

HBV Oral Therapies and Interferons

Michael Fried, MD

*University of North Carolina
Chapel Hill, NC*

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Post-AASLD
Symposium**

SOUTHERN
CALIFORNIA
SOCIETY OF
GASTROENTEROLOGY

Commercial Disclosures

Michael W. Fried, M.D.

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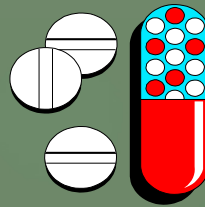
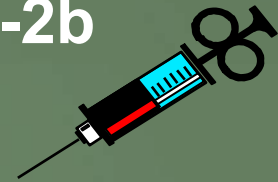
AASLD2010: Themes

- Reassurance about long-term efficacy
- Reassurance about long-term safety
- Reassurance that treatments work in the real world
- Confirming optimal dosing

Current therapeutic options for chronic hepatitis B in US

- **FDA-approved medications**

- Peginterferon alfa-2a, Interferon alpha-2b
- Lamivudine
- Adefovir
- Entecavir
- Tenofovir
- Telbivudine



- **Medications approved for HIV infection, also active against HBV**

- Tenofovir/FTC

- **Active but not approved: Peginterferon alfa-2b**

Responses to Approved Antiviral Therapies HBeAg-Positive CHB

Table 8. Responses to Approved Antiviral Therapies Among Treatment-Naive Patients with HBeAg-Positive Chronic Hepatitis B

	Placebo/ Control Groups from Multiple Studies	Standard IFN- α 5 MU qd or 10 MU tiw 12-24 wk	Lamivudine 100 mg qd 48-52 wk	Adefovir 10 mg qd 48 wk	Entecavir 0.5 mg qd 48 wk	Tenofovir 300 mg qd 48 wk	Telbivudine 600 mg qd 52 wk	PegIFN α 180 mcg qw 48 wk	Peg IFN α 180 mcg qw + Lamivudine 100 mg 48 wk
Loss of serum HBV DNA*	0%-17%	37%	40%-44%	21%	67%	76%	60%	25%	69%
Loss of HBeAg	6%-12%	33%	17%-32%	24%	22%	na	26%	30%/34%†	27%/28%†
HBeAg seroconversion	4%-6%	Difference of 18%	16%-21%	12%	21%	21%	22%	27%/32%†	24%/27%†
Loss of HBsAg	0%-1%	7.80%	1%	0	2%	3.2%	0%	3%	3%
Normalization of ALT	7%-24%	Difference of 23%	41%-75%	48%	68%	68%	77%	39%	46%
Histologic improvement	na	na	49%-56%	53%	72%	74%	65%	38%‡	41%‡
Durability of response		80%-90%	50%-80%§	~90%§	69%§	na	~80%	na	na

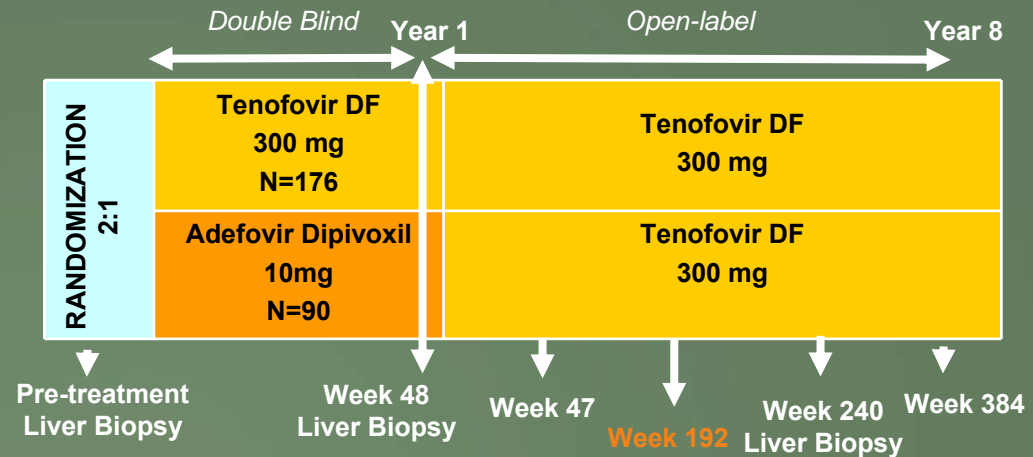
Responses to Approved Antiviral Therapies HBeAg-Negative

Table 9. Responses to Approved Antiviral Therapies Among Treatment-Naive Patients with HBeAg-Negative Chronic Hepatitis B

	Control/Placebo Groups from Multiple Studies	Standard IFN- α 5 Mu qd or 10 MU tiw 6-12 mo	Lamivudine 100 mg qd 48-52 wk	Adefovir 10 mg qd 48 wk	Entecavir 0.5 mg qd 48 wk	Telbivudine 600 mg qd 52 wk	Tenofovir 300 mg qd 48 wk	Peg IFN α 180 mcg qw 48 wk	PegIFN- α 180 mcg qw+ Lamivudine 100 mg qd 48 wk
Loss of serum HBV DNA*	0%-20%	60%-70%	60%-73%	51%	90%	88%	93%	63%	87%
Normalization of ALT	10%-29%	60%-70%	60%-79%	72%	78%	74%	76%	38%	49%
Histologic improvement	33%	na	60%-66%	64%	70%	67%	72%	48%	38%†
Durability of response	Control	10%-20%	<10%	~5%	3%	na	na	~20%	~20%

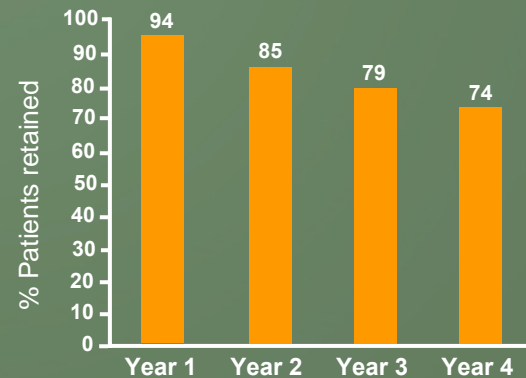
Abstract 477: Tenofovir Provides Effective and Sustained Virologic Suppression in HBeAg-Positive HBV-Infected Patients Through 192 Weeks (Study 103)

- Tenofovir approved in 2008 for the treatment of HBV
- Methods: Patients with HBeAg+ CHB mono-infection were randomized 2:1 to once daily, double-blind TDF 300 mg (N=176) or adefovir dipivoxil (ADV) 10 mg (N=90)
- After week (W) 48, patients with a W 48 liver biopsy were switched to open-label TDF for 7 additional years
- Option to add emtricitabine (FTC) confirmed HBV DNA ≥ 400 copies (69 IU/mL).



- On/After week 72, patients with confirmed HBV DNA > 400 copies/ml were eligible to add FTC in a fixed dose combination table.
- 39 patients who were eligible to add FTC, 34 added and 5 did not.

Figure 2. Patient Retention

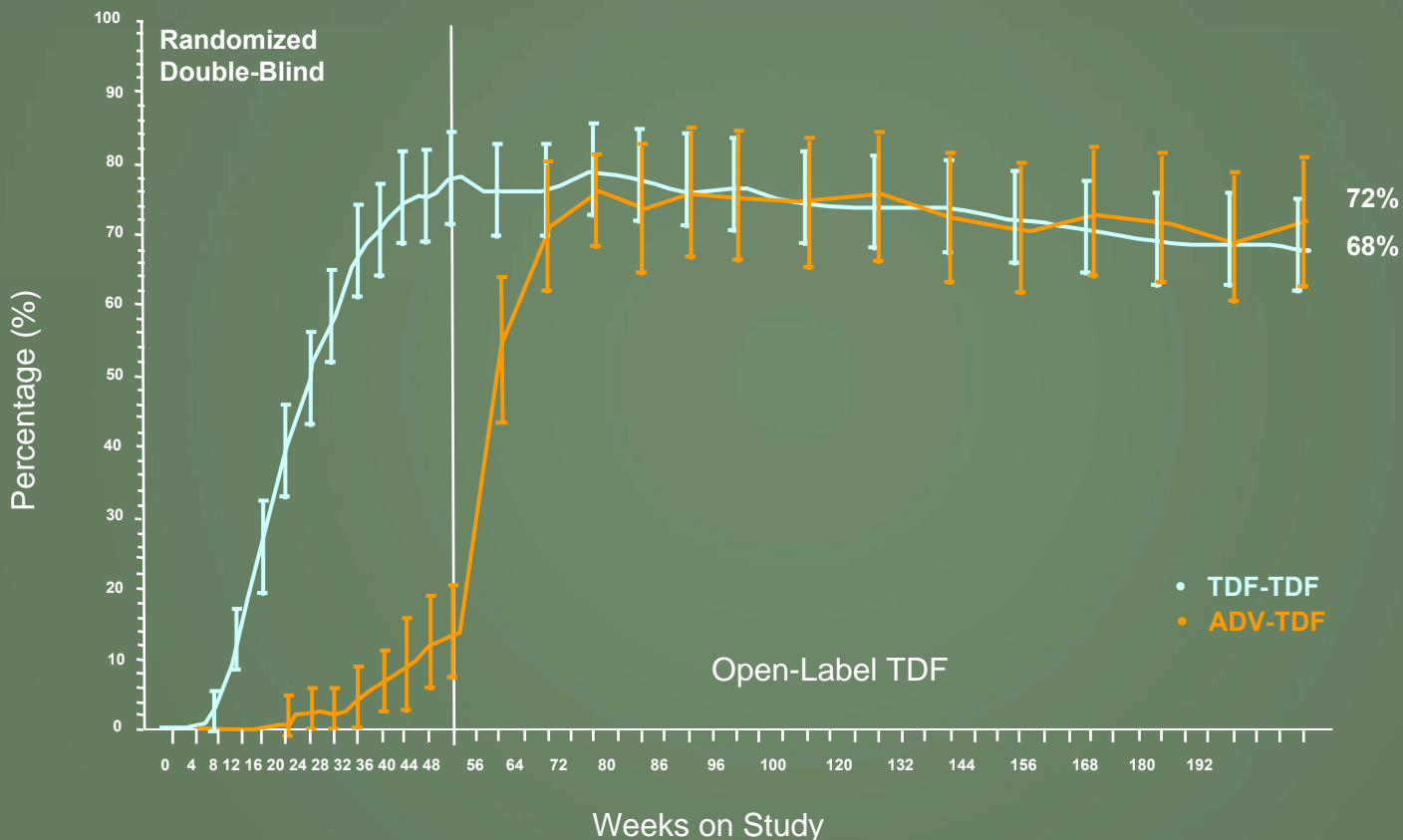


% Patients completing at the end of each year

Abstract 477: Tenofovir Provides Effective and Sustained Virologic Suppression in HBeAg-Positive HBV-Infected Patients Through 192 Weeks (Study 103)

Figure 3. HBV DNA remains Suppressed with up to 4 Years of TDF Treatment (% Patients with HBV DNA <400 copies/mL)

Figure 3a. LTE-TDF ANALYSIS: Long Term Evaluation, TDF



OLE-TDF: % Patients with HBV DNA <400 Copies/mL was 71% TDF-TDF and 71% ADV-TDF

Abstract 477: Tenofovir Provides Effective and Sustained Virologic Suppression in HBeAg-Positive HBV-Infected Patients Through 192 Weeks (Study 103)...(Contd)

Figure 3. HBV DNA remains Suppressed with up to 4 Years of TDF Treatment (% Patients with HBV DNA <400 copies/mL)

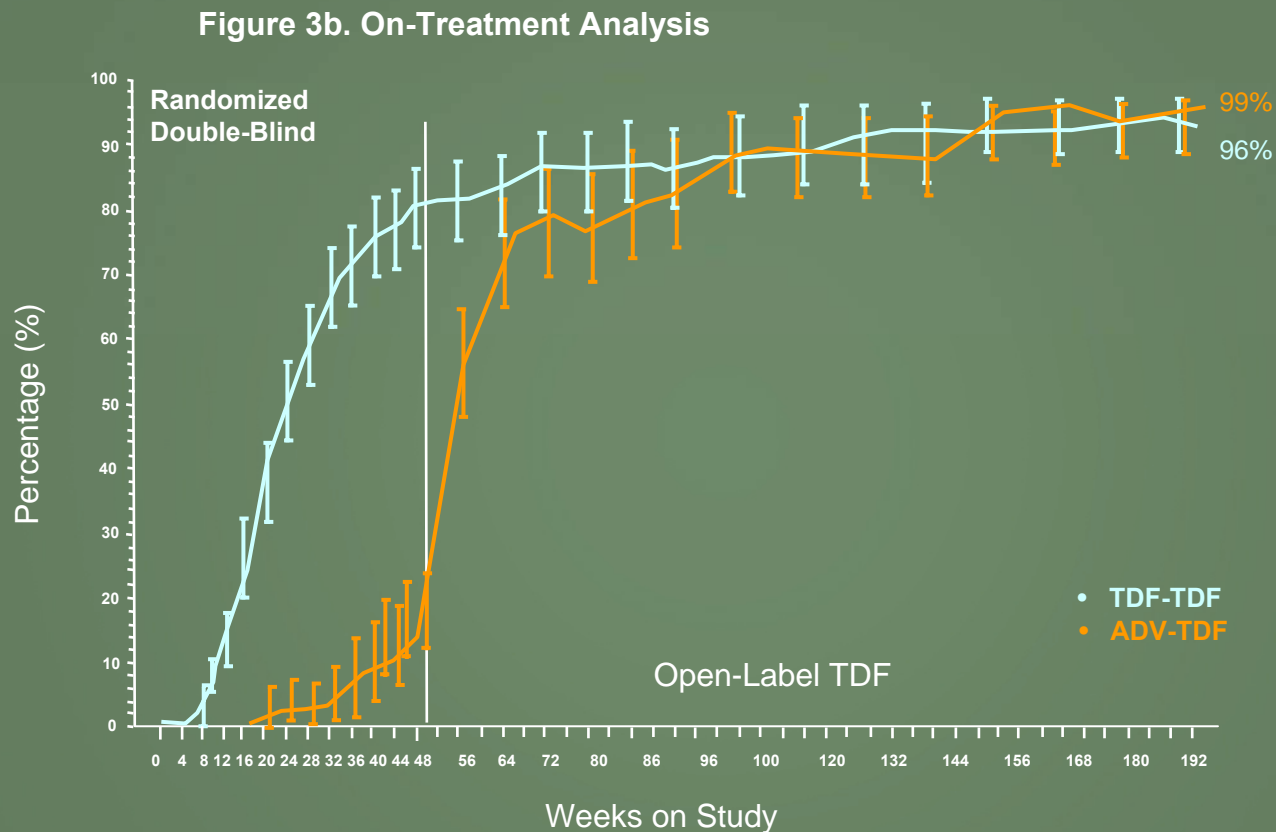


Illustration includes 19 patients who added FTC and had
HBV DNA <400 copies/mL at week 192

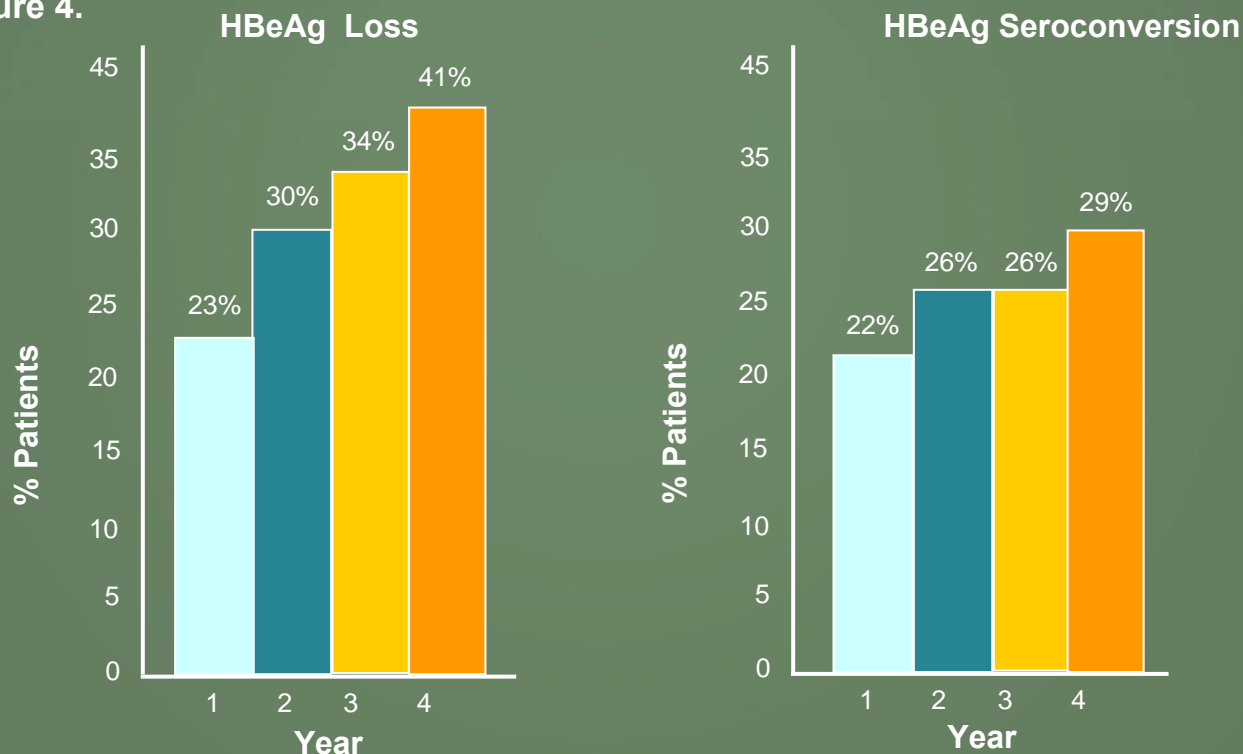
Abstract 477: Tenofovir Provides Effective and Sustained Virologic Suppression in HBeAg-Positive HBV-Infected Patients Through 192 Weeks (Study 103)

Figure 4. Week 192 Biochemical Response

	TDF-TDF	ADV-TDF
Mean ALT (U/L)	36.3	32.5
% Normalized (on-treatment)	77%	80%

a. ALT ULN = 34 for females and ULN = 43 for males

Figure 4. % Patients with HBeAg Loss and Seroconversion (On-Treatment) TDF-TDF

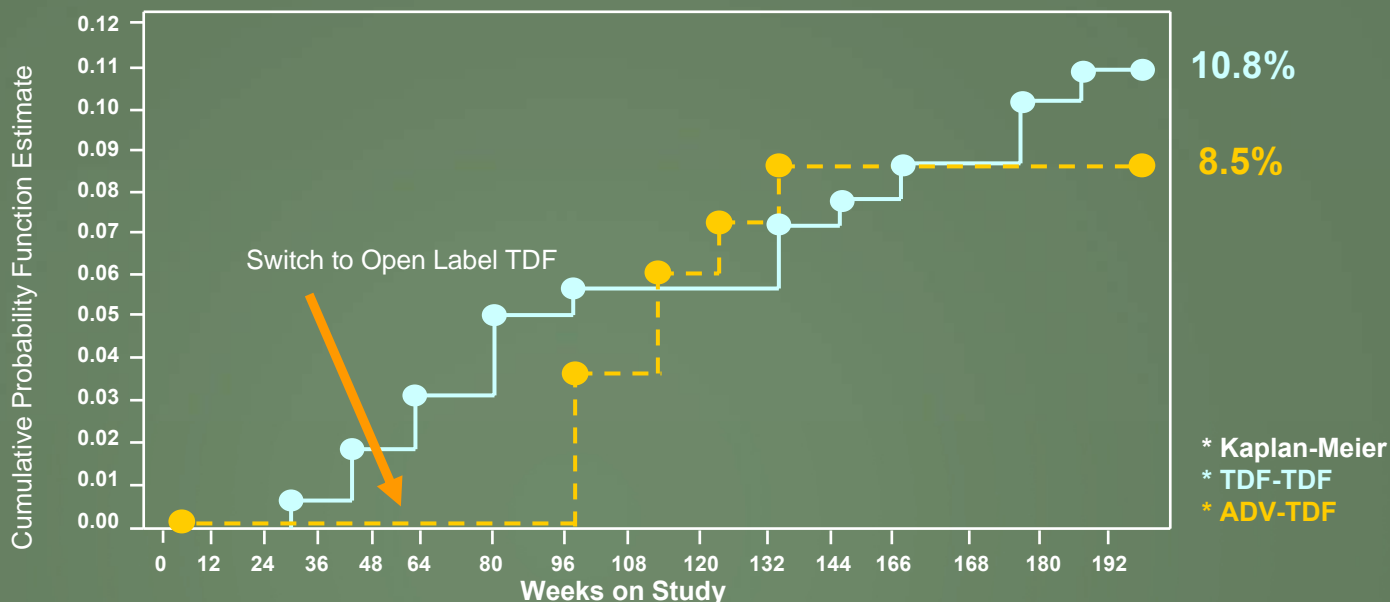


48 of the 49 patients with HBeAg loss at week 192 were on TDF monotherapy

Abstract 477: Tenofovir Provides Effective and Sustained Virologic Suppression in HBeAg-Positive HBV-Infected Patients Through 192 Weeks (Study 103)

Figure 5.

Cumulative Probability* of HBsAg Loss



- Cumulative probability of seroconversion to anti-HBs: 7.7% TDF-TDF and 7.3% ADV-TDF
- 18/23 patients discontinued treatment for HBsAg loss; 3 patients regained HBsAg off treatment (1 patient was lost to follow up, 1 patient restarted therapy and subsequently lost HBsAg, and 1 patient remained off treatment based on HBsAg negative local laboratory results)

Table 3. Percentage of TDF-TDF Patients with HBsAg Loss

Key Characteristic	HBsAg Clearance by year 4 n/N(%)
Genotype A or D	14/95(15%)
HBV DNA $\geq 9 \log_{10}$ copies/ml	12/75(16%)
HBsAg $\geq 4.5 \log_{10}$ IU/mL	14/90(16%)
Knodell Necroinflammatory Score ≥ 9	13/114(11%)

Abstract 477: Tenofovir Provides Effective and Sustained Virologic Suppression in HBeAg-Positive HBV-Infected Patients Through 192 Weeks (Study 103)

- TDF was well tolerated and produced potent, continuous viral suppression
- Increasing HBeAg and HBsAg loss
- No mutations developed in association with TDF resistance in this HBeAg+ patient population.
- Similar long-term results in HBeAg-negative population (Abstract 476): HBsAg loss= 0
- Major question: When do you stop therapy and what happens to virological response?

Abstract 369: Effectiveness and safety of Tenofovir disoproxil fumarate in field practice: a multicenter European cohort study of 737 patients with chronic hepatitis B

- Background and Aim: Test effectiveness and safety in “field” practice
- Methods: 737 patients on either mono or combo therapy with TDF were enrolled in a retrospective/prospective cohort study conducted in 17 Centers.
- Included were all patients with chronic hepatitis B starting TDF in each center
 - HIV co-infected were excluded
 - Median follow-up was 16 months (range 0-52).
- Virological response was defined as undetectable HBV DNA by sensitive assays; safety analysis focused on renal and tubular function.

Abstract 369: Effectiveness and safety of Tenofovir disoproxil fumarate in field practice: a multicenter European cohort study of 737 patients with chronic hepatitis B

- Baseline features:
 - Median age 56 years, 75% males,
 - 77% HBeAg negative
 - 42% with cirrhosis
 - 9% with HCC
 - 30% with previous IFN treatment,
 - 71% NUC experienced or resistant and 29% NUC-naïve patients.
- TDF was given as a monotherapy in 27% of the patients and in combination, with lamivudine in 72%
- 14% of the patients started on reduced TDF dose because of reduced creatinine clearance.

Abstract 369: Effectiveness and safety of Tenofovir disoproxil fumarate in field practice: a multicenter European cohort study of 737 patients with chronic hepatitis B

- NUC naïve patients, with a median baseline viremia of 5.9 log IU/ml, virological response rates (PCR undetectable) were 37%, 66%, 72% and 89% at 12, 24, 36, 48 weeks
 - Time to PCR negativity significantly affected by baseline viral load.
- In NUC-experienced or resistant patients, viremia remained undetectable in those who switched from ADV to TDF
 - HBV DNA became undetectable in 74% of those with baseline ongoing HBV replication (median HBV DNA 4.1 log IU/ml, range 1->9 log), independently of the treatment strategy.

Abstract 369: Effectiveness and safety of Tenofovir disoproxil fumarate in field practice: a multicenter European cohort study of 737 patients with chronic hepatitis B

- In pooled safety assessment, a greater than 0.3 or 0.5 mg/dl increase of serum creatinine in the last visit versus baseline occurred in 3% and <1% of the patients, respectively.
- Blood phosphorus levels dropped below 2.3 mg/dl in 8% of the patients and urinary phosphate absorption, as assessed by estimated TmPI/GFR, decreased below 0.7 mmol/L in 37%: most of these patients had long-term previous exposure to ADV.
- Overall, TDF dose was reduced in 6% of the patients because of worsened creatinine clearance: most of these patients were older than 60 years, with previous exposure to ADV and with concomitant potentially nephrotoxic diseases/medications.

Conclusions. TDF suppressed HBV replication in most NUC-naïve and NUC-experienced or resistant patients in field practice. Few patients showed an impaired renal and tubular function of multifactorial origin.

Abstract 391: Long-term Suppression of HBV Replication in Nuc-naïve Patients with Chronic HBV treated with Entecavir in Field Practice: The Italian Multicenter Experience

- Aim: Assess the long-term effectiveness and safety of Entecavir (ETV) in NUC-naïve patients treated in field practice.
- Study Design: 418 consecutive NUC-naïve patients with chronic HBV recruited in 18 Liver Units in Italy
- Treated with ETV 0.5 mg for 30 months (2-38)
- LFT's, HBV DNA q 3 months. Virological breakthrough was defined as > 1 log U increase of viremia.
- Results:
 - Median age 58 years, 76% males, 83% HBeAg(-), 49% cirrhotics, 56% with concomitant diseases/medications.
 - Median HBV DNA was 6.0 log IU/ml (range 1.5- \rightarrow 9.0) and ALT were elevated in 85% of the patients.

Abstract 391: Long-term Suppression of HBV Replication in Nuc-naïve Patients with Chronic HBV treated with Entecavir in Field Practice: The Italian Multicenter Experience

- **Results:**
 - On ETV treatment, 90% of the patients achieved undetectable HBV DNA
 - Primary nonresponse at week 12 (<1%)
 - Partial virological response at week 48 (14%)
 - Virological breakthroughs (<1%)
 - TDF was added to ETV in 17 patients with pVR. Of the 39 pVR not rescued with TDF, 20 (50%) cleared viremia in follow-up (6-9mo).
 - A greater than 0.3 or 0.5 mg/dl increase of Cr occurred in 3% and 0.6% of pts, respectively.
- **Conclusions:** The vast majority of NUC-naïve patients treated with ETV monotherapy in field practice achieved and maintained a virological response through 30 mo and treatment was well tolerated.

Dosing Recommendations for Interferon-based HBV Therapy

Dose Regimens

26. IFN- α and pegIFN- α are administered as subcutaneous injections.

a. The recommended dose of standard IFN- α for adults is 5 MU daily or 10 MU thrice weekly. The recommended dose of pegIFN- α 2a is 180 mcg weekly.

(I)

b. The recommended IFN- α dose for children is 6 MU/m² thrice weekly with a maximum of 10 MU. (I) PegIFN- α has not been approved for treatment of chronic hepatitis B in children.

c. The recommended treatment duration for HBeAg-positive chronic hepatitis B is 16 weeks for standard IFN- α and 48 weeks for pegIFN- α . (I)

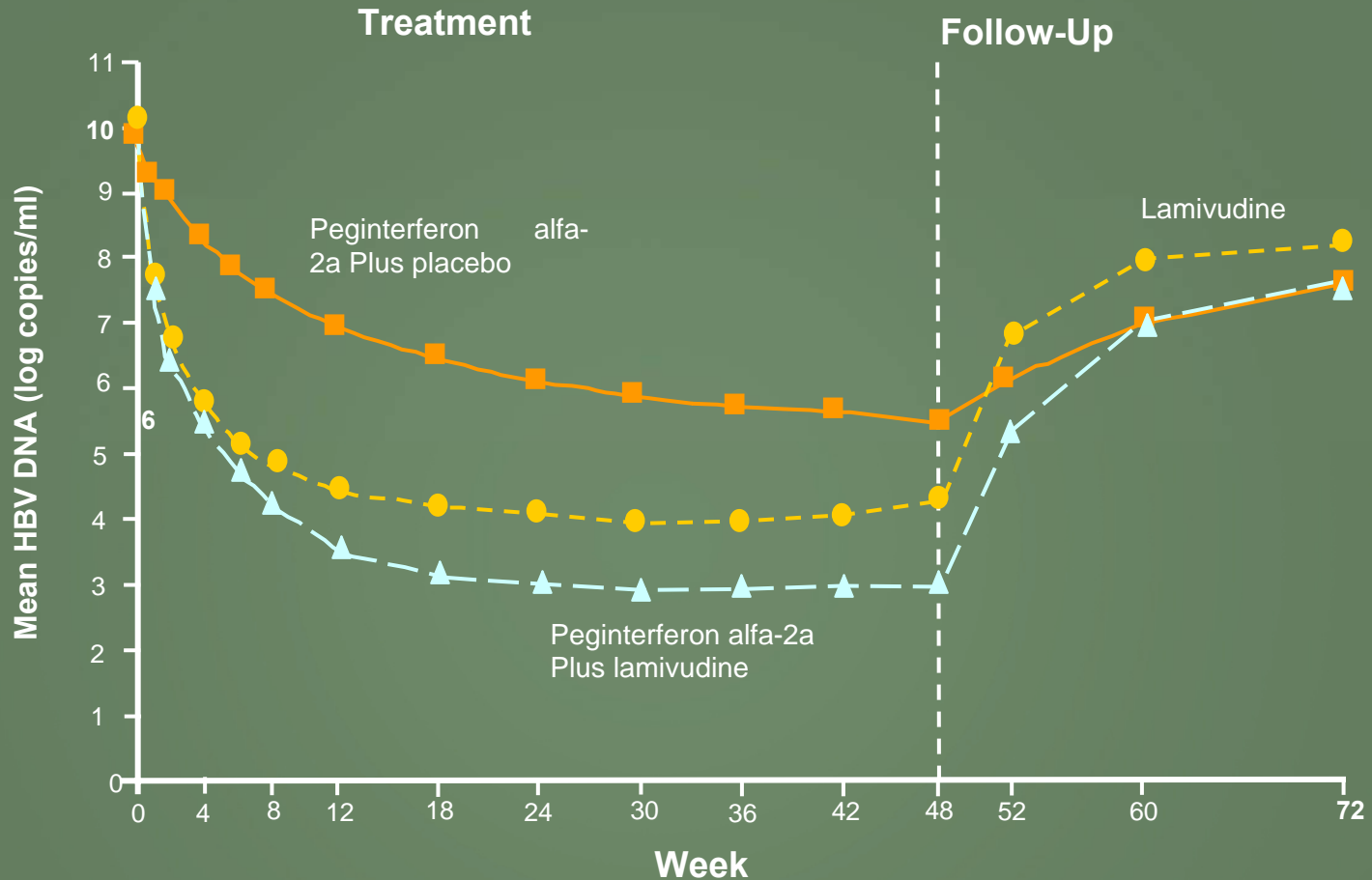
d. The recommended treatment duration for HBeAg-negative chronic hepatitis B is 48 weeks for both standard and pegIFN- α (II-3)

Summary of Guidelines: Peginterferon for HBV

Guideline	Dose	Duration
EASL	No dose stated	48 weeks/1 year
AASLD	180 µg/week 90 µg/week may be suitable for HBeAG-positive patients	48 weeks 24 weeks may be suitable for HBeAG-positive patients
APASL	90-180 µg/week	In HBeAG-positive: 6-12 months(longer in genotype C) In HBeAG-negative: 12 months

Peginterferon alfa-2a +/- Lamivudine for HBV

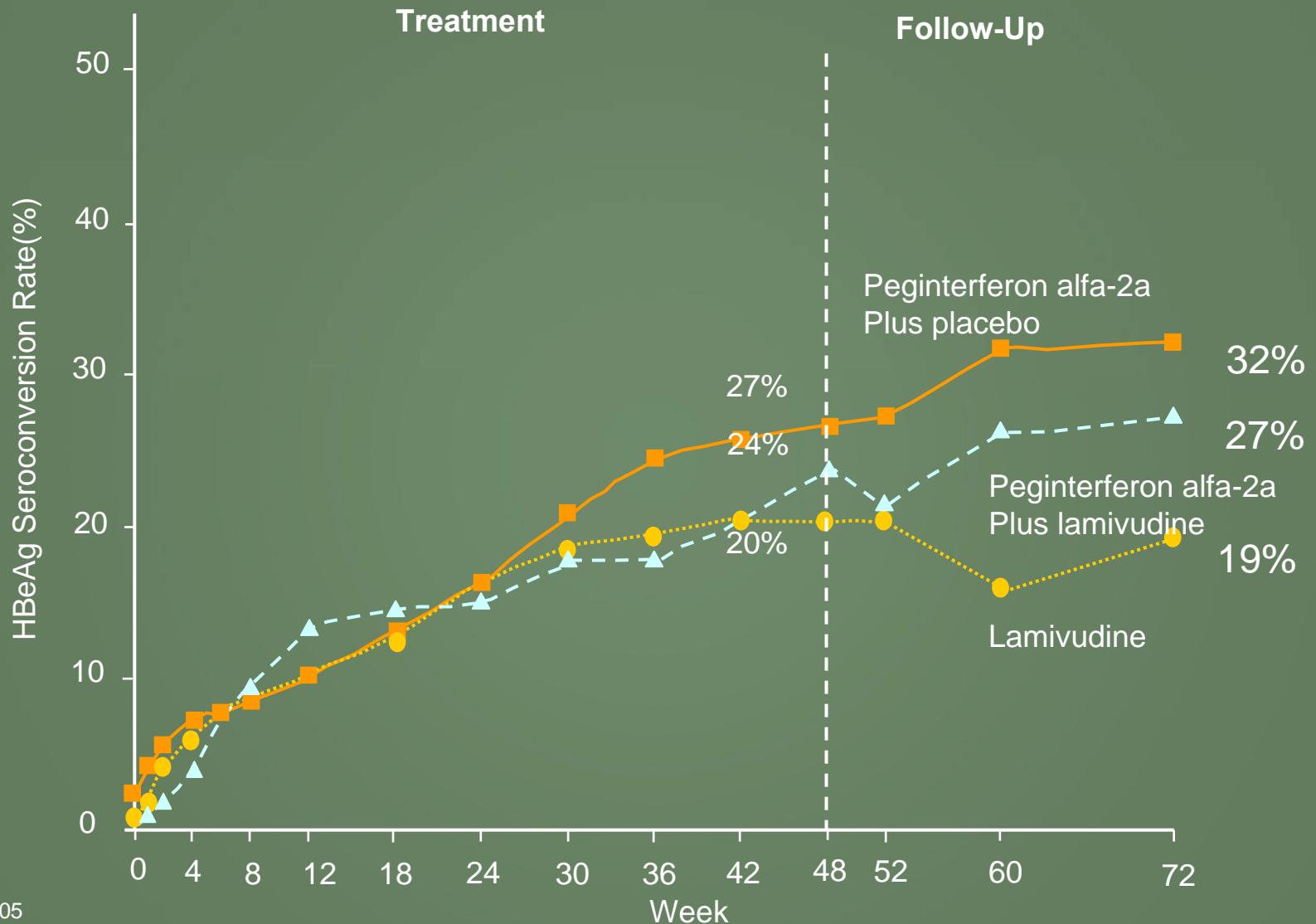
Change in HBV DNA



Us placebo	271	269	265	265	262	263	259	258	255	248	254	241	248
Us lamivudine	271	268	268	267	268	263	259	254	255	249	254	244	254
	272	267	267	267	263	263	259	260	244	249	248	228	241

Peginterferon alfa-2a +/- Lamivudine for HBV

HBeAg Seroconversion Over Time



Peginterferon alfa-2a +/- Lamivudine for HBV

HBeAg Seroconversion After 24 Weeks Follow-up

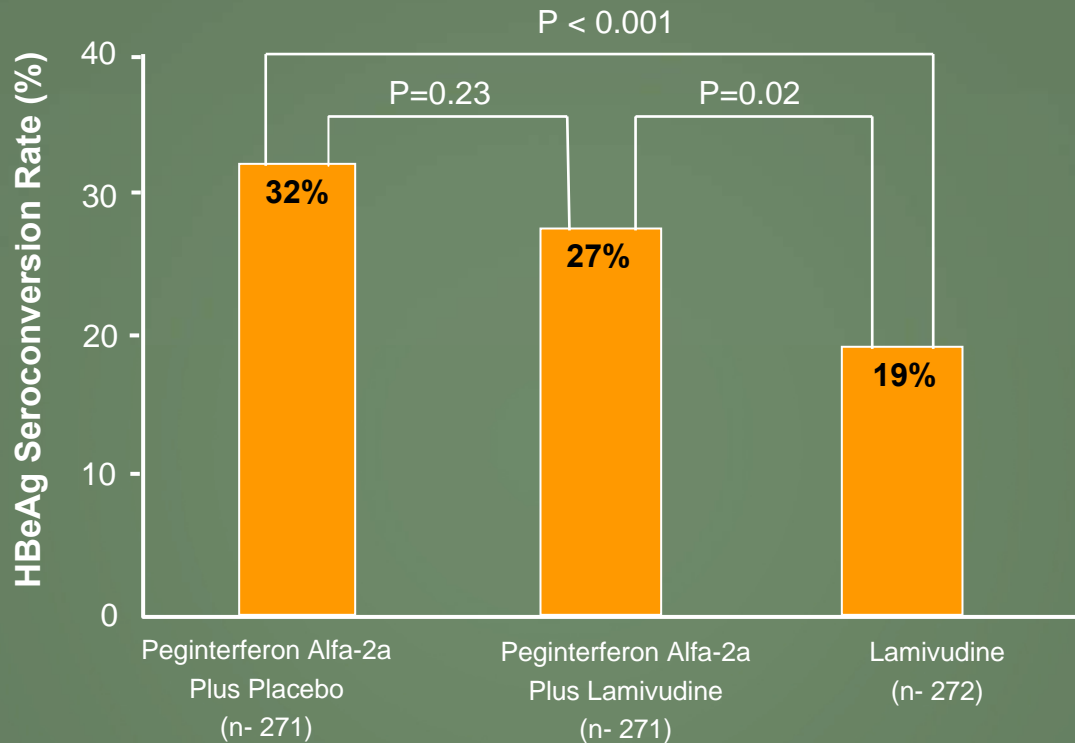
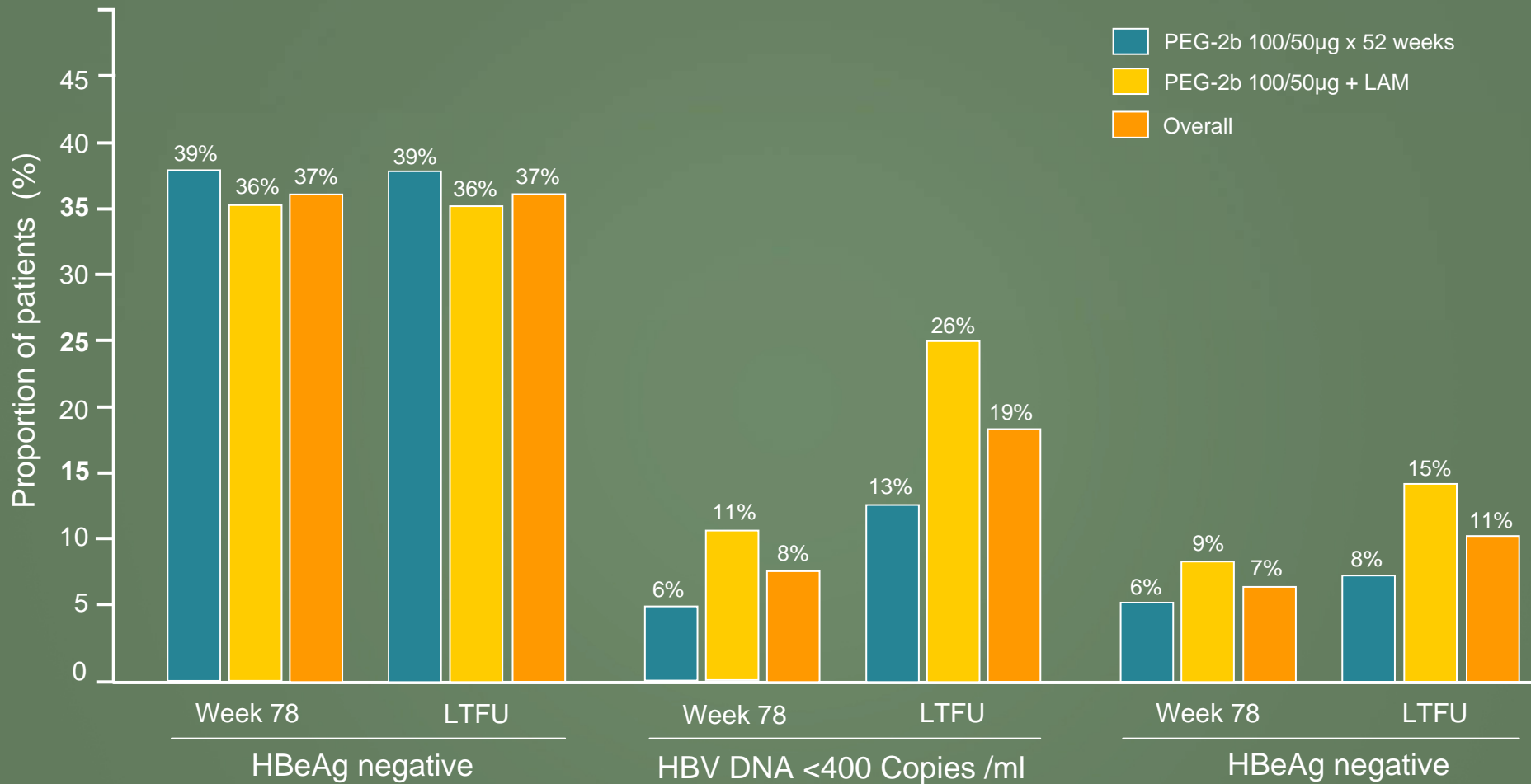


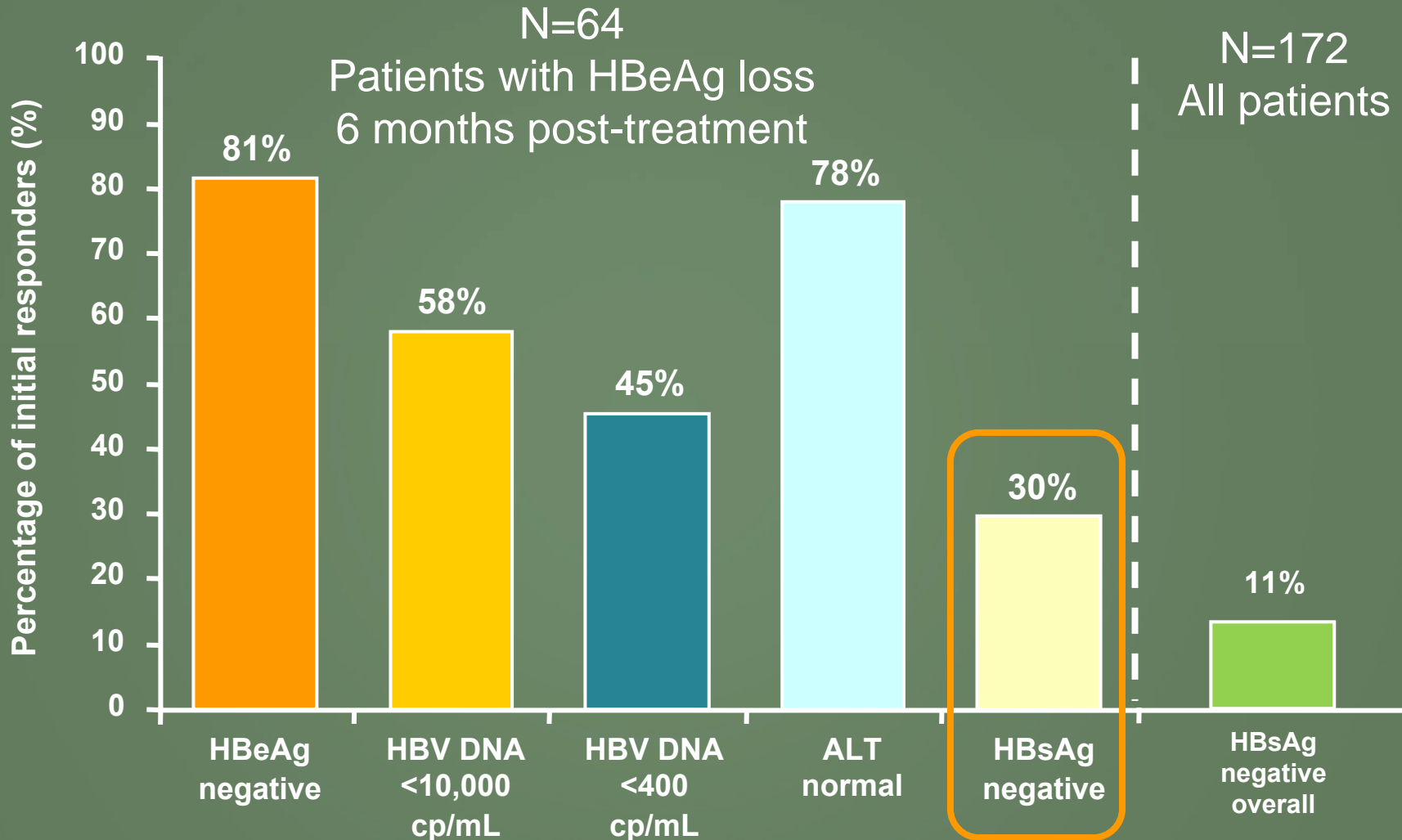
Figure 2. Rates of HBeAg Seroconversion after 24 Weeks

The Percentage of patients with seroconversion in each group is shown at the top of the corresponding bar.

3-year follow up of HBeAg responders to PEG-IFN α -2b: HBeAg-positive CHB: Initial Outcomes

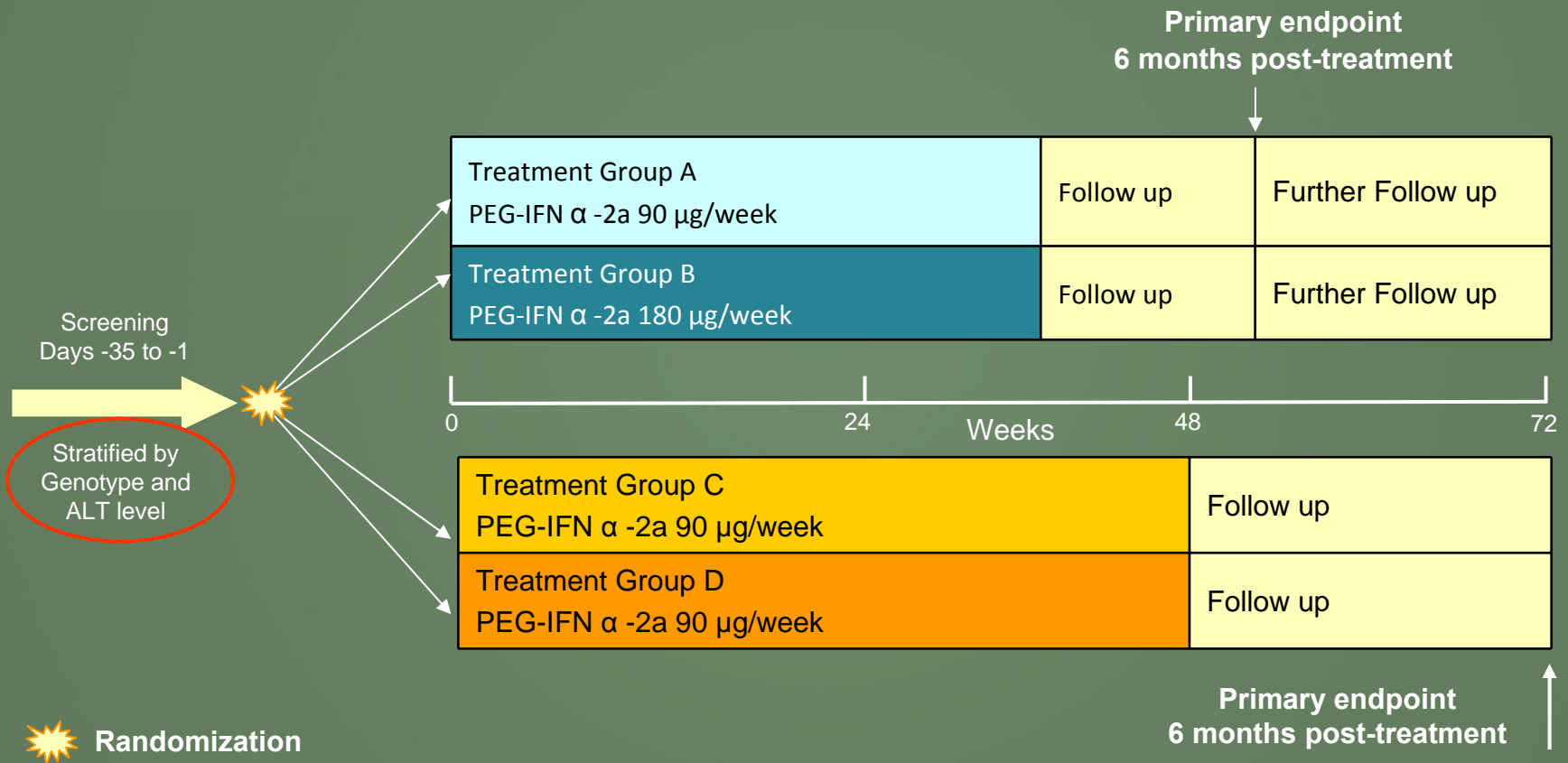


3-year follow up of HBeAg responders to PEG-IFN α -2b: HBeAg-positive CHB



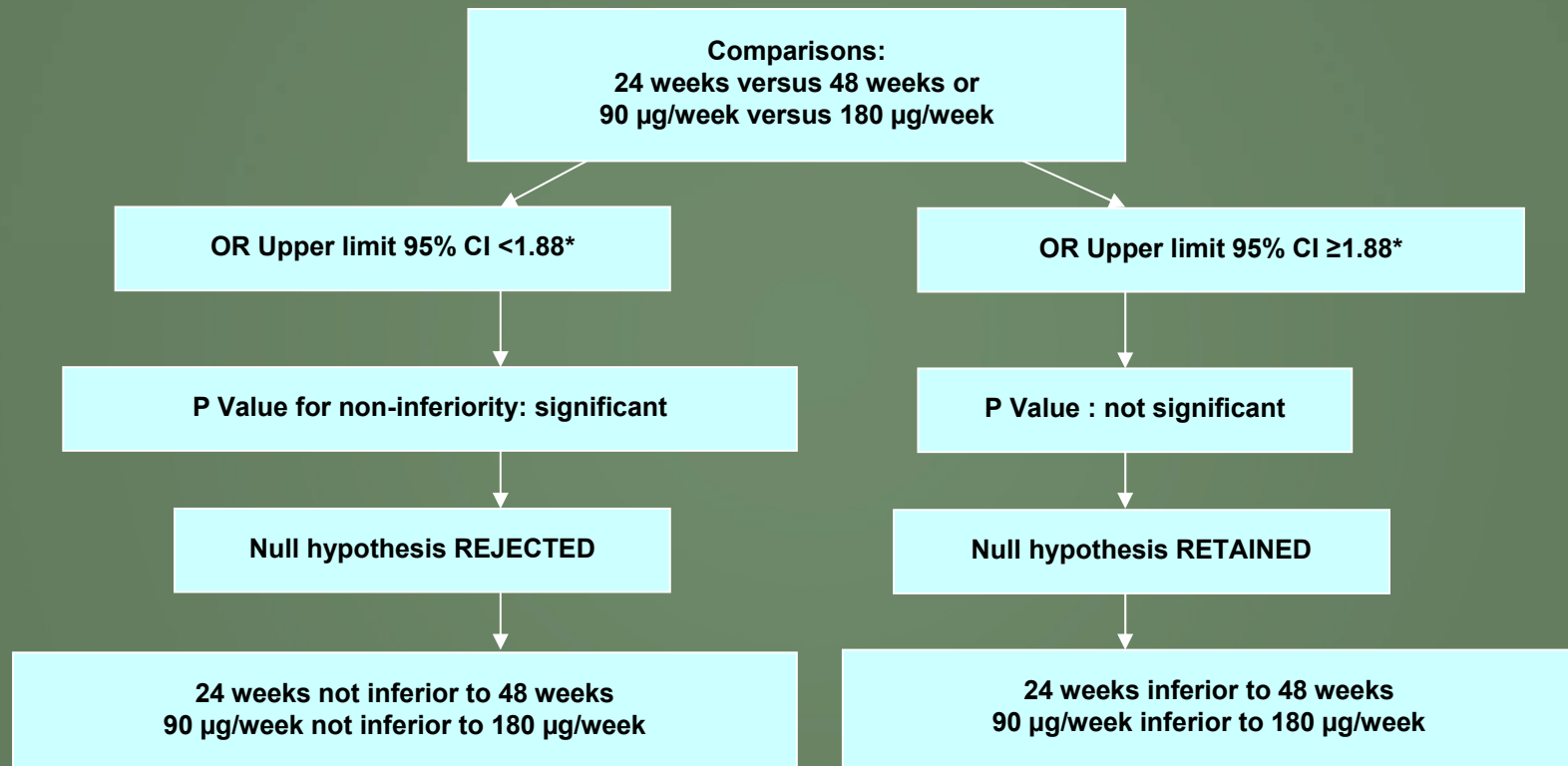
Shorter duration and lower dose of peginterferon alfa-2a therapy results in inferior HBeAg seroconversion rates compared with the duration and dose of 48 weeks and 180 µg: NEPTUNE study

NEPTUNE Study: a 2 x 2 factorial design non-inferiority study in HBeAg-positive patients (n=524)



Shorter duration and lower dose of peginterferon alfa-2a therapy results in inferior HBeAg seroconversion rates compared with the duration and dose of 48 weeks and 180 µg: NEPTUNE study

Testing the Main Effects



*Pre-specified non inferiority margin for odds ratio

Shorter duration and lower dose of peginterferon alfa-2a therapy results in inferior HBeAg seroconversion rates compared with the duration and dose of 48 weeks and 180 µg: NEPTUNE study

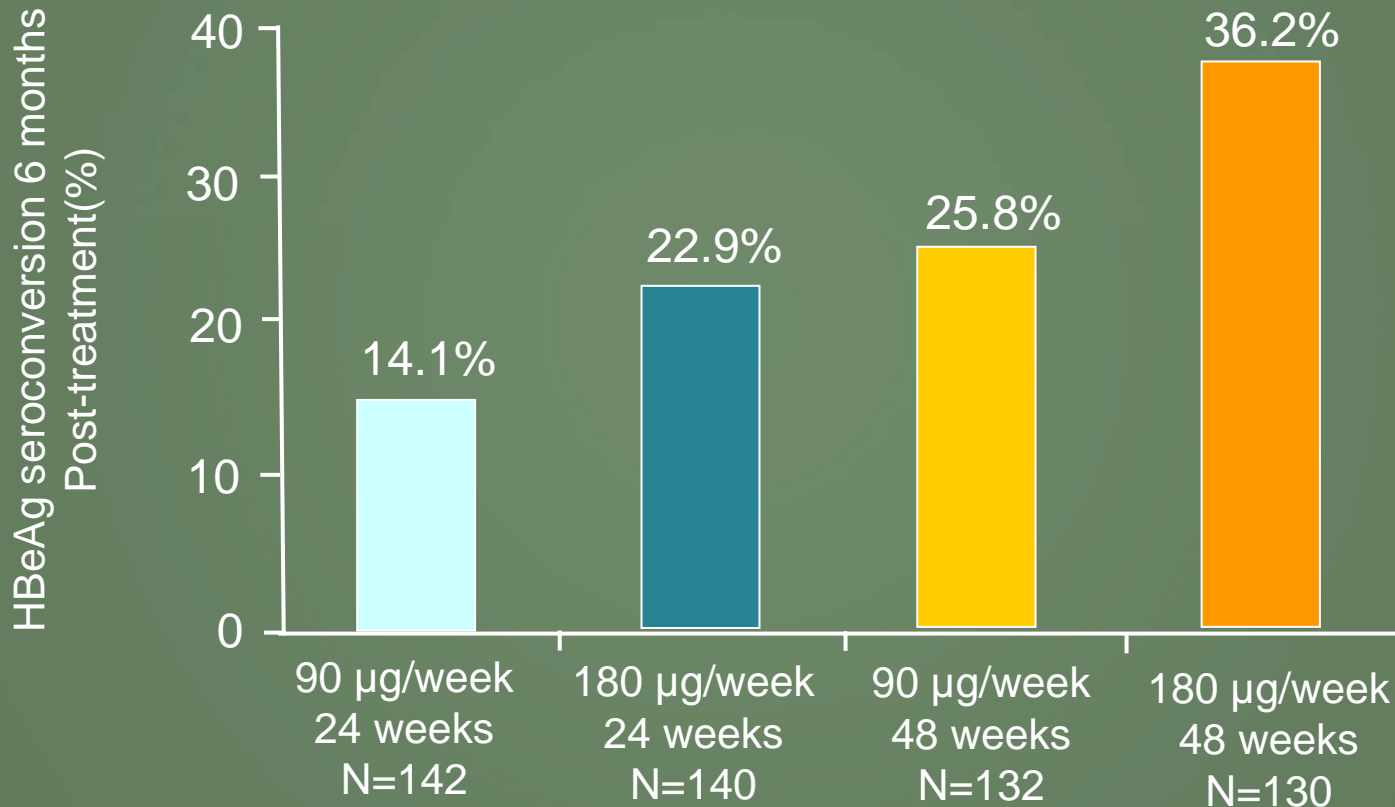
Baseline characteristics are similar across groups

- ≈70% male, 84-88% Oriental
- Mean age: ≈ 32-34 years
- Genotype A= 2-6%; B= 34-35%; C= 49-54%; D= 4-8%

	90 µg / 24 weeks n=140	180 µg / 24 weeks n=140	90 µg / 48 weeks n=136	180 µg / 48 weeks n=136
Baseline HBV DNA (log₁₀ IU/mL)	7.8 ± 1.1	7.7 ± 1.1	8.0 ± 0.9	7.6 ± 1.1
Baseline ALT (IU/L)	160.7 ± 120.2	174.1 ± 147.6	155.8 ± 117.7	161.5 ± 155.3

Shorter duration and lower dose of peginterferon alfa-2a therapy results in inferior HBeAg seroconversion rates compared with the duration and dose of 48 weeks and 180 µg: NEPTUNE study

Highest HBeAg seroconversion rate in the 180 µg/week for 48 weeks group

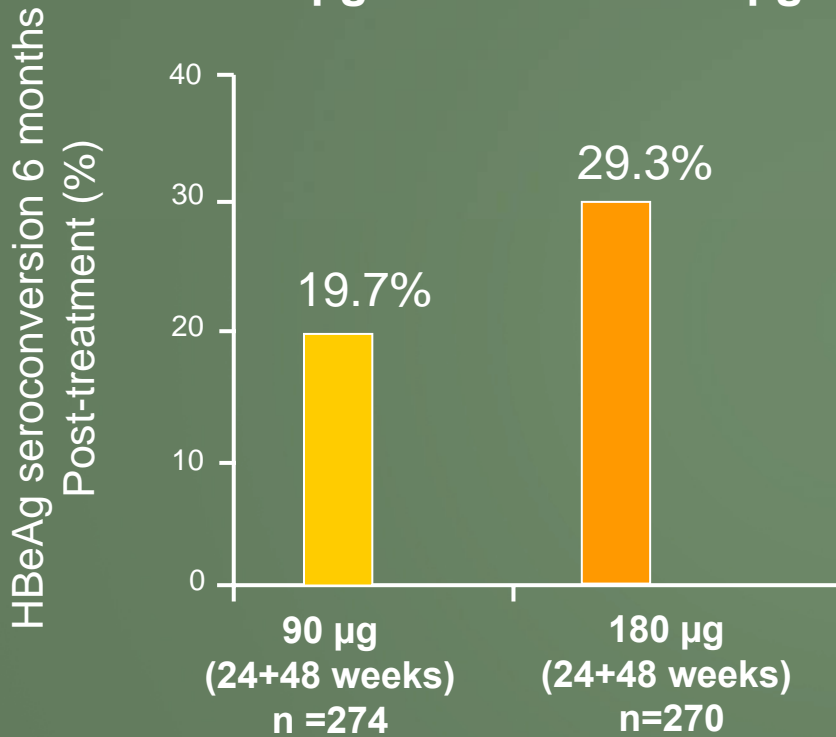


No interaction between dose and duration: P=0.8959

Shorter duration and lower dose of peginterferon alfa-2a therapy results in inferior HBeAg seroconversion rates compared with the duration and dose of 48 weeks and 180 µg: NEPTUNE study

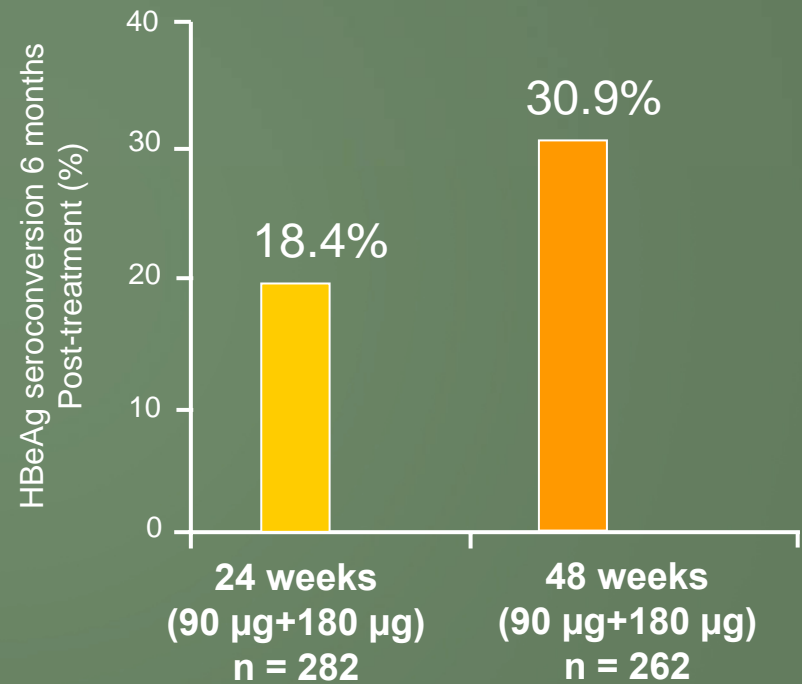
90 µg/week is inferior to 180 µg/week
24 weeks is inferior to 48 weeks

180 µg/week versus 90 µg/week



OR(95% CI):1.79(1.13,2.72); P=0.410

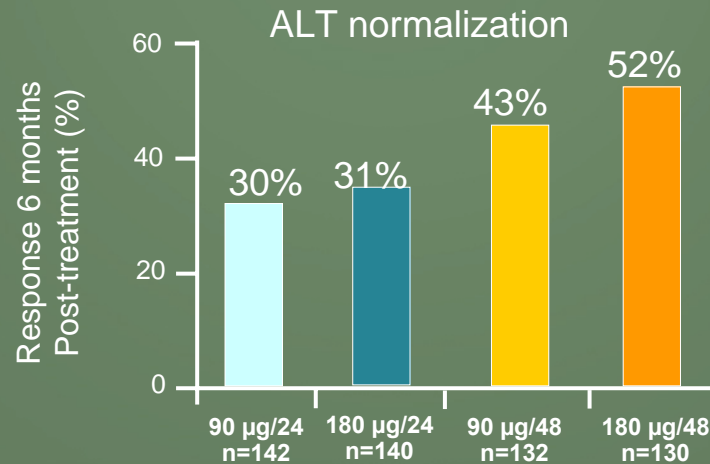
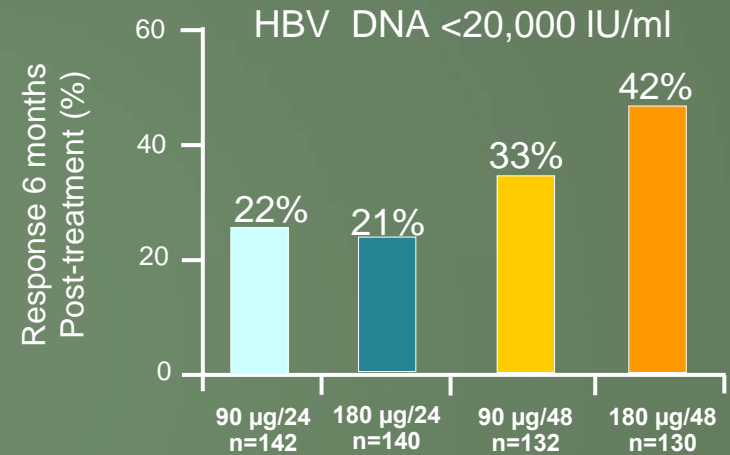
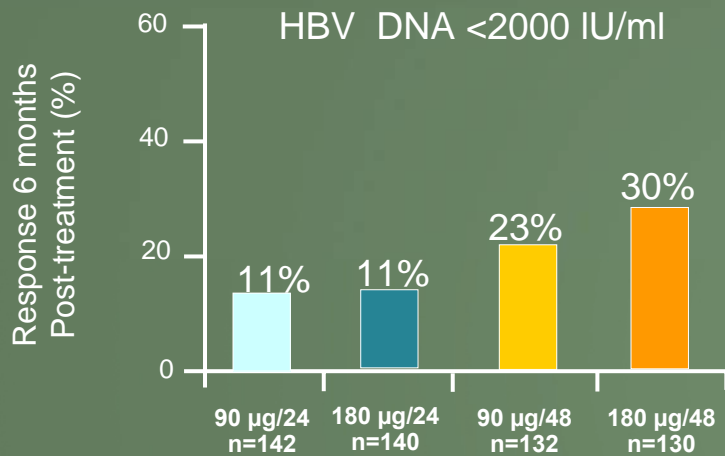
48 week versus 24 weeks



OR(95% CI):2.17(1.43,3.31); P=0.749

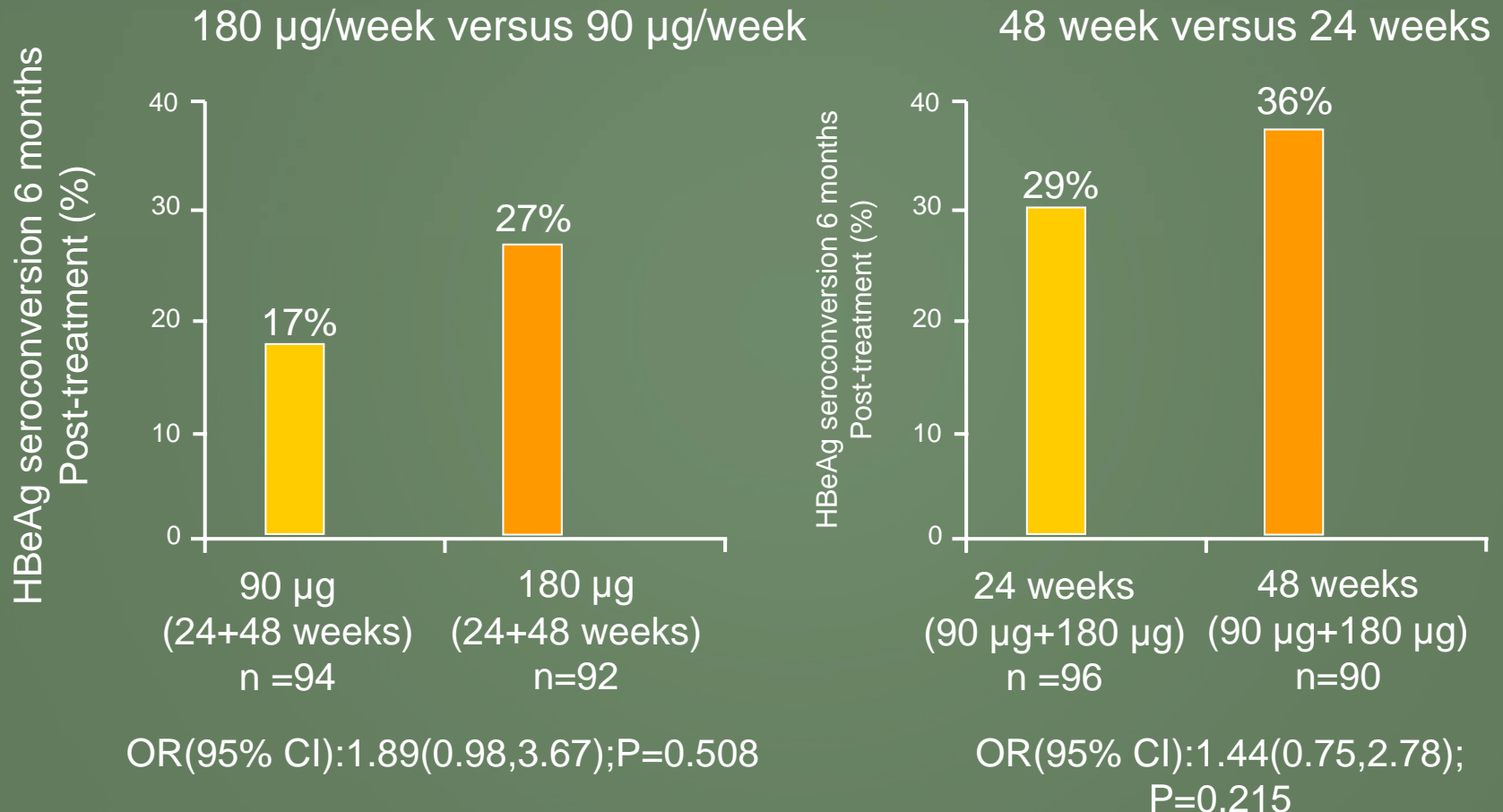
Shorter duration and lower dose of peginterferon alfa-2a therapy results in inferior HBeAg seroconversion rates compared with the duration and dose of 48 weeks and 180 µg: NEPTUNE study

Secondary endpoint results are consistent with the primary efficacy endpoints



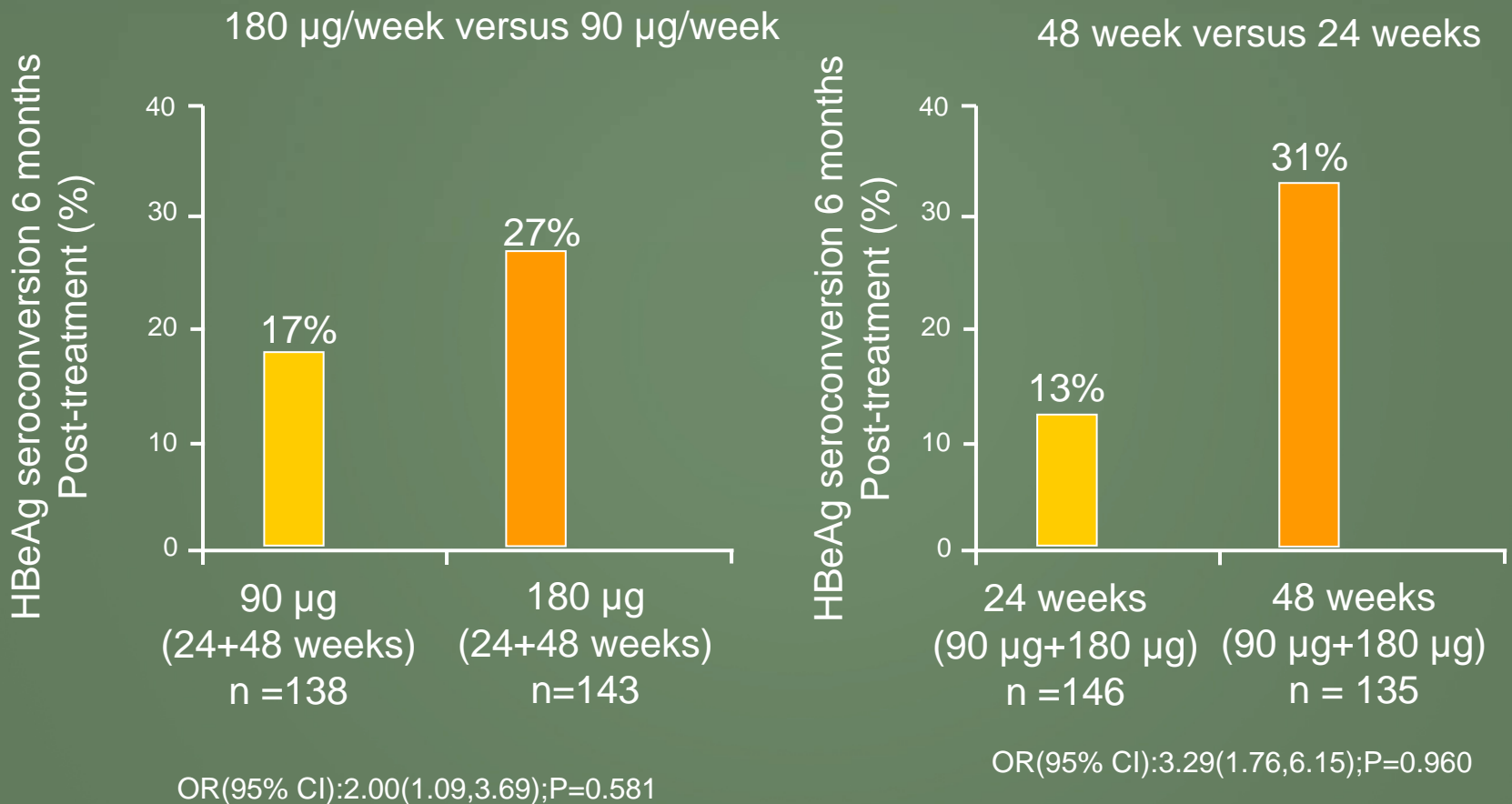
Shorter duration and lower dose of peginterferon alfa-2a therapy results in inferior HBeAg seroconversion rates compared with the duration and dose of 48 weeks and 180 µg: NEPTUNE study

90 µg/week is inferior to 180 µg/week 24 weeks is inferior to 48 weeks in genotype B



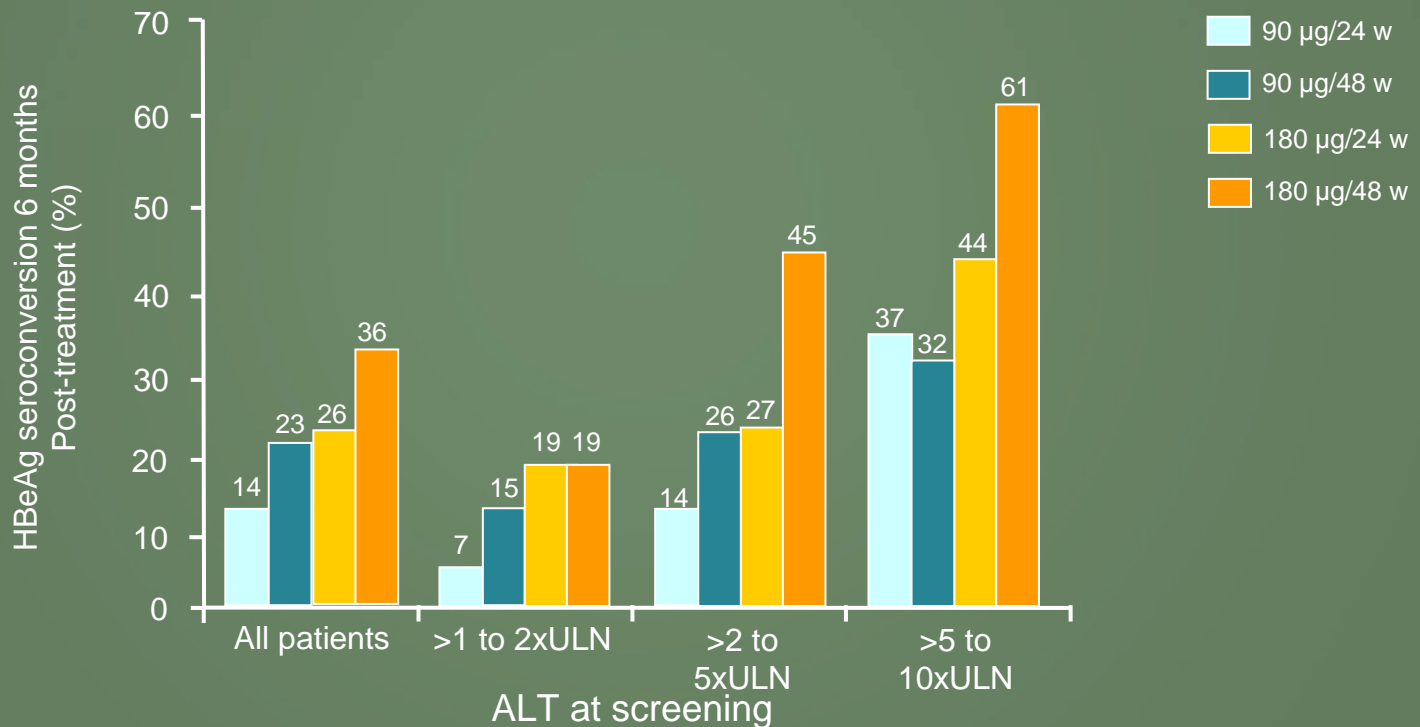
Shorter duration and lower dose of peginterferon alfa-2a therapy results in inferior HBeAg seroconversion rates compared with the duration and dose of 48 weeks and 180 µg: NEPTUNE study

90 µg/week is inferior to 180 µg/week 24 weeks is inferior to 48 weeks in genotype C



Shorter duration and lower dose of peginterferon alfa-2a therapy results in inferior HBeAg seroconversion rates compared with the duration and dose of 48 weeks and 180 µg: NEPTUNE study

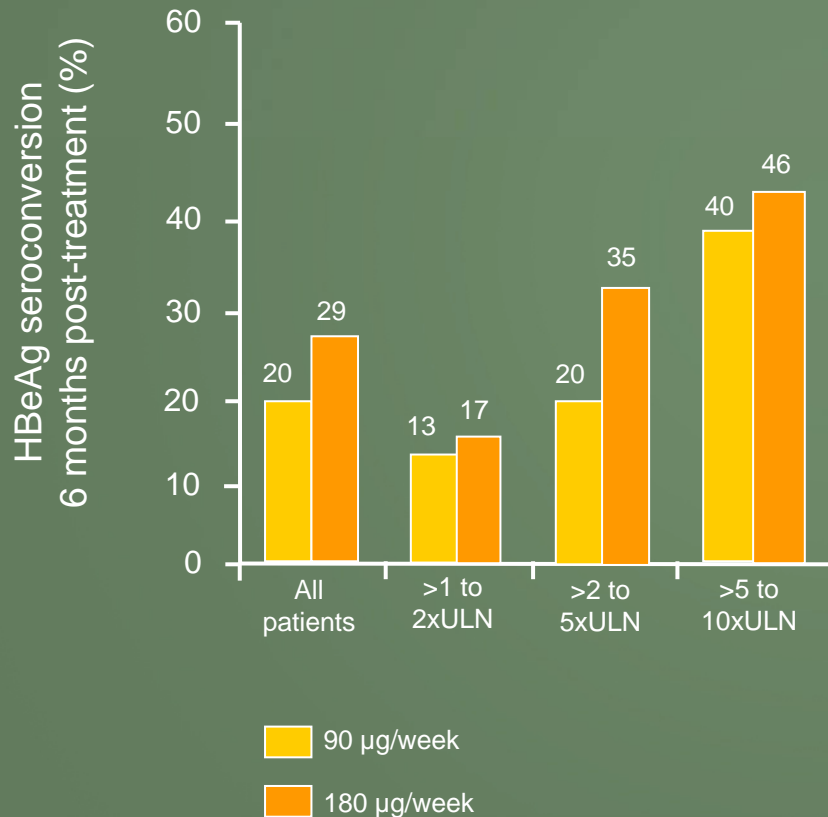
Highest HBeAg seroconversion rates in the 180 µg/week for 48 weeks group for the majority of screening ALT strata



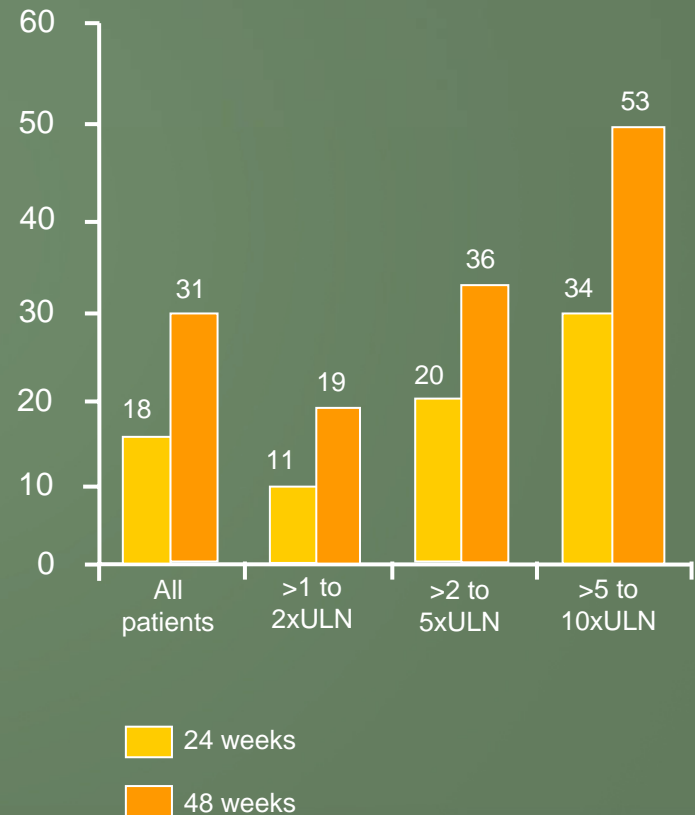
Shorter duration and lower dose of peginterferon alfa-2a therapy results in inferior HBeAg seroconversion rates compared with the duration and dose of 48 weeks and 180 µg: NEPTUNE study

90 µg is inferior to 180 µg and 24 weeks is inferior to 48 weeks in each ALT strata

180 µg/week versus 90 µg/week



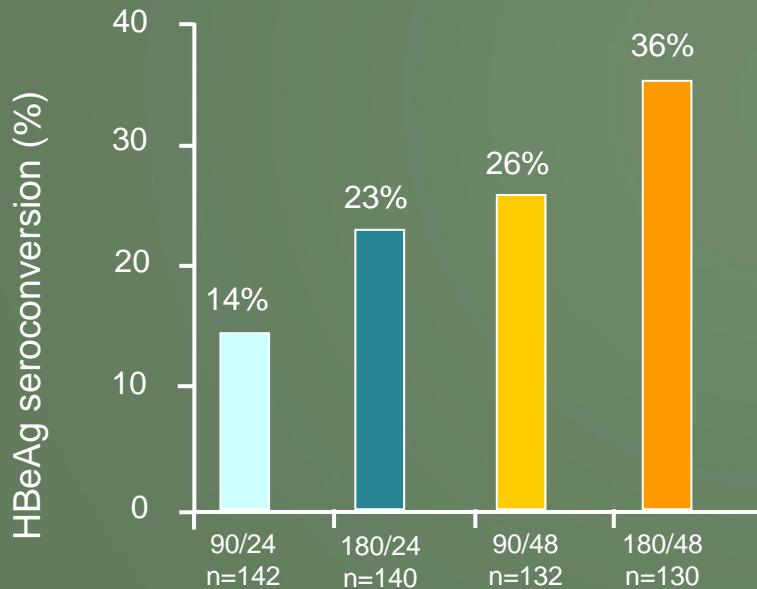
48 weeks versus 24 weeks



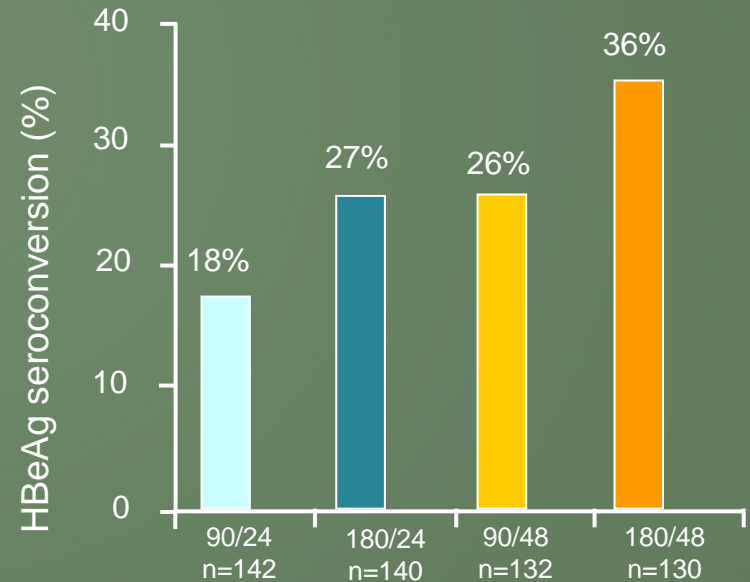
Shorter duration and lower dose of peginterferon alfa-2a therapy results in inferior HBeAg seroconversion rates compared with the duration and dose of 48 weeks and 180 µg: NEPTUNE study

Highest post-treatment HBeAg seroconversion rates in the 180 µg/week for 48 weeks group

6 months post-treatment



72 weeks time point



Shorter duration and lower dose of peginterferon alfa-2a therapy results in inferior HBeAg seroconversion rates compared with the duration and dose of 48 weeks and 180 µg: NEPTUNE study

- High rates of treatment completion in all groups (86-93%)
- Mean doses received were 94-98% of total planned dose
- Safety data was consistent with the known safety profile of PEG-IFN α -2 α in CHB
- 180 µg of PEG-IFN α -2 α for 48 weeks was well tolerated
- Incidence of AEs leading to withdrawal or dose modifications, serious AEs were low and similar across all treatment groups

Shorter duration and lower dose of peginterferon alfa-2a therapy results in inferior HBeAg seroconversion rates compared with the duration and dose of 48 weeks and 180 µg: NEPTUNE study

NEPTUNE: Summary and conclusion

- The highest rates of response were achieved in the 180 µg/week for 48 week group: 36% for HBeAg seroconversion
 - 24 weeks was inferior to 48 weeks of treatment
 - 90 µg/week was inferior to 180 µg/week dose
 - Secondary endpoints were consistent
- The NEPTUNE study data confirm that compared with lower doses and shorter durations, the licensed dose of 180 µg and duration for 48 weeks of PEG-IFN α-2a is the most efficacious and beneficial treatment regimen for CHB patients

Abstract 416: Long-term Response to Lamivudine Monotherapy in Patients with HBeAg neg Chronic Hepatitis B: To Change or Not to Change?

- **Background and aims: Lamivudine (LAM) is the first nucleoside analogue approved for treatment of chronic hepatitis B (CHB)**
 - High rate of drug-resistance (about 20% per year); in fact, after a 5-year LAM-monotherapy, only 25-30% patients maintain sustained virologic response.
- In these long-term LAM-responder patients, it is unclear if LAM-monotherapy should be continued or switched to a high-genetic-barrier analogue.
- The efficacy of long-term LAM-monotherapy, its rate of drug resistance and its safety profile were evaluated in a prospective cohort of CHB-patients successfully treated for at least 60 months.

Abstract 416: Long-term Response to Lamivudine Monotherapy in Patients with HBeAg neg Chronic Hepatitis B: To Change or Not to Change?

- **Patients and Methods:**
- **74 nucleos(t)ide analogue naïve patients with chronic anti-HBeAg-positive hepatitis B treated with LAM monotherapy for at least 60 months with a durable virologic response were enrolled**
- **17/74 patients initially received LAM plus IFN α for 12-24 months and subsequently continued monotherapy**
- **All patients had periodic biochemical and virological tests every 3 months**
 - **In virologic breakthrough patients (HBV DNA ≥ 1 log₁₀ increased), molecular analysis of RT region was performed by direct sequencing using a commercially available assay (Trugene HBV, Siemens Diagnostics). I**
- **In 53/74 patients, quantitative detection of serum HBsAg was performed yearly with Architect Assay (Abbott Diagnostic).**

Abstract 416: Long-term Response to Lamivudine Monotherapy in Patients with HBeAg neg Chronic Hepatitis B: To Change or Not to Change?

- **Results:** All 74 long-term LAM-responder patients (57 male, median age 53 years, median BMI 25, 21 cirrhotics) were treated for a median period of 90 months (range 60-144).
- 59/74 patients (80%) maintained virological response
- HBsAg clearance was observed in 9/53 (17%) tested patients
- Virologic breakthrough was noted in 15/74 patients (20%) within a 76-month median treatment (range 63-101).
- In 8/15 patients, the analysis of RT region showed the presence of LAM-resistant mutations at position 180, 181 and 204 in 7/8 patients (2 rtL180M+rtM204V, 3 rtM204I, 1 rtL180M+rtM204I, 1 rtA181T+rtM204I).

Abstract 416: Long-term Response to Lamivudine Monotherapy in Patients with HBeAg neg Chronic Hepatitis B: To Change or Not to Change?

- **Conclusions: In the majority of our long-term LAM-responder patients, continuation of LAM-monotherapy was safe and effective, resulting in HBsAg clearance in 17%.**
- **However, selection of LAM resistant mutants can still occur even after a five-year therapy, although less frequently.**
- **Therefore, LAM monotherapy could be continued in CHB-patients without cirrhosis while a treatment switch should be considered for cirrhotic patients.**
- **Ongoing surveillance is required for patients continuing on LAM**

Abstract 212. A Prospective and Open-Label Study for the Efficacy and Safety of Telbivudine(Ltd) in Pregnancy for the Prevention of Perinatal Transmission of Hepatitis B Virus (HBV) to the Infants

- Despite the use of HBIg and HBV vaccination, HBV perinatal transmission (PT) occurs in ~10-30% of infants born to highly viremic mothers.
- We evaluated the efficacy and safety of Ltd use during late pregnancy in reducing HBV transmission in highly viremic HBeAg+ mothers

Methods:

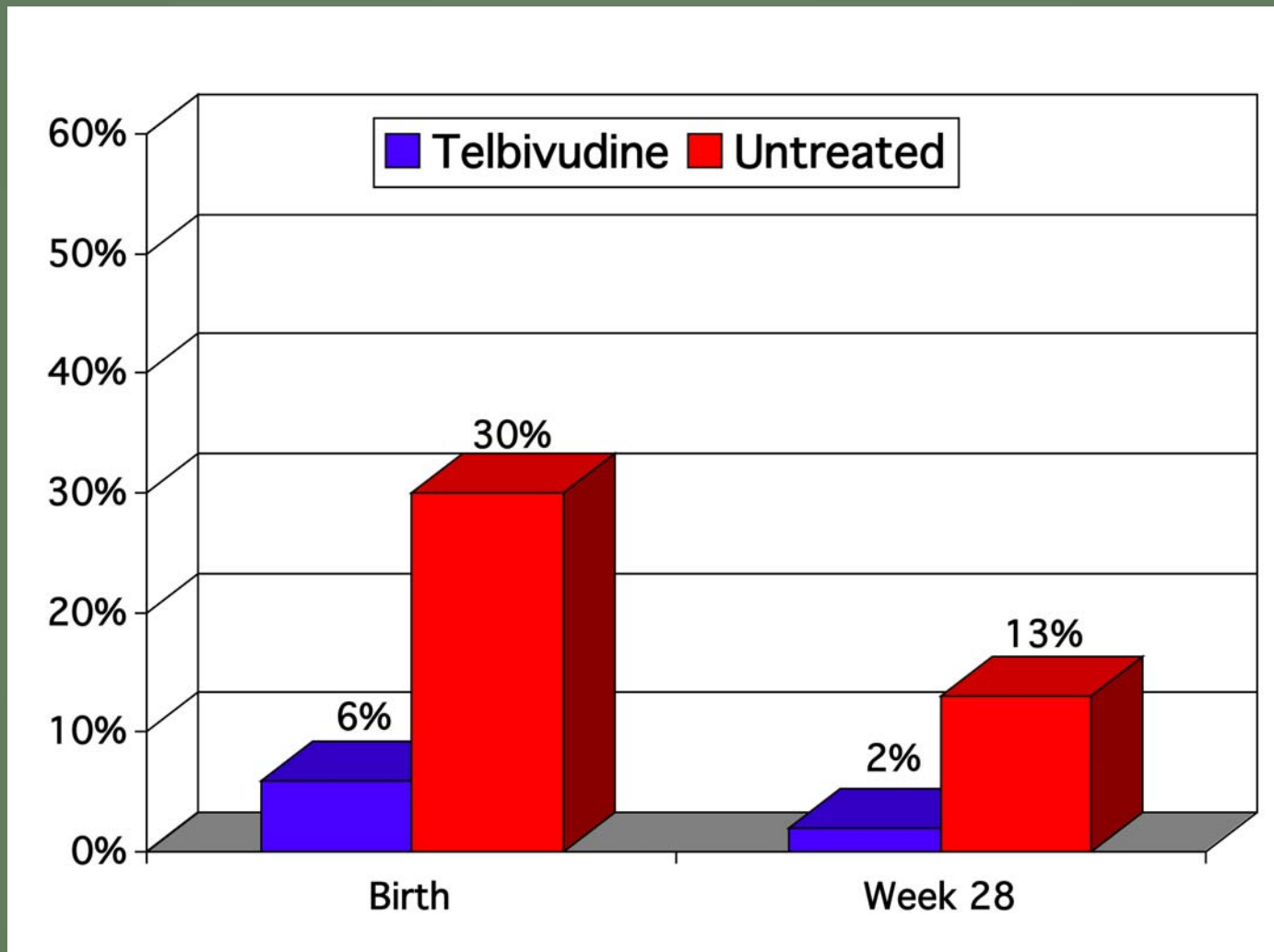
- **HBeAg+ mothers between Weeks 20-32 of gestation with HBV DNA > 1.0 x 10⁶ c/mL were eligible for enrollment**
- Treated with either Ltd 600 mg/d from W20-32 of gestation to W4 postpartum or no treatment.
- Subjects with active CHB in Ltd arm continued Ltd until W28 postpartum.
- All infants in both arms received 200 IU of HBIg within 24 hrs postpartum and recombinant HBV vaccine of 20 ug at 0,1 and 6m
- **HBsAg and HBV DNA results from infants at W28 were used to determine perinatal transmission rate**
- **RANDOMIZED?**

Abstract 212. A Prospective and Open-Label Study for the Efficacy and Safety of Telbivudine(Ltd) in Pregnancy for the Prevention of Perinatal Transmission of Hepatitis B Virus (HBV) to the Infants

Baseline Characteristics of Mothers	Telbivudine (n=94)	Controls (n=92)	p
Age	27	26	NS
ALT	23	28	NS
ALT > ULN	33%	38%	NS
HBV DNA (log copies)	8.2	8.0	NS
HBV DNA at delivery	2.4	7.8	

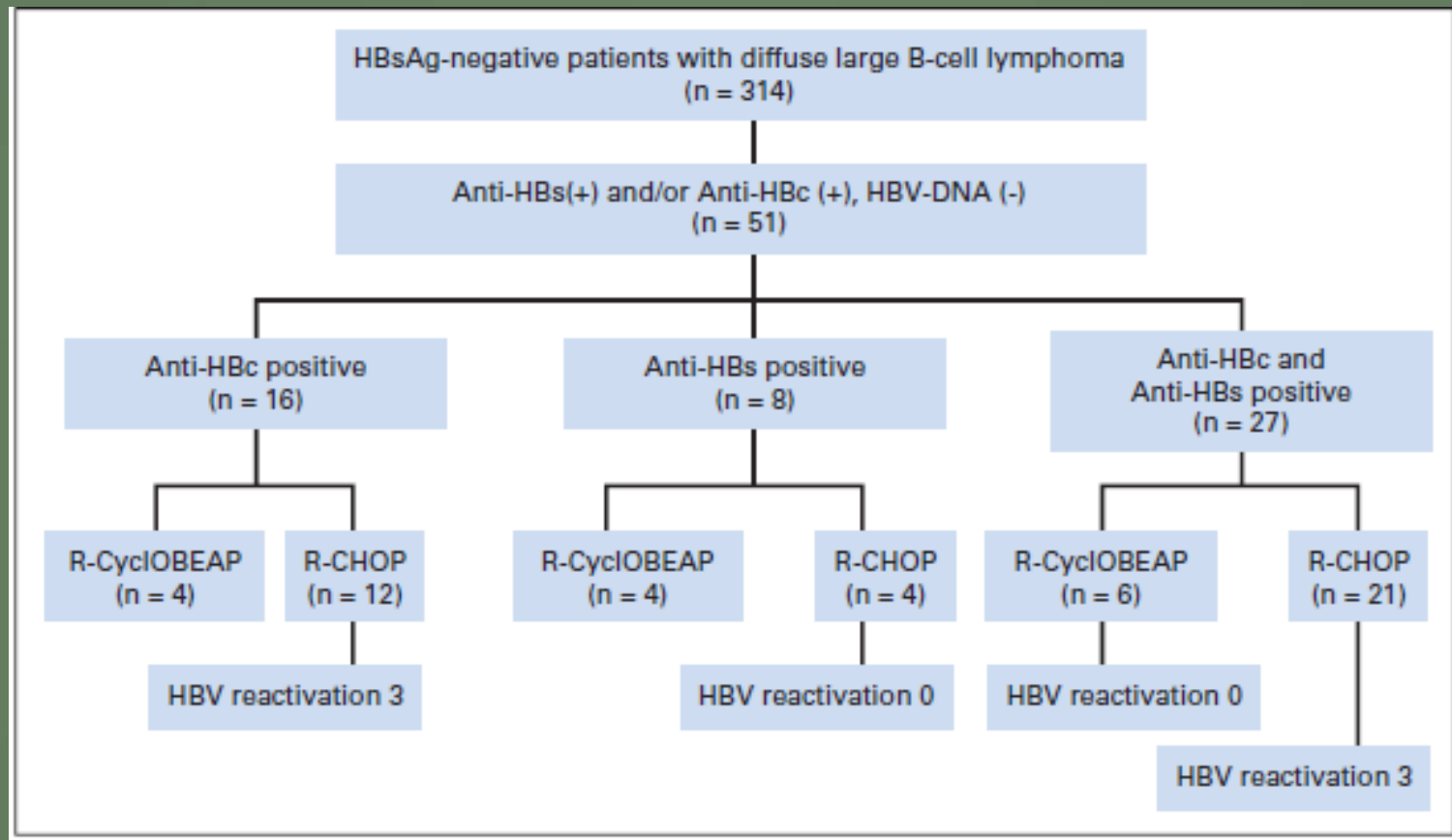
Abstract 212. A Prospective and Open-Label Study for the Efficacy and Safety of Telbivudine(Ltd) in Pregnancy for the Prevention of Perinatal Transmission of Hepatitis B Virus (HBV) to the Infants

%HBsAg+



No maternal adverse events occurred

Prospective Analysis of Hepatitis B Virus Reactivation in Patients With Diffuse Large B-Cell Lymphoma After Rituximab Combination Chemotherapy



ICAAC abstract V-1786 - Lymphoma Chemotherapy Can Cause Severe Hepatitis B Reactivation

- Background:
 - Reactivation of HBV is a serious complication in lymphoma pts receiving chemotherapy (CHT) and/or immunotherapy (e.g. rituximab).
 - HBsAg+ pts should receive prophylaxis with lamivudine (LAM) or other nucleos(t)ide analogues for at least 1 year after cessation of CHT but the optimal duration of is unknown.
 - The risk of HBV reactivation during CHT in HBsAg-/ hepatitis B core antibody (HBcAb)+ pts remains to be elucidated.
- Study Design:
 - Retrospectively analyzed 630 lymphoma pts and identified 13 (2%) who were HBsAg+ and 59 (9.6%) who were HBcAb+/sAg-.
 - Lymphoma pts receiving CHT who were HBcAb+/sAg- after 4/2007 received PRO with LAM (Italian guidelines).
 - HBV reactivation: detectable HBV DNA with ALT elevation.

ICAAC abstract V-1786 - Lymphoma Chemotherapy Can Cause Severe Hepatitis B Reactivation

- Results:
 - All 13 HBsAg+ pts received PRO with LAM . Median duration 16mo post CHT.
 - During PRO, 4 pts developed HBV hepatitis (9,12,15 and 16 mo after completion of CHT), with LAM-resistant HBV in 2pts (1 died).
 - 59 pts were HBsAg -/ HBcAb+: 47 received PRO with LAM and none of them had HBV reactivation while 12 pts did not receive PRO with LAM and 3 (25%) had a severe HBV reactivation.
- Conclusions:
 - In HBsAg+ lymphoma pts receiving CHT, severe HBV reactivation may occur after 1 year of PRO with LAM ; in this setting, the role of other NA should be evaluated.
 - HBV reactivation was observed in HBsAg-/HBcAb+ pts; PRO with LAM seems efficacious for this group of pts.

HBV AASLD Update 2010: Summary

- Extended duration of therapy with tenofovir and entecavir remain safe and effective (annual updates)
- Results from “field practice” appear similar to registration trials
- Peginterferon-2a- 180 μ g x 48 weeks is superior to lower dose and shorter duration
- LAM responders may be maintained on LAM but late breakthrough may occur-ongoing vigilance
- Perinatal transmission is decreased by telbivudine during last trimester of pregnancy
- HBV reactivation during chemo important concern