Hepatitis B Medications

Tenofovir Alafenamide (*Vimlidy*)

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Tenofovir alafenamide (TAF)
Summary of Key Studies

- Phase 3 Trials
  - Study 108: TAF versus TDF in HBeAg-Negative
  - Study 110: TAF versus TDF in HBeAg-Positive

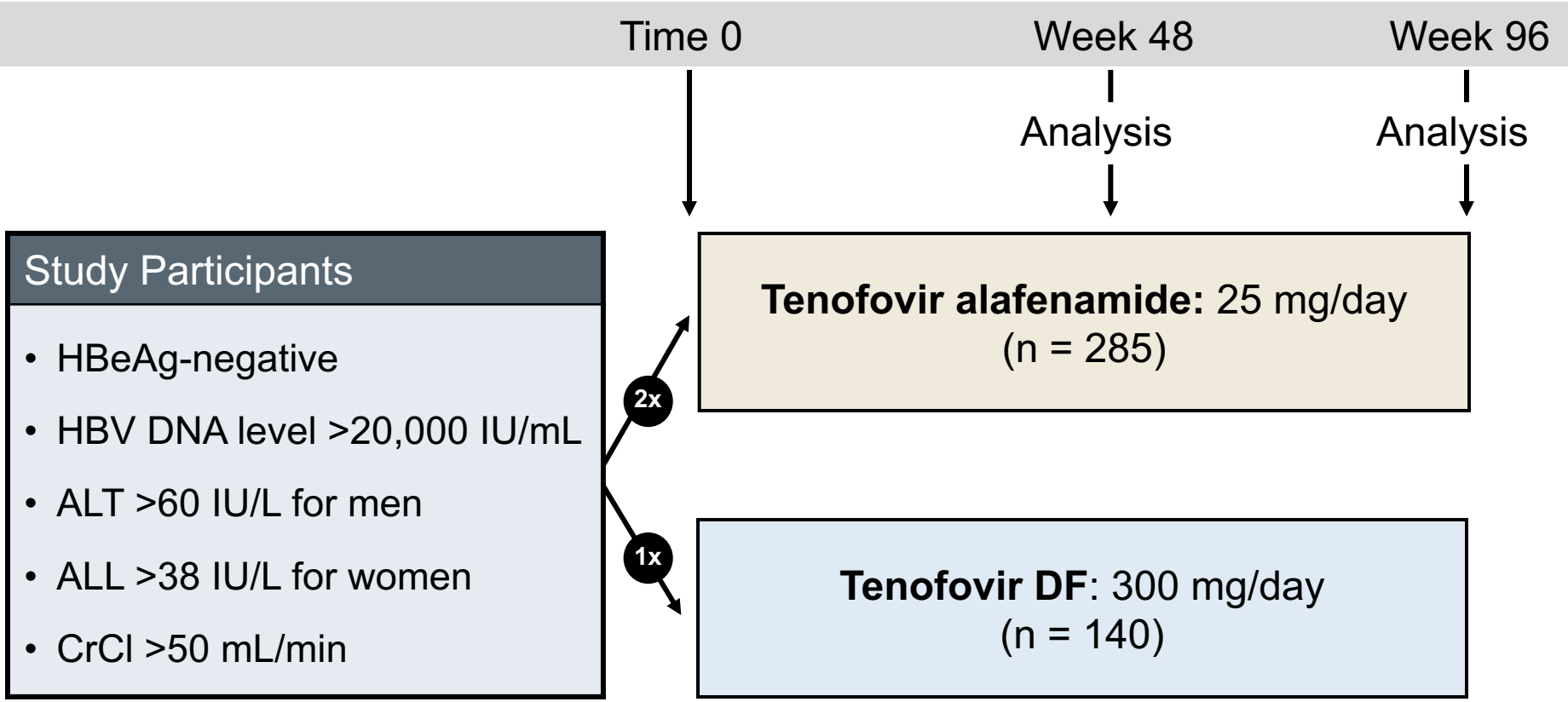
Tenofovir AF vs Tenofovir DF in HBeAg-Negative Study 108

Tenofovir AF vs Tenofovir DF for HBeAg-Negative Study 108: Design

- **Background**
  - Randomized double-blind placebo-controlled non-inferiority trial of tenofovir alafenamide (TAF) versus tenofovir disoproxil fumarate (TDF) in HBeAg-negative adults with chronic hepatitis B
- **Subjects (n = 426)**
  - Age ≥18 years
  - Chronic HBeAg-negative
  - HBV DNA level >20,000 IU/mL
  - ALT >60 IU/L in men, >38 IU/L in women; ALT <10 x ULN for both
- **Regimen**
  - Tenofovir AF: 25 mg once daily with matching placebo
  - Tenofovir DF: 300 mg once daily with matching placebo
- **Study End-Point**
  - HBV DNA level <29 IU/mL at week 48

Source: Buti M, et. al. Lancet Gastroenterol Hepatol. 2016;1:196-206.

Tenofovir AF vs Tenofovir DF for HBeAg-Negative Study 108: Design



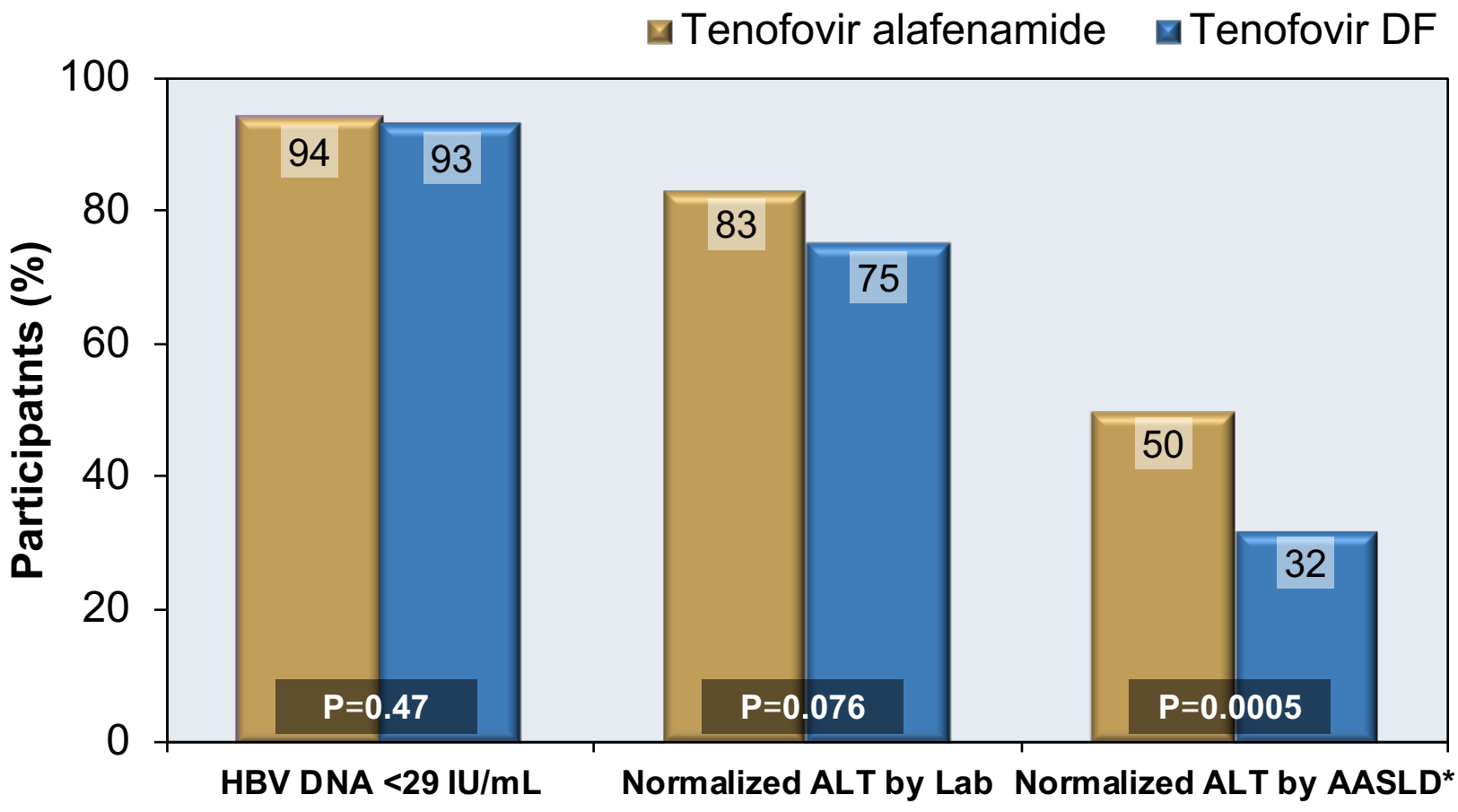
Source: Buti M, et. al. Lancet Gastroenterol Hepatol. 2016;1:196-206.

Tenofovir AF vs Tenofovir DF for HBeAg-Negative Study 108: Baseline Characteristics

Baseline Characteristic	Tenofovir AF (n = 285)	Tenofovir DF (n = 140)
Age, mean (±SD), years	45 (12)	48 (10)
Male, no. (%)	173 (61)	86 (61)
Race, no. (%)		
Asian	205 (72)	101 (72)
White	71 (25)	35 (25)
Black	5 (2)	3 (2)
Other	4 (2)	1 (1)
ALT > ULN by central lab, no. (%)	236 (83)	121 (86)
HBV DNA, $\log_{10}$ IU/mL (±SD)	5.7 (1.3)	5.8 (1.3)
FibroTest score ≥0.75, no. (%)	31/280 (11)	20/139 (14)
Previous nucleos(t)ide therapy, no. (%)	60 (21)	31 (22)
Previous interferon therapy, no. (%)	29 (10)	19 (14)

Source: Buti M, et. al. Lancet Gastroenterol Hepatol. 2016;1:196-206.

Tenofovir AF vs Tenofovir DF for HBeAg-Negative Study 108: Results at Week 48

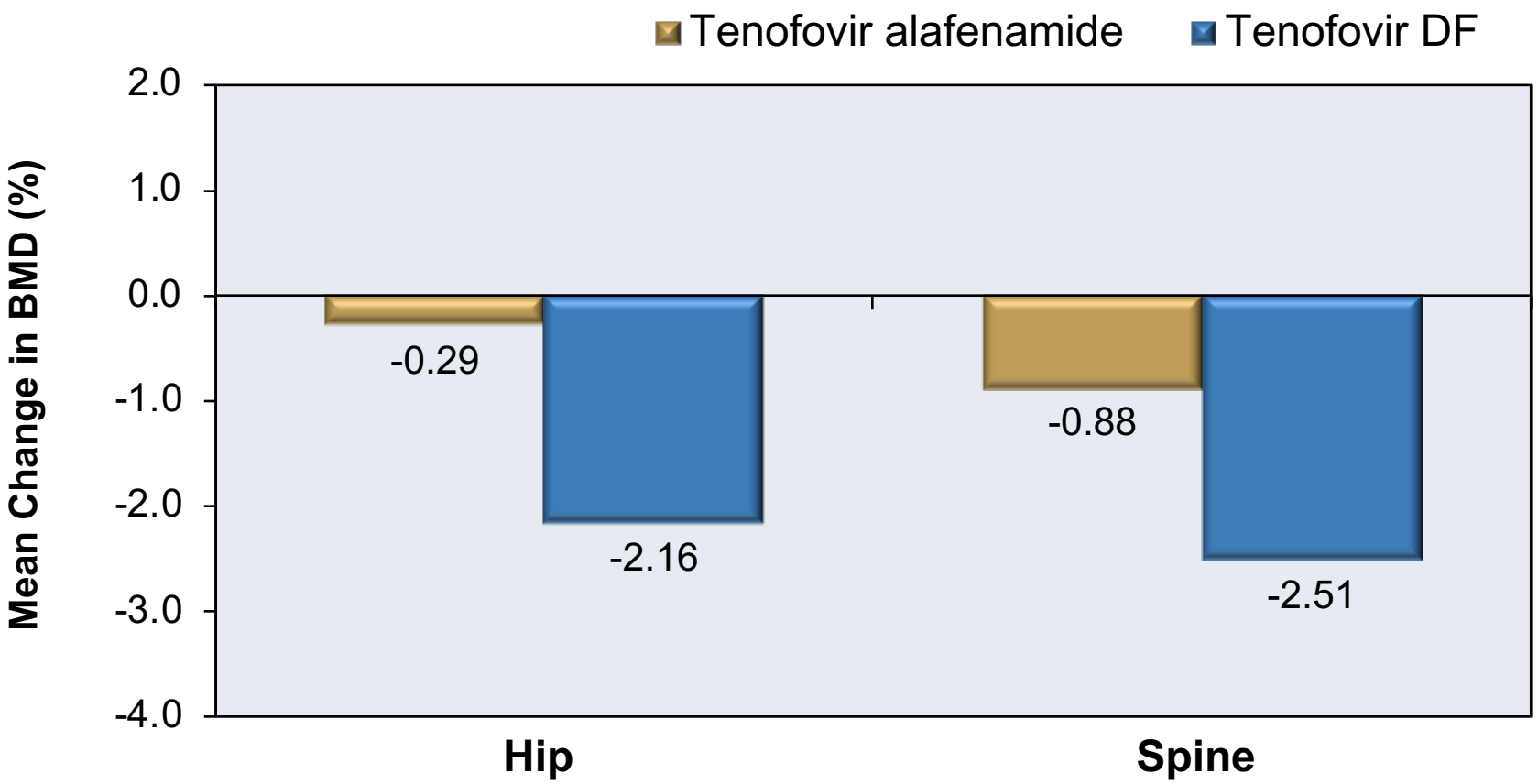


*Using normal ranges of ≤30 U/L for men and ≤19 U/L for women

Source: Buti M, et. al. Lancet Gastroenterol Hepatol. 2016;1:196-206.

Tenofovir AF vs Tenofovir DF for HBeAg-Negative Study 108: Adverse Effects

Week 48 Changes in Bone Mineral Density (BMD)



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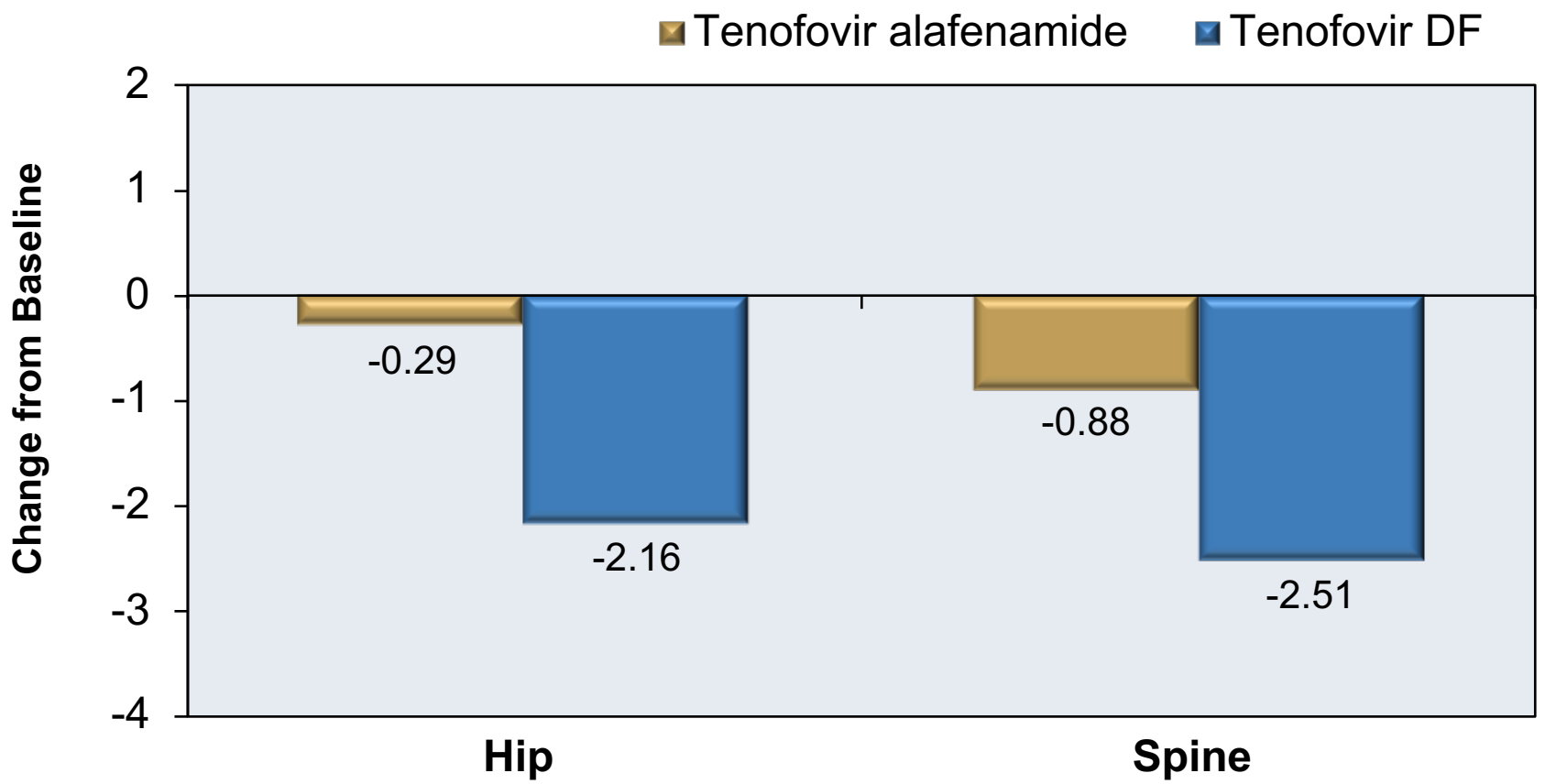

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Tenofovir AF vs Tenofovir DF for HBeAg-Negative Study 108: Results

Interpretation: “In patients with HBeAg-negative chronic HBV, the efficacy of tenofovir alafenamide was non-inferior to that of tenofovir disoproxil fumarate, and had improved bone and renal effects. Longer term follow-up is needed to better understand the clinical impact of these changes.”

Source: Buti M, et. al. Lancet Gastroenterol Hepatol. 2016;1:196-206.

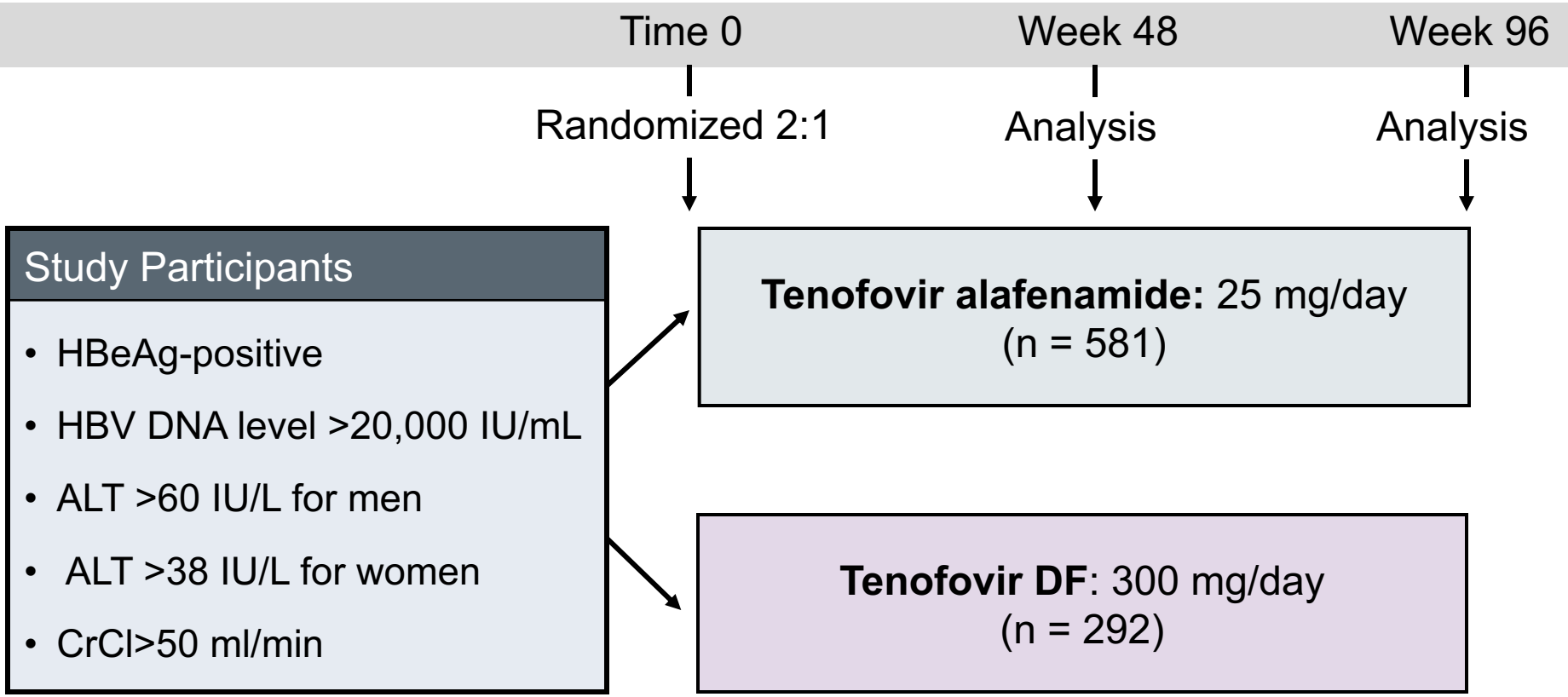
Tenofovir AF vs Tenofovir DF in HBeAg-Positive Study 110

Tenofovir AF vs Tenofovir DF for HBeAg-Positive Study 110: Design

- **Background**
  - Randomized double-blind placebo-controlled non-inferiority trial of tenofovir alafenamide (TAF) versus tenofovir disoproxil fumarate (TDF) in HBeAg-positive chronic hepatitis B patients
- **Subjects**
  - N = 1473 with chronic hepatitis B eAg-positive infection
  - HBV DNA level >20,000 IU/mL
  - ALT >60 IU/L in men, >38 IU/L in women; <10 x ULN for both
- **Regimens**
  - Tenofovir AF 25 mg once daily with matching placebo
  - Tenofovir DF 300 mg once daily with matching placebo
- **Study End-Point**
  - HBV DNA level <29 IU/mL at week 48

Source: Chan HL, et. al. Lancet Gastroenterol Hepatol. 2016;1:185-95.

Tenofovir AF vs Tenofovir DF for HBeAg-Positive Study 110: Design



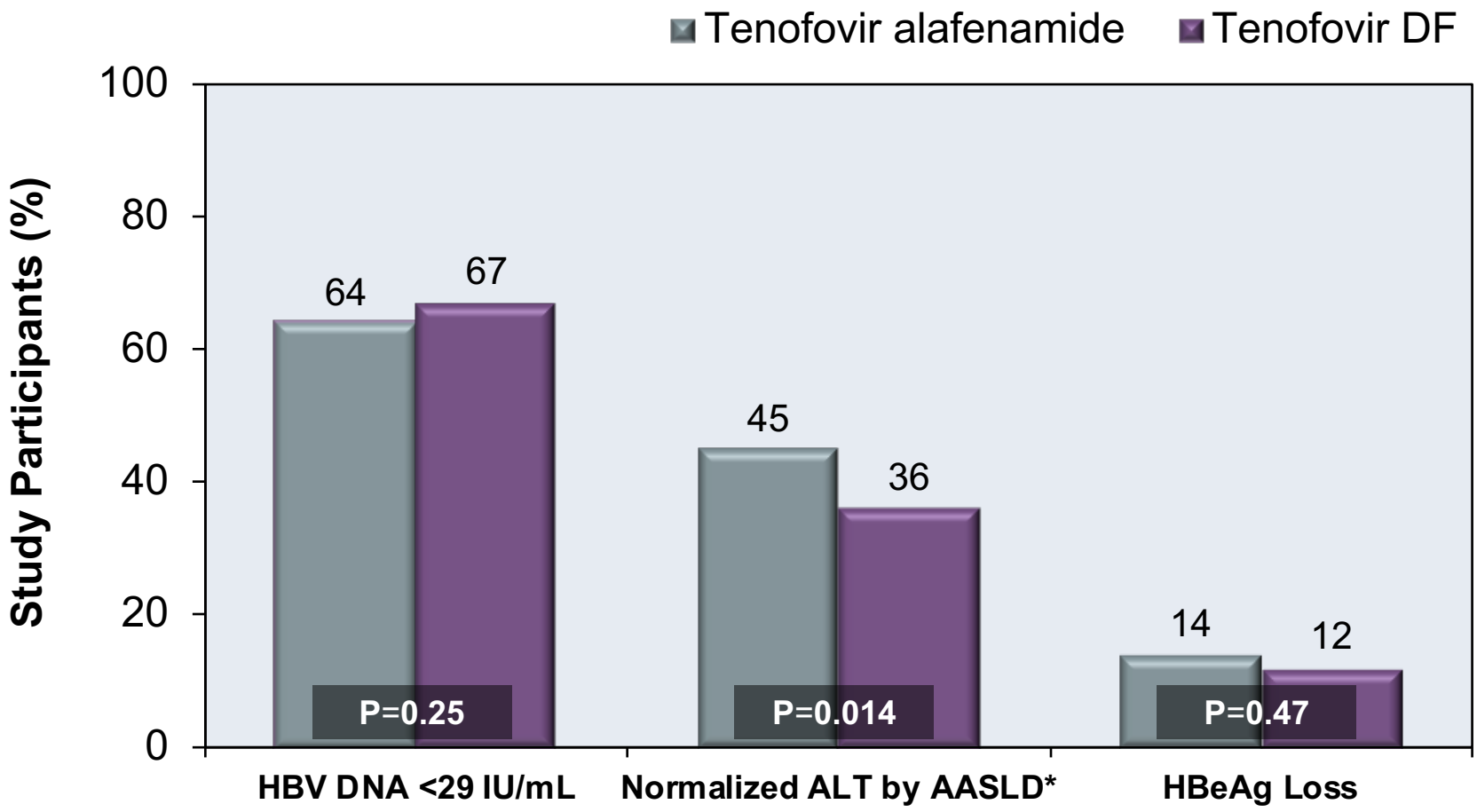
Source: Chan HL, et. al. Lancet Gastroenterol Hepatol. 2016;1:185-95.

Tenofovir AF vs Tenofovir DF for HBeAg-Positive Study 110: Baseline Characteristics

Baseline Characteristic	Tenofovir AF (n = 581)	Tenofovir DF (n = 292)
Age, mean (±SD), years	38 (11)	38 (12)
Male, no. (%)	371 (64)	189 (65)
Race, no. (%)		
Asian	482 (83)	232 (79)
White	96 (17)	53 (18)
Other	3 (1)	7 (2)
ALT > ULN by central lab, no. (%)	537 (98)	288 (99)
HBV DNA, $\log_{10}$ IU/mL (±SD)	7.6 (1.3)	7.6 (1.4)
FibroTest score, mean (±SD)	0.34 (0.23)	0.32 (0.22)
Cirrhosis, no. (%)	41 (7)	24 (8)
Serum creatinine, mean (±SD)	0.81 (0.17)	0.82 (0.16)

Source: Chan HL, et. al. Lancet Gastroenterol Hepatol. 2016;1:185-95.

Tenofovir AF vs Tenofovir DF for HBeAg-Positive Study 110: Results at Week 48



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Tenofovir AF vs Tenofovir DF for HBeAg-Positive Study 110: Adverse Effects

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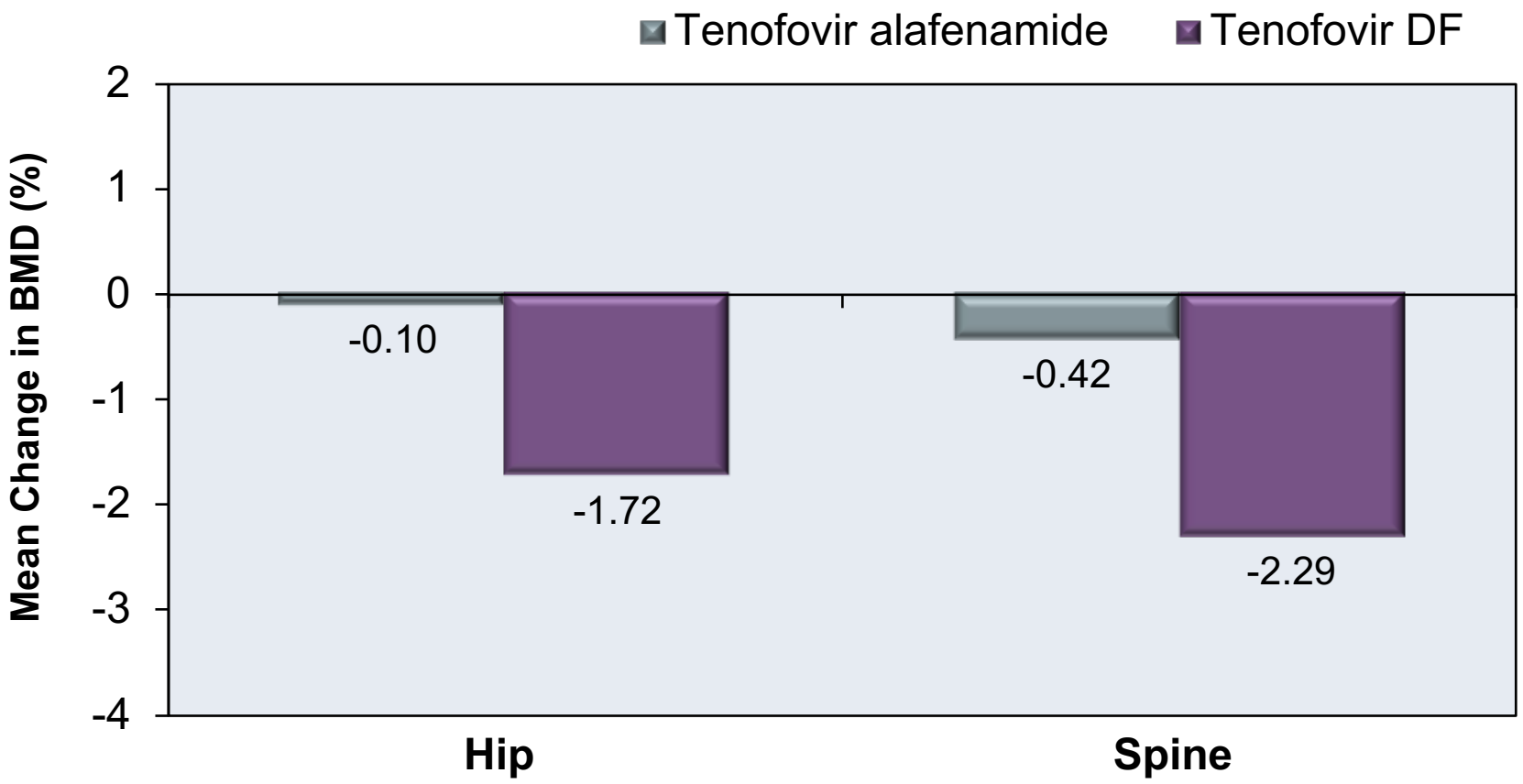

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Tenofovir AF vs Tenofovir DF for HBeAg-Positive Study 110: Conclusion

Interpretation: “In patients with HBeAg-positive HBV infection, tenofovir alafenamide was non-inferior to tenofovir disoproxil fumarate, and had improved bone and renal effects. Longer term follow-up is needed to better understand the clinical impact of these changes.”

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