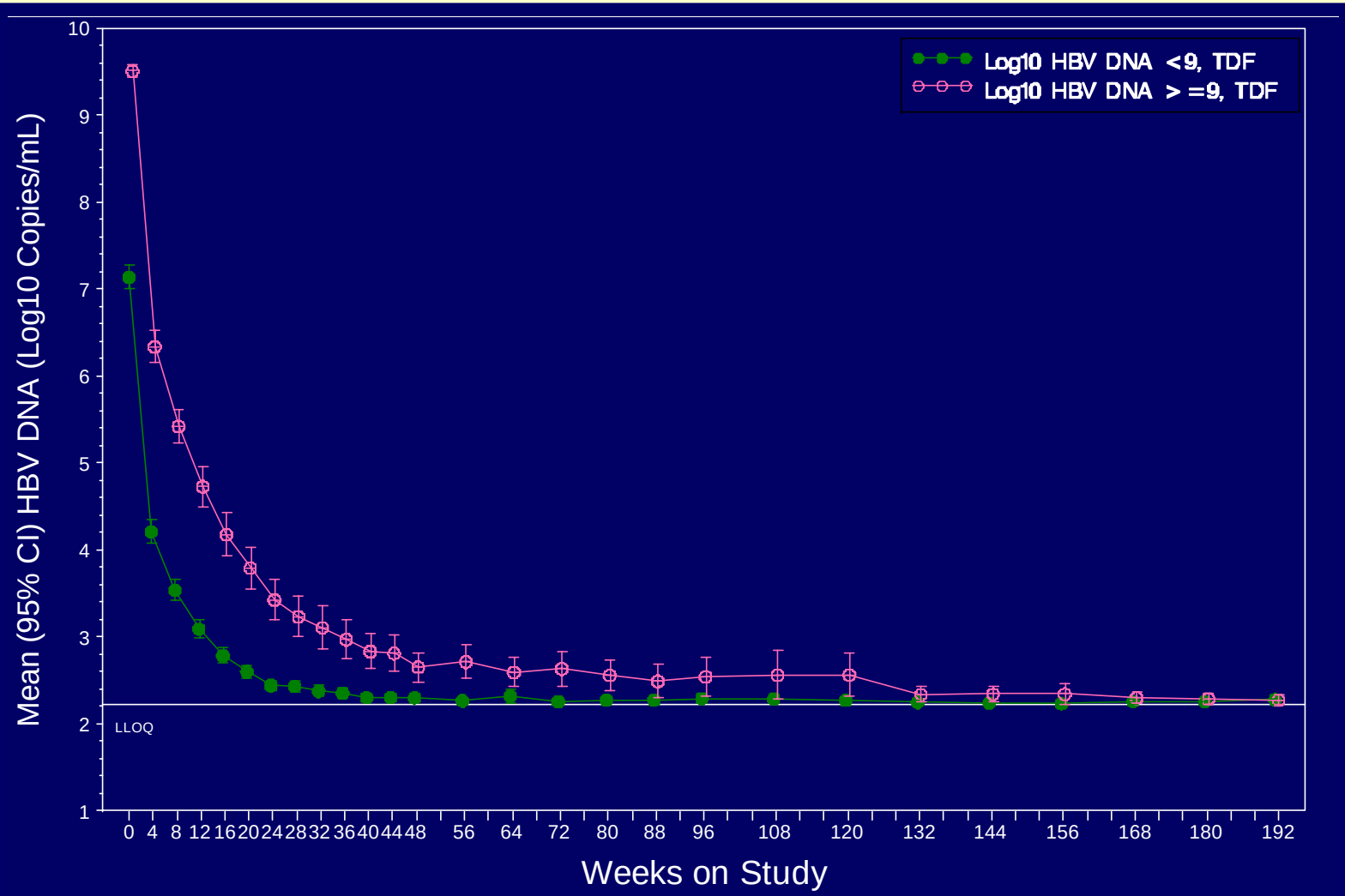
Baseline Characteristics

	Patients with Baseline HBV DNA ≥9 log_{10}copies/mL		Patients with Baseline HBV DNA <9 log_{10}copies/mL	
Original Randomized Treatment Group	TDF (N=82)	ADV (N=47)	TDF (N=344)	ADV (N=168)
Mean HBV DNA (log_{10} copies/mL)	9.51	9.59	7.14	7.27
HBeAg Positive	93%	89%	29%	29%
Mean Age (years)	33	31	42	42
Mean HBsAg (log_{10} IU/mL)	4.87	4.86	3.81	3.83
Mean ALT (U/L)	136.9	168.0	132.8	158.0
Race Asian Caucasian	 20% 71%	 28% 60%	 32% 57%	 29% 59%
Male	74%	74%	73%	75%
Mean Knodell necroinflammatory score Mean Knodell fibrosis score	7.9 2.0	8.0 2.2	8.0 2.4	8.1 2.5
Knodell fibrosis score = 4 (cirrhosis)	14%	20%	21%	20%
Viral Genotype A B C D	22% 7% 12% 53%	22% 13% 20% 41%	16% 12% 19% 49%	14% 13% 17% 54%

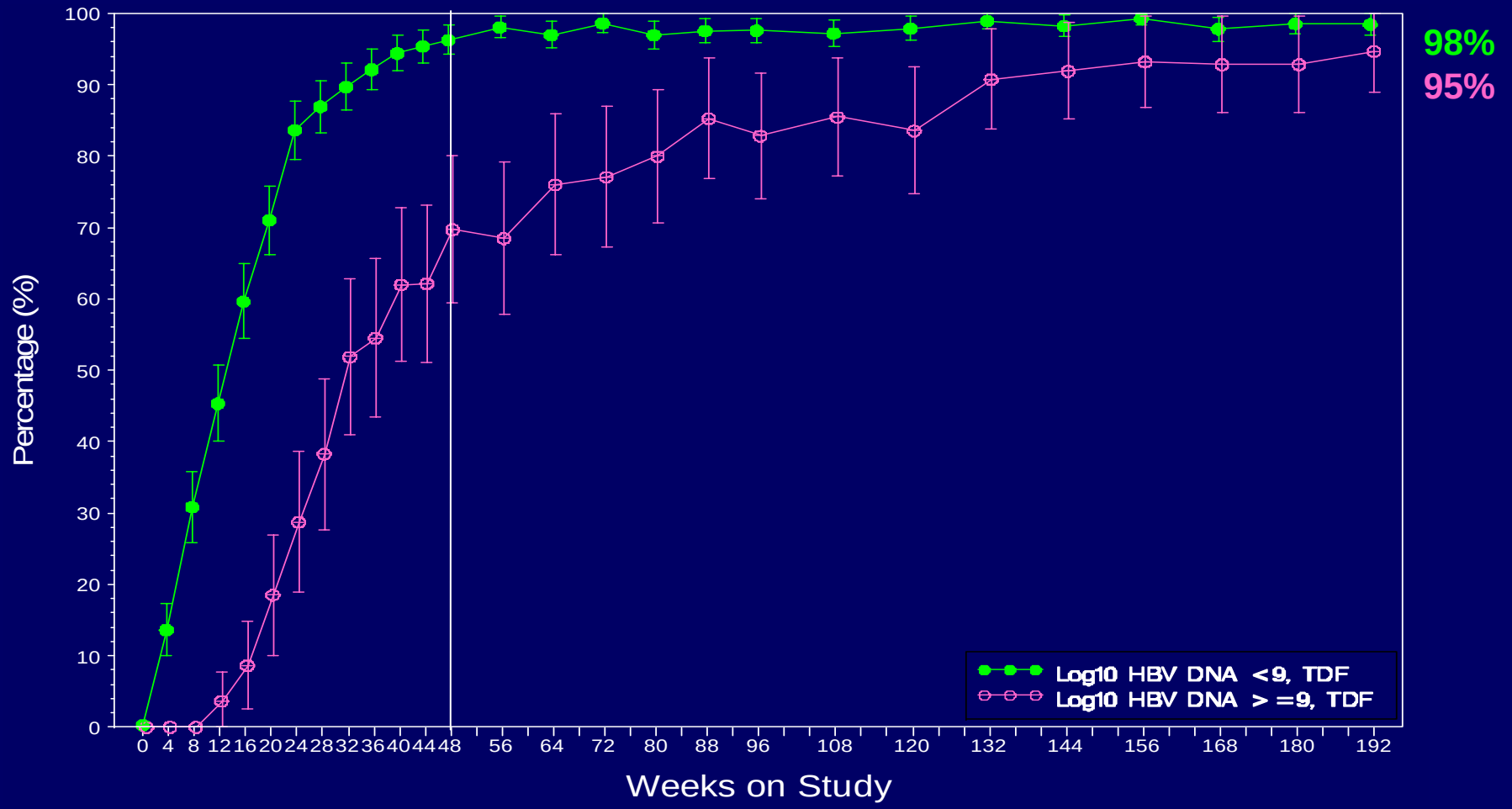
Proportion of High Viral Load Patients with HBV DNA <400 copies/mL: ITT Analysis



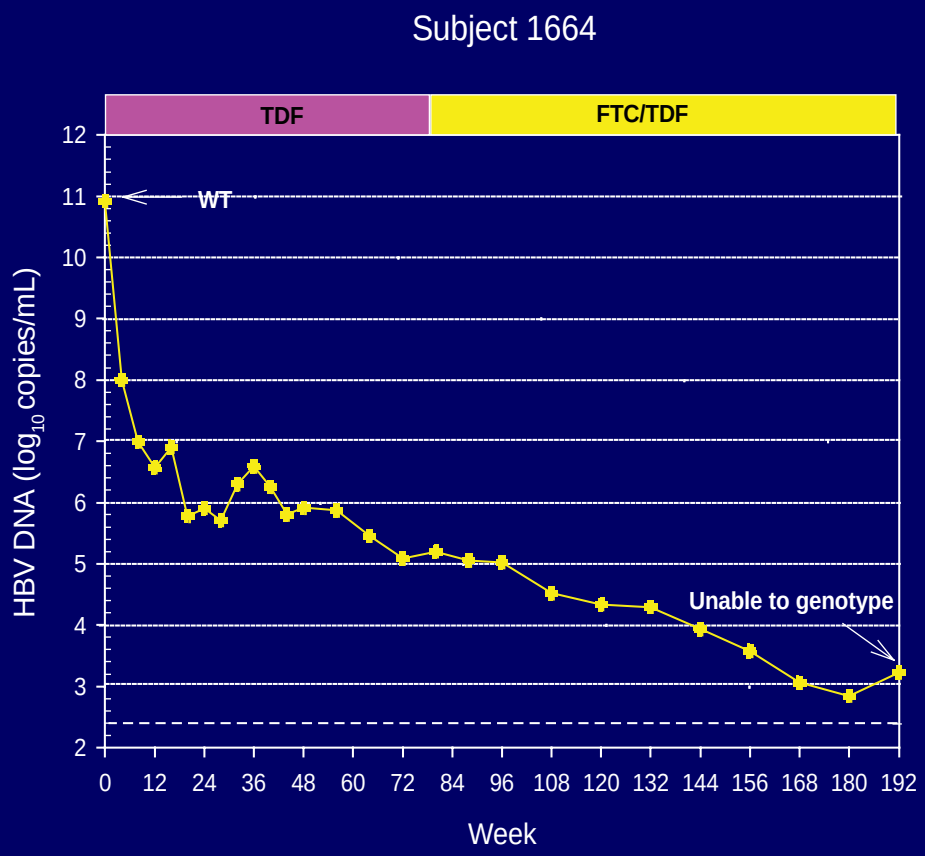
HBV DNA Over Time for Patients Treated with TDF for 192 Weeks: HBV DNA < 9 vs ≥ 9 log_{10}copies/mL

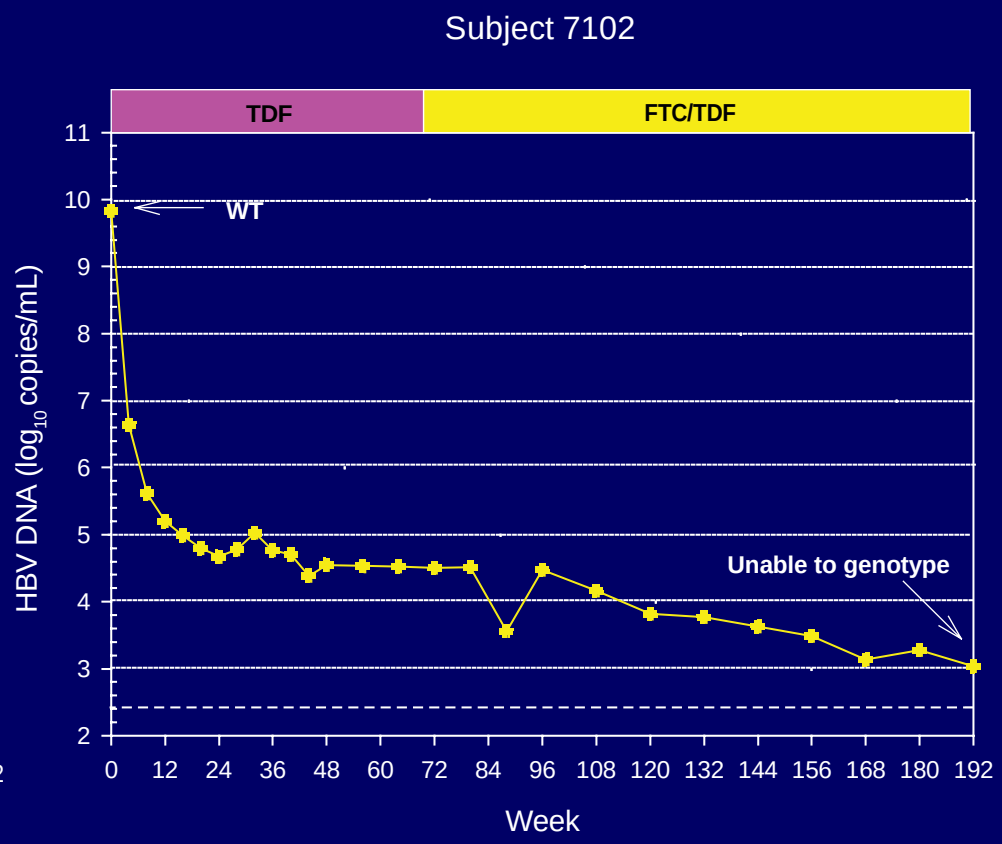


Proportion of Patients with HBV DNA < 400 copies/mL Treated with TDF for 192 Weeks: On-Treatment Analysis

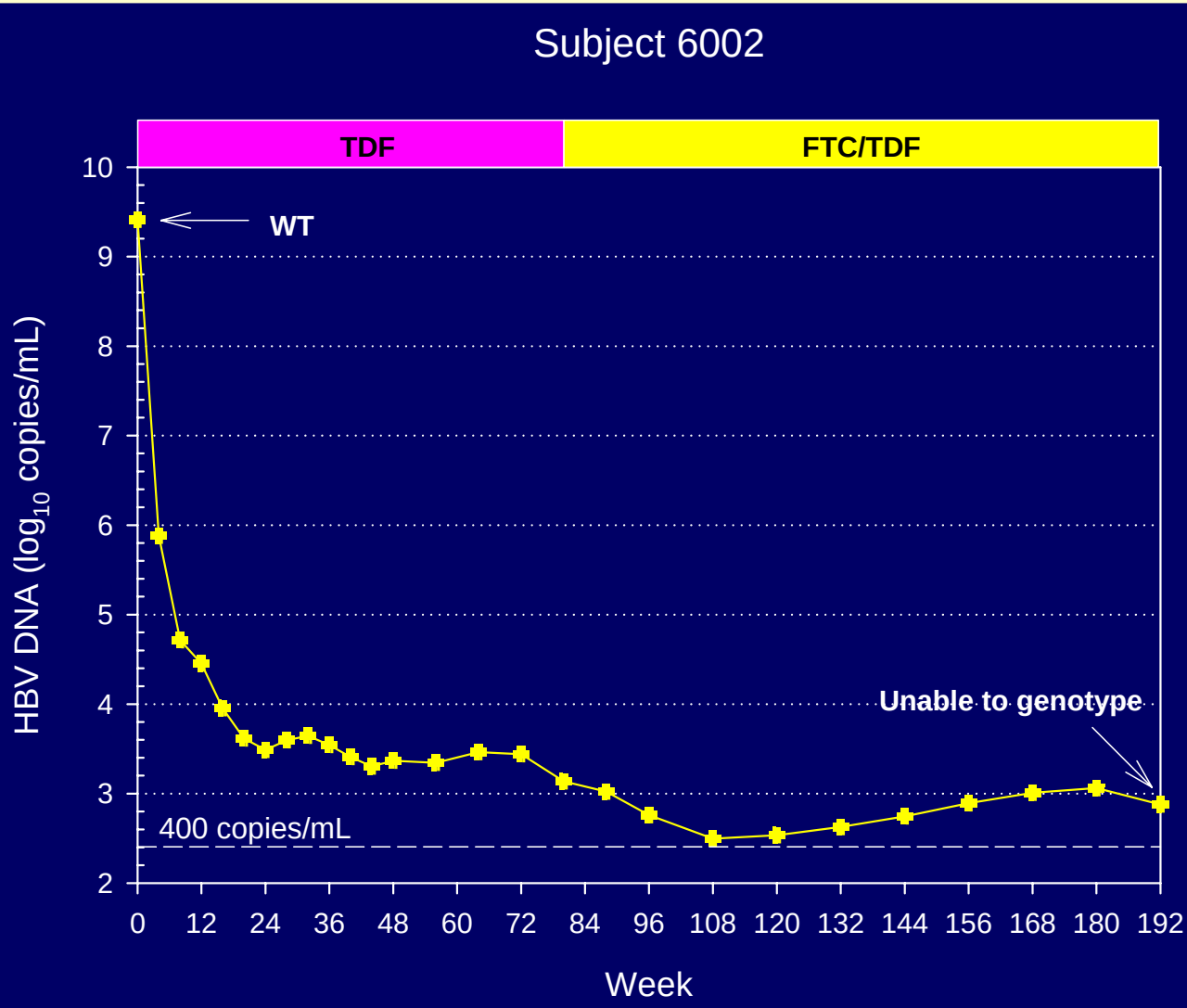


HBV DNA Profiles for Patients with HBV DNA ≥ 400 copies/mL at Week 192

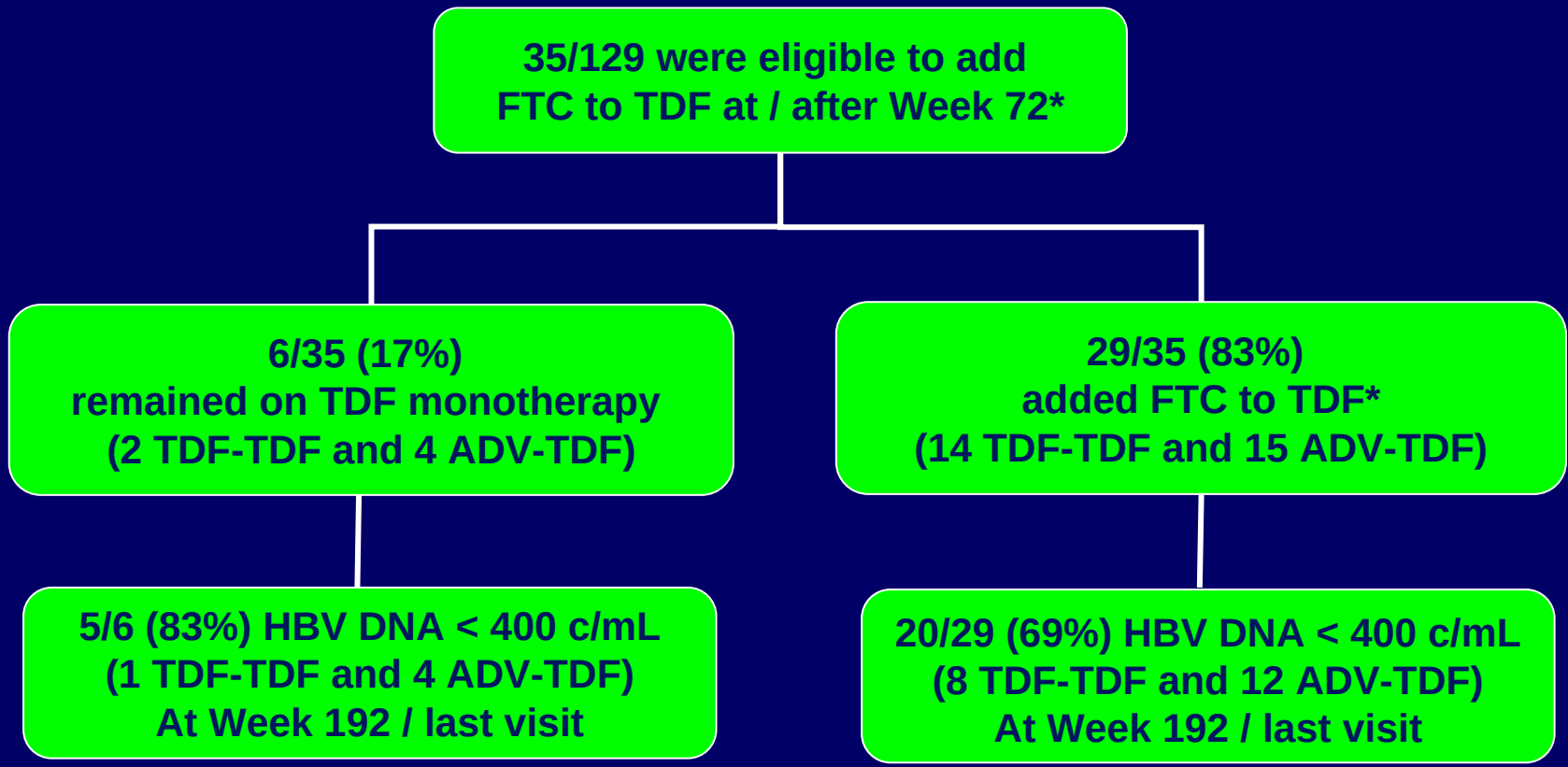




HBV DNA Profiles for Patients with HBV DNA ≥ 400 copies/mL at Week 192 (cont'd)

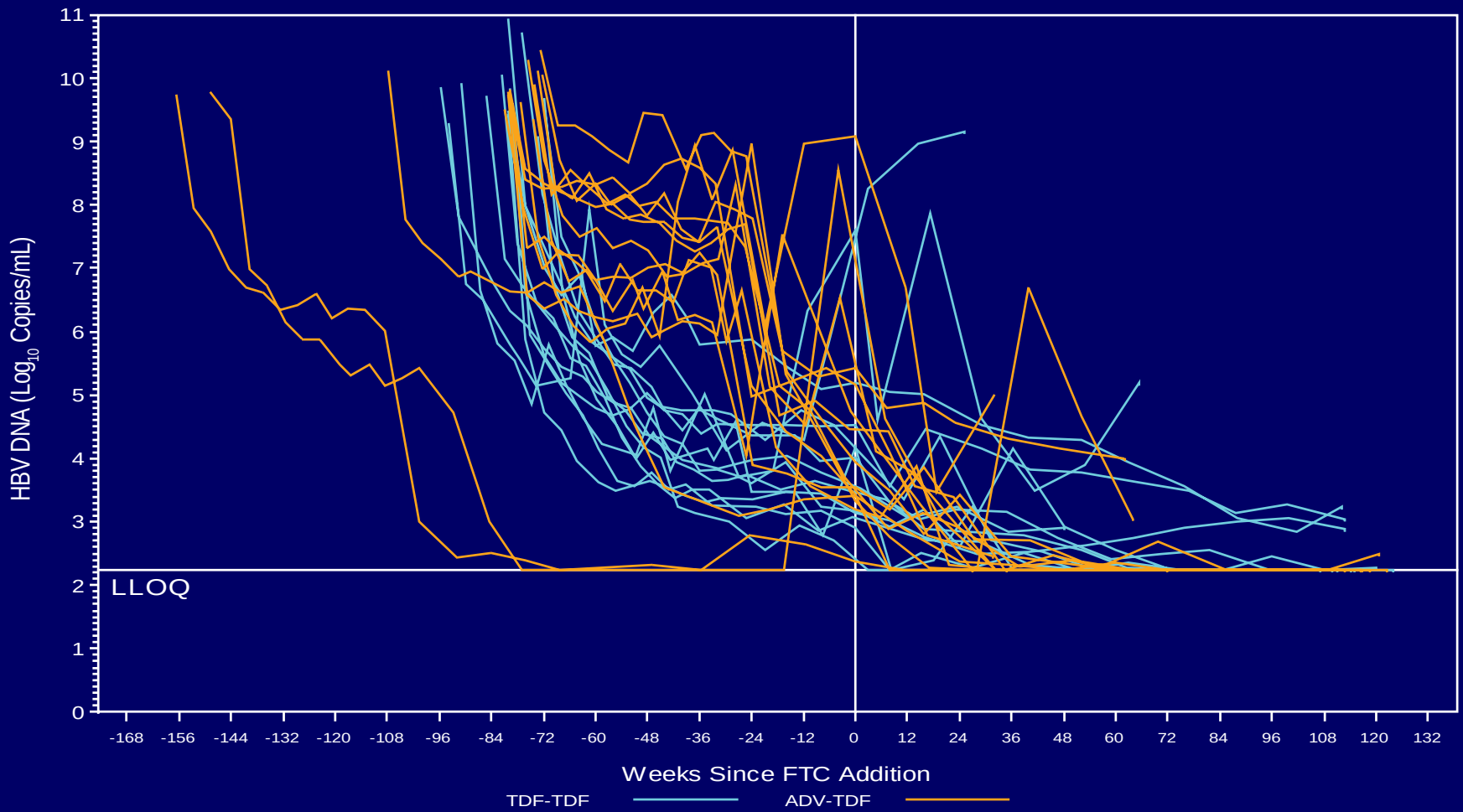


The Majority of Patients who remained on TDF Monotherapy or added FTC to TDF Between Weeks 72-192 Achieved HBV DNA < 400 copies/mL

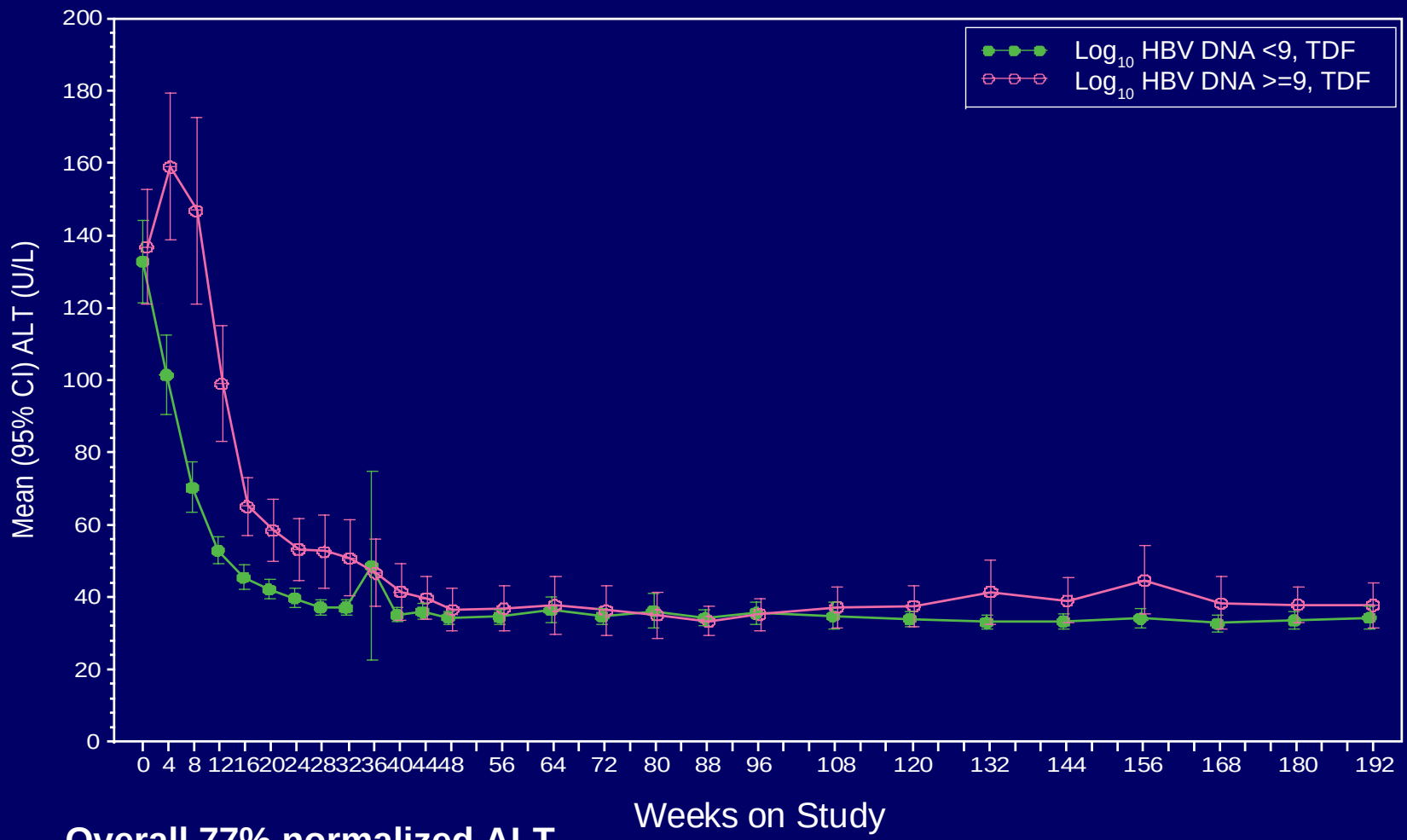


*Most patients (N=26) added FTC to TDF on or before the week 96

29 High Viral Load Patients Who Added FTC

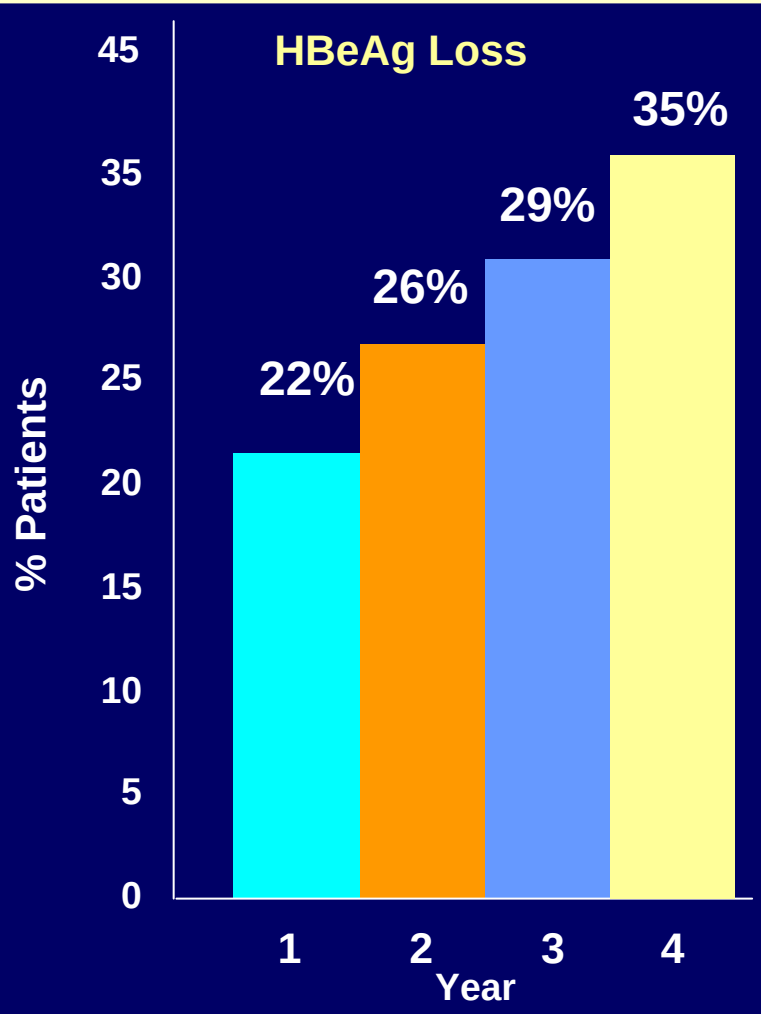


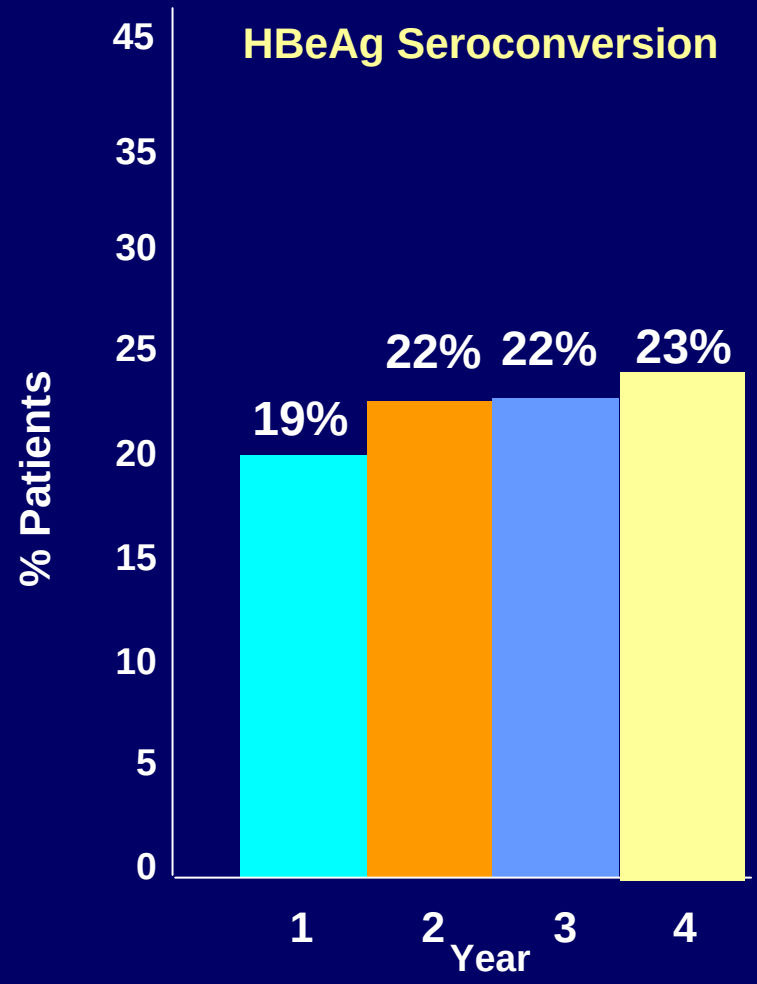
ALT Over Time by Baseline HBV DNA ≥ 9 vs < 9 Log_{10} copies/mL (TDF-TDF)



Overall 77% normalized ALT

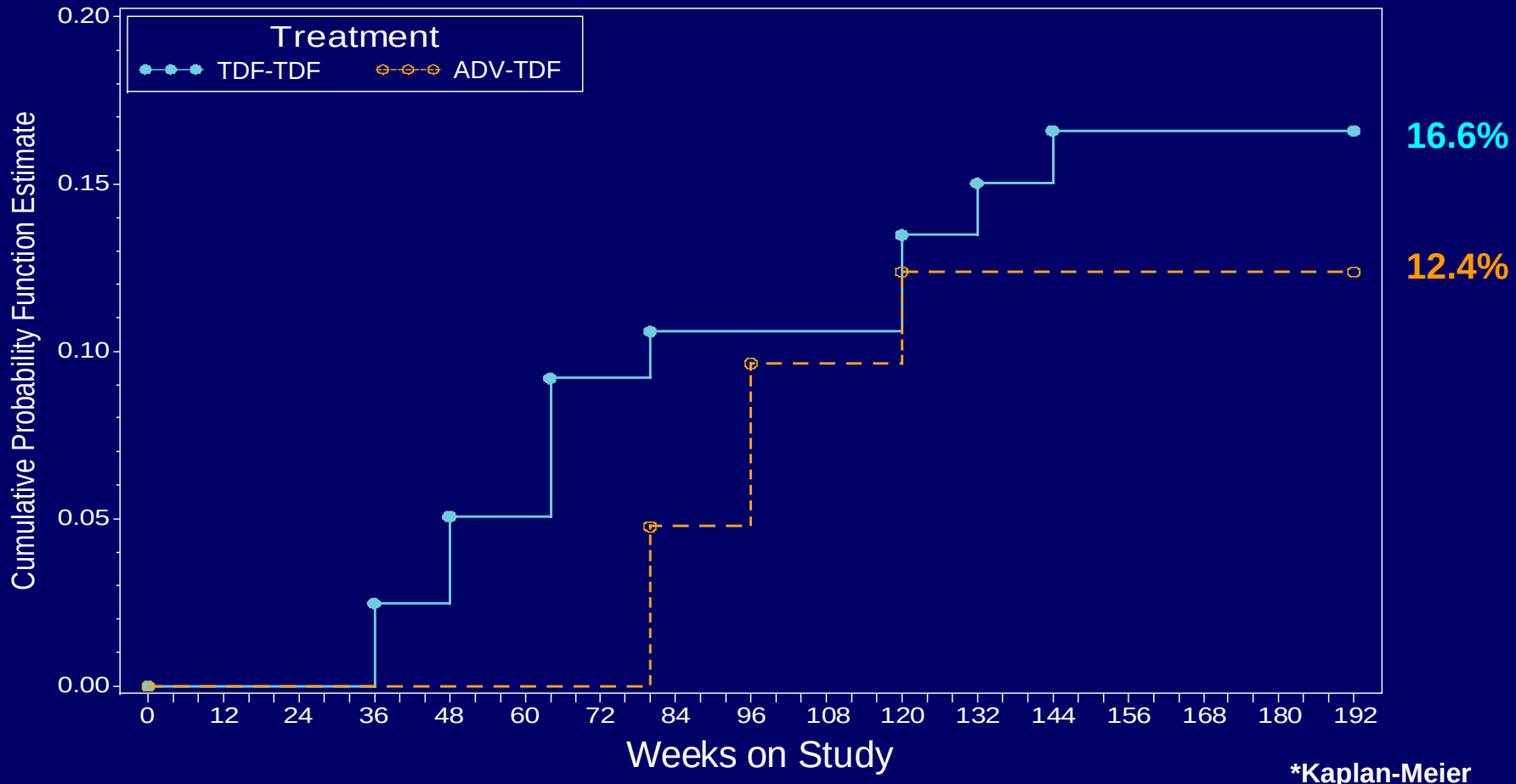
% High Viral Load Patients with HBeAg Loss and HBeAg Seroconversion*





*On-Treatment-Data for year 1 is for double-blind TDF only and thereafter includes all patients on open-label TDF

Cumulative Probability* of HBsAg Loss through Week 192 in Patients with High Viral Load



*Kaplan-Meier

- **Cumulative probability of seroconversion to anti-HBs: 11.8% TDF-TDF and 10.0% ADV-TDF**
- **A total of 17 HVL patients lost HBsAg, 12 of whom seroconverted to anti-HBs**

Surveillance for Resistance Results

- No HBV pol/RT amino acid substitutions associated with tenofovir resistance were detected through 192 weeks of TDF in patients with high viral load

For complete details on the Week 192 Resistance Surveillance see Poster # 1365 by Snow-Lampart et al No Resistance to Tenofovir Disoproxil Fumarate (TDF) Detected Following up to 192 Weeks of Treatment in Subjects Mono-Infected with Chronic Hepatitis B Virus

Conclusions

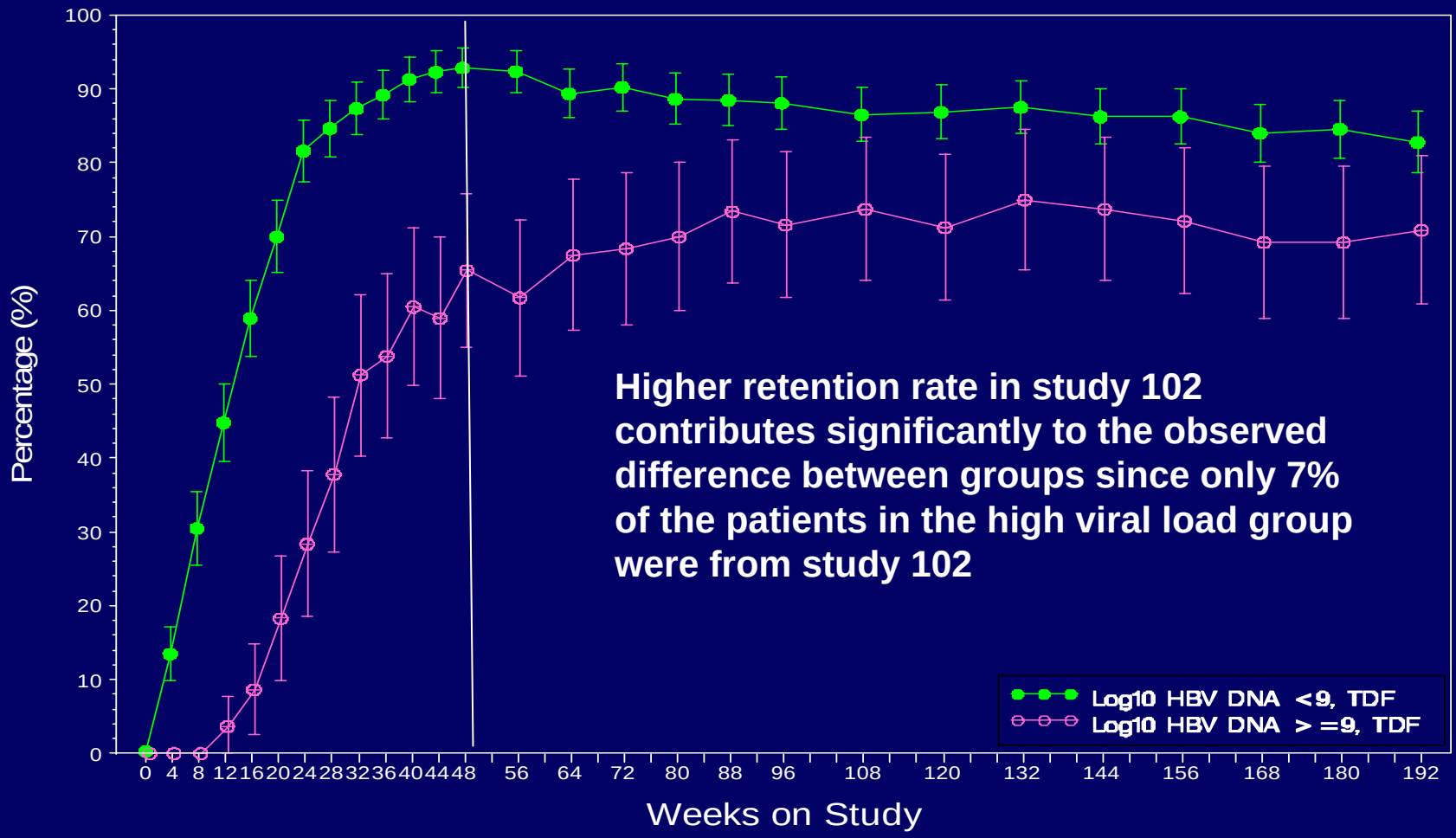
Patients with high viral load, i.e., HBV DNA ≥ 9 $\log_{10}$copies/mL enrolled in the pivotal studies 102 and 103 achieved:

- **Potent and durable antiviral activity: > 95% of patients on treatment at week 192 had HBV DNA < 400 copies/mL**
- **Increasing percentage of patients with HBeAg loss**
- **Increasing percentage of patients with HBsAg loss**
- **No resistance to TDF**

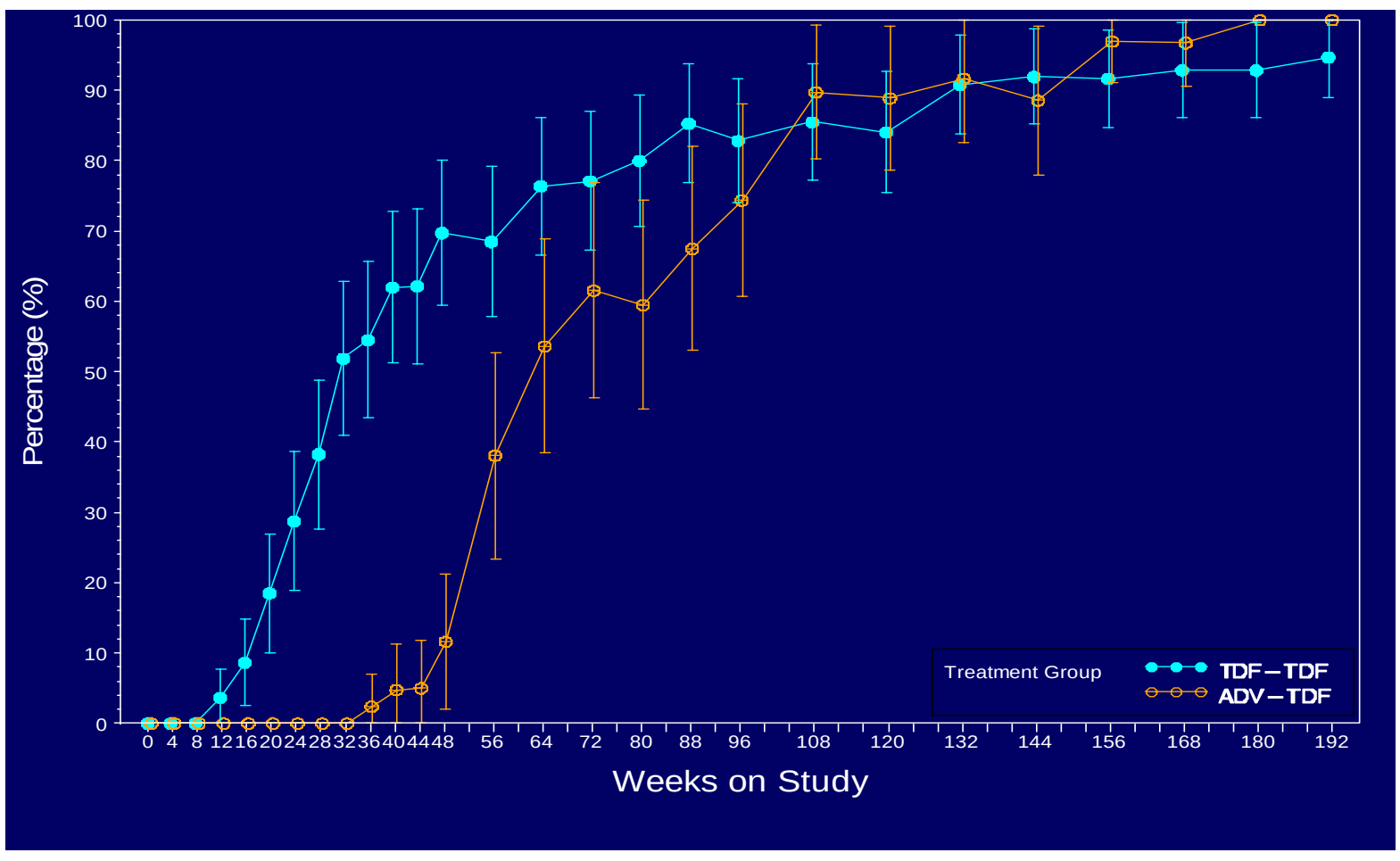
TDF is an effective treatment option for patients with high viral load

Backup

Proportion of Patients with HBV DNA <400 copies/mL Treated with TDF for 192 Weeks: ITT Analysis



Proportion of High Viral Load Patients with HBV DNA <400 copies/mL: On-Treatment Analysis



100%
95%

Overall Virological Response in Studies 102 and 103: HBV DNA <400 copies/mL at Week 192