KRONİK HEPATİT B TEDAVİSİNDE TAF KULLANIMI: ETKİNLİK & GÜVENİLİRLİK

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İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD.
Afyonkarahisar,2019.

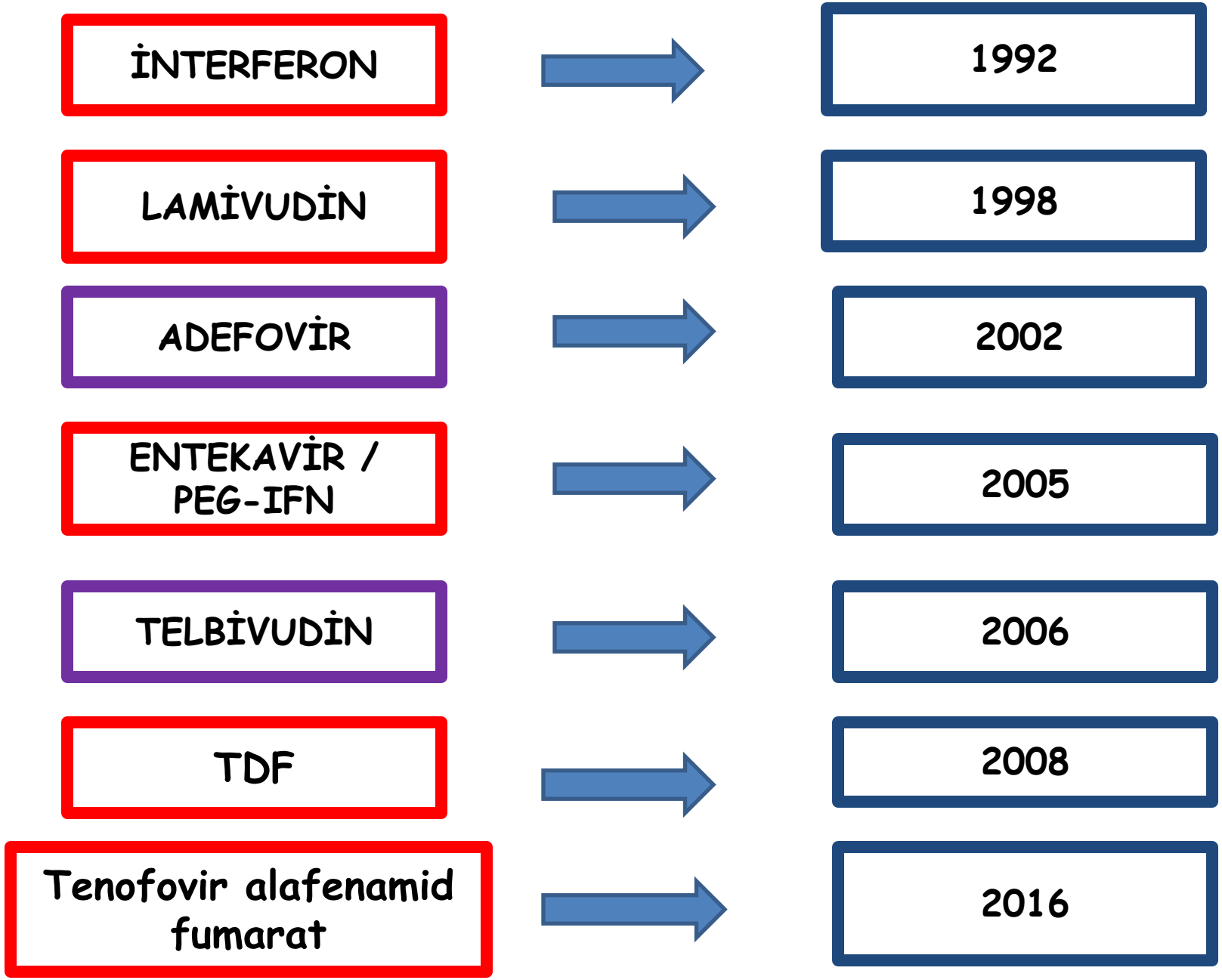
İNTERFERON
1992
LAMİVUDİN
1998
ADEFOVİR
2002
ENTEKAVİR / PEG-IFN
2005
TELBİVUDİN
2006
TDF
2008
Tenofovir alafenamid fumarat
2016

TABLE 1. Approved Antiviral Therapies in Adults and Children

Drug	Dose in Adults*	Use in Children*	Pregnancy Category†	Potential Side Effects†	Monitoring on Treatment‡
Preferred					
Peg-IFN-α-2a (adult) IFN-α-2b (children)	180 mcg weekly	≥1 year dose: 6 million IU/m^2 three times weekly§	C	Flu-like symptoms, fatigue, mood disturbances, cytopenia, autoimmune disorders in adults, anorexia and weight loss in children	Complete blood count (monthly to every 3 months) TSH (every 3 months) Clinical monitoring for autoimmune, ischemic, neuropsychiatric, and infectious complications
Entecavir	0.5 mg daily‖	≥2 years dose: weight-based to 10-30 kg; above 30 kg: 0.5 mg daily‖	C	Lactic acidosis (decompensated cirrhosis only)	Lactic acid levels if there is clinical concern Test for HIV before treatment initiation
Tenofovir dipovoxil fumarate	300 mg daily	≥12 years	B	Nephropathy, Fanconi syndrome, osteomalacia, lactic acidosis	Creatinine clearance at baseline If at risk for renal impairment, creatinine clearance, serum phosphate, urine glucose, and protein at least annually Consider bone density study at baseline and during treatment in patients with history of fracture or risks for osteopenia Lactic acid levels if there is clinical concern Test for HIV before treatment initiation
Tenofovir alafenamide	25 mg daily	—	There are insufficient human data on use during pregnancy to inform a drug-associated risk of birth defects and miscarriage.	Lactic acidosis	Lactic acid levels if clinical concern Assess serum creatinine, serum phosphorus, creatinine clearance, urine glucose, and urine protein before initiating and during therapy in all patients as clinically appropriate Test for HIV before treatment initiation

Update of prevention, diagnosis and treatment of CHB; AASLD 2018 Hepatiti B Guidance

KHB hastalarında TAF

- 2015; faz I çalışmalar
- TAF 8 -25 - 40 ve 120 mg/gün & 300mg/gün TDF
- 28 günlük değerlendirme
- Farmakokinetik ve güvenilirlik

- SONUÇ; Etkin ve güvenli

Agarwal K et al. J Hepatol, 2015

Faz III çalışmalar: 108 ve 110

Tenofovir alafenamide versus tenofovir disoproxil fumarate for the treatment of HBeAg-positive chronic hepatitis B virus infection: a randomised, double-blind, phase 3, non-inferiority trial

Henry L Y Chan, Scott Fung, Wai Kay Seto, Wan-Long Chuang, Chi-Yi Chen, Hyung Joon Kim, Aric Josun Hui, Harry L A Janssen, Abhijit C[illegible] Tak Yin Owen Tsang, Rajiv Mehta, Edward Gane, John F Flaherty, Benedetta Massetto, Anuj Gaggar, Kathryn M Kitrinos, Lanjia Lin, G Mani Subramanian, John G McHutchison, Young-Suk Lim, Subrat K Acharya, Kosh Agarwal, and the GS-US-320-0110 Investigators*

Lancet Gastroenterol Hepatol 2016; 1: 185–95
Published Online September 22, 2016
http://dx.doi.org/10.1016/S2468-1253(16)30024-3

Tenofovir alafenamide versus tenofovir disoproxil fumarate for the treatment of patients with HBeAg-negative chronic hepatitis B virus infection: a randomised, double-blind, phase 3, non-inferiority trial

Maria Buti, Edward Gane, Wai Kay Seto, Henry L Y Chan, Wan-Long Chuang, Tatjana Stepanova, Aric-Josun Hui, Young-Suk Lim, Rajiv Mehta, Harry L A Janssen, Subrat K Acharya, John F Flaherty, Benedetta Massetto, Andrea L Cathcart, Kyungpil Kim, Anuj Gaggar, G Mani Subramanian, John G McHutchison, Calvin Q Pan, Maurizia Brunetto, Namiki Izumi, Patrick Marcellin, and the GS-US-320-0108 Investigators*

Lancet Gastroenterol Hepatol 2016; 1: 196–206

Research Article
Viral Hepatitis

JOURNAL OF HEPATOLOGY

96 weeks treatment of tenofovir alafenamide *vs.* tenofovir disoproxil fumarate for hepatitis B virus infection

Kosh Agarwal[1,*], Maurizia Brunetto[2], Wai Kay Seto[3], Young-Suk Lim[4], Scott Fung[5], Patrick Marcellin[6], Sang Hoon Ahn[7], Namiki Izumi[8], Wan–Long Chuang[9], Ho Bae[10], Manoj Sharma[11], Harry L.A. Janssen[12,13], Calvin Q. Pan[14], Mustafa Kemal Çelen[15], Norihiro Furusyo[16], Dr. Shalimar[17], Ki Tae Yoon[18], Huy Trinh[19], John F. Flaherty[20], Anuj Gaggar[20], Audrey H. Lau[20], Andrea L. Cathcart[20], Lanjia Lin[20], Neeru Bhardwaj[20], Vithika Suri[20], G. Mani Subramanian[20], Edward J. Gane[21], Maria Buti[22], Henry L.Y. Chan[23,*], and the GS-US-320-0110 and GS-US-320-0108 Investigators

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Keywords: Chronic hepatitis B virus; Bone safety; Renal safety.
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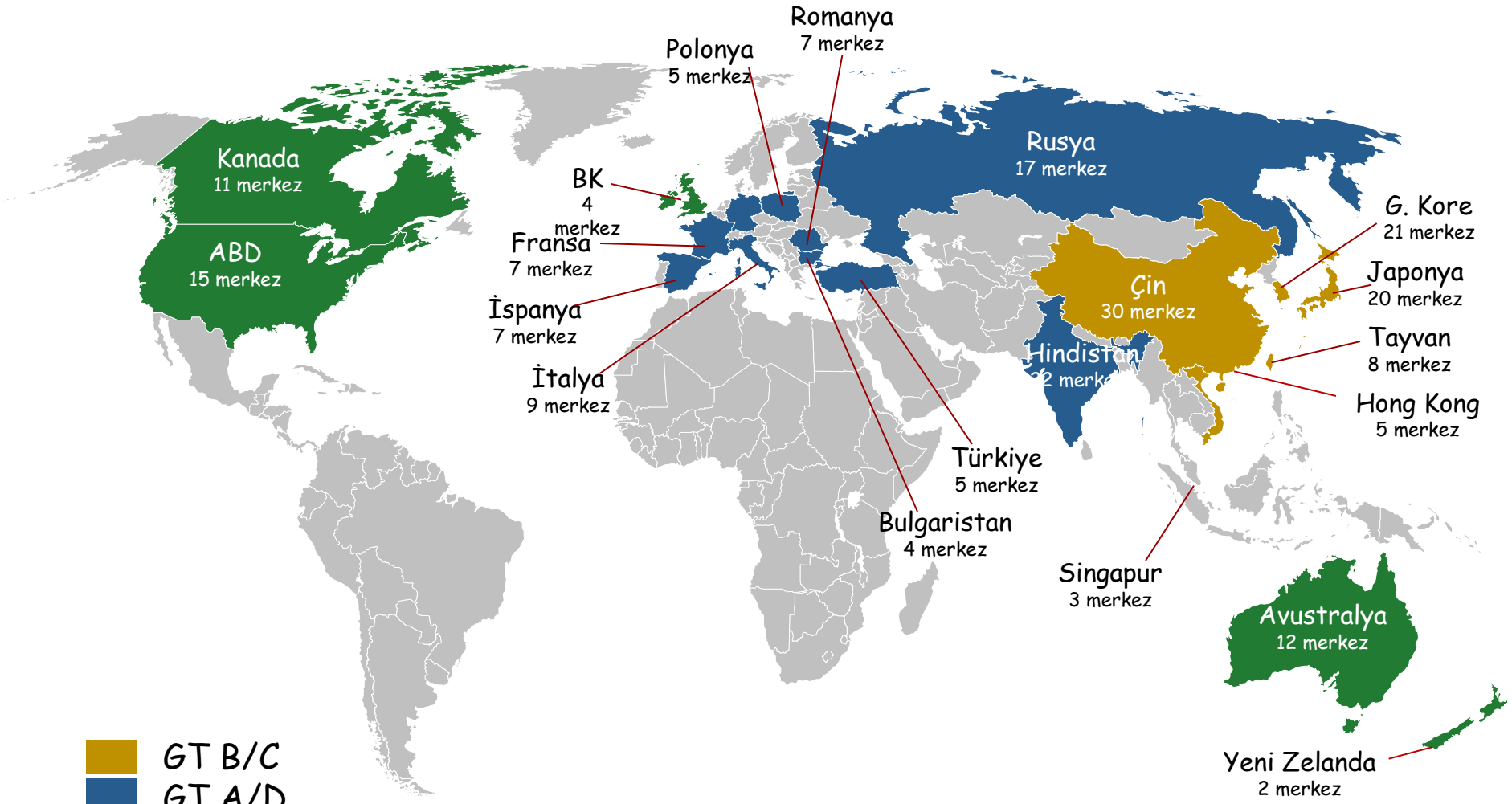
Global Faz 3 Program: 191 merkez, 19 ülke

875 HBeAg+, 426 HBeAg- KHB hastası*



Çalışmaya dahil ve hariç tutma kriterleri

Dahil etme

- HBV DNA seviyeleri >20,000 IU/ml,
- Erkeklerde ALT >60 U/L ya da kadınlarda >38 U/L
- eGFR Cockcroft-Gault method: >50 ml/dak.

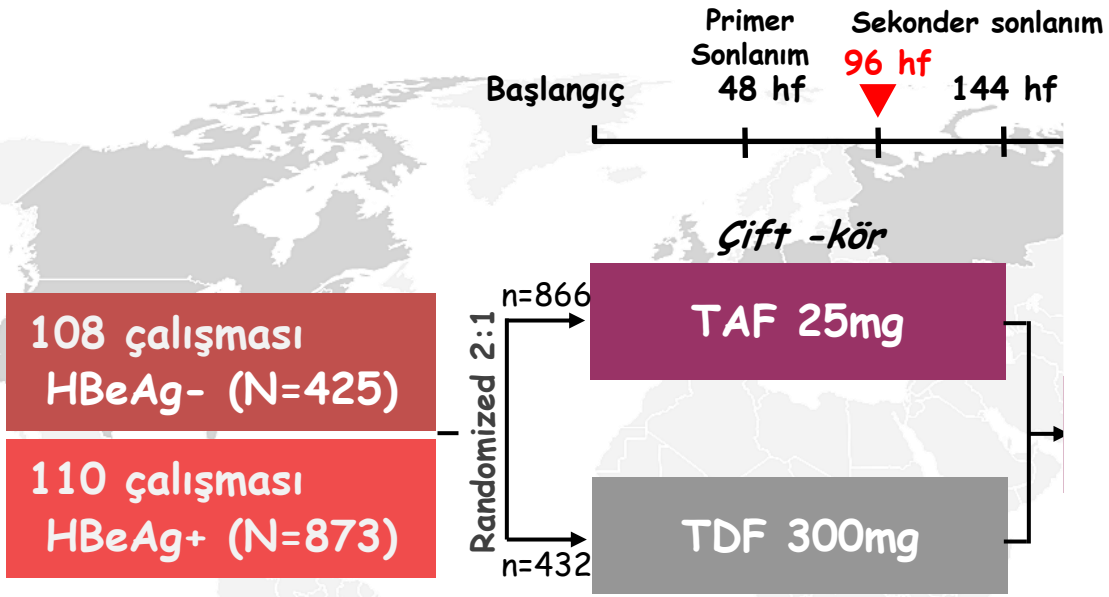
Hariç tutma

- Trombosit ≤50,000 hücre/µl,
- Hemoglobin <10 g/dl,
- Albumin <3 g/dl,
- Direk bilirubin >2.5 ULN,
- ALT >10 ULN
- Dekompansasyon bulgusu; assit, ensefalopati ya da varis kanaması
- Hepatosellüler kanser

Agarwal K, Brunetto M, Seto WK, et al. J Hepatol. 2018;68(4):672-681

Study 108 and 110:

Tenofovir Alafenamide HBV Faz 3 Program



- **Primer sonlanım noktası**
  - 48. haftada HBV DNA <29 IU/mL
- **Önemli sekonder sonlanım noktaları**
  - 96. haftada HBV DNA <29 IU/mL
  - ALT normalizasyonu (merkezi lab ve AASLD kriterleri)
  - Seroloji (HBeAg ve HBsAg kaybı/serokonversiyon)

Agarwal K, Brunetto M, Seto WK, et al. J Hepatol. 2018;68(4):672-681

- Takip protokolu

- İlk 48 hafta boyunca 4 haftada bir
- Takiben 96 haftaya kadar 8 haftada bir
  - Hematolojik inceleme
  - Biyokimyasal inceleme; lipid parametreleri ve renal testler (kreatinin, GFR ve proteinüri)
- Başlangıçtan itibaren 24 hafta bir KMD ölçümü
- En az 24 hafta tedavi almış hastalarda 96 haftada HBV DNA ≥ 69 IU/ml ise direnç analizi

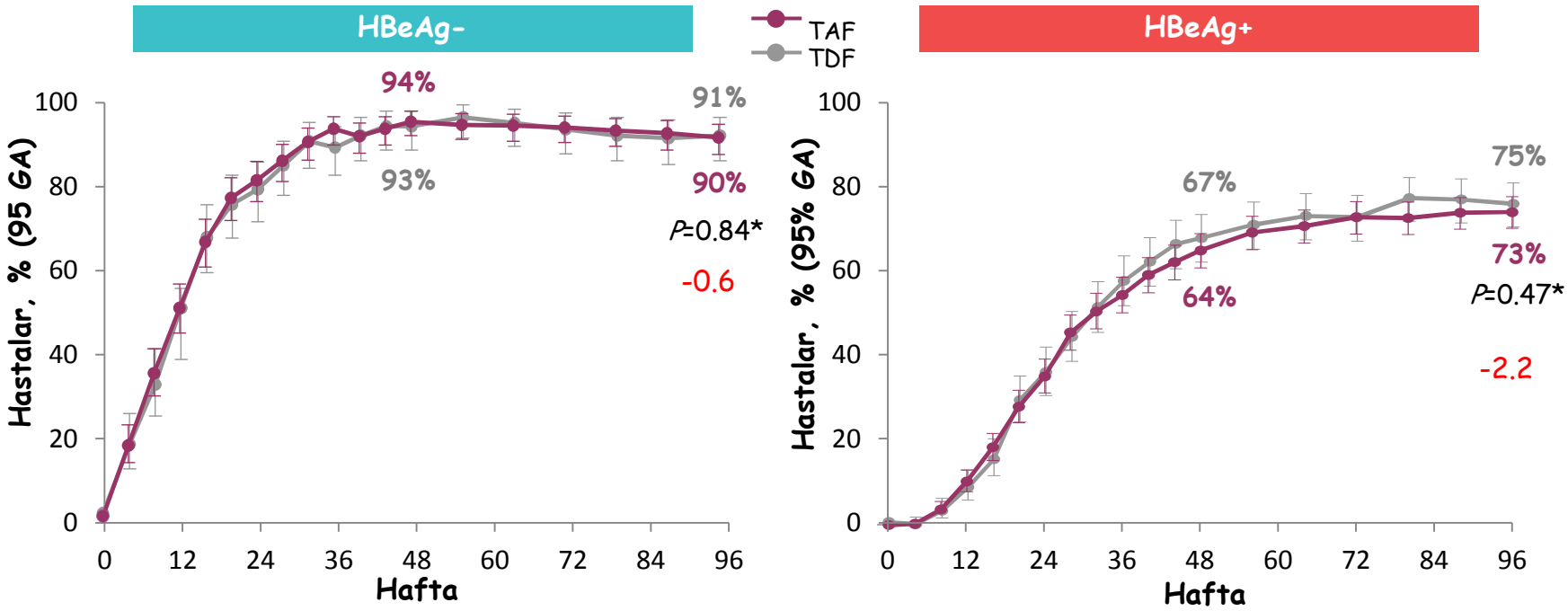
Demografik bulgular

	108 Çalışması (HBeAg-) (N=425)		110 Çalışması (HBeAg+) (N=873)	
	TAF n=285	TDF n=140	TAF n=581	TDF n=292
Ortalama yaş (aralık)	45 (19–80)	48 (25–72)*	38 (18–69)	38 (18–68)
Erkek, n (%)	173 (61)	86 (61)	371 (64)	189 (65)
Asyalı, n (%)	205 (72)	101 (72)	482 (83)	232 (79)
HBV Genotip (A, B, C, D), %	5, 21, 40, 32	4, 29, 34, 30	7, 17, 52, 23	9, 16, 52, 22
Ortalama VKİ, kg/m^2 (SD)	25 (4)	25 (4)	24 (4)	24 (4)
Tedavi deneyimi, n (%)	60 (21)	31 (22)	151 (26)	77 (26)
Ortalama HBV DNA, log_{10} IU/mL (SD)	5.7 (1.34)	5.8 (1.32)	7.6 (1.3)	7.6 (1.4)
Yüksek HBV DNA, n (%) HBeAg- (≥7 log_{10} IU/mL) HBeAg+ (≥8 log_{10} IU/mL)	55 (19)	24 (17)	272 (47)	142 (49)
Medyan ALT, U/L (Q1, Q3)	67 (44, 102)	67 (47, 102)	85 (61, 139)	86 (57, 137)
FibroTest skoru ≥0.75, n/n (%)	31/280 (11)	20/139 (14)	45/566 (8)	22/282 (8)
Siroz hikayesi	24/285 (8)	14/140 (10)	41/581 (7)	24/292 (8)

*P=0.011 comorbid %13
†East Asia region denotes Hong Kong, Japan, Singapore (Study 110 only), South Korea, and Taiwan
Q, quartile; SD, standard deviation; Buti M et al. Lancet G&H 2016; doi: 10.1016/S2468-1253(16)30107-8; Chan HLY et al. Lancet G&H 2016; doi: /10.1016/S2468-1253(16)30024-3; Agarwal, EASL 2017, FRI-153; Brunetto, EASL 2017, PS-042

96. haftada TAF ve TDF'in antiviral etkinliği

Viral Supresyon oranları HBV DNA <29 IU/mL



- 96 haftaya kadar hiç direnç saptanmadı
- TAF ve TDF karşılaştırıldığında 96. haftaya kadar benzer HBV DNA baskılanması elde edildi

*Adjusted for baseline HBV DNA level and oral antiviral treatment status strata
ITT, M=F, intention-to-treat analysis where missing equals failure 10% marrgin used to determine noninferiority
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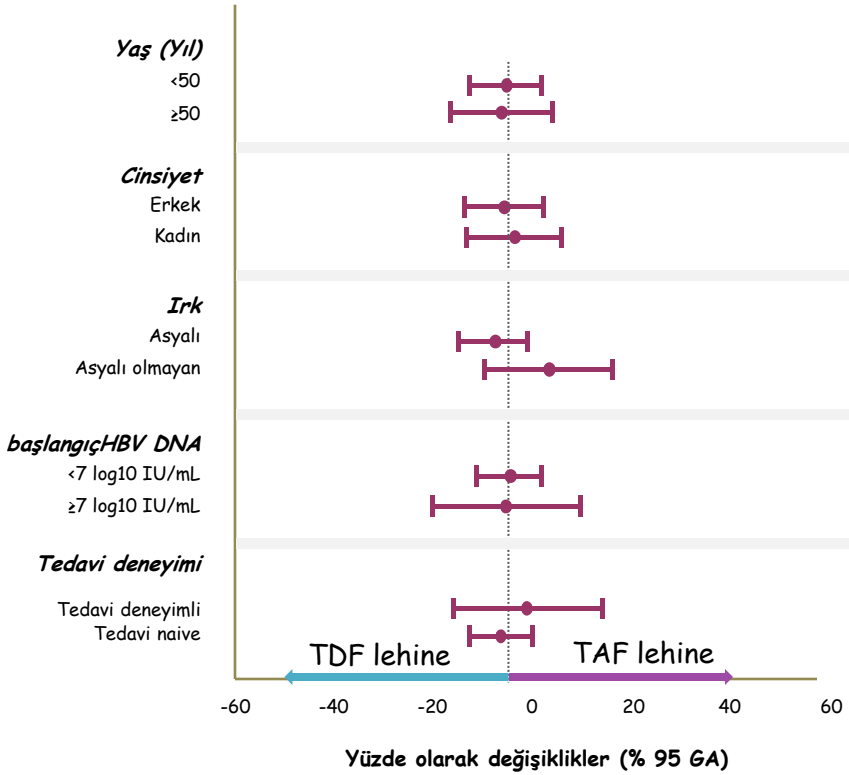
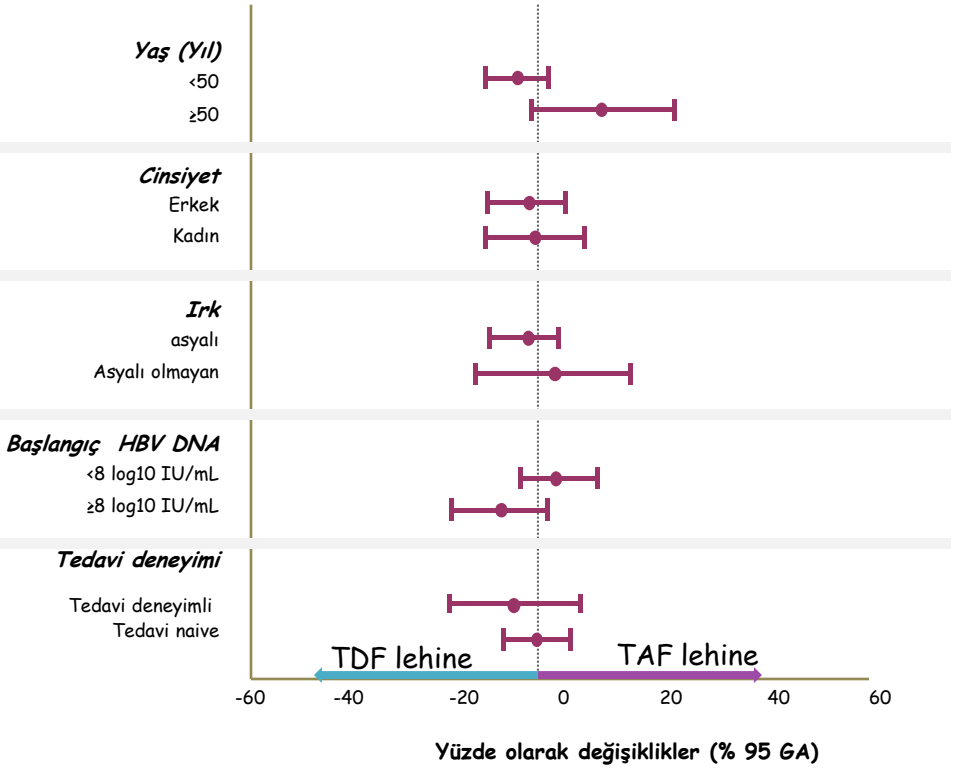
Sekonder sonlanım noktasında hedefe ulaşan hastaların (*96. haftada HBV DNA <29 IU/mL*) analizi ‡

108 (HBeAg negatif)



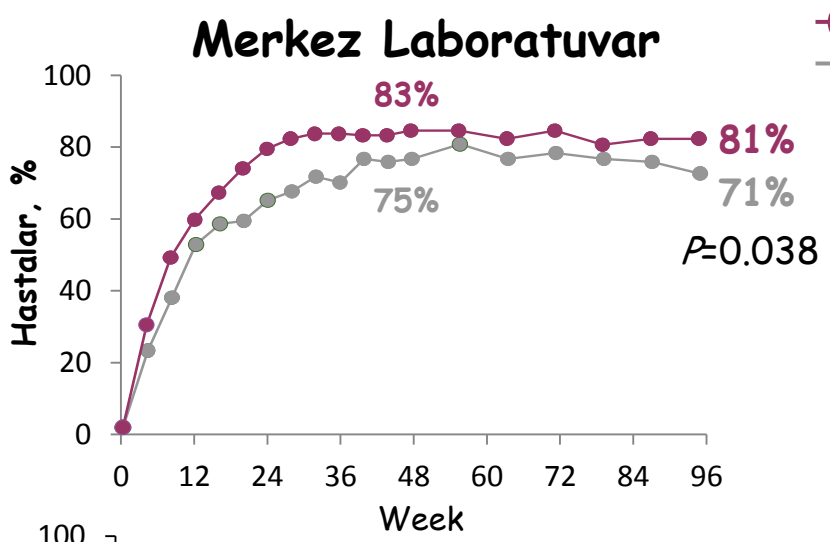
110 (HBeAg pozitif)

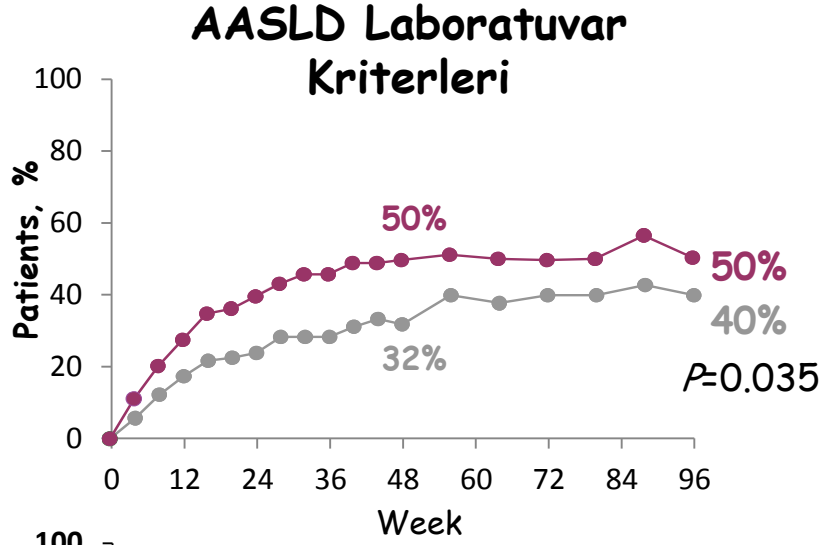


Gilead Science, Data on File.

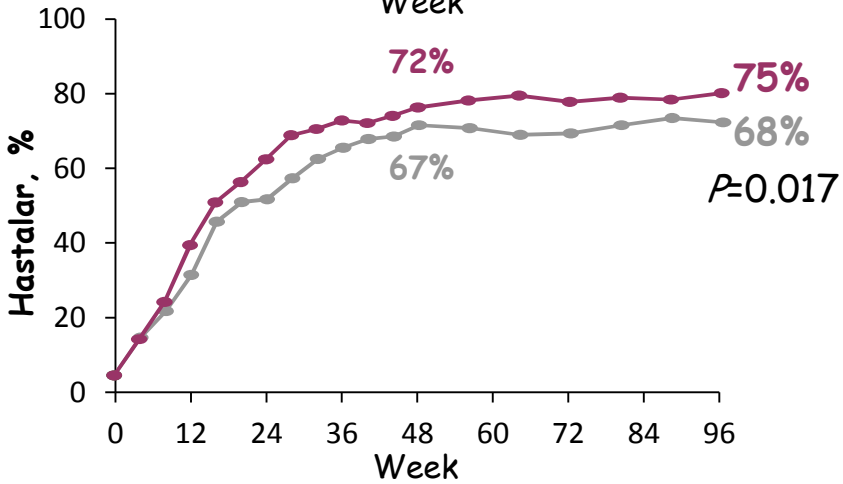
96. haftada ALT normalizasyonu

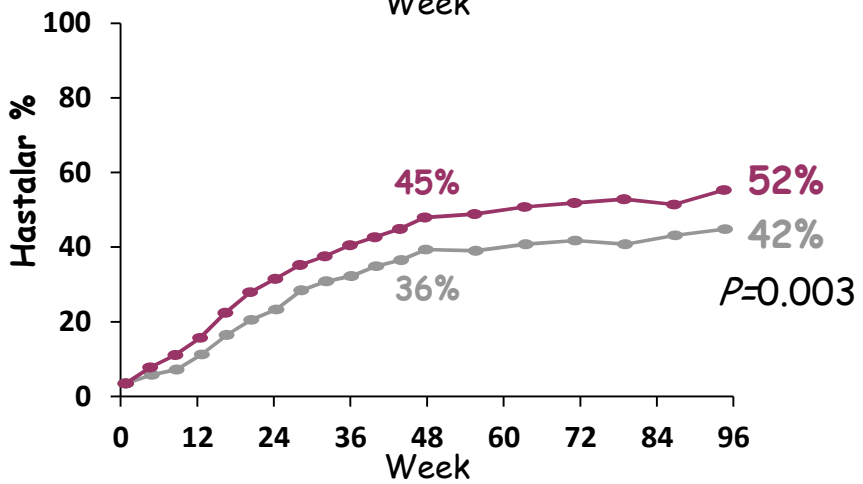
HBeAg-





HBeAg+





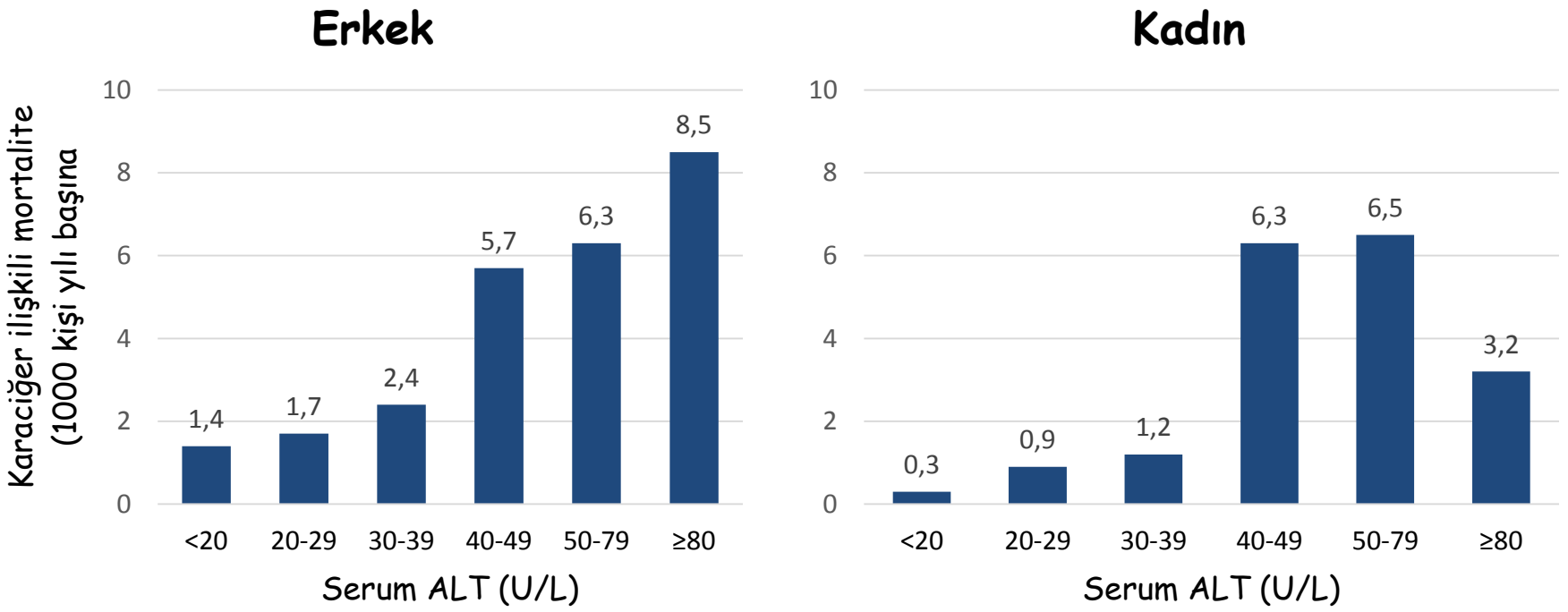
Anlamlı olarak TAF ile yüksek ALT normalizasyonu

Central lab upper limit of normal (ULN): males ≤43 U/L and females ≤34 U/L (≥69 y: males ≤35 U/L and fem
U/L); AASLD criteria ULN: males ≤30 U/L and females ≤19 U/L.

Agarwal K, Brunetto M, Seto WK, et al. J Hepatol. 2018;68(4):672-681; Buti M et al. Lancet G&H 2016; Chan HLY et

KHB hastalarında ALT ve karaciğer-ilişkili mortalite

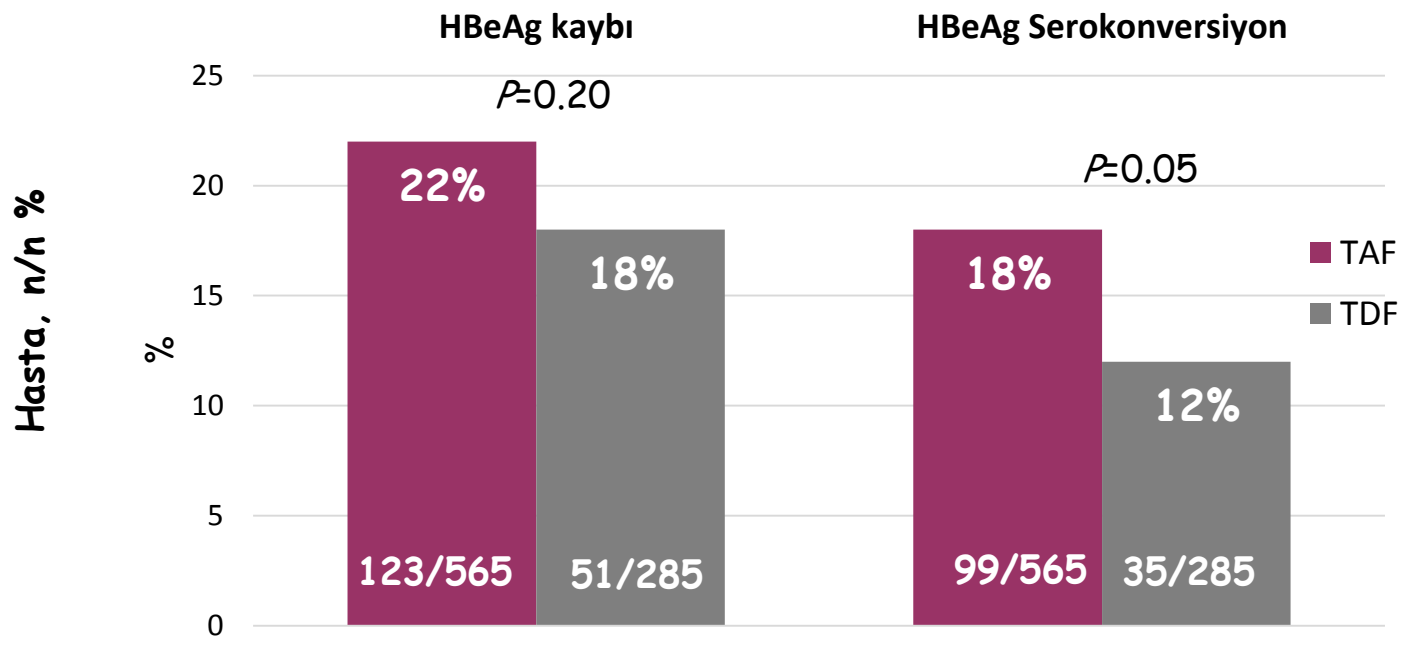
Kore'den 2002–2003 arasında 12 486 KHB hastası analiz edilmiştir



Serum ALT seviyesi (> 40 U/L) karaciğer ilişkili mortalite ile olumlu yönde ilişkilidir

Shim J-J, AASLD 2017, Poster 1905

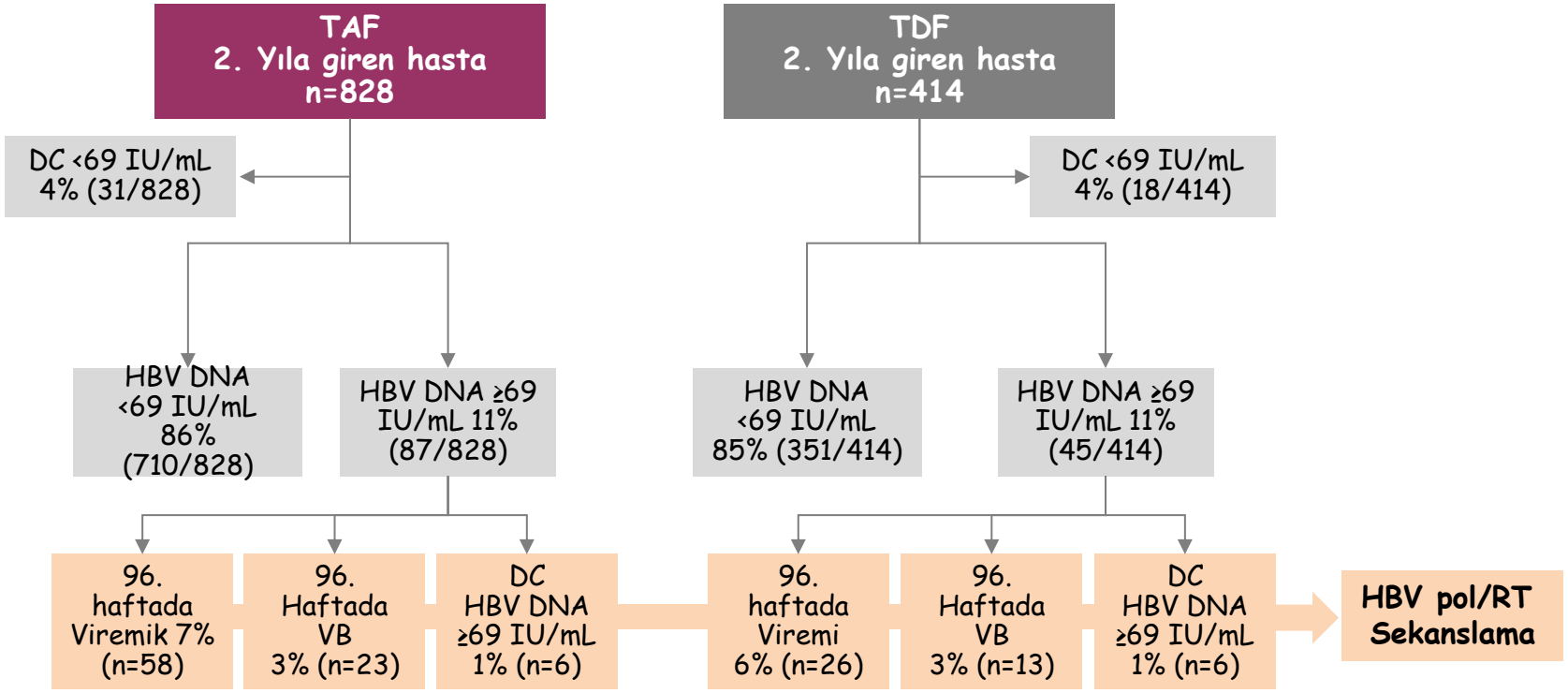
96. haftada serolojik yanıt



HBeAg negatiflerde 96 tedavi haftasında bir hastada HBsAg kaybı
HBeAg pozitiflerde

- HBsAg kaybı: TAF 7/576 hasta vs TDF 4/288, *P*=0.88
- HBsAg serokonversiyon: TAF 6/576 hasta vs TDF 0/288 hasta, *P*=0.08

96. hafta direnç analizi



DC = early discontinuation; VB = virologic breakthrough (HBV DNA increase 1 $\log_{10}$IU/mL above nadir or ≥69 IU/mL after being <69 IU/mL for 2 consecutive visits); Viremic = patients with viremia in absence of VB

Chan, AASLD 2017, Oral 26

TAF ve TDF'e 96. haftaya kadar direnç saptanmadı

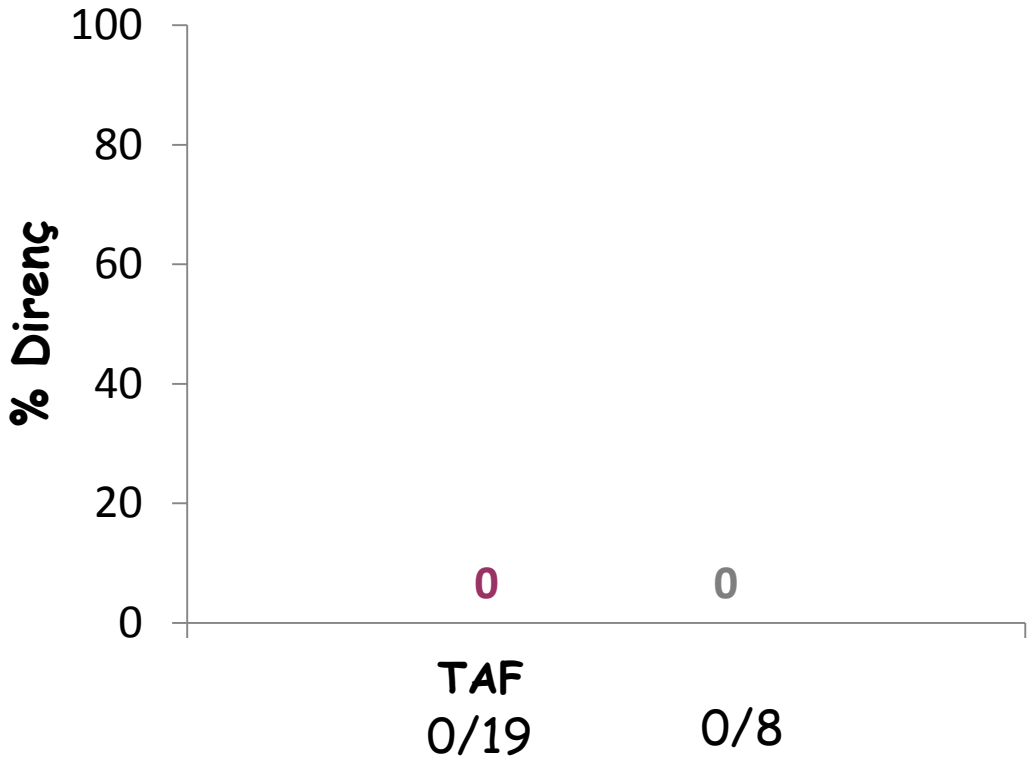
Sekanslama†
(HBV pol/RT'in doğrudan sekanslaması)

TAF	TDF
87/828	45/414
%11	%11

Fenotipleme*‡
in vitro analiz

TAF	TDF
19/87	8/45
%22	%18

Fenotipik analizde direnç oranı



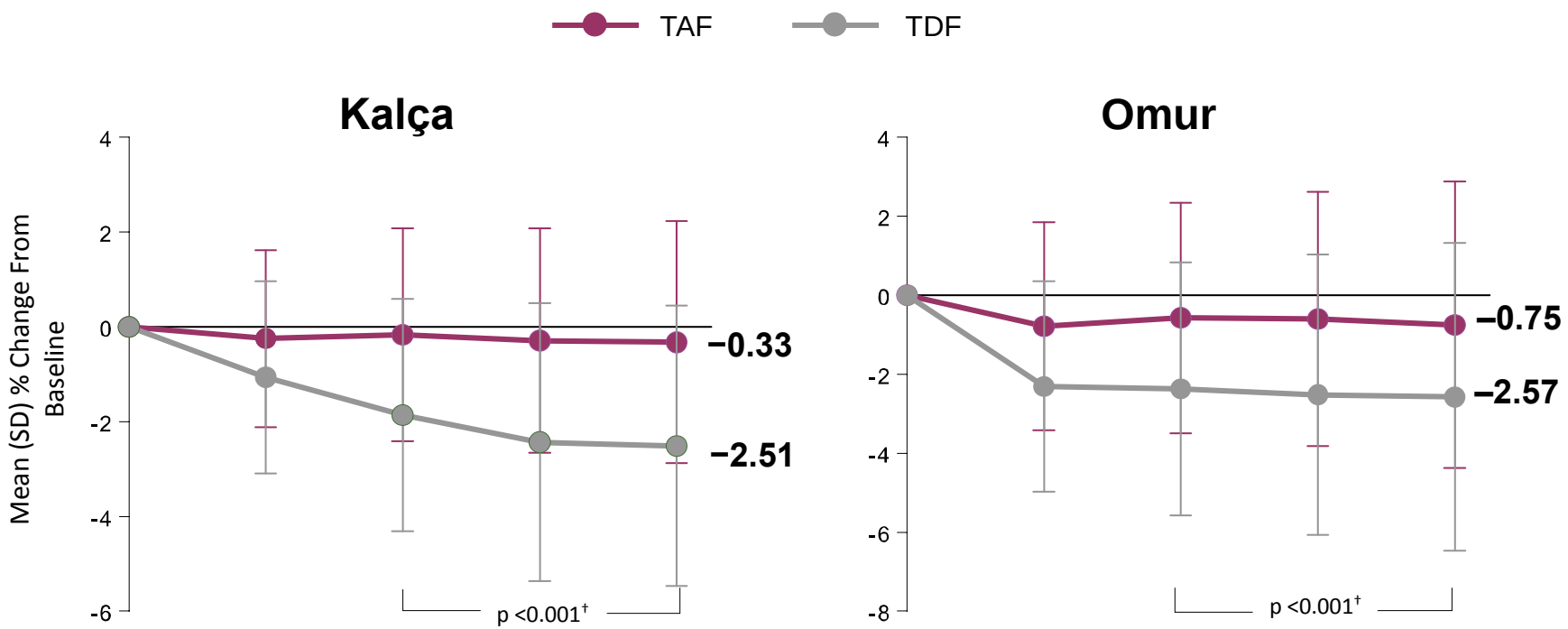
†Limit of sequencing assay = 69 IU/mL, consensus level results are reported (15% cutoff)
* Each patient pool or clone was tested at least twice; on-treatment patient samples were compared to the corresponding baseline sample.
‡ Established assay cutoff of 2-fold change EC_{50}. Includes results from patient pools and isolated clones

Agarwal K, Brunetto M, Seto WK, et al. J Hepatol. 2018;68(4):672-681; Chan, AASLD 2017, Oral 26

Table 3. Safety data.

	TAF 25 mg (n = 866)	TDF 300 mg (n = 432)
Patients with any adverse event	670 (77%)	327 (76%)
Adverse event leading to study drug discontinuation	13 (2%)	4 (1%)
Deaths	0	0
Patients with grade 3 or 4 adverse events	58 (7%)	22 (5%)
Patients with serious adverse event	60 (7%)	29 (7%)
Adverse events occurring in ≥5% of patients in any treatment group		
Headache	104 (12%)	43 (10%)
Nasopharyngitis	105 (12%)	44 (10%)
Upper respiratory tract infection	98 (11%)	45 (10%)
Cough	70 (8%)	34 (8%)
Back pain	54 (6%)	27 (6%)
Fatigue	52 (6%)	23 (5%)
Nausea	52 (6%)	24 (6%)
Dyspepsia	43 (5%)	22 (5%)
Diarrhea	47 (5%)	22 (5%)
Grade 3 or 4 laboratory abnormalities in ≥1% of patients in any treatment group*		
Alanine aminotransferase >5× ULN	72 (8%)	41 (10%)
Aspartate aminotransferase >5× ULN	30 (3%)	23 (5%)
Amylase >2×ULN	28 (3%)	13/427 (3%)
Creatine kinase ≥10× ULN	28 (3%)	13 (3%)
Fasting cholesterol >300 mg/dl	10/857 (1%)	0
Fasting LDL cholesterol >190 mg/dl	50/843 (6%)	3/418 (1%)
Gamma glutamyl transferase >5x ULN	4 (<1%)	6 (1%)
Hemoglobin <9.0 g/dl	7 (1%)	9/426 (2%)
Segmented neutrophils <750/mm^3	9 (1%)	3 (1%)
Fasting glucose >250 mg/dl	11 (1%)	0
Nonfasting glucose >250 mg/dl	31/856 (4%)	7/426 (2%)
Occult blood	81 (9%)	39/426 (9%)
Urine erythrocytes	75/798 (9%)	39/397 (10%)
Urine glucose	44/859 (5%)	7/426 (2%)

96 hafta boyunca BMD'de değişiklikler



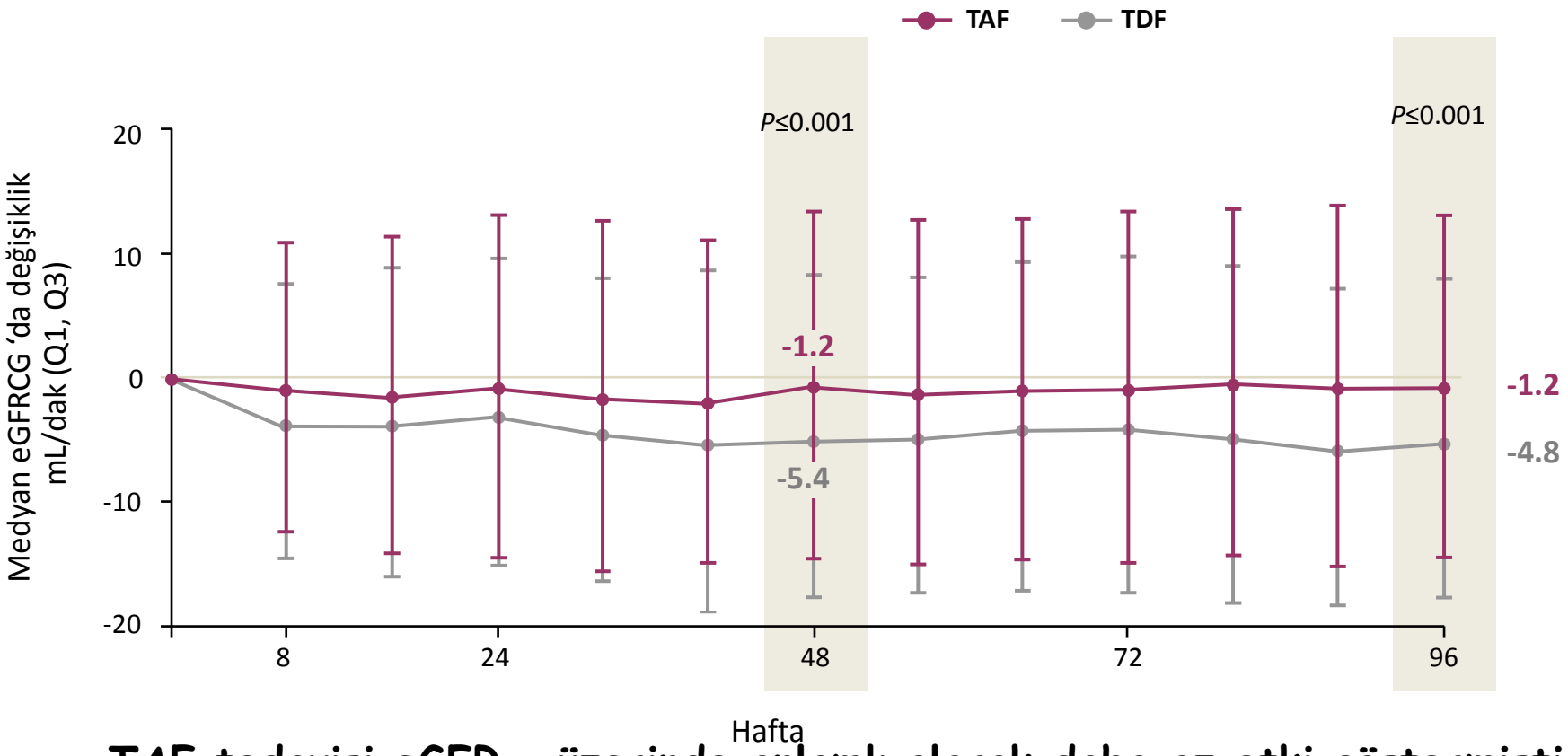
Hafta	0	24	48	72	96	0	24	48	72	96
TAF, n	851	822	807	792	740	856	830	814	799	746
TDF, n	426	405	404	391	369	426	410	407	393	371

TAF tedavisi ile kemik mineral dansitesindeki azalmanın anlamlı olarak daha düşük düzeyde olduğu görülmüştür.

* All p-values from Week 24-96 are < 0.001; p-values from analysis of variance model including treatment as a fixed effect;
† p-values from mixed model repeated measures
Agarwal K, Brunetto M, Seto WK, et al. J Hepatol. 2018;68(4):672-681; Fung, EASL 2017, SAT-162

96. haftaya kadar renal güvenlilik

Medyan $eGFR_{CG}$ 'da değişiklik



TAF tedavisi $eGFR_{CG}$ üzerinde anlamlı olarak daha az etki göstermiştir

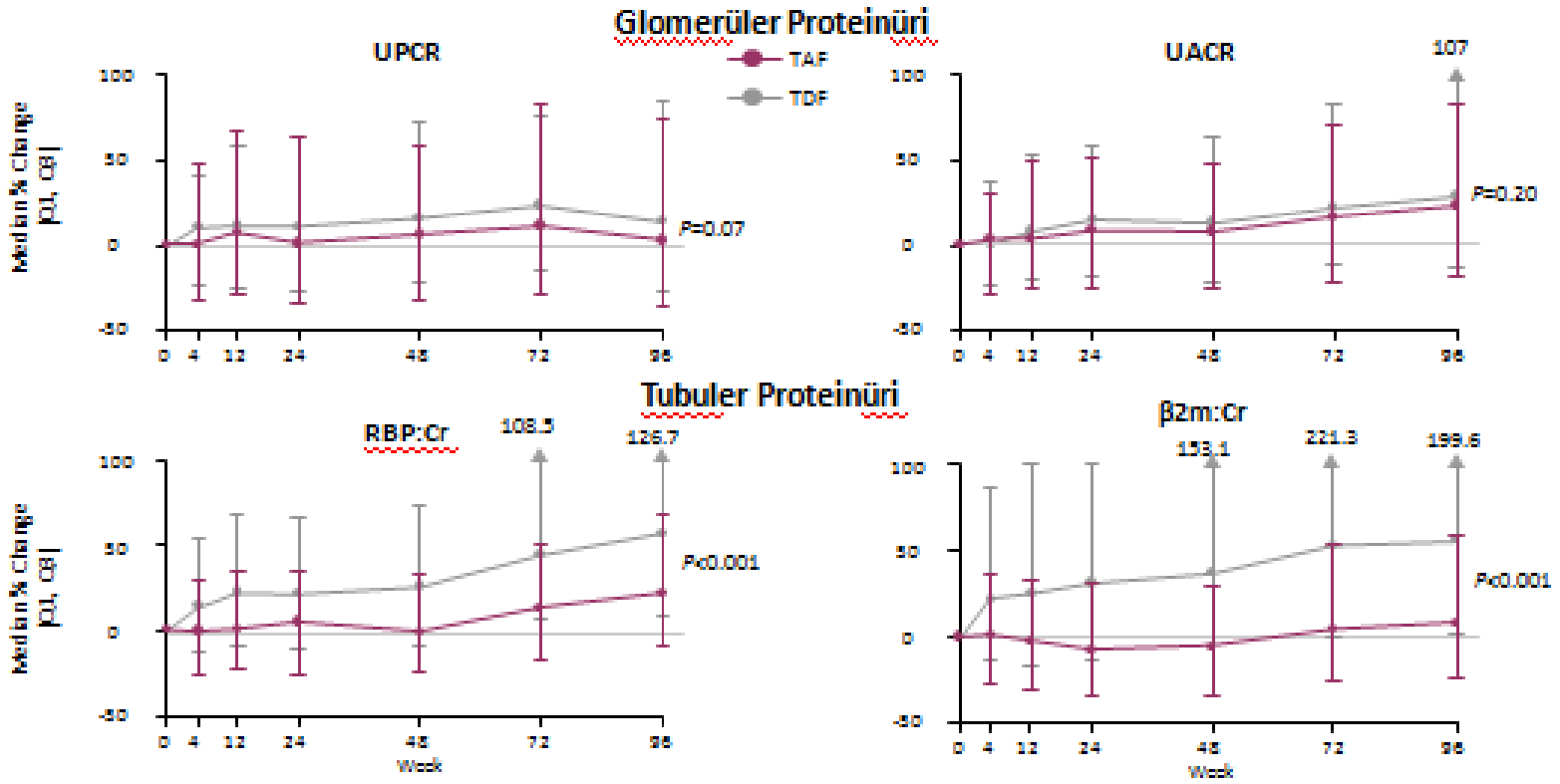
- 96 haftada GFR < 50ml/dk olan hasta oranı
  - TAF %0.1 (bir hasta) & TDF %1.2 (beş hasta)
    p=0.017

- Başlangıca göre 96 haftada GFR %25 azalan hasta oranı
  - TAF %10 & TDF %18 *p<0.001*
  - Belirleyici kriterler;
    - DM
    - TDF alıyor olmak
    - vit D < bazal düzey
    - başlangıç ALT > x5ULN

Agarwal K, Brunetto M, Seto WK, et al. J Hepatol. 2018;68(4):672-681

96 haftada proksimal tubuler disfonksiyon belirteçlerindeki değişiklikler

96. haftada kantitatif proteinüri değişiklikleri



TAF ve TDF arasında renal tubuler belirteçlerde anlamlı farklılık

UPCR, urine protein-to-creatinine ratio; UACR, urine albumin-to-creatinine ratio; RBP:Cr, retinol binding protein-to-creatinine ratio; B2M:Cr, β2 microglobulin-to-creatinine ratio

* p-values from 2-sided Wilcoxon rank-sum test

Chuang, EASL 2017, SAT-171

Faz III çalışma sonuçları

- TAF güvenli bulunmuştur ve iyi tolere edilmiştir.
  - Tedaviye bağlı yan etkiler benzerdir.
  - Kemik mineral yoğunluğunda TDF ile daha fazla düşüş gözlenmiştir.
  - eGFR'deTAF ile daha az düşüş gözlenirken tubuler disfonksiyon belirleyicilerin klerensinde de iyileşme saptanmıştır.

Agarwal K, Brunetto M, Seto WK, et al. J Hepatol. 2018;68(4):672-681

★ 381

Three Year Efficacy and Safety of Tenofovir Alafenamide (TAF) Compared to Tenofovir Disoproxil Fumarate (TDF) in Hbeag-Negative and Hbeag-Positive Patients with Chronic Hepatitis B

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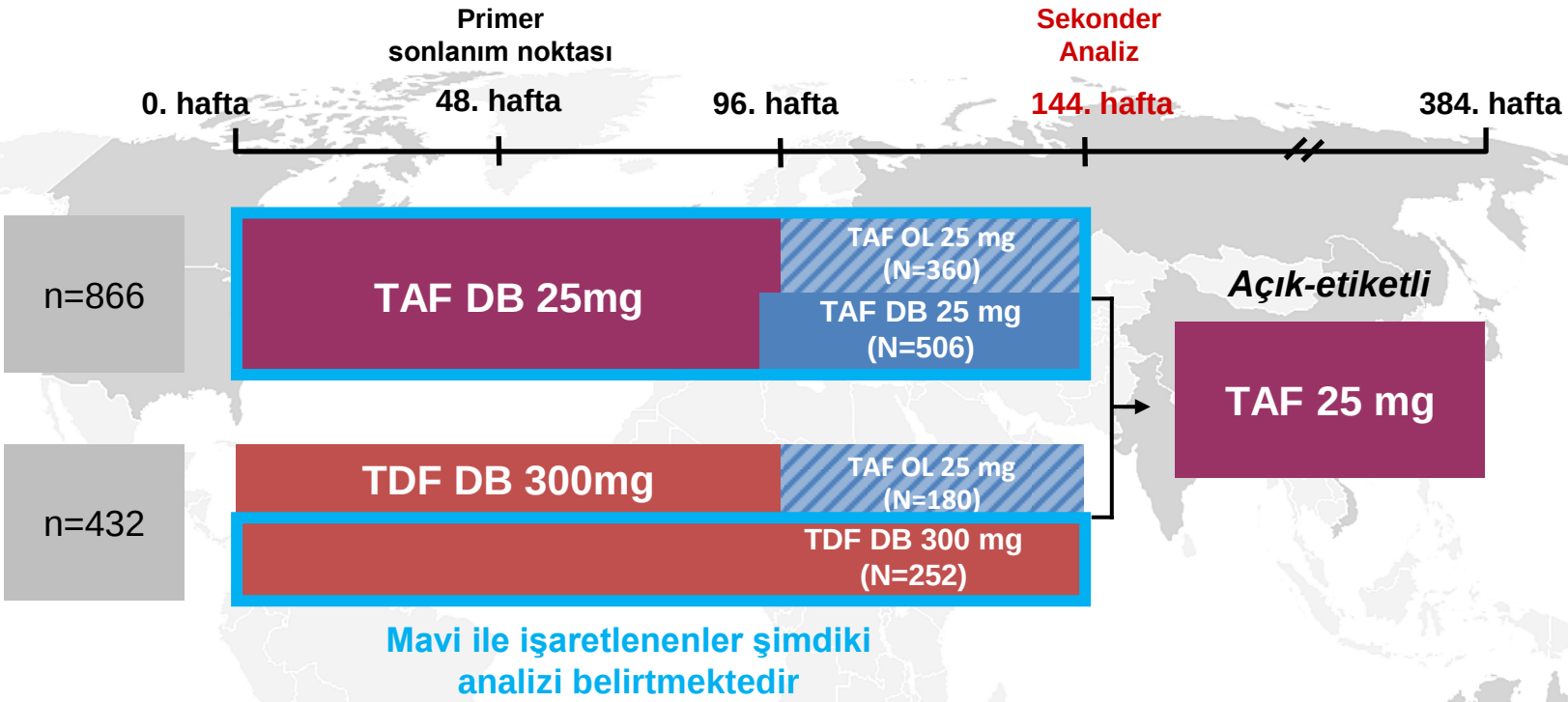
Background: In 2 identically-designed double-blind, randomized (2:1), Phase 3 studies, TAF has shown efficacy non-inferior to that of TDF at Weeks 48 and 96, with a superior renal and bone safety profile. Following a protocol amendment, 50% of enrolled patients had their double-blind (DB) treatment extended for 1 additional year, while the remainder rolled over to open-label (OL) TAF at Week 96 (Year 2). Here we evaluated the comparative safety and efficacy of TAF and TDF in patients receiving treatment with these agents for 3 years. **Methods**: 1298 patients (425 HBeAg-negative [Study 108] and 873 HBeAg-positive [Study 110]) with CHB were randomized and treated with TAF 25 mg QD or TDF 300 mg QD. Included in this analysis, were 1118 patients (759 HBeAg-positive and 359 HBeAg-negative); 866 of whom received TAF (both DB and OL) and 252 who were treated with DB TDF for 3 years, had early discontinuation, and who did not enter the OL TAF phase at Week 96. Efficacy analyses were performed by study and included virologic, biochemical, and serologic responses, while safety assessments including changes in hip and spine bone mineral density (BMD), and changes in serum creatinine and estimated GFR by Cockcroft- Gault method ($eGFR_{CG}$) were performed in a pooled fashion. **Results**: Baseline characteristics were similar between groups and among studies and included (pooled data): mean age 40 years, 63% males, 78% Asian, mostly genotypes C (48%) and D (26%); mean HBV DNA was 7.0 $\log_{10}$ IU/mL (34% of patients had HBV DNA ≥ 8 $\log_{10}$ IU/mL), and 25% previously treated with oral nucleos(t)ides. High rates of virologic control were maintained at week 144 in TAF vs. TDF treated patients in each study; a greater proportion of patients receiving TAF achieved ALT normalization at Year 3 (Table). In HBeAg-

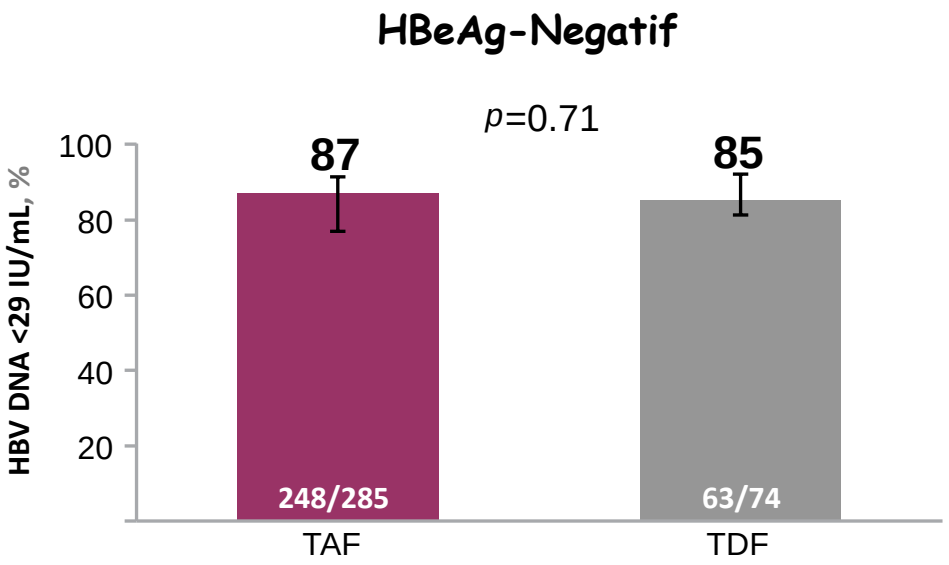
Çalışma tasarımı

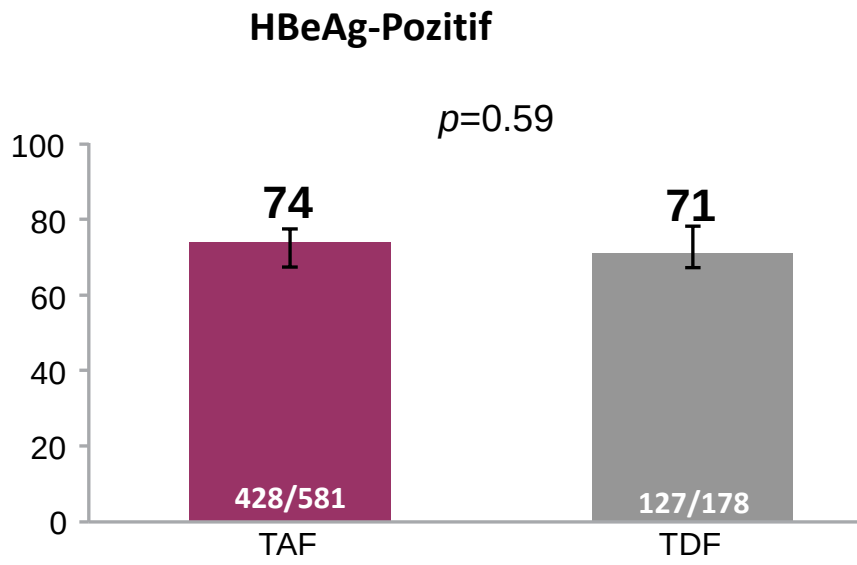


Çalışmanın amacı :

- 144 hafta boyunca TAF ve TDF alan hastalarının etkililiği ve güvenliliği (96. hafta TAF'a geçen hastaları dışarıda tutan bir analiz)

144. hafta HBV DNA <29 IU/mL



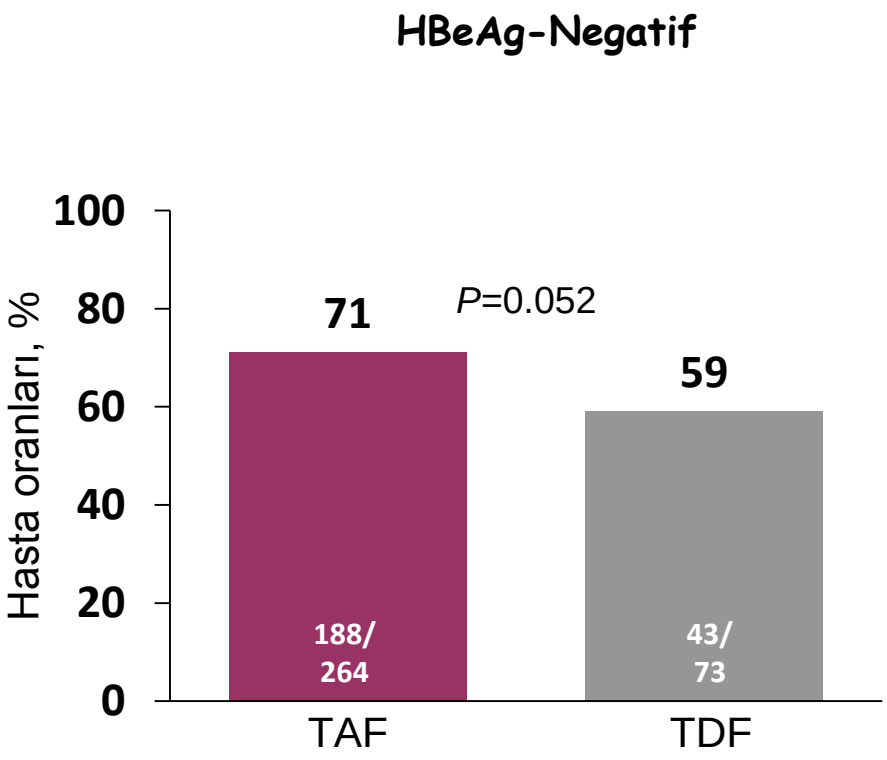


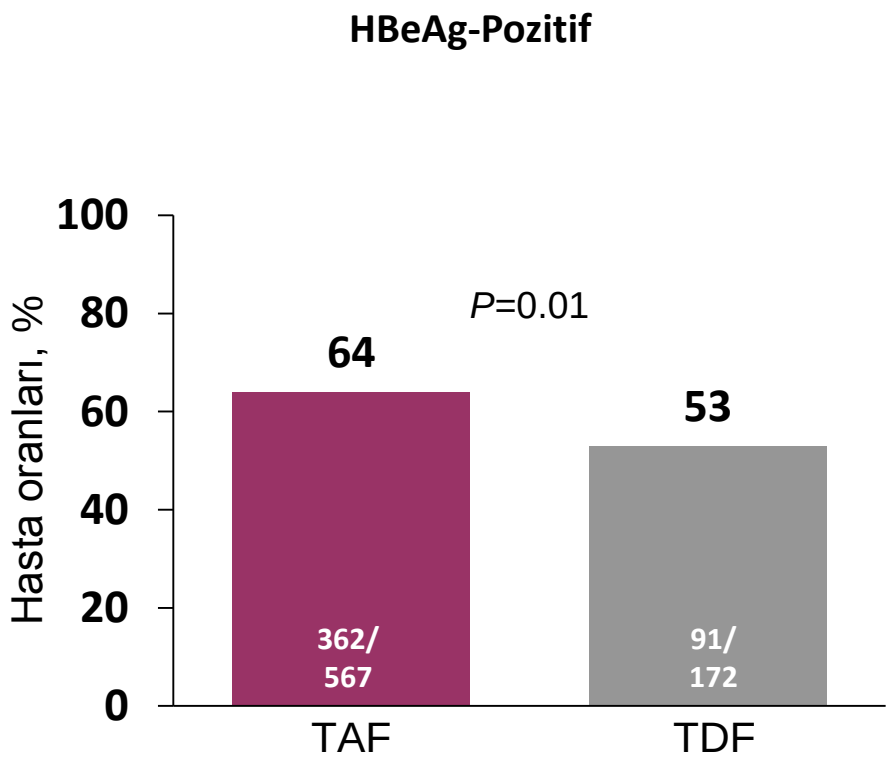
	TAF	TDF
HBeAg kaybı, n/N (%)	135/565 (24)	39/175 (22)
HBeAg serokonversiyon, n/N (%)	105/565 (19)	23/175 (13)
HBsAg kaybı, n/N (%)	9/857 (1)	3/251 (1)
HBsAg serokonversiyon, n/N (%)	2/857 (<1)	0/251 (0)

TAF ve TDF'e 144. haftaya kadar direnç saptanmadı

144. haftada ALT normalizasyonu (AASLD 2018 kriterlerine göre

AASLD 2018 kriterleri ULN: erkek ≤ 35 U/L, kadın ≤ 25 U/L

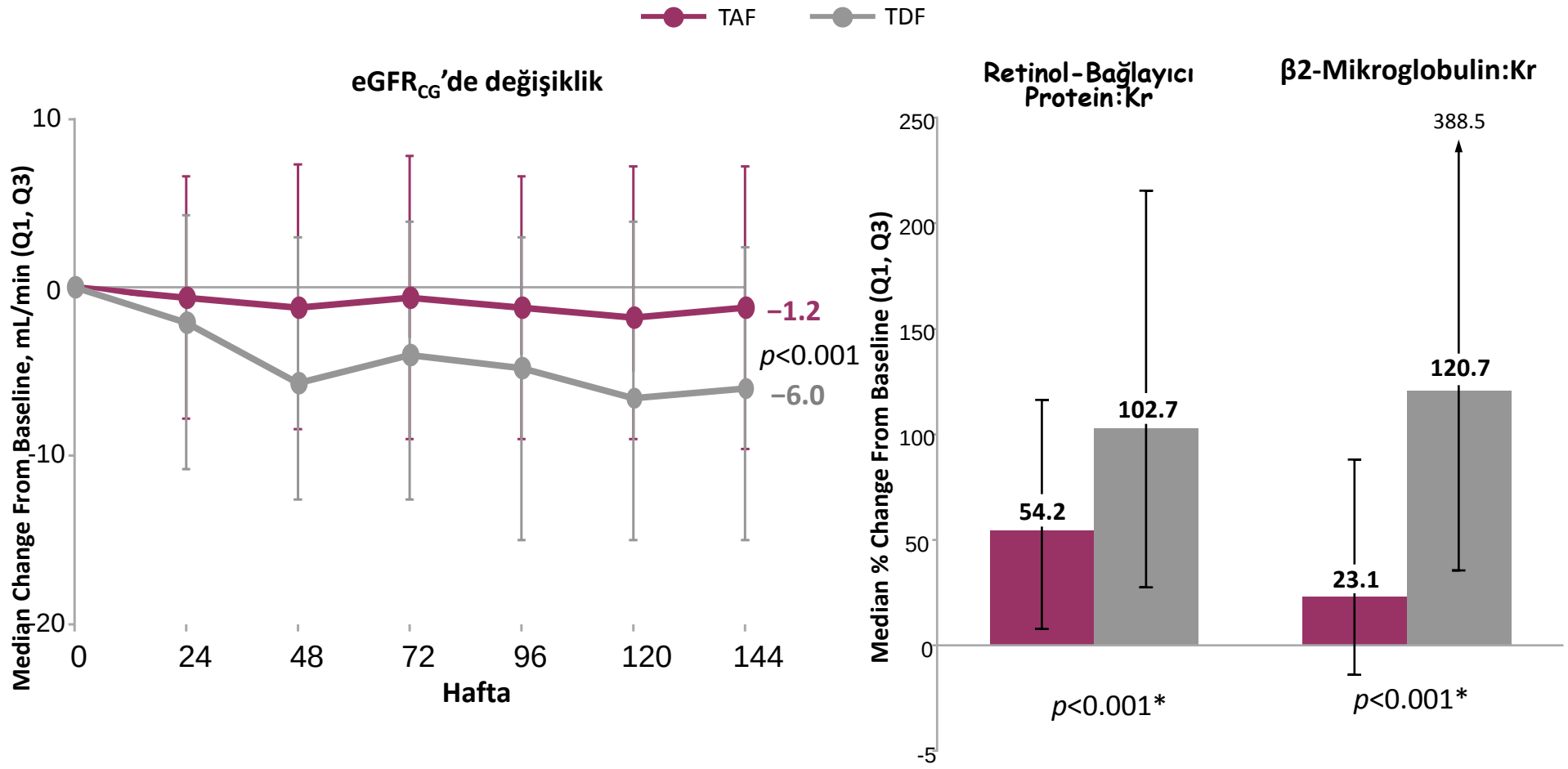




TAF ile AASLD 2018 ALT normalizasyon kriterlerine göre daha yüksek oran elde edilmiştir

Chan, AASLD 2018, 0381

144. hafta renal parametrelerde değişiklik



TAF ile 144. haftada anlamlı olarak daha küçük eGFR$_{CG}$ azalışları ve proksimal tubul belirteçlerinde değişiklik gözlendi.

*From 2-sided Wilcoxon rank-sum test

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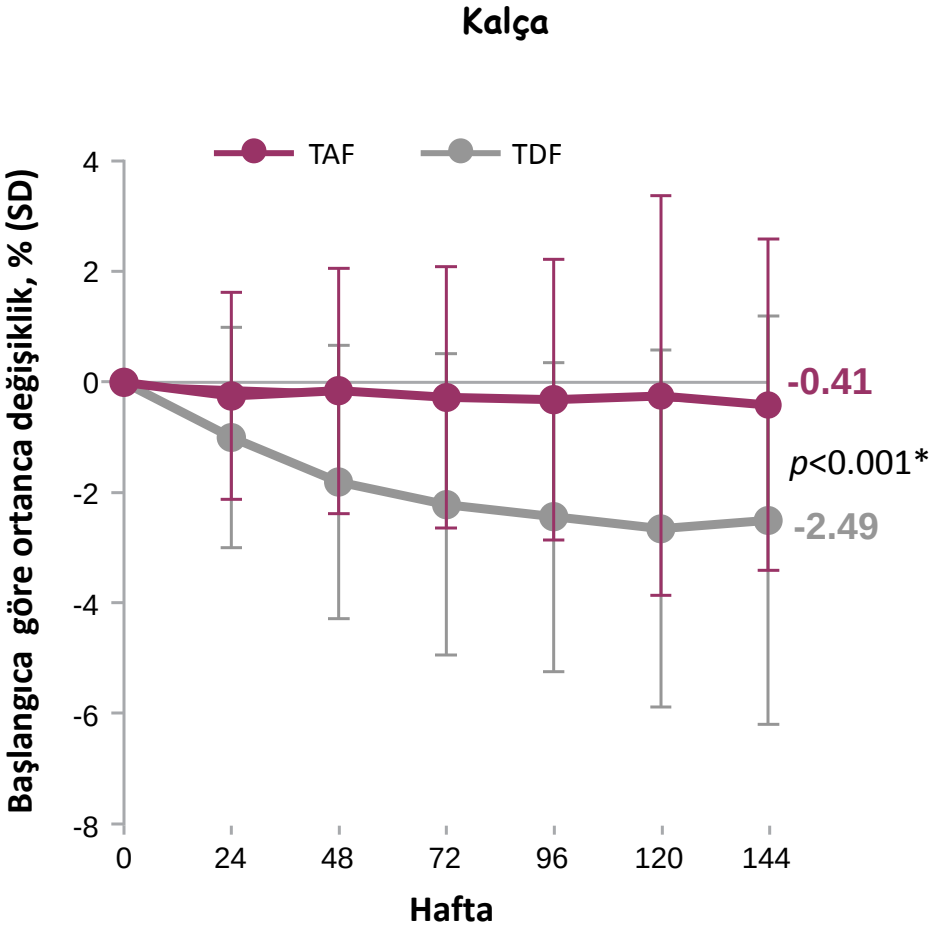
144. haftaya kadar KMD'deki değişiklikler



TAF ile daha az kalça kemik mineral younluğundan anlamlı azalma

*From analysis of variance model including treatment as fixed effect
† From Cochran-Mantel-Haenszel test for ordinal data (row mean scores differ statistic was used).

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904

Improved Bone and Renal Safety at 1 Year after Switching from Tenofovir Disoproxil Fumarate (TDF) to Tenofovir Alafenamide (TAF): Results from 2 Phase 3 Studies in HBeAg-positive and HBeAg-negative Patients with Chronic Hepatitis B (CHB)

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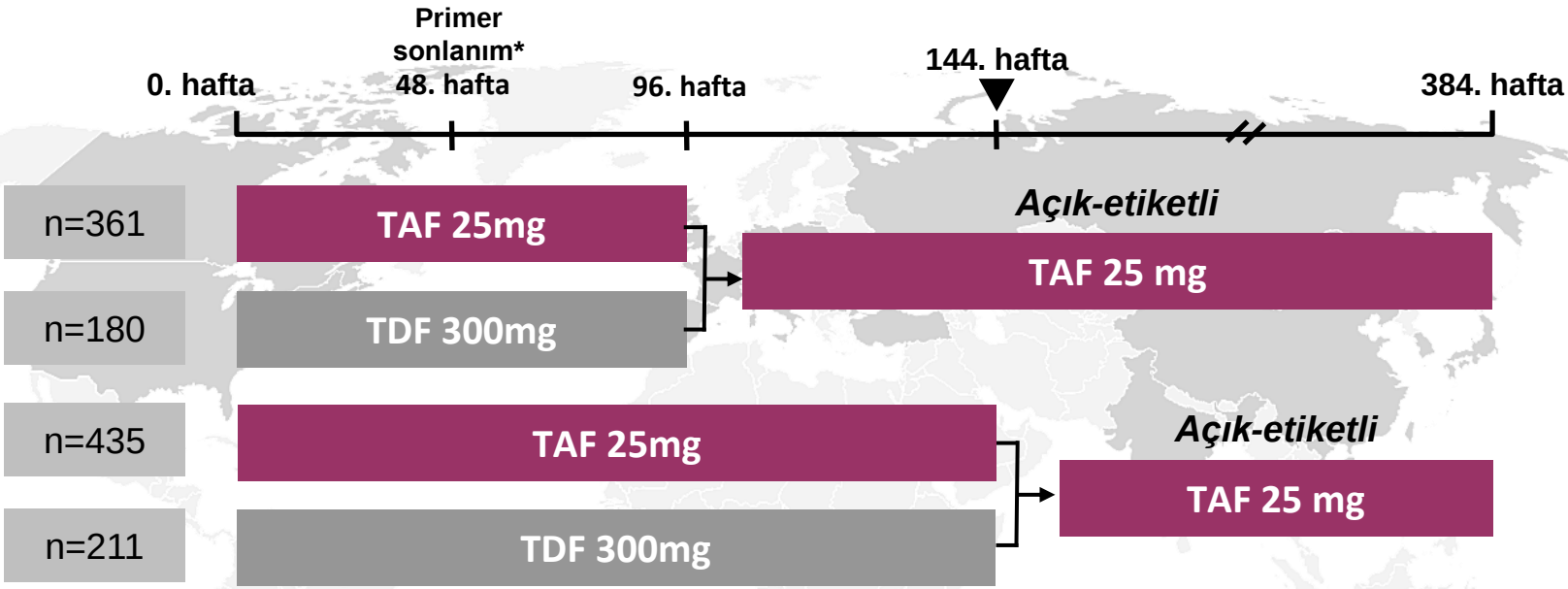
Background: TAF has shown less bone and renal effects with similar efficacy rates compared to TDF in two large multinational Phase 3 studies after 96 weeks of double-blind (DB) treatment. We evaluated patients who completed 96 weeks of DB treatment with TAF or TDF and switched to open label (OL) treatment with TAF, including those with 1 year of data (through Week 144) to determine changes in bone mineral density (BMD), creatinine clearance (CrCL), and the maintenance of viral suppression.

Methods: In two identically-designed studies, 1298 CHB patients who were HBeAg-negative (Study 108; N=425) or HBeAg-positive (Study 110; N=873) were randomized and treated with TAF 25 mg QD or TDF 300 mg QD. At Week 96, 541 (42%; TAF 361; TDF 180) patients enrolled in these ongoing 8 year studies had completed DB treatment with TAF or TDF and switched to OL TAF 25 mg QD. DXA scans were evaluated every 24 weeks as were serial assessments of CrCL and viral suppression. Analyses included subjects with values at Week 96 and at Week 144 for creatinine clearance (n=401), spine BMD (n=288) or hip BMD (n=287), HBV DNA (n=394) and ALT normalization by AASLD criteria (n=398). **Results:** CrCL improved significantly in patients who switched from DB TDF to OL TAF at Week 144 compared to Week 96 (n=122, median (Q1, Q3) change = +3.6 (-4.2, +8.4) ml/min, $p<0.001$); and remained stable in those previously receiving TAF (Figure A). BMD also showed improvements at Week 144 from Week 96 among patients switched from DB TDF to OL TAF (hip: n=88, mean (SD) % change = +0.94% (1.825), $p<0.001$; spine: n=88, mean (SD) % change = +1.54% (2.680), $p<0.001$). BMD changes in hip and spine for DB TAF patients entering the OL TAF period were relatively stable (Figure B). Compared to results at Week 96, high rates of virologic control (HBV DNA <29 IU/mL) were maintained across patients in both treatment groups at Week 144 (TDF 87% vs 88% and TAF 91% vs 89%). One year after switching the rate of ALT normalization increased in the TDF group relative to Week 96 (n=122; 65% vs 47%; $p<0.001$) and did not differ from the TAF group (65% vs 66%; p=0.83) at Week 144. **Conclusions**: Patients who switched from TDF to TAF demonstrated continued improvements in BMD and CrCL over 48 weeks of treatment, virologic control was maintained, and rates of ALT normalization increased. Longer term data is required to establish the benefits of switching to TAF for treatment of CHB.

108 ve 110 Çalışmaları
TDF'ten TAF'a Geçiş (geçiş sonrası 48 hafta analizi)

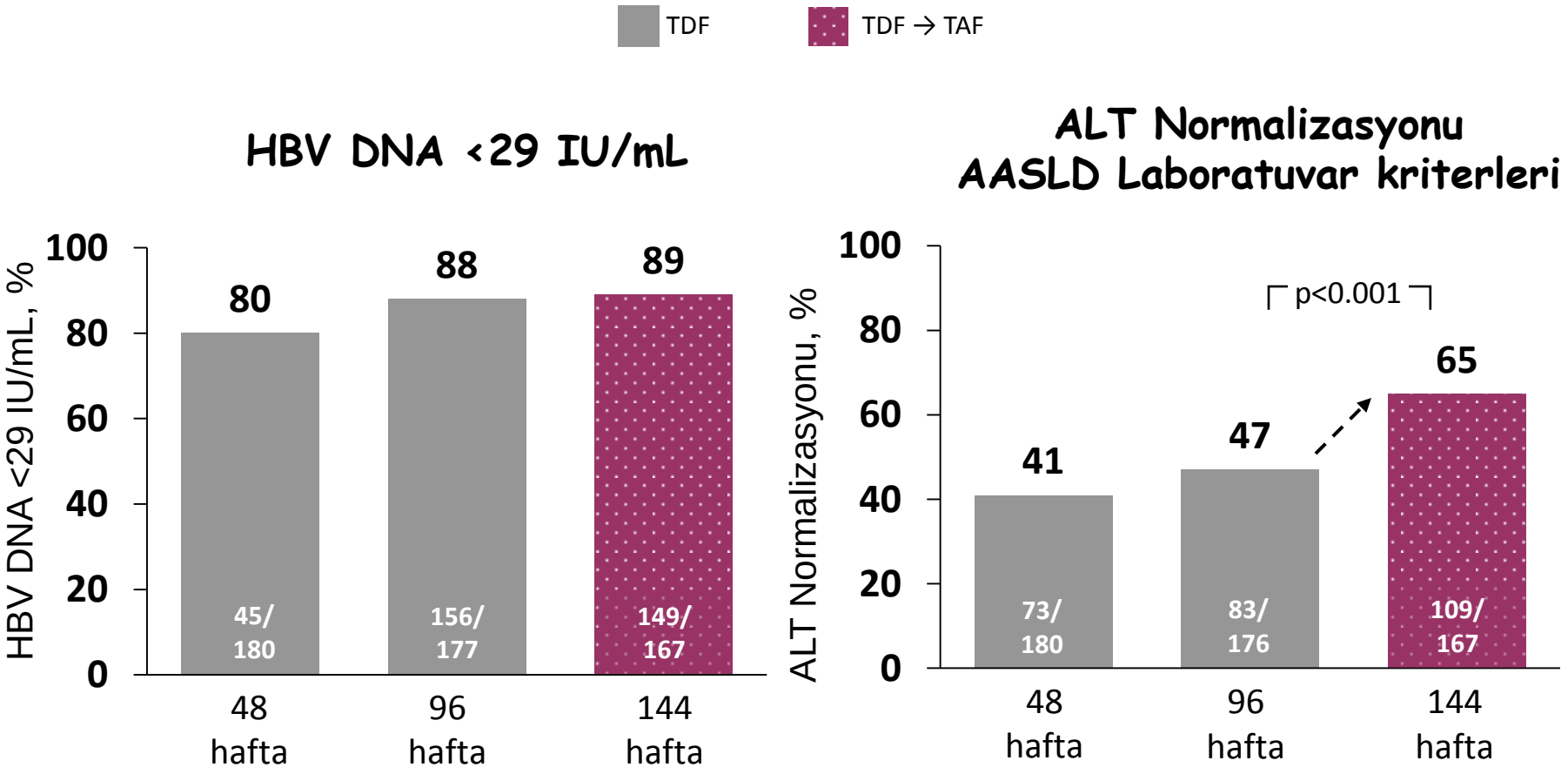
Çalışma tasarımı



- 2 faz 3, randomize, çift-kör, aktif kontrollü çalışma
  - 108 çalışması (N=425): HBeAg-negatif hastalar
  - 110 çalışması (N=873): HBeAg-pozitif hastalar
- Önemli dahil etme kriterleri (her iki çalışma için de)
  - HBV DNA ≥20,000 IU/mL; ALT >60 U/L (erkekler) >38 U/L (kadın); eGFR ≥50 mL/dak
- 2:1 randomizasyon
  - HBV DNA seviyelerine ve tedavi deneyimlerine göre sınıflandırma

Pan, AASLD 2017, Poster 904

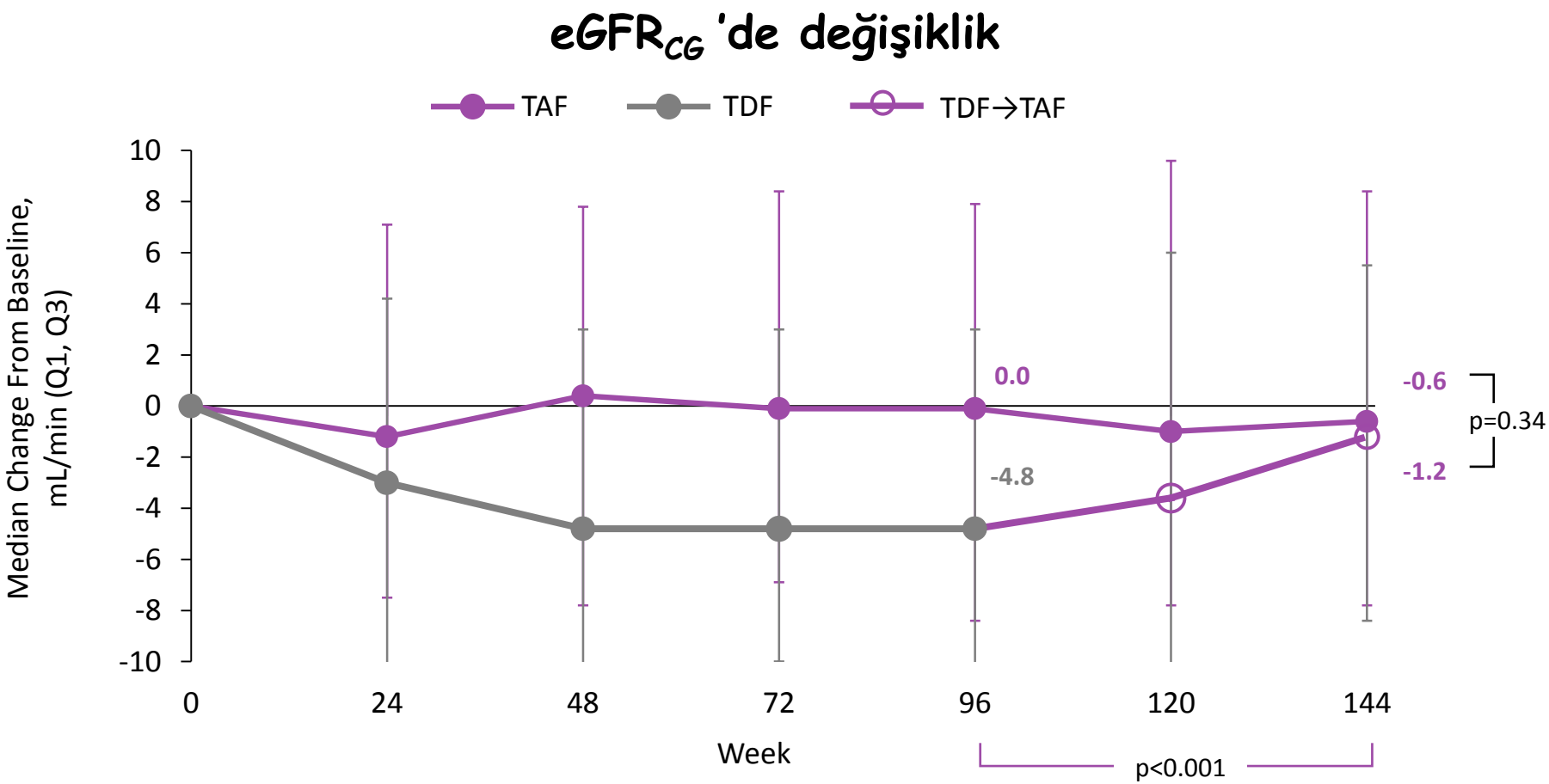
Virolojik ve biyokimyasal etkinlik



TDF'ten TAF'a geçince viral baskılama korundu, ALT normalizasyonu arttı

Pan, AASLD 2017, Poster 904; Chan, AASLD 2017, Oral 26
Data on file, Gilead Sciences, Inc.

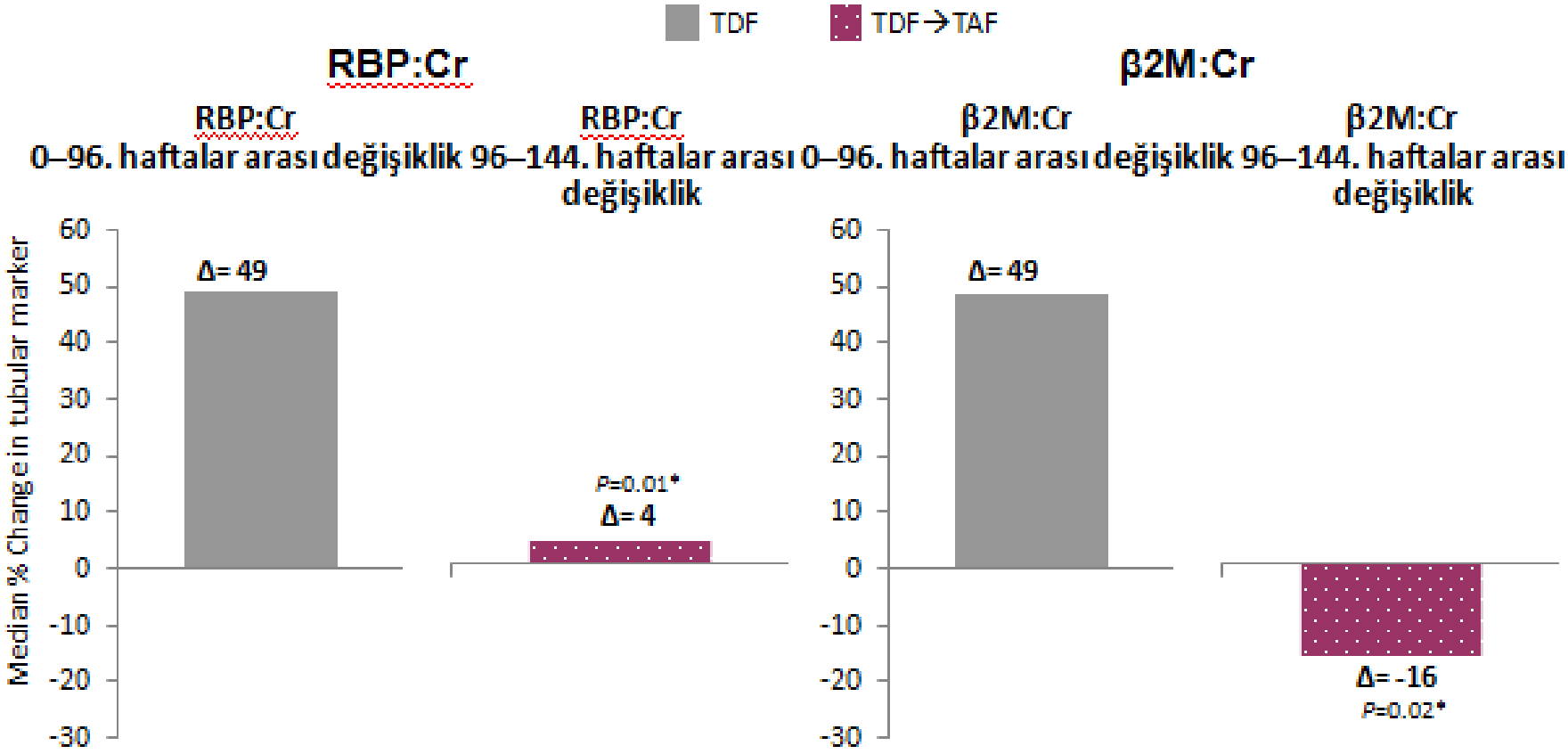
TAF ya da TDF ile tedavi edilen hastalarda renal laboratuvar parametreleri



96. Haftadan sonra 144. haftaya kadar TDF'ten TAF'a geçen hastalarda anlamlı eGFR$_{CG}$ artışı

eGFR$_{CG}$, estimated glomerular filtration rate as measured by the Cockcroft-Gault equation
Pan, AASLD 2017, Poster 904

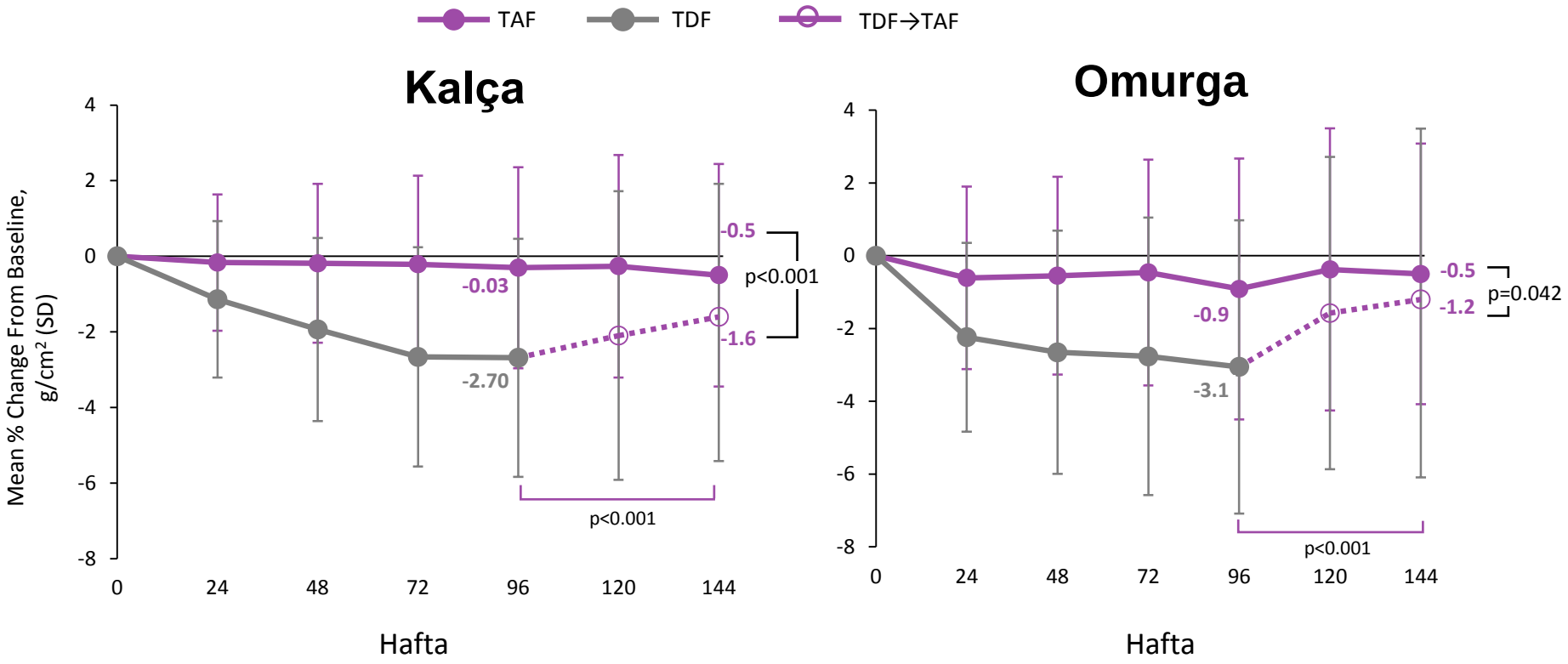
TDF'ten TAF'a geçen hastalarda renal tubuler belirteçlerde değişiklik



TDF'ten TAF'a geçen hastalarda 48. haftada anlamlı tubuler parametrelerde iyileşme

RBP, retinol binding protein; B2M, Beta-2-microglobulin
* P-value is for comparison of Week 144 vs open-label baseline (Week 96)
Fan, AASLD 2017, Poster 904

TDF'ten TAF'a geçen hastalarda KMD'deki değişiklikler



TDF'ten TAF'a geçen hastalarda 48. haftada kalça ve omurga KMD'de anlamlı iyileşme saptandı

Pan, AASLD 2017, Poster 904

SONUÇ

- Kronik hepatit B hastalarında en az TDF kadar etkin.
- Yan etki profili açısından TDF'a göre daha güvenli.
- TDF ile bozulan KMD ve renal fonksiyonlarda TAF'a geçiş ile iyileşme elde edilebiliyor.

TEŞEKKÜR EDERİM…