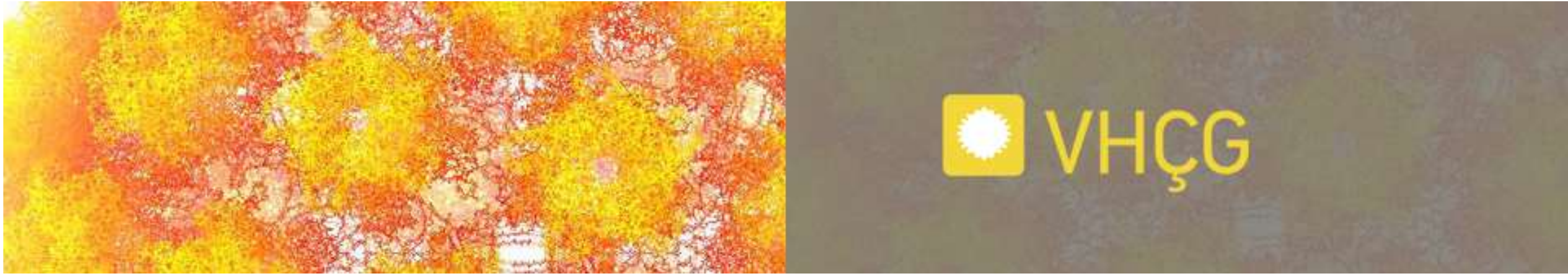
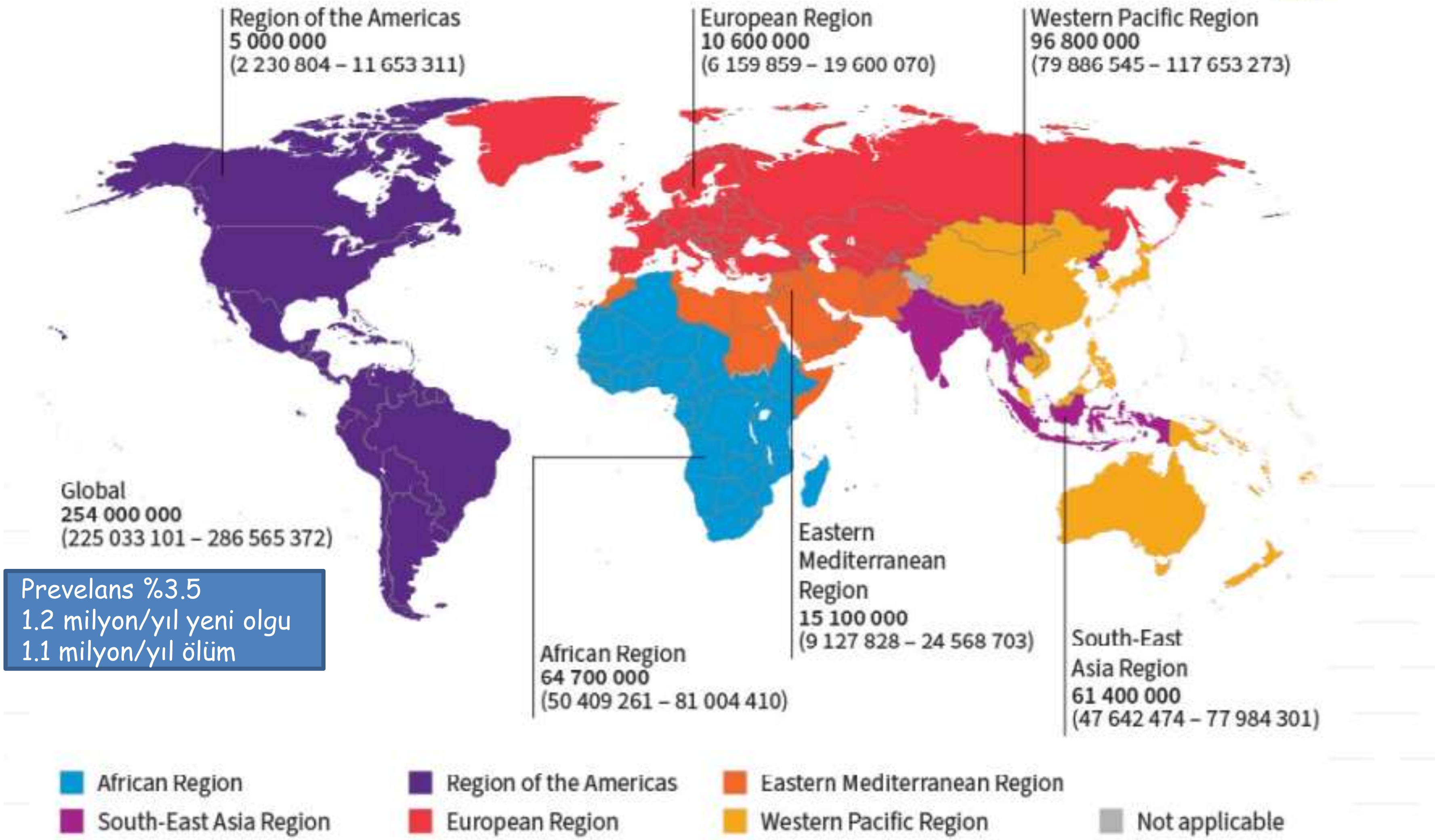


KRONİK HEPATİT B'DE TEDAVİYİ KESELİM Mİ?

Dr. Neşe DEMİRTÜRK
Afyonkarahisar Sağlık Bilimleri Üniversitesi Tıp Fakültesi
İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD.
Afyonkarahisar, 2024.

Fig. 2.3. Prevalent cases of chronic hepatitis B by WHO region, 2022



Prevelans %3.5
1.2 milyon/yıl yeni olgu
1.1 milyon/yıl ölüm

WHO, Global Hepatitis Report 2024

Kronik Hepatit B İnfeksiyonunun Yönetimi: Türk Klinik Mikrobiyoloji ve İnfeksiyon Hastalıkları Derneği Viral Hepatit Çalışma Grubu Uzlaşı Raporu-2023 Güncellemesi

Tedavi Endikasyonları

Öneriler

1. HBeAg pozitif kronik infeksiyonlu hastalar (HBeAg pozitif, HBV DNA $>10^7$ İÜ/ml ve devamlı normal düzeyde ALT'si olanlar, genellikle 40 yaş altındadır) antiviral tedavi verilmeksizin izlenmelidir.
2. Normal ALT'si olup HBeAg pozitif kronik infeksiyon evresinde olduğu düşünülen olgularda, eğer hastanın yaşı >30-40 yıl ise, HBV DNA $<10^7$ İÜ/ml ise veya ALT düzeyi üst sınıra yakınsa invazif olmayan fibroz değerlendirme testleri veya karaciğer biyopsisi ile değerlendirme önerilir; söz konusu yöntemlerle orta-şiddetli nekroinflamasyon ve/veya orta-ciddi fibroz bulgusu elde edilirse antiviral tedavi başlanabilir.
3. HBeAg pozitif ya da negatif KHB infeksiyonlu hastalarda akut alevlenme gelişme durumunda antiviral tedavi mutlaka başlanmalıdır.

Öneriler

7. HBeAg pozitif ve HBV DNA düzeyi ≥20 000 İÜ/ml olan KHB hastaları ile HBeAg negatif ve HBV DNA düzeyi ≥2000 İÜ/ml olan KHB hastaları, ALT düzeyinden bağımsız olarak tedavi edilmelidir.
8. HBV DNA düzeyleri, ilk öneride belirtilen eşik değerlerin altında olan ancak ALT düzeyi >normalin üst sınırı x 1-2 kat olan hastalarda, karaciğer histolojisi biyopsi ya da invazif olmayan tanı testleri ile değerlendirilmeli ve karaciğerde orta-ağır düzeyde nekroinflamasyon ya da fibroz varlığında tedavi düşünülmelidir.

5.1 Recommendations

New recommendations – who to treat

Treatment is recommended for all adults and adolescents (aged ≥12 years) with CHB[a] (including pregnant women and girls and non-pregnant women of reproductive age) with:

1. Evidence of significant fibrosis (≥F2)[b] based on an APRI score of >0.5 or transient elastography[c] value of >7 kPa or evidence of cirrhosis (F4) (based on clinical criteria (or an APRI score of >1 or transient elastography value of >12.5 kPa[b]), regardless of HBV DNA or ALT levels.

(adults: strong recommendation, moderate-certainty evidence; adolescents: strong recommendation, low-certainty evidence)

OR

2. HBV DNA >2000 IU/mL and an ALT level above the upper limit of normal (ULN) (30 U/L for men and boys and 19 U/L for women and girls). For adolescents, this should be based on ALT>ULN on at least two occasions in a 6- to 12-month period.[d]

(adults: strong recommendation, high-certainty evidence [HBV DNA >20 000 IU/mL] and low-certainty evidence [HBV DNA 2000–20 000,]; adolescents: conditional recommendation, low-certainty evidence)

OR

3. Presence of **coinfections** (such as HIV, hepatitis D or hepatitis C); **family history** of liver cancer or cirrhosis; **immune suppression** (such as long-term steroids, solid organ or stem cell transplant); **comorbidities** (such as diabetes or metabolic dysfunction—associated steatotic liver disease); or **extrahepatic manifestations** (such as glomerulonephritis or vasculitis), regardless of the APRI score or HBV DNA or ALT levels.

(adults: strong recommendation, moderate-certainty evidence; adolescents: conditional recommendation, low-certainty evidence)

OR

In the absence of access to an HBV DNA assay:

4. Persistently abnormal ALT levels (defined as two ALT values above the ULN at unspecified intervals during a 6- to 12-month period), regardless of APRI score.[e]

(adults and adolescents: conditional recommendation, very-low-certainty evidence)

Guidelines for the prevention, diagnosis, care and treatment for people with chronic hepatitis B infection, WHO 2024.

NE İLE TEDAVİ ÖNERİYORUZ?

Klimik Dergisi 2023; 36(Özel Sayı 1): 1-22

UZLAŞI RAPORU CONSENSUS REPORT

Kronik Hepatit B İnfeksiyonunun Yönetimi: Türk Klinik Mikrobiyoloji ve İnfeksiyon Hastalıkları Derneği Viral Hepatit Çalışma Grubu Uzlaşı Raporu-2023 Güncellemesi

Management of Chronic Hepatitis B Infection: A Consensus Report of the Study Group for Viral Hepatitis of the Turkish Society of Clinical Microbiology and Infectious Diseases-2023 Update

Neşe Demirtürk[1], Adem Köse[2], Onur Ural[3], Ali Asan[4], Şener Barut[5], Şua Sümer[3], Funda Şimşek[6], Nesrin Türker[7]

[1]Afyonkarahisar Sağlık Bilimleri Üniversitesi Tıp Fakültesi, İnfeksiyon Hastalıkları ve Klinik M
Türkiye; [2]İnönü Üniversitesi Tıp Fakültesi, İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Ana
Tıp Fakültesi, İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı, Konya, Türkiye; [4]
İhtisas Sağlık Uygulama ve Araştırma Merkezi, İnfeksiyon Hastalıkları ve Klinik Mikrobiyolo
Bakanlığı Tepecik Eğitim ve Araştırma Hastanesi, İnfeksiyon Hastalıkları ve Klinik Mikrobiyo
Üniversitesi Prof. Dr. Cemil Taşçıoğlu Şehir Hastanesi, İnfeksiyon Hastalıkları ve Klinik Mikr
Bilimleri Üniversitesi, Atatürk Eğitim ve Araştırma Hastanesi, İnfeksiyon Hastalıkları ve Klini

Öneriler

1. KHB tedavisinde, ilk seçenek olarak PEG-INF-α ya da genetik bariyeri yüksek NA kullanılır.
2. Antiviral direnç için yüksek genetik bariyerli ilaçlar; entekavir, TDF ve TAF olup; NA ile tedavi başlanacaksa, ilk seçenek bu ilaçlardan biri olmalıdır. Besifovir, ABD Gıda ve İlaç Dairesi (FDA) onaylı olmasına karşın henüz uluslararası rehberlerde ilk seçenek tedaviler arasında yer almamakta ve ülkemizde bulunmamaktadır.
3. Kompanse sirotik hastalarda, yüksek genetik bariyerli NA öncelikli olarak önerilir. Ancak karaciğer fonksiyonu iyi korunmuşsa, karaciğer fonksiyonlarının ve yan etkilerin yakın takibi koşulu ile PEG- INF-α da kullanılabilir.
4. Dekompanse sirotik hastalarda PEG- INF-α kontrendikedir.

TEDAVİDE HEDEFLERİMİZ

Primer hedef

- Biyokimyasal yanıt
- Kalıcı HBV DNA negatifliği
  Kalıcı virolojik yanıt
- HBeAg pozitif hastalarda serokonversiyon

Sekonder hedefler

- Histolojik yanıt
- HBsAg kaybı ya da serokonversiyonu;
  Fonsiyonel Kür
- Genoma entegre olmuş olan HBVDNA ve cccDNA kaybı;
  Steril Kür

Fonksiyonel kür ne kadar başarılıyor ?

- Peg-IFN
  - HBeAg negatif hastalarda 48 hafta tedavi ile, tedaviden 6 ay ve 3 yıl sonra HBsAg klirensi %4 ve %8-%14
  - HBeAg pozitif hastalarda 48 hafta tedavi ile, tedaviden 6 ay sonra %3-%7, tedaviden 3 yıl sonra %11

- NA Tedavisi
  - ETV; HBeAg pozitif hastalarda 7-10 yıllık tedavi ile %4
  - TDF;HBeAg pozitif hastalarda 10 yıllık tedavi ile %3
  - TAF; HBeAg pozitif 5 yıllık tedavi ile %1
- HBeAg negatif hastalarda NA ile HBsAg serokonversiyon olasılığı çok düşük <%1

EASL Guideline, 2017.
Jeng WJ et al. Lancet, 2023.
Demirtürk N ve ark. KLİMİK Uzlaşı Raporu, KLİMİK Derg, 2023.

ORIGINAL ARTICLE

Korean J Intern Med 2017;32:636-646
https://doi.org/10.3904/kjim.2016.096

KJIM

Long-term real-world entecavir therapy in treatment-naïve hepatitis B patients: base-line hepatitis B virus DNA and hepatitis B surface antigen levels predict virologic response

Ju-Yeon Cho[1,2], Won Sohn[1,3], Dong-Hyun Sinn[1], Geum-Youn Gwak[1], Yong-Han Paik[1], Moon Seok Choi[1], Kwang Cheol Koh[1], Seung Woon Paik[1], Byung Chul Yoo[1], and Joon Hyeok Lee[1]

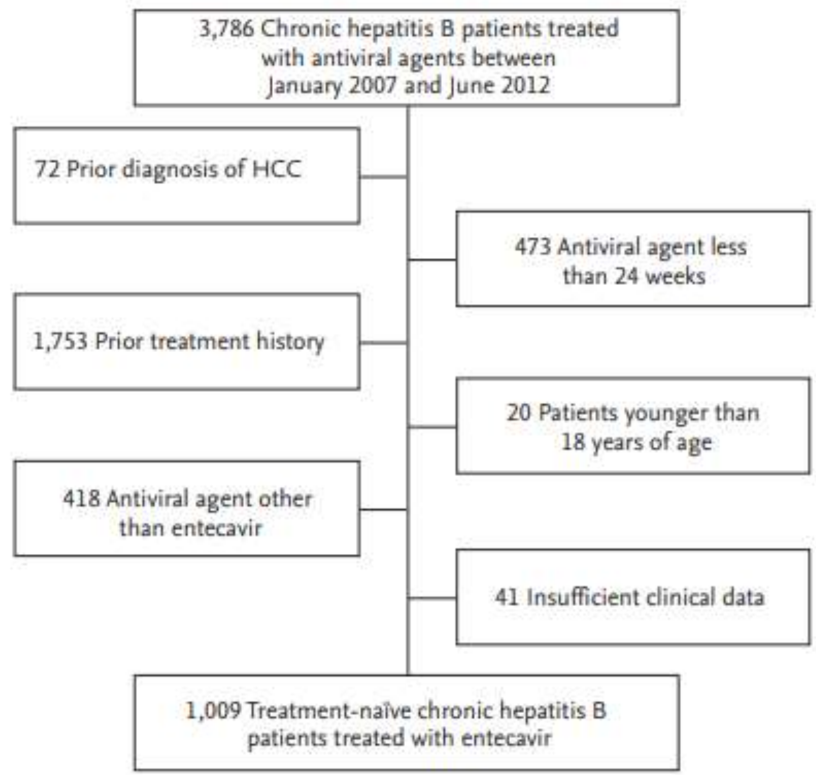


Figure 1. Flow chart of patients included in the study.

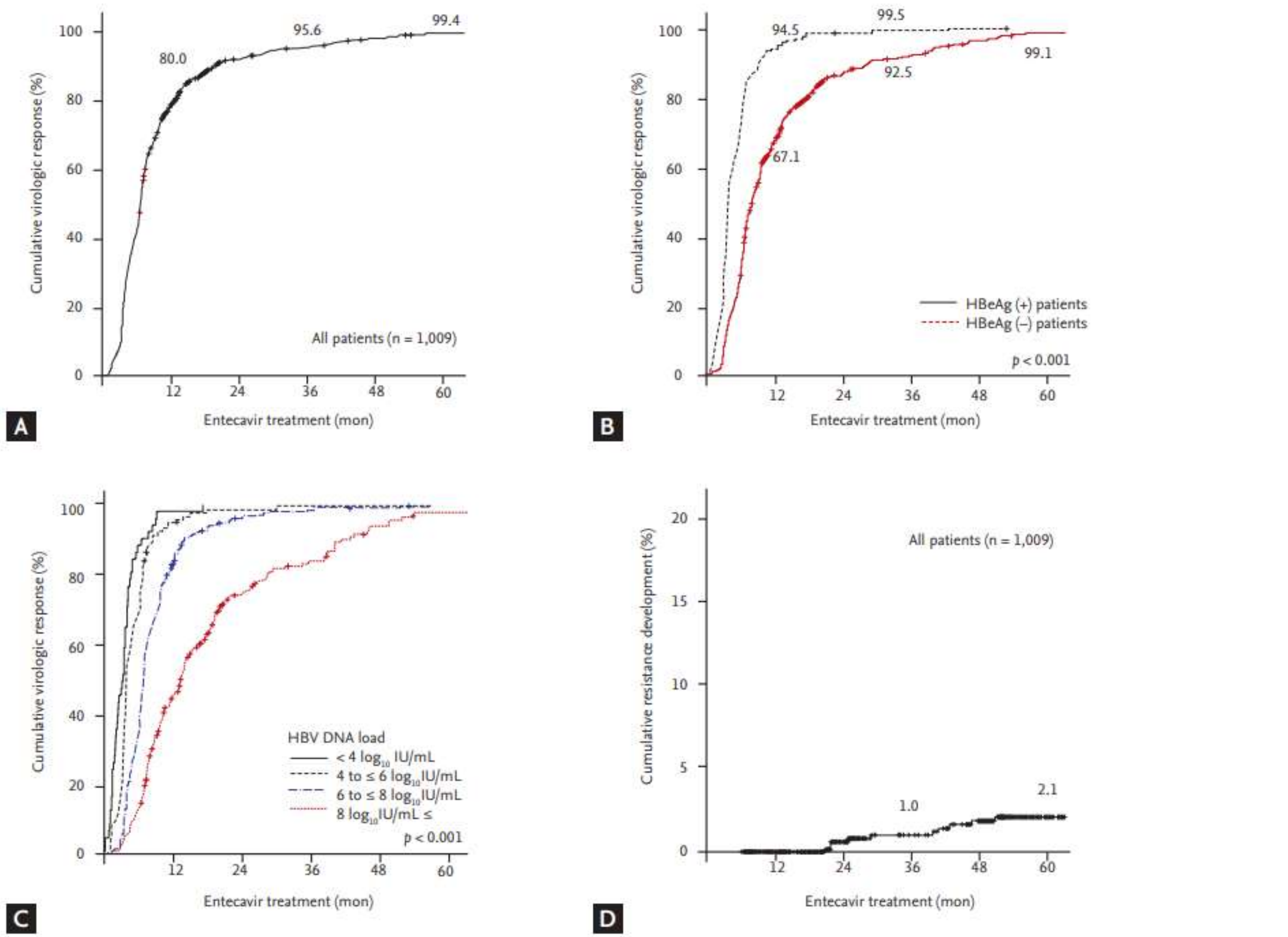
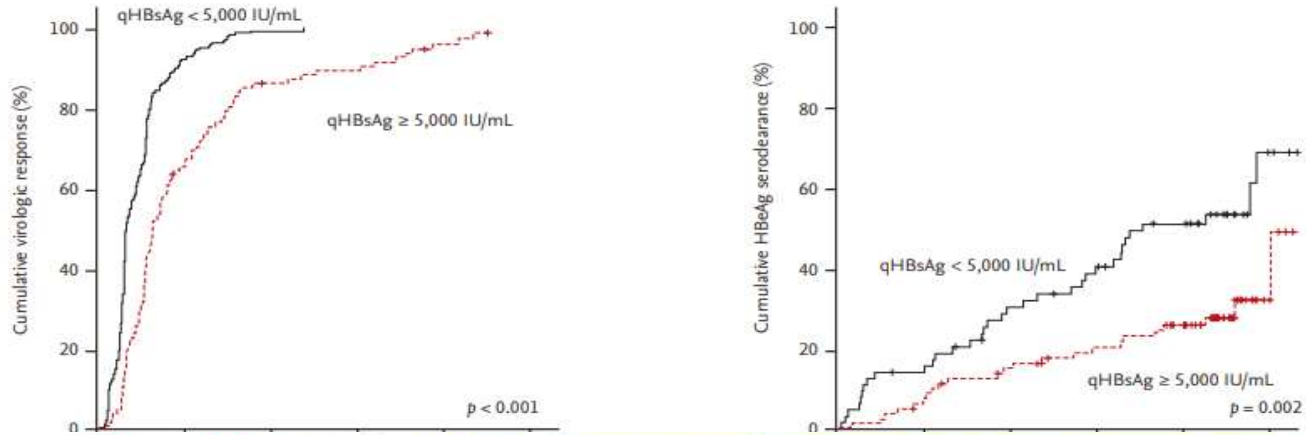


Figure 2. Virologic response of patients on continuous entecavir treatment. (A) The cumulative virologic response rate increased with time, reaching 99.4% at year 5. (B) Hepatitis B e antigen (HBeAg)-negative patients had a statistically higher rate of virologic response at year 1, 3, and 5. (C) The cumulative virologic response rate in patients with high hepatitis B virus (HBV) DNA loads, compared to patients with HBV DNA loads < 4 $\log_{10}$ IU/mL resulted in a significantly lower virologic response. (D) The log-rank test was used to compare the differences in the viral responses between each group. The cumulative entecavir resistance rates were 0% after 1 year, 1.0% after 3 years, and 2.1% after 5 years.



The cumulative HBsAg seroclearance rates were 0.4%, 0.7%, and 1.6% in years 1, 3, and 5, respectively. Among the 571 HBeAg-positive patients, the cumulative HBeAg seroclearance rates at years 1, 3, and 5 were 4.1%, 19.2%, and 40.2%, respectively.

Figure 3. Virologic response and hepatitis B e antigen (HBeAg) seroclearance based on quantitative hepatitis B surface antigen (qHBsAg) level. (A) The cumulative virologic response rate was significantly greater in patients with baseline qHBsAg < 5,000 IU/mL. (B) In HBeAg-positive patients, baseline qHBsAg < 5,000 IU/mL was associated with a significantly greater cumulative rate of HBeAg seroclearance. (C) The cumulative virologic response rate was not statistically different among patients with low viral loads (≤ 6 $\log_{10}$ IU/mL), regardless of qHBsAg levels. (D) In the high viral load group (high hepatitis B virus [HBV] DNA > 6 $\log_{10}$ IU/mL), patients with low qHBsAg (≤ 5,000 IU/mL) had a significantly greater virologic response compared to patients with high qHBsAg levels (qHBsAg > 5,000 IU/mL, $p < 0.001$).

Dig Dis Sci (2016) 61:3072–3083
DOI 10.1007/s10620-015-4027-8

ORIGINAL ARTICLE

Effectiveness and Safety of Tenofovir Disoproxil Fumarate in Chronic Hepatitis B: A 3-Year, Prospective, Real-World Study in France

Patrick Marcellin[1] · Fabien Zoulim[2] · Christophe Hézode[3] · Xavier Causse[4] · Bruno Roche[5] · Régine Truchi[6] · Arnaud Pauwels[7] · Denis Ouzan[8] · Jérôme Dumortier[9] · Georges-Philippe Pageaux[10] · Marc Bourlière[11] · Ghassan Riachi[12] · Jean-Pierre Zarski[13] · Jean-François Cadranel[14] · Valérie Tilliet[15] · Christiane Stern[15] · Pascal Pétour[15] · Olivier Libert[15] · Silla M. Consoli[16] · Dominique Larrey[10]

Received: 26 June 2015 / Accepted: 28 December 2015 / Published online: 28 January 2016

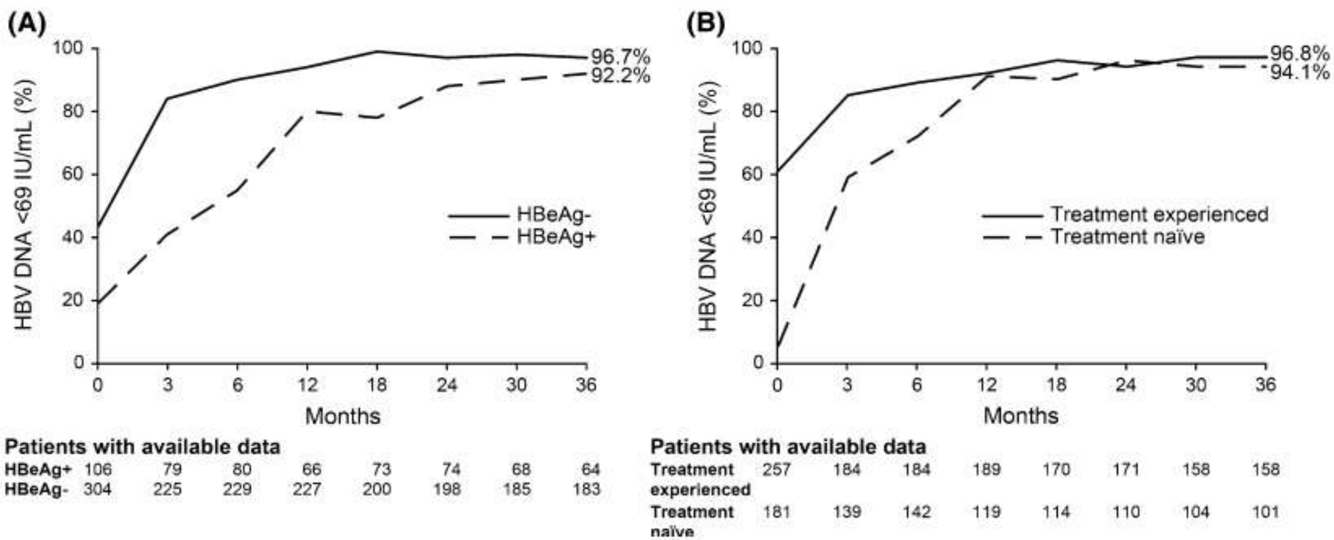


Fig. 1 Virologic response over time. **a** By HBeAg status; **b** by prior treatment status. *HBeAg* hepatitis B e antigen

- 14 hastada HBsAg kaybı saptanmış
  Fonksiyonel kür %3

- HBeAg pozitif hastalarda
  - HBeAg kaybı %45
  - HBeAg serokonversiyonu %25

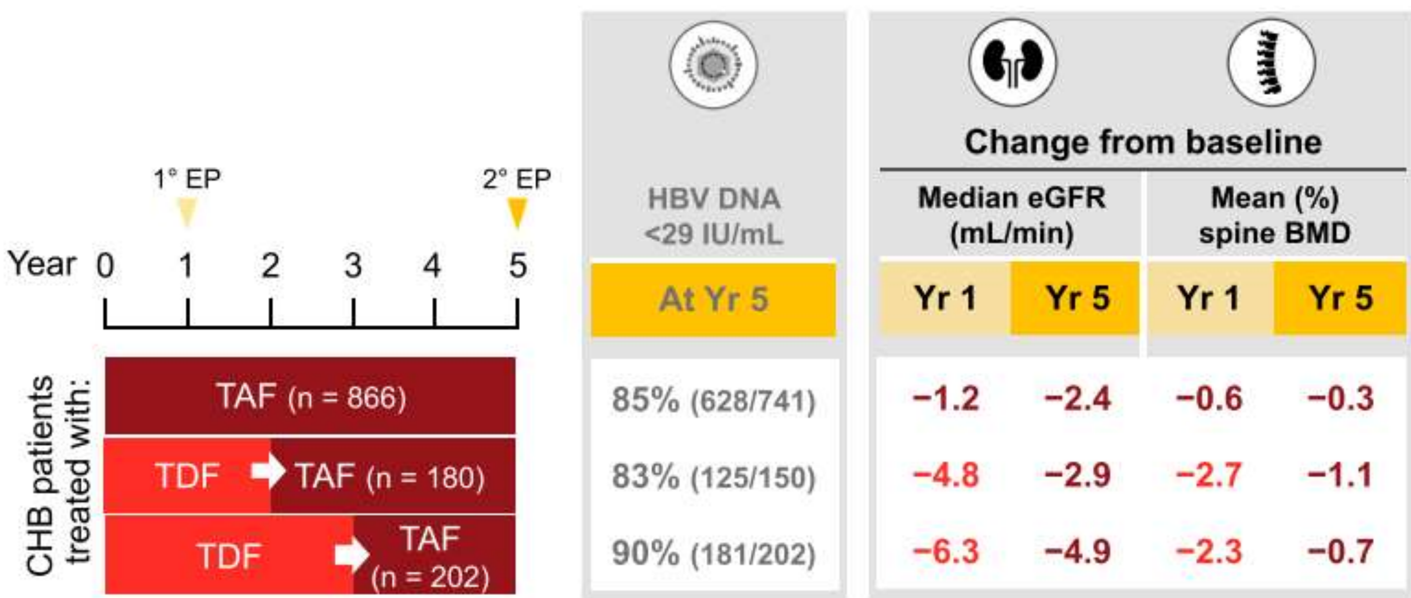
Long-Term Treatment With Tenofovir Alafenamide for Chronic Hepatitis B Results in High Rates of Viral Suppression and Favorable Renal and Bone Safety

Henry L.Y. Chan, MD[1], Maria Buti, MD, PhD[2], Young-Suk Lim, MD, PhD[3], Kosh Agarwal, MD[4], Patrick Marcellin, MD, PhD[5], Maurizia Brunetto, MD[6], Wan-Long Chuang, MD, PhD[7], Harry L.A. Janssen, MD, PhD[8,9], Scott Fung, MD, FRCPC[10], Namiki Izumi, MD, PhD[11], Dzhamal Abdurakhmanov, MD, PhD[12], Maciej Jabłkowski, MD, PhD[13], Mustafa K. Celen, MD[14], Xiaoli Ma, MD[15], Florin Caruntu, MD, PhD[16], John F. Flaherty, PharmD[17], Frida Abramov, DMSc, PA-C[17], Hongyuan Wang, PhD[17], Gregory Camus, PhD[17], Anu Osinusi, MD[17], Calvin Q. Pan, MD[18], Shalimar, MBBS[19], Wai-Kay Seto, MD[20] and Edward Gane, MBChB, MD[21], on behalf of the GS-US-320-0110 and GS-US-320-0108 investigators

Am J Gastroenterol. 2024. doi:10.14309/ajg.0000000000002468

AJG The American Journal of GASTROENTEROLOGY

Tenofovir Alafenamide (TAF) vs Tenofovir Disoproxil Fumarate (TDF) for Chronic Hepatitis B (CHB): 5-Year Results From 2 Phase 3 Studies



Supplemental Table 1. Efficacy results at year 5 by study, M = F analysis

n/N (%)	TAF	TDF→TAF3y	TDF→TAF2y
Study 108			
HBV DNA < 29 IU/mL	230/249 (92.4)	47/53 (88.7)	61/63 (96.8)
HBV DNA < 29 IU/mL with TND	143/249 (57.4)	30/53 (56.6)	35/63 (55.6)
HBV DNA ≥ 29 IU/mL (nonmissing)	4/249 (1.6)	2/53 (3.8)	1/63 (1.6)
Normalized ALT (central lab)[a]	171/206 (83.0)	37/45 (82.2)	43/55 (78.2)
Normalized ALT (2018 AASLD)[b]	171/229 (74.7)	37/49 (75.5)	47/62 (75.8)
HBeAg loss	N/A	N/A	N/A
HBeAg seroconversion	N/A	N/A	N/A
HBsAg loss	3/245 (1.2)	0/52	0/63
HBsAg seroconversion	2/245 (0.8)	0/52	0/63
FibroTest, mean (SD)	−0.05 (0.132)	−0.03 (0.144)	0.00 (0.134)
Study 110			
HBV DNA < 29 IU/mL	398/492 (80.9)	78/97 (80.4)	120/139 (86.3)
HBV DNA < 29 IU/mL with TND	169/492 (34.3)	41/97 (42.3)	48/139 (34.5)
HBV DNA ≥ 29 IU/mL (nonmissing)	43/492 (8.7)	9/97 (9.3)	6/139 (4.3)
Normalized ALT (central lab)[a]	336/453 (74.2)	69/91 (75.8)	96/126 (76.2)
Normalized ALT (2018 AASLD)[b]	313/479 (65.3)	58/95 (61.1)	91/134 (67.9)
HBeAg loss	164/484 (33.9)	30/93 (32.3)	48/136 (35.3)
HBeAg seroconversion	114/484 (23.6)	17/93 (18.3)	28/136 (20.6)
HBsAg loss	4/490 (0.8)	1/94 (1.1)	5/139 (3.6)
HBsAg seroconversion	3/490 (0.6)	1/94 (1.1)	2/139 (1.4)
FibroTest, mean (SD)	−0.06 (0.146)	−0.04 (0.155)	−0.03 (0.138)

Fonksiyonel kür olana kadar tedaviye devam edelim mi?


Kronik Hepatit B İnfeksiyonunun Yönetimi: Türk Klinik Mikrobiyoloji ve İnfeksiyon Hastalıkları Derneği Viral Hepatit Çalışma Grubu Uzlaşı Raporu-2023 Güncellemesi

Management of Chronic Hepatitis B Infection: A Consensus Report of the Study Group for Viral Hepatitis of the Turkish Society of Clinical Microbiology and Infectious Diseases-2023 Update

Öneriler

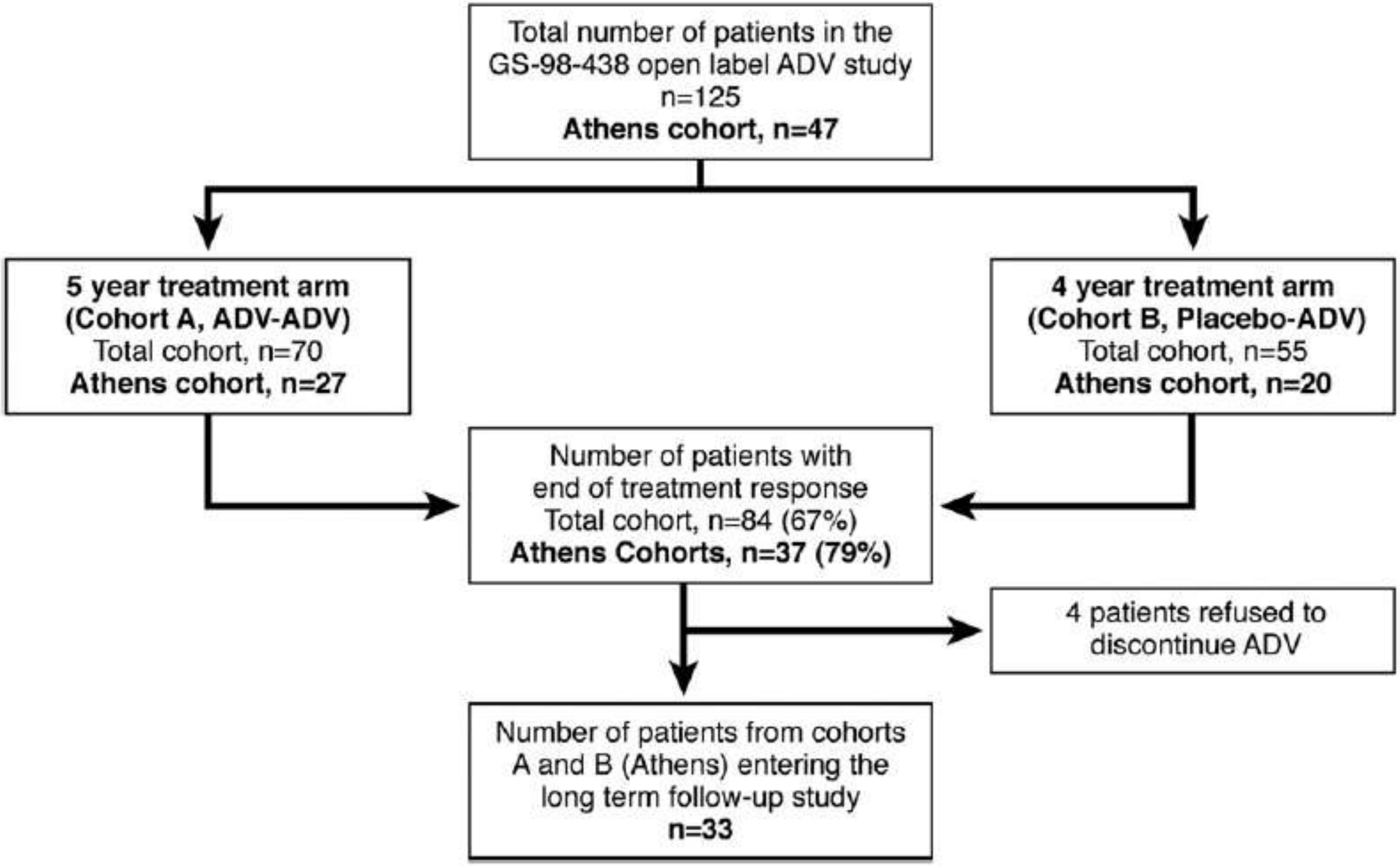
1. PEG- INF-α tedavisi 48 hafta uygulandıktan sonra kesilir.
2. Nükleoz(t)id anoloğu ilaçlar ile antiviral tedavinin sonlandırılması için en kesin nokta HBsAg negatifleşmesidir.
3. HBeAg pozitif hastalarda, NA ile tedavi sırasında HBeAg kaybı ya da anti-HBe serokonversiyonu gelişirse, tedavi 12 ay daha sürdürüldükten sonra kesilebilir.
4. NA ile antiviral tedavinin sonlandırılmasında kullanılabilecek tanımlanmış biyobelirteçler HBsAg kantitasyonu, HBV DNA ve yeni tanımlanan HBcrAg'dir. HBeAg negatif hastalarda HBsAg <100 İÜ/ml ise tedavinin kesilmesi denenebilir. HBcrAg için kesinleşmiş bir kantitatif değer yoktur. HBeAg negatif, sirotik olmayan hastalarda üç yıldan uzun HBV DNA negatifliği durumunda, yakın takibin sürdürülmesi koşuluyla hastalar, tedavinin kesilmesi açısından değerlendirilebilir.
5. Özellikle dekompansasyon gelişmiş sirotik hastalarda tedavi HBsAg negatif olmadan kesilmemelidir.

Sustained Responses and Loss of HBsAg in HBeAg-Negative Patients With Chronic Hepatitis B Who Stop Long-Term Treatment With Adefovir

STEPHANOS J. HADZIYANNIS,[*,‡] VASSILIOS SEVASTIANOS,[*] IRENE RAPTI,[*] DIMITRIOS VASSILOPOULOS,[§] and EMILIA HADZIYANNIS[§]

GASTROENTEROLOGY 2012;143:629–636

[*]Department of Medicine and Hepatology, Henry Dunant Hospital, [§]2nd Academic Department of Medicine, Hippokration Hospital, and the [‡]Molecular Biology Laboratory of the Liver Unit at the Evgenidion Hospital, National and Kapodistrian University of Athens, Athens, Greece



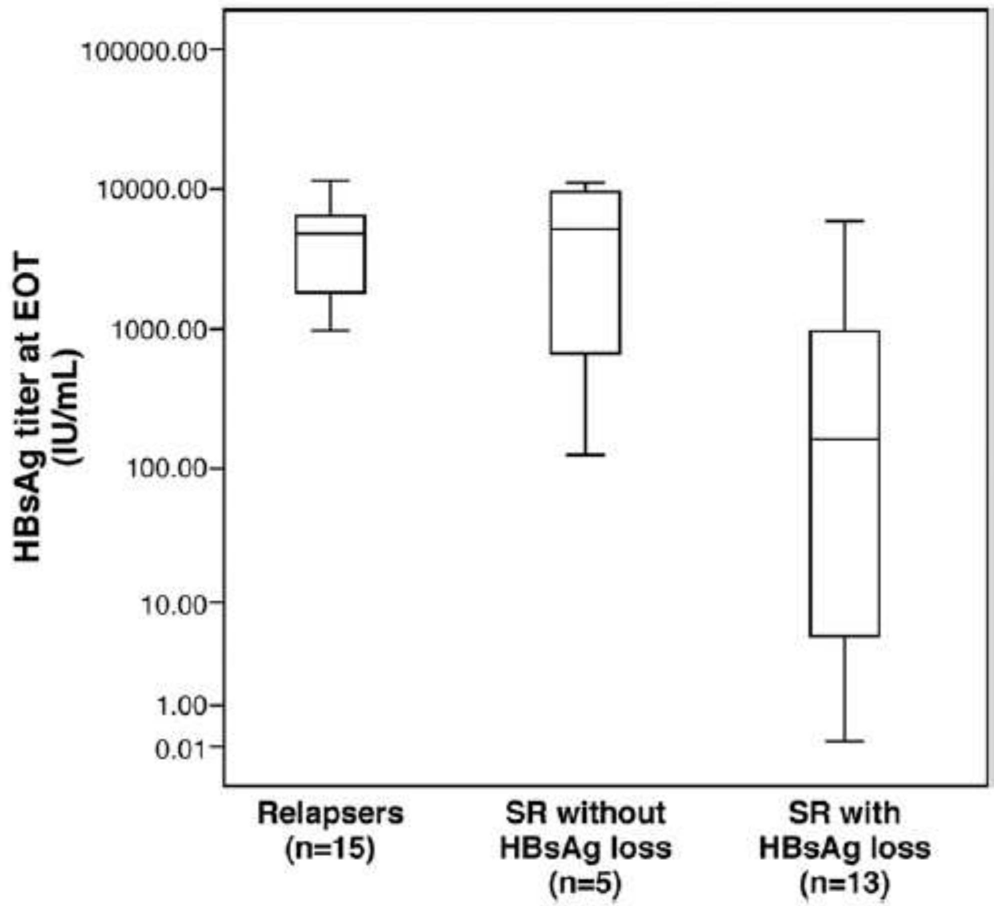


Figure 4. EOT HBsAg levels in patients with SR and HBsAg loss (n = 13) vs patients with virological and biochemical relapse (n = 15; *P* = .002) or patients with SR without HBsAg loss (n = 5; *P* = .07). SR indicates persistently not detectable HBV DNA or <2000 IU/mL combined with persistently normal ALT level following posttreatment month 6 sustained until the end of follow-up.

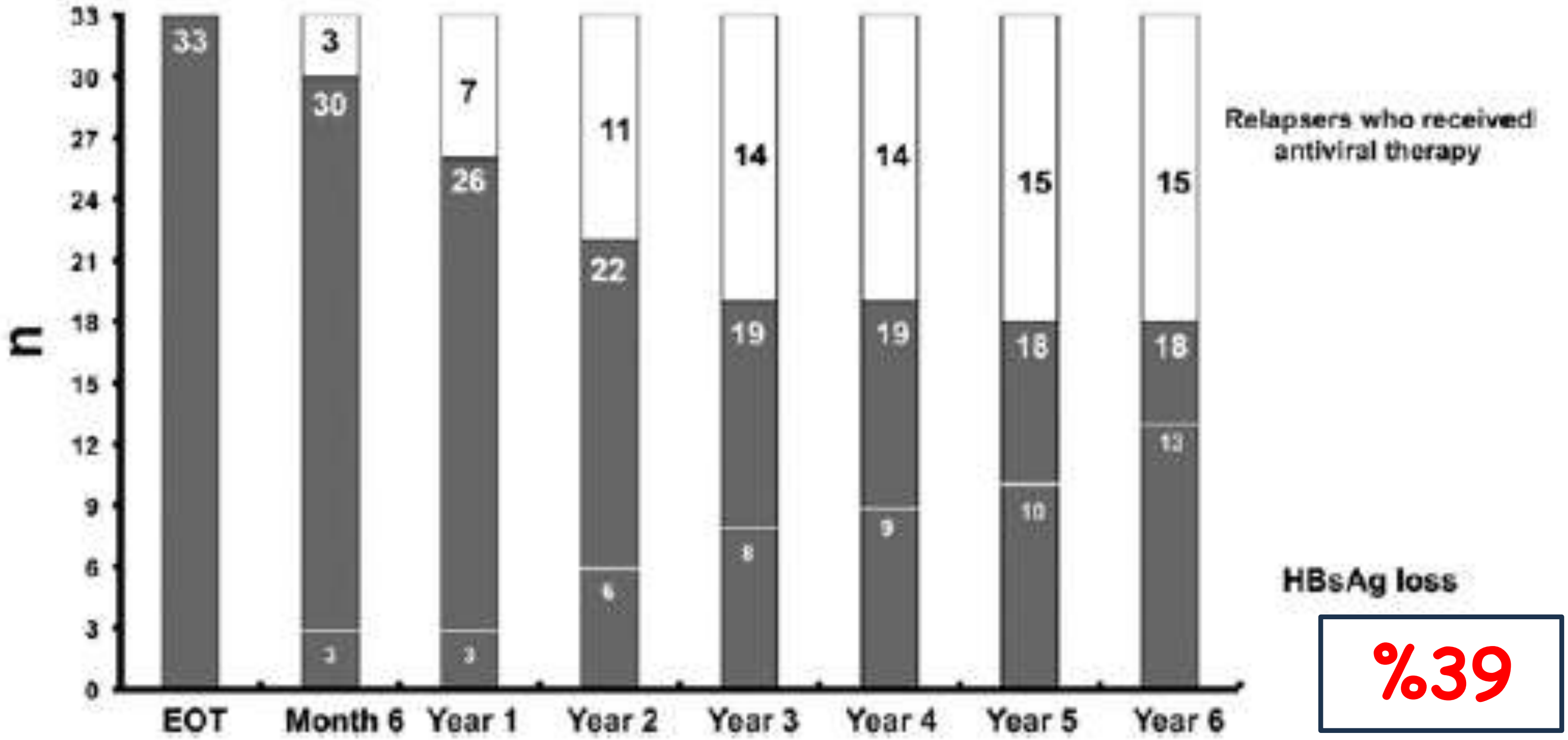


Figure 2. The number of patients who experienced a relapse and received antiviral therapy (relapsers) or lost HBsAg among the remaining patients during follow-up.

Table 2. Comparison Between Patients Without (n = 19) and With HBsAg Loss (n = 14) Among the Whole Patient Population (N = 33)

Characteristic	No HBsAg loss (n = 19)	HBsAg loss (n = 14)	P value	Univariate analysis OR (95% CI)	Univariate analysis P value	Multivariate analysis[a] OR (95% CI)	Multivariate analysis[a] P value	Multivariate analysis (P < .1)[b] OR (95% CI)	Multivariate analysis (P < .1)[b] P value	Multivariate analysis[c] OR (95% CI)	Multivariate analysis[c] P value
Before/during ADV treatment											
Age	53.7 ± 12.2	55.3 ± 11	.71	1.012 (0.95–1.08)	.701	1.341 (0.90–2.00)	.151				
Previous interferon treatment (yes/no)	**15/4**	**3/11**	**.002**	0.073 (0.01–0.39)	.002	0.000 (0.00–2.21)	.067	**0.025 (0.00–0.48)**	**.015**	0.015 (0.00–0.74)	.084
ALT (*U/L*)	121.7 ± 63.7	138.3 ± 103.3	.9	1.003 (0.99–1.01)	.562	1.048 (0.99–1.11)	.108	**1.022 (1.00–1.41)**	**.027**	1.019 (1.00–1.39)	.066
HBV DNA (*IU/mL*), median (range)	6.38 (3.90–6.91)	5.93 (3.93–6.55)	.06	0.999 (0.99–1.00)	.043	0.999 (0.99–1.00)	.095	**0.999 (0.99–0.99)**	**.033**	0.999 (0.99–1.00)	.094
Liver necroinflammation (Knodell)[d]	7.6 ± 2.5	8.1 ± 2.8	.78	1.077 (0.81–1.42)	.604	2.374 (0.63–8.95)	.201				
Liver fibrosis (Knodell)[d]	2.2 ± 1.2	2.5 ± 1.2	.44	1.267 (0.69–2.33)	.447	24.267 (0.36–1637.80)	.138	2.718 (0.85–8.74)	.093	9.027 (0.73–111.92)	.087
Duration of ADV therapy (4/5 years)	6/13	6/8	.5	1.625 (0.39–6.82)	.507	0.001 (0.00–16.90)	.165				
Duration of HBV DNA undetectability (*mo*)	48.5 ± 6.7	48.6 ± 7.8	.78	1.003 (0.91–1.11)	.945	1.847 (0.85–4.01)	.122				
End of ADV treatment (EOT)											
ALT (*U/L*)	**23.7 ± 6.6**	**32.6 ± 8.5**	**.007**	**1.182 (1.05–1.34)**	**.007**	1.485 (0.92–2.39)	.103	**1.295 (1.04–1.61)**	**.019**		
HBsAg titer (*IU/mL*)	**4905 ± 3783**	**1733 ± 2457**	**.02**	**1.000 (0.99–1.00)**	**.022**	0.999 (0.99–1.00)	.137	**0.999 (0.99–0.99)**	**.040**		
Liver necroinflammation (Ishak)[e]	3.2 ± 1	2.6 ± 0.6	.14	0.422 (0.15–1.20)	.105	0.185 (0.02–2.15)	.178				
Liver fibrosis (Ishak)[e]	2.7 ± 0.7	2.5 ± 1.5	.68	0.806 (0.40–1.61)	.540	1.615 (0.47–5.58)	.449				
Post-ADV treatment follow-up											
Peak ALT after stopping ADV (first year)	175.5 ± 218.5	128.5 ± 110.2	.83	0.998 (0.99–1.00)	.110	1.054 (0.99–1.13)	.346				
Timing of peak ALT (*mo*)	3.95 ± 2.88	3.14 ± 3.46	.23	0.915 (0.72–1.16)	.860	1.042 (0.66–1.64)	.432				
Peak HBV DNA (*IU/mL*), median (range)	5.15 (3.65–7.11)	4.67 (2.28–5.58)	.08	0.999 (0.99–1.00)	.128	0.999 (0.99–1.00)	.185				
Timing of peak HBV DNA (*mo*)	3.42 ± 3.7	1.43 ± 0.85	.09	0.648 (0.36–1.16)	.344	0.496 (0.12–2.12)	.123				
Re-treatment after stopping ADV (yes/no)	**14/5**	**1/13**	**.0003**	**0.027 (0.00–0.27)**	**.002**	0.000 (0.00–3.92)	.993	**0.027 (0.00–0.27)**	**.002**	0.002 (0.00–0.29)	.093

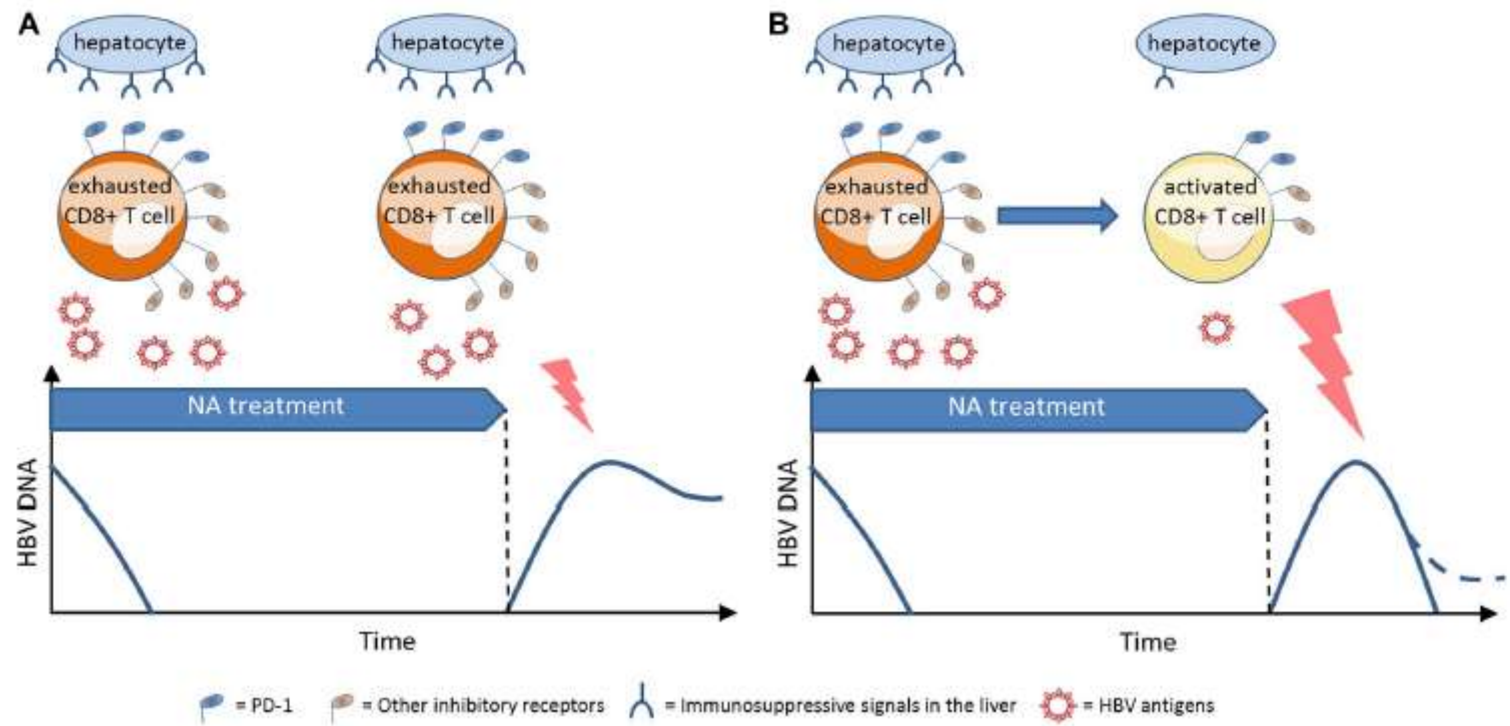


FIG. 1. Immunological and viral factors that are believed to determine response to NA treatment discontinuation. (A) CD8+ T cells that are chronically overstimulated by viral antigens (e.g., HBV DNA, HBsAg) and inhibited by excessive immunosuppressive microenvironment in the liver (e.g., PD-L1) express high levels of inhibitory receptors, such as PD-1, TIM-3, LAG-3, and CTLA-4. The rebound of HBV replication after treatment discontinuation results in a relapse of high levels of HBV-DNA replication in those patients who cannot establish sufficient immune control due to persisting T-cell exhaustion. (B) Patients who overcome T-cell exhaustion during NA treatment may respond to the HBV-DNA rebound by establishing immune control with low or undetectable levels of HBV DNA, ideally followed by HBsAg loss. Abbreviations: CTLA-4, cytotoxic T-lymphocyte antigen 4; LAG-3, lymphocyte-activation gene 3; TIM-3, T-cell immunoglobulin mucin family member 3.

van Bömmel F, Berg T. Hepatol Commun, 2021.

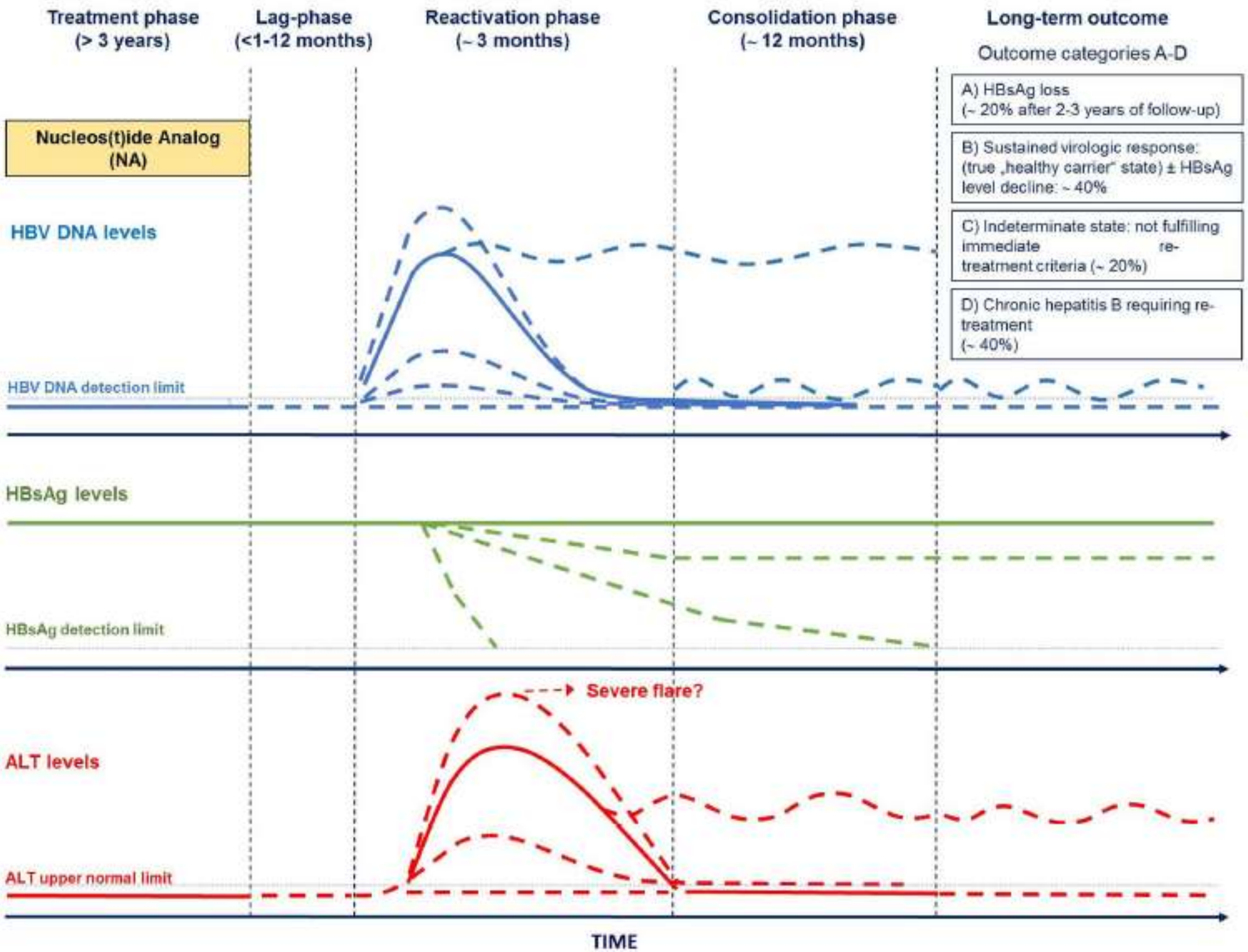


FIG. 2. Proposed phases of hepatitis B reactivation after NA discontinuation and possible long-term outcomes. (Adapted from Ref. 89.)

van Bömmel F, Berg T. Hepatol Commun, 2021.

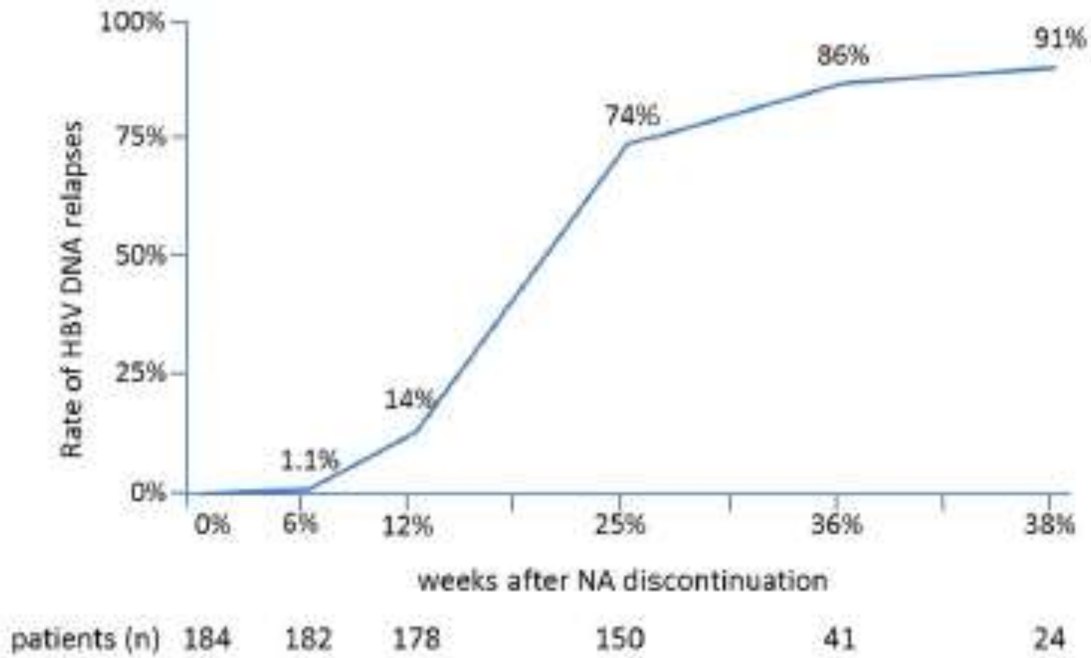


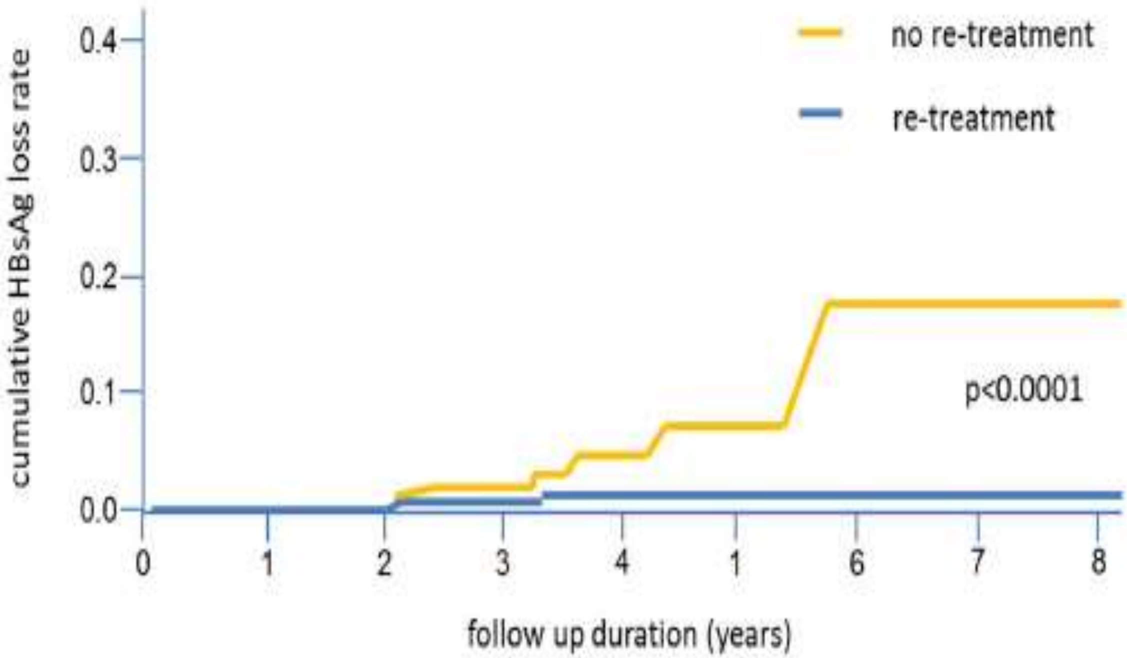
FIG. 3. Increase of HBV-DNA relapses greater than 2,000 IU/mL in HBeAg-negative patients after discontinuing treatment with ETV. Most virologic relapses occurred between weeks 12 and 24. At 48 weeks after NA discontinuation, a virologic relapse had appeared in almost all patients. (Adapted from Fig. 1 of Ref. 59.)

TABLE 1. SELECTED PROSPECTIVE STUDIES ASSESSING NA DISCONTINUATION IN HBeAg-NEGATIVE PATIENTS

Study	Region	Design	HBeAg-Negative Patients With NA Discontinued (n)	Endpoint(s)	NA	Mean NA Treatment Duration, Range (Months)	Mean Post-NA Follow-up, Range (Months)	HBV-DNA Relapses (%)	HBsAg Loss (%)	No Retreatment (%)
Liu et al.[41]	China	Prospective	61	HBV-DNA relapse; HBsAg loss	LMV +/− PEG-IFN	30 (24-66)	22 (1-84)	56	10	N/A
Ha et al.[45]	China	Prospective	145	HBV-DNA relapse; HBsAg loss	ADV +/− IFN-α	26 (24-66)*	16 (1-88)*	65.5	8.3	N/A
Seto et al.[59]	China	Prospective	184	HBV-DNA relapse; HBsAg loss; immune control	ETV	≥24	12	91.4	0	8.4†
Karakaya et al.[60]	Turkey	Prospective	23	HBV-DNA relapse; HBsAg loss	LMV	>60	12-60	45	9	9
Cao et al.[61]	China	Prospective	22	HBV-DNA relapse; HBsAg loss	ETV, ADV, LdT, LMV	47 (29-77)	N/A	53	N/A	N/A
Berg et al.[62]	Germany	Prospective, randomized	21	HBsAg loss; retreatment	TDF	33	36	100	19	43
Rivino et al.[26]	Great Britain	Prospective	21/27	HBV-DNA relapse	TDF, LMV	≥24/≥24	12	N/A	0	19/51
Papatheodoridis et al.[63]	Greece	Prospective	57	HBV-DNA relapse; retreatment	ETV, TDF	>48	18	72	25	74†
Liem et al.[68]	Asian patients (98%)	Prospective, randomized	27	HBV DNA < 2,000 IU/mL; HBsAg loss	TDF, ETV	91	18	100	1 (2.2)	17 (38%)
van Bömmel et al.[70]	European patients	Prospective, randomized	79	HBsAg loss	TDF, ETV, LdT, LMV	>48	24	100	8 (10.3)	53 (67.9%)

*Any ALT increase.
†Any HBV-DNA increase.
Abbreviations: ADV, adefovir dipivoxil; IFN, interferon; N/A, not applicable; PEG-IFN, pegylated interferon.

van Bömmel F, Berg T. Hepatol Commun, 2021.



%1.7 & %19

FIG. 5. Cumulative HBsAg loss rate in 519 patients with clinical relapse and retreatment (blue line; n = 269) or patients with clinical relapse but no retreatment (yellow line; n = 150). (Adapted from Fig. 3 of Ref. 65.)

AP&T Alimentary Pharmacology and Therapeutics

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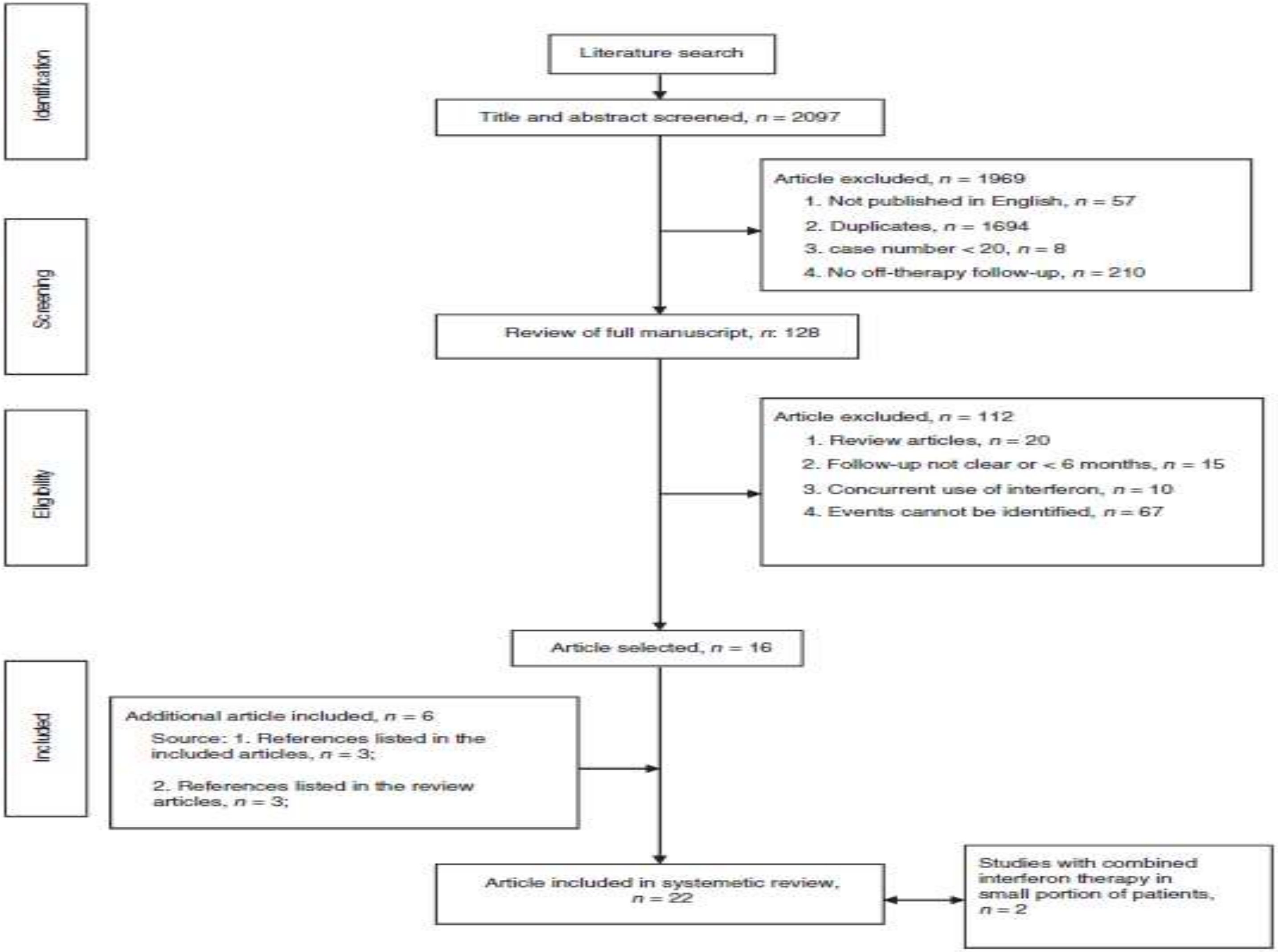

1995-2014 yılları arası taranmış
22 çalışma ve 1732 hasta değerlendirilmiş
LAM, ADV ve ETV alan hastalar

- Tedavi süresi 6 ay-8 yıl
- HBeAg pozitiflerde serokonversiyon sonrası konsolidasyon tedavisi 4-96 hafta
- Tedavi kesildikten sonra takip süresi 6 ay-80 ay

- Tedaviden 1 yıl sonra
  - Virolojik relaps (HBV DNA >2000 IU/mL) oranı %70
  - Klinik relaps (HBV DNA > 2000 IU/mL + ALT yükselmesi) oranı %50
  - Yeniden tedavi %40

- Kısa süreli tedavi, kısa süre konsolidasyon tedavisi ve daha az potent ilaç kullanma relaps ile ilişkili bulunmuş

- Değerlendirilen çalışmaların 11'inde takipte HBsAg klerensi araştırılmış
- 6 çalışmada HBsAg kaybı %0; beşinde tedavi süresi <2 yıl
- HBsAg seroklerensi gösteren çalışmalar için, HBsAg kaybı oranı bir çalışmada 48 haftalık NA tedavisi sırasında %0.4
- Tedavi süresi >2 yıl olan kalan dört çalışmada HBsAg seroklerensi %2 -%42
- İki çalışmada, NA tedavisi kesildiği anda HBsAg <200 IU/mL olması HBsAg kaybı ile ilişkili bulunmuş

Research Article

EASL | JOURNAL OF HEPATOLOGY

Long-term response after stopping tenofovir disoproxil fumarate in non-cirrhotic HBeAg-negative patients – FINITE study☆

Thomas Berg[1,*], Karl-Georg Simon[2], Stefan Mauss[3], Eckart Schott[4], Renate Heyne[5], Dietmar M. Klass[6], Christoph Eisenbach[7], Tania Mara Welzel[8], Reinhart Zachoval[9], Gisela Felten[10], Julian Schulze-zur-Wiesch[11], Markus Cornberg[12], Marjoleine L. Op den Brouw[13], Belinda Jump[14], Hans Reiser[14], Lothar Gallo[15], Tobias Warger[15], Jörg Petersen[16], On behalf of the FINITE CHB study investigators [First investigation in stopping TDF treatment after long-term virological suppression in HBeAg-negative chronic hepatitis B]

[1]Section of Hepatology, Clinic for Gastroenterology and Rheumatology, University Clinic Leipzig, Leipzig, Germany; [2]Gastroentrologische Gemeinschaftspraxis, Leverkusen, Germany; [3]Zentrum für HIV und Hepatogastroenterologie, Düsseldorf, Germany; [4]Charite Universitätsmedizin, Berlin, Germany; [5]Leberzentrum Checkpoint, Berlin, Germany; [6]Klinikum Lüneburg, Lüneburg, Germany; [7]Dept. Gastroenterology, GRN-Klinik Weinheim, Weinheim, Germany; [8]Klinikum der J.W. Goethe-Universität Frankfurt am Main, Germany; [9]Klinikum der Ludwig-Maximilians München University, München, Germany; [10]Gastroenterologische Gemeinschaftspraxis, Herne, Germany; [11]Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany; [12]Hannover Medical School, Hannover; German Center for Infection Research (DZIF), partner site Hannover-Braunschweig, Germany; [13]Gilead Sciences Europe Ltd., Uxbridge, United Kingdom; [14]Gilead Sciences Inc., Foster City, USA; [15]Gilead Sciences, Martinsried, Germany; [16]IFI Institute for Interdisciplinary Medicine at the Asklepios Klinik St. George, University of Hamburg, Hamburg, Germany

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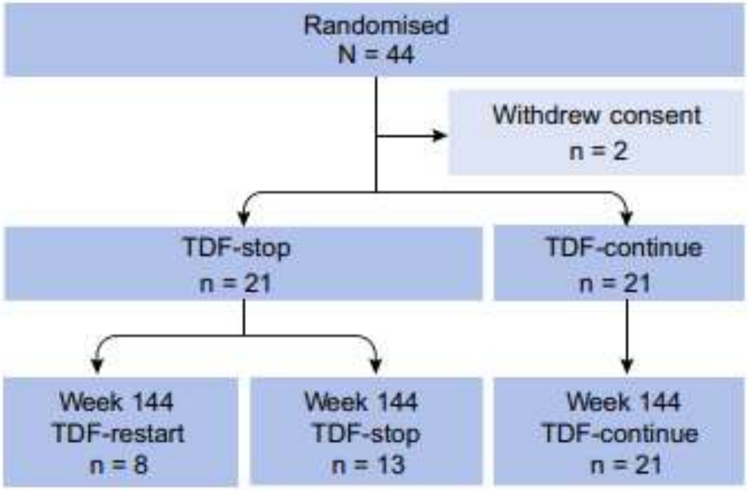


Fig. 1. Patient flow diagram up to Week 144.

En az 4 yıl süreyle TDF alan ve en az 3.5 yıl boyunca virolojik yanıt alınmış olan HBeAg negatif ve sirozu olmayan hastalar

- Tedavi kesilen kolda %14 HBsAg kaybı , tedaviye devam eden kolda 96. haftada bir hastada;%5 HBsAg kaybı

- TDF tedavisi kesilen tüm hastalarda virolojik relaps Takip süresi sonunda tedavisiz takip edilebilen hasta oranı%69
  - %47 HBV DNA saptanamaz düzeyde.

ARTICLE IN PRESS

Research Article
Viral Hepatitis

JOURNAL OF HEPATOLOGY

A multicenter randomized-controlled trial of nucleos(t)ide analogue cessation in HBeAg-negative chronic hepatitis B

Florian van Bömmel[1,*], Kerstin Stein[2], Renate Heyne[3], Jörg Petersen[4], Peter Buggisch[4], Christoph Berg[5], Stefan Zeuzem[6], Andreas Stallmach[7], Martin Sprinzl[8], Eckart Schott[9,10], Anita Pathil-Warth[6,11], Ulrike von Arnim[12], Verena Keitel[12,13], Jürgen Lohmeyer[14], Karl-Georg Simon[15], Christian Trautwein[16], Andreas Trein[17], Dietrich Hüppe[18], Markus Cornberg[19,20], Frank Lammert[19,21], Patrick Ingiliz[22,23], Reinhart Zachoval[24], Holger Hinrichsen[25], Alexander Zipprich[7,26], Hartmuth Klinker[27], Julian Schulze zur Wiesch[28], Anett Schmiedeknecht[29], Oana Brosteanu[29,‡], Thomas Berg[1,‡]

Journal of Hepatology **2023**. vol. ■ | 1–11

- Güncel bir çalışma, prospektif
- En az 4 yıl bir NA tedavisi alan ve 4 yıl sonunda HBV DNA <172 IU/ml hastalar dahil edilmiş.
- Hastaların tümünde tedavi öncesi HBV DNA > 2000 IU/ml ve non sirotik
- Ortalama takip süresi 37 hafta (9-74 hafta)

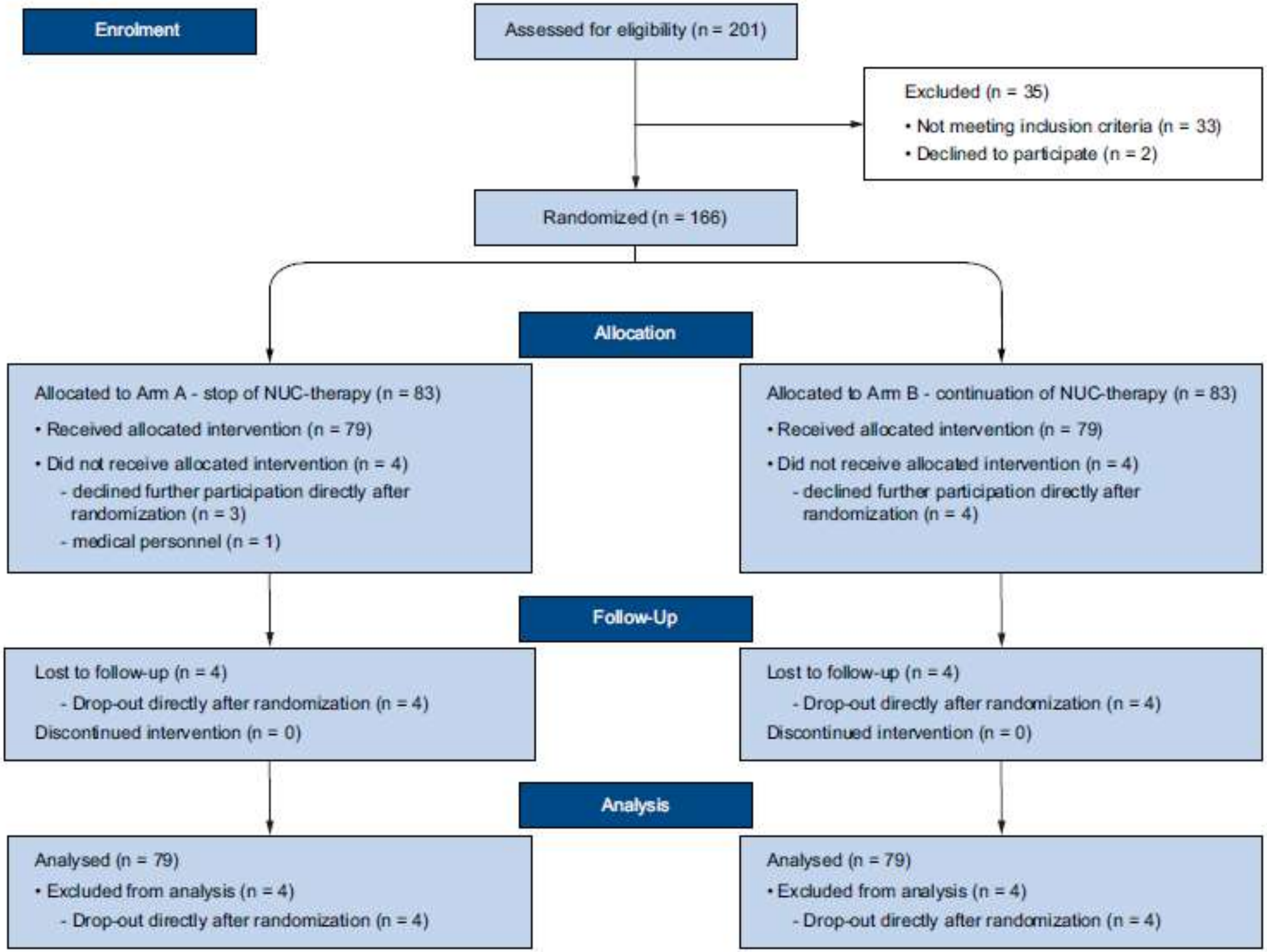
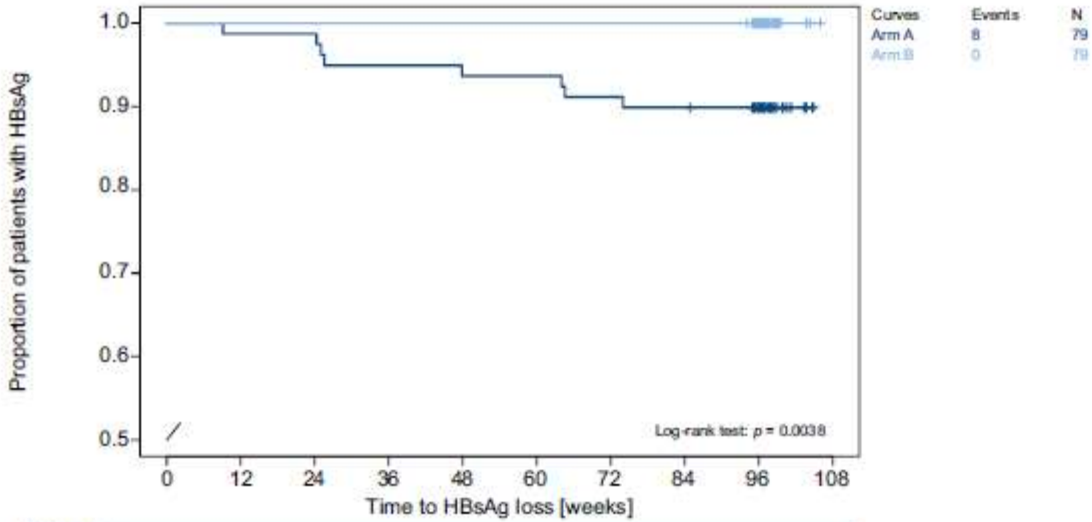


Fig. 1. CONSORT diagram showing enrolment and randomization of patients.

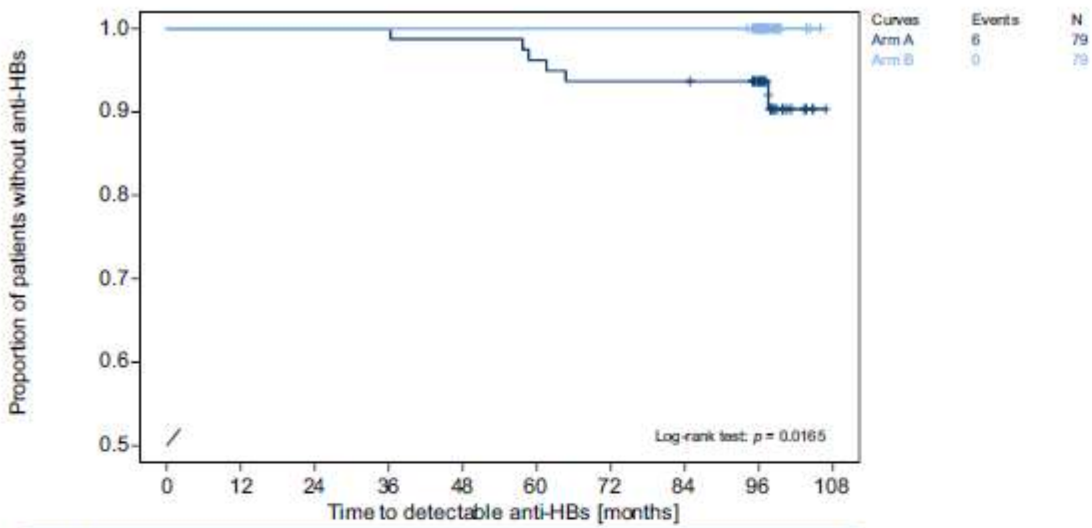
Table 1. Patient characteristics at baseline.

Characteristic	Arm A (n = 79)	Arm B (n = 79)	*p* value[5]
Age, years[1]	53 (28-66)	51 (28-75)	0.964
Female sex, n (%)	29 (36.7)	28 (35.4)	1
Body mass index[1]	26.7 (18.6-36.8)	25.4 (18.3-41.7)	0.205
Ethnicity, n (%)			
Caucasian	62 (78.5)	65 (82.3)	
Asian	9 (11.4)	6 (7.6)	
African	2 (2.5)	5 (6.3)	
Other	6 (7.6)	3 (3.8)	0.398
Duration of HBV infection, years[1]	13.0 (4-52)	13.5 (5-57)	0.744
NUC treatment, n (%)			
Entecavir	27 (34.2)	35 (44.3)	0.428
Tenofovir disoproxil fumarate	44 (55.7)	37 (46.8)	
Lamivudine	2 (2.5)	4 (5.1)	
Telbivudine	6 (7.6)	3 (3.8)	
Log_{10} (HBsAg, IU/ml)[1]	3.2 (-0.9 to 4.4)	3.3 (-0.1 to 4.5)	0.523
HBsAg, n (%)			
<10 IU/ml	3 (3.8)	1 (1.3)	0.733
≥10 IU/ml – <100 IU/ml	7 (8.9)	7 (8.9)	
≥100 IU/ml – <1,000 IU/ml	15 (19.0)	18 (22.8)	
≥1,000 IU/ml	54 (68.4)	53 (67.1)	
ALT, xULN[1,2]	0.6 (0.2-1.3)	0.6 (0.2-1.1)	0.727
Liver elastography, kPa[1,3,4]	5.7 (2.4-10.4)	5.7 (2.3-14.4)	0.644



N° at risk									
Arm A	79	78	78	75	74	74	72	71	61
Arm B	79	79	79	79	79	79	79	79	69

%10.1



N° at risk									
Arm A	79	79	79	79	78	76	74	74	64
Arm B	79	79	79	79	79	79	79	79	69

%7.6

Gastroenterology 2022;162:757–771

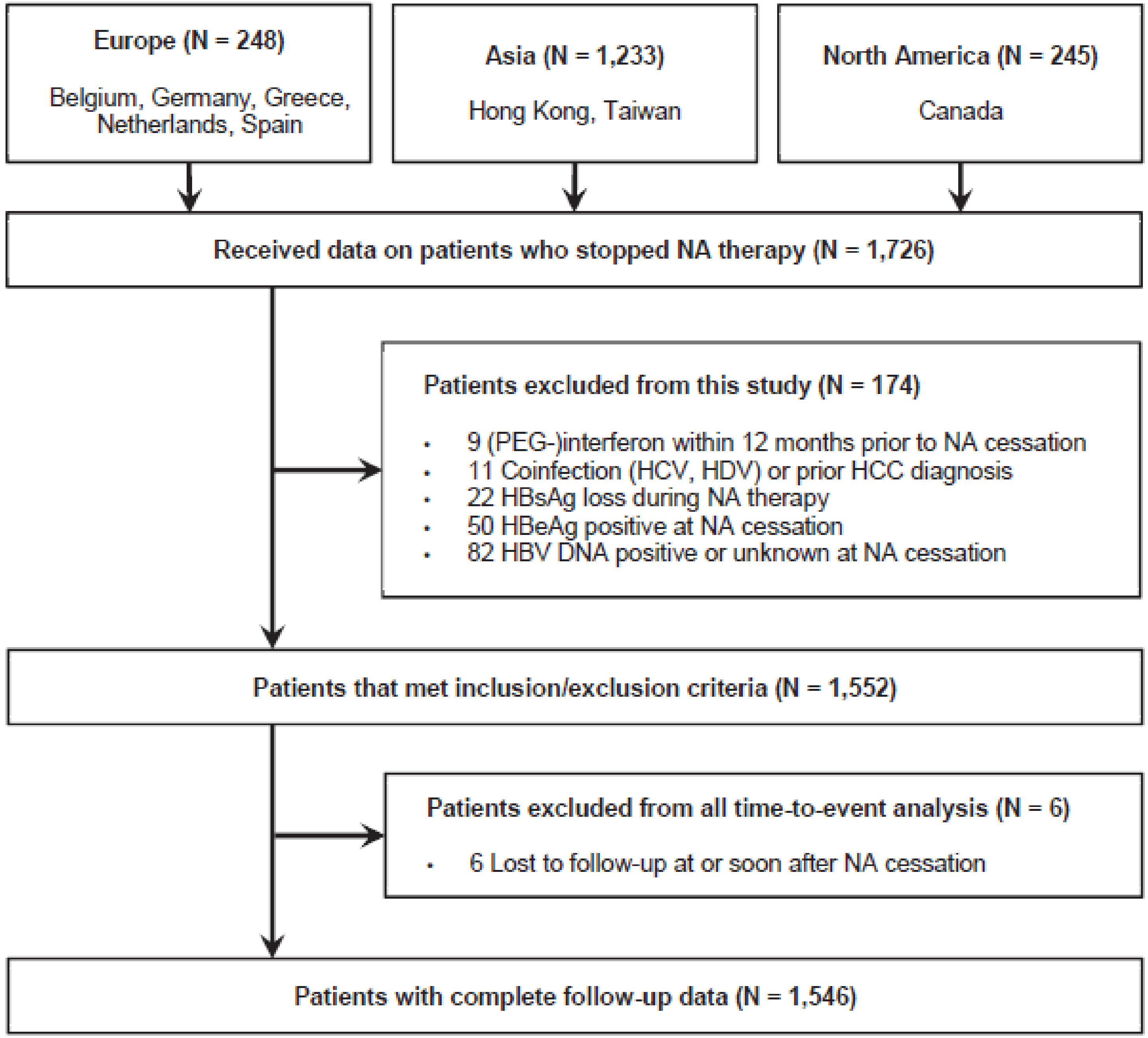
CLINICAL—LIVER

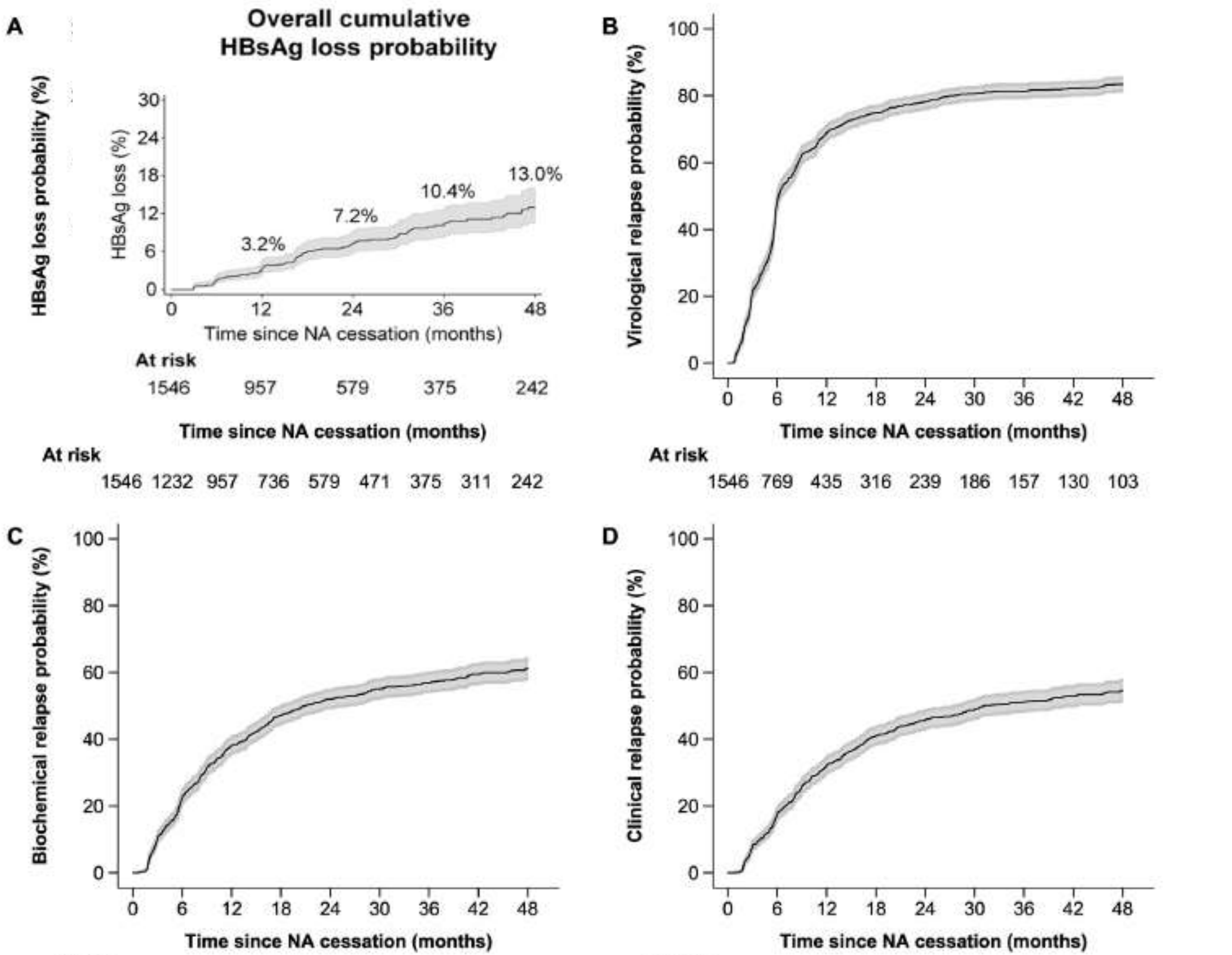
Off-Therapy Response After Nucleos(t)ide Analogue Withdrawal in Patients With Chronic Hepatitis B: An International, Multicenter, Multiethnic Cohort (RETRACT-B Study)

Grishma Hirode,[1,2,3] Hannah S. J. Choi,[1,2] Chien-Hung Chen,[4] Tung-Hung Su,[5] Wai-Kay Seto,[6] Stijn Van Hees,[7] Margarita Papatheodoridi,[8] Sabela Lens,[9] Grace Wong,[10] Sylvia M. Brakenhoff,[11] Rong-Nan Chien,[12] Jordan Feld,[1,2,3] Milan J. Sonneveld,[11] Henry L. Y. Chan,[10] Xavier Forns,[9] George V. Papatheodoridis,[8] Thomas Vanwolleghem,[7] Man-Fung Yuen,[6] Yao-Chun Hsu,[13] Jia-Horng Kao,[5] Markus Cornberg,[14] Bettina E. Hansen,[1,3] Wen-Juei Jeng,[12] and Harry L. A. Janssen,[1,2,3] on Behalf of the RETRACT-B Study Group

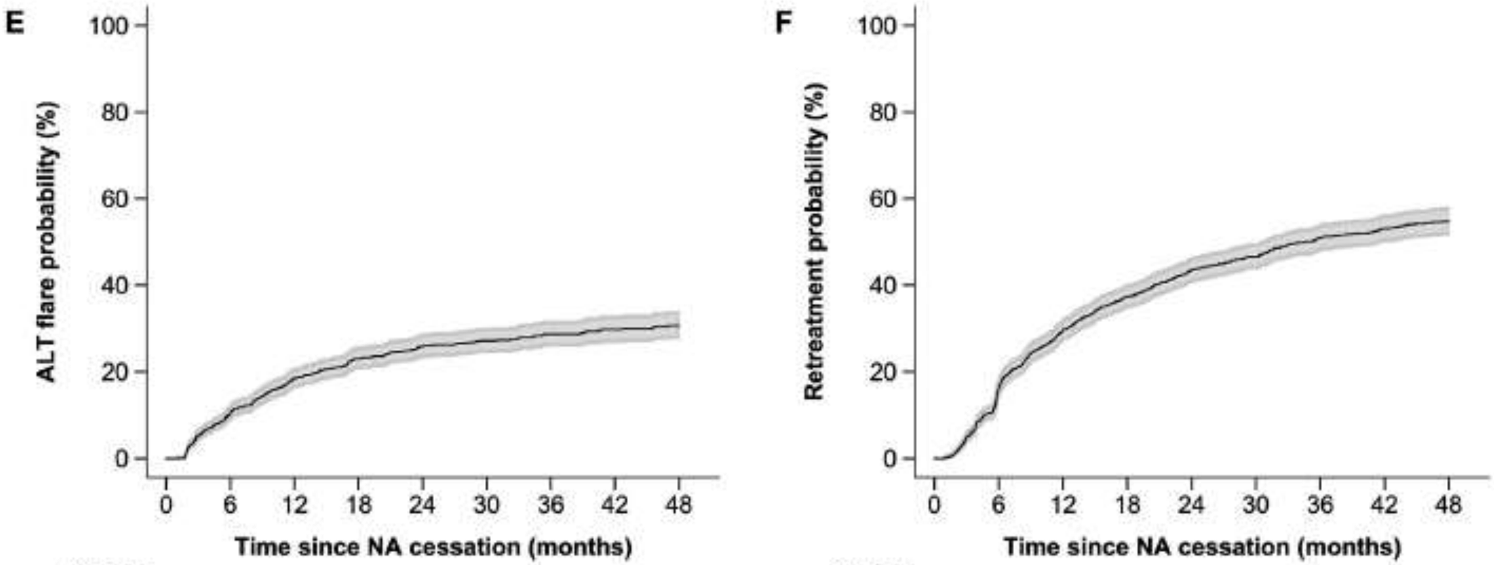
[1]Toronto Centre for Liver Disease, Toronto General Hospital, University Health Network, Toronto, Canada; [2]Institute of Medical Science, University of Toronto, Toronto, Canada; [3]The Toronto Viral Hepatitis Care Network, Toronto, Canada; [4]Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan; [5]National Taiwan University Hospital, Taipei, Taiwan; [6]Department of Medicine and State Key Laboratory of Liver Research, The University of Hong Kong, Hong Kong, Special administrative regions of China; [7]Department of Gastroenterology and Hepatology, Antwerp University Hospital, Antwerp, Belgium; [8]Medical School of National and Kapodistrian University of Athens, Athens, Greece; [9]Hospital Clinic Barcelona, IDIBAPS and CIBEREHD, University of Barcelona, Barcelona, Spain; [10]The Chinese University of Hong Kong, Hong Kong, Special administrative regions of China; [11]Department of Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, the Netherlands; [12]Department of Gastroenterology and Hepatology, Chang Gung Memorial Hospital Linkou Medical Center, Chang Gung University, Linkou, Taiwan; [13]E-Da Hospital/I-Shou University, Kaohsiung, Taiwan; and [14]Department of Gastroenterology, Hepatology and Endocrinology, Hannover Medical School, Germany; Centre for Individualized Infection Medicine, Hannover, Germany

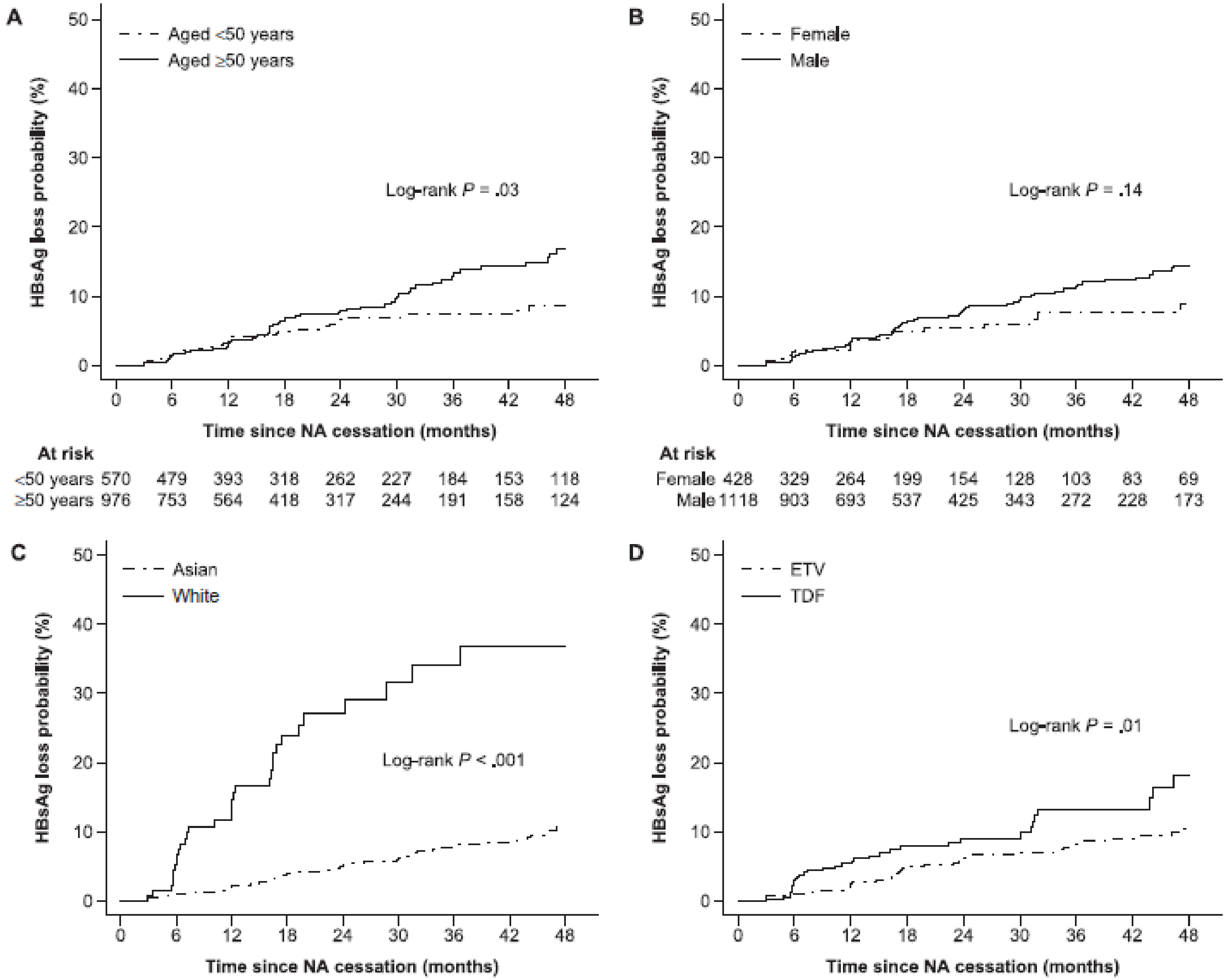
- Prospektif, çok merkezli ve multi-etnik bir çalışma
- HCC ve koinfeksiyonu olanlar ya da tedavi kesilmeden önceki 12 ay içinde IFN almış olanlar çalışma dışı ancak sirotik hastalar dahil edilmiş
- Tedavi kesilip çalışmaya alınan hastaların tamamı, o anda HBeAg negatif olan hastalar


Europe (N = 248)
Belgium, Germany, Greece, Netherlands, Spain
Asia (N = 1,233)
Hong Kong, Taiwan
North America (N = 245)
Canada
Received data on patients who stopped NA therapy (N = 1,726)
Patients excluded from this study (N = 174)
9 (PEG-)interferon within 12 months prior to NA cessation
11 Coinfection (HCV, HDV) or prior HCC diagnosis
22 HBsAg loss during NA therapy
50 HBeAg positive at NA cessation
82 HBV DNA positive or unknown at NA cessation
Patients that met inclusion/exclusion criteria (N = 1,552)
Patients excluded from all time-to-event analysis (N = 6)
6 Lost to follow-up at or soon after NA cessation
Patients with complete follow-up data (N = 1,546)

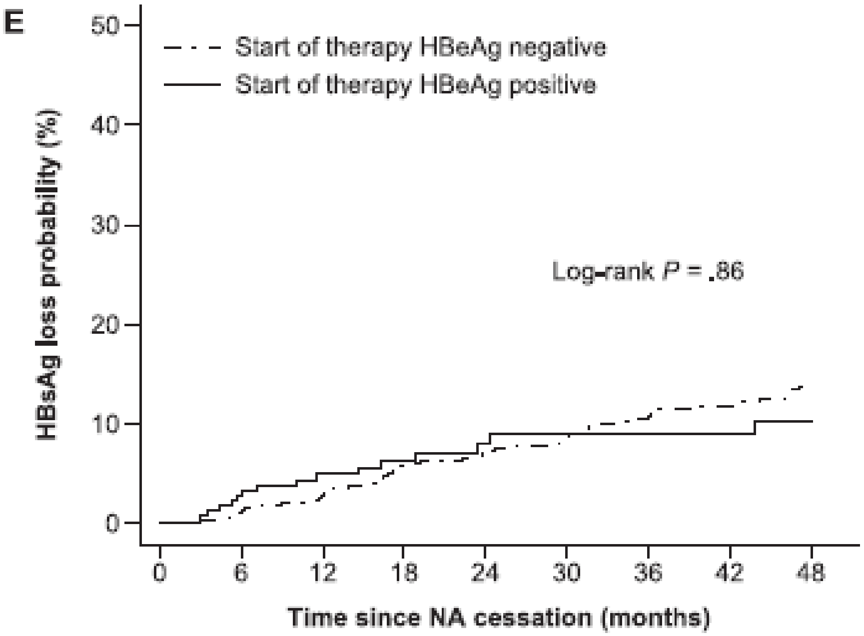


A
Overall cumulative
HBsAg loss probability
HBsAg loss probability (%)
HBsAg loss (%)
30
24
18
12
6
0
3.2%
7.2%
10.4%
13.0%
0
12
24
36
48
Time since NA cessation (months)
At risk
1546 957 579 375 242
Time since NA cessation (months)
At risk
1546 1232 957 736 579 471 375 311 242
B
Virological relapse probability (%)
100
80
60
40
20
0
0 6 12 18 24 30 36 42 48
Time since NA cessation (months)
At risk
1546 769 435 316 239 186 157 130 103
C
Biochemical relapse probability (%)
100
80
60
40
20
0
0 6 12 18 24 30 36 42 48
Time since NA cessation (months)
D
Clinical relapse probability (%)
100
80
60
40
20
0
0 6 12 18 24 30 36 42 48
Time since NA cessation (months)

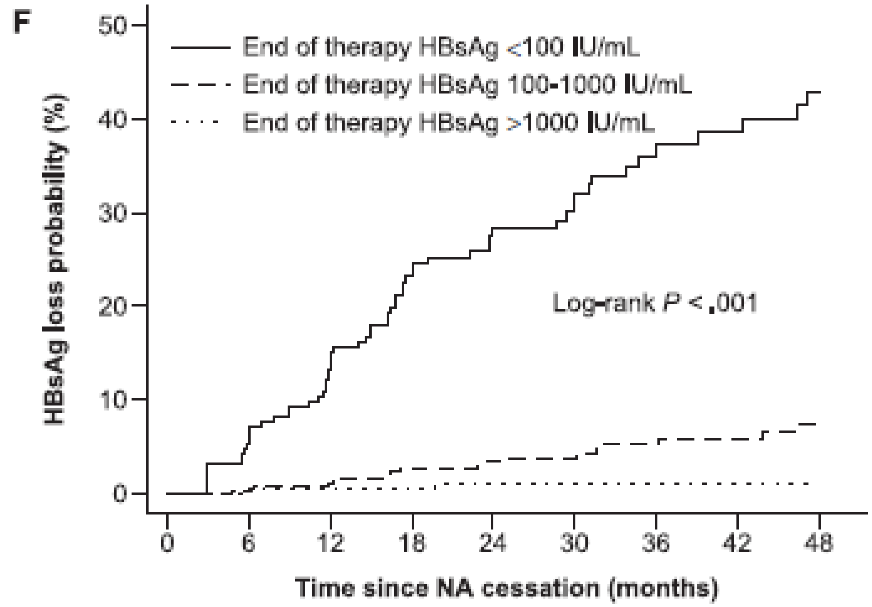

E
F
ALT flare probability (%)
Retreatment probability (%)
100
80
60
40
20
0
0 6 12 18 24 30 36 42 48
Time since NA cessation (months)



A
Aged <50 years
Aged ≥50 years
Log-rank P = .03
HBsAg loss probability (%)
Time since NA cessation (months)
At risk
<50 years 570 479 393 318 262 227 184 153 118
≥50 years 976 753 564 418 317 244 191 158 124
B
Female
Male
Log-rank P = .14
HBsAg loss probability (%)
Time since NA cessation (months)
At risk
Female 428 329 264 199 154 128 103 83 69
Male 1118 903 693 537 425 343 272 228 173
C
Asian
White
Log-rank P < .001
HBsAg loss probability (%)
Time since NA cessation (months)
D
ETV
TDF
Log-rank P = .01
HBsAg loss probability (%)
Time since NA cessation (months)



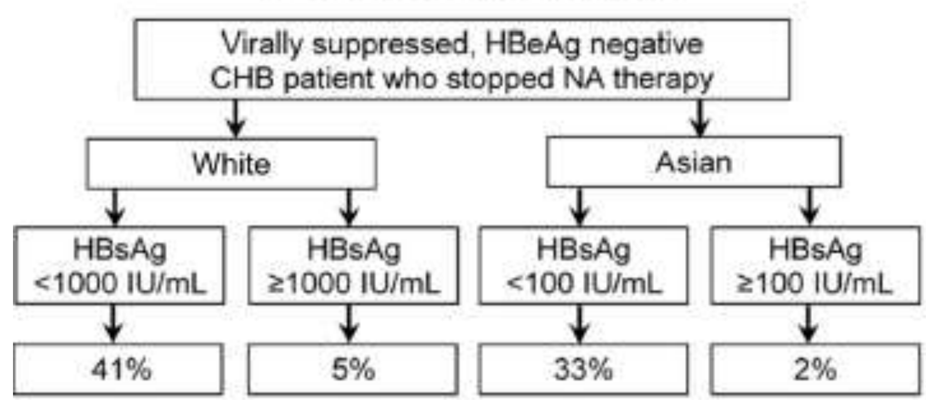
At risk	0	6	12	18	24	30	36	42	48
Negative	1304	1027	797	610	479	380	298	243	187
Positive	231	198	156	122	97	89	75	66	53



At risk	0	6	12	18	24	30	36	42	48
<100	223	190	149	117	95	72	55	45	34
100-1000	682	549	423	327	250	204	164	140	105
>1000	463	344	263	201	158	131	101	77	60

En önemli belirleyici faktör tedavi kesildiği andaki HBsAg kantitasyonu

Predicted 4-year HBsAg loss probability



- Tedavi kesildikten sonra 19 hastada hepatik dekompansasyon gelişmiş
  - Sirotiklerde %4.3 (8/184)
  - Nonsirotiklerde %0.8 (11/1368) *$p < 0,001$*

- Bu hastaların 1/19'unda (%5.3) HBsAg kaybı
- 16/19'unda (%84.2) yeniden tedavi
- 7/19'unda (%36.8) ölüm ; 6'sı yeniden tedaviye başladıktan sonra
  - 4'ünde (%57.1) ölüm hepatit B'ye bağlı alevlenmeden
  - 3'ünde (%42.9) diğer nedenler; 1'i ürosepsis ve septik şok, 1'i lenfoma ve 1'i kolanjiokarsinom

Clinical Microbiology and Infection 24 (2018) 997–1003

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Original article

Long-term incidence and predictors of hepatitis B surface antigen loss after discontinuing nucleoside analogues in noncirrhotic chronic hepatitis B patients

C.-H. Chen*, C.-H. Hung, J.-H. Wang, S.-N. Lu, T.-H. Hu, C.-M. Lee

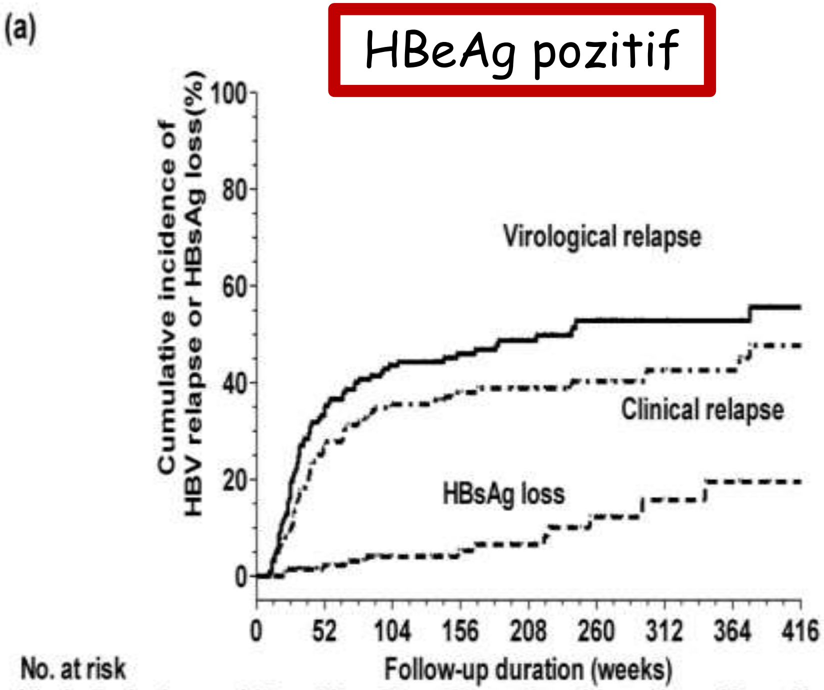
Department of Internal Medicine, Division of Hepatogastroenterology, Kaohsiung Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Taiwan

Table 1
Baseline features of study population

Characteristic	HBeAg positive ($n = 148$)	HBeAg negative ($n = 263$)	p
Age (years)	36.9 ± 10.7	49.7 ± 11.0	<0.001
Sex (male:female)	106:42	214:49	0.022
ALT (U/L)	347 (15–2686)	170 (16–2859)	<0.001
Total bilirubin (mg/dL)	1.1 (0.3–19)	1.1 (0.3–23)	0.69
HBV DNA (log copies/mL)	7.3 ± 1.4	6.3 ± 1.6	<0.001
HBV genotype			<0.001
B	81 (54.7%)	210 (79.8%)	
C	67 (45.3%)	53 (20.2%)	
Treatment duration (weeks) (range)	142.6 ± 59.7 (52–409)	152.9 ± 49.8 (76–346)	0.062
LAM vs. ETV	52:96	58:205	0.004
NA-naive status	126 (85.1%)	218 (82.9%)	0.55
HBsAg at baseline (log IU/mL)	3.71 ± 0.76	3.05 ± 0.88	<0.001
HBsAg at 12 months	3.12 ± 0.63	2.70 ± 0.75	<0.001
HBsAg at end of treatment (log IU/mL)	3.02 ± 0.76	2.54 ± 0.88	<0.001

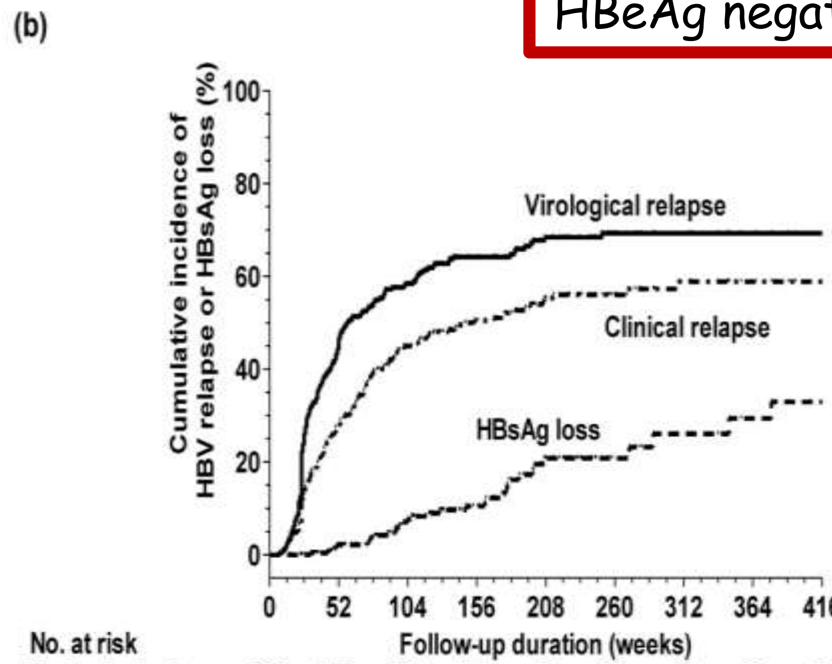
Data are presented as median (range) or mean ± standard deviation unless otherwise indicated.
ALT, alanine aminotransferase; ETV, entecavir; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; LAM, lamivudine.

HBeAg pozitif



No. at risk									
Virological relapse	148	98	78	63	49	31	19	18	13
Clinical relapse	148	107	90	72	58	40	24	23	18
HBsAg loss	148	118	96	78	61	39	23	21	18

HBeAg negatif



No. at risk									
Virological relapse	263	146	101	71	47	29	19	13	9
Clinical relapse	263	189	130	97	64	38	26	19	14
HBsAg loss	263	219	152	108	61	34	26	20	16

The cumulative incidences of virologic relapse at 1, 3, 5 and 8 years were 35.2%, 45.8%, 52.8% and 55.6%, while the clinical relapse rates were 27.1%, 38%, 40.3% and 47.7%, respectively.

HBsAg loss at 1, 3, 5 and 8 years were 2.2%, 5.2%, 12.2% and 19.6%, while those of anti-HBs seroconversion were 1.5%, 3.5%, 6.3% and 16.5%, respectively.

The cumulative incidences of virologic relapse at 1, 3, 5 and 8 years were 46.8%, 64.2%, 69.3% and 69.3%, while the clinical relapse rates were 27.8%, 50.5%, 56.0% and 58.9%, respectively.

HBsAg loss at 1, 3, 5 and 8 years were 2.2%, 10.5%, 20.8% and 33.1%, and those of HBsAg seroconversion were 0%, 4.2%, 11.3% and 21.2%, respectively.

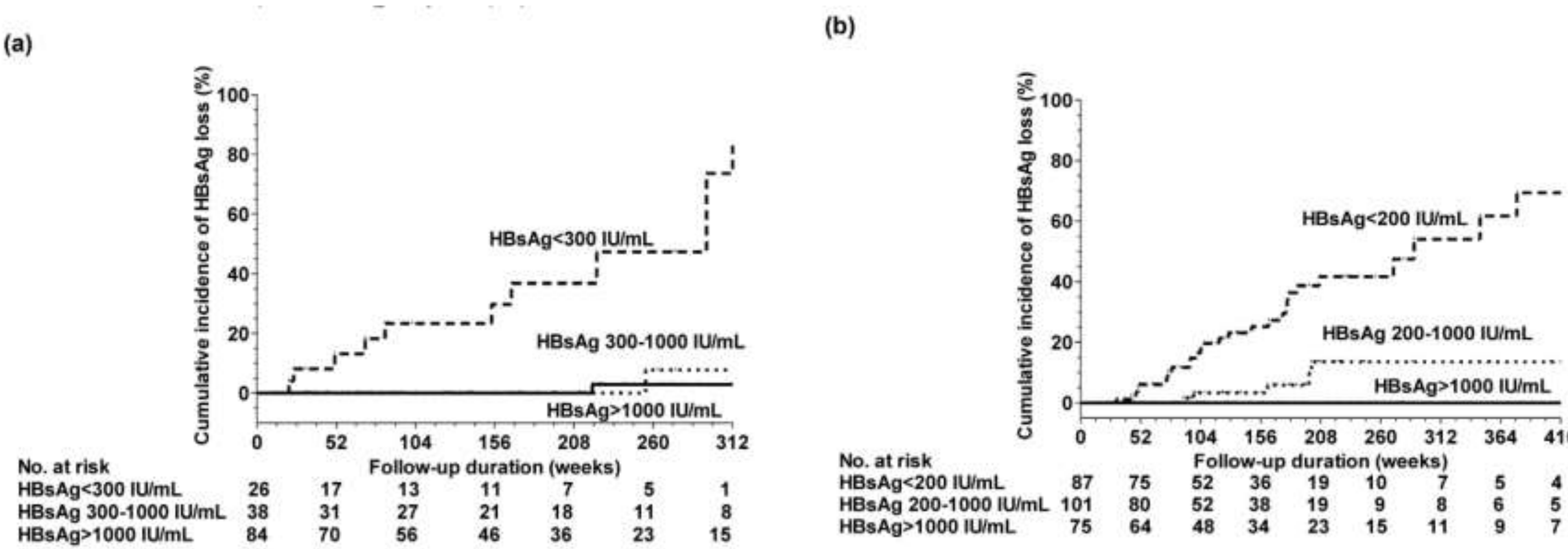


Fig. 2. Cumulative incidence of HBsAg loss according to end-of-treatment HBsAg levels in (a) HBeAg-positive and (b) HBeAg-negative patients. HBeAg, hepatitis B e antigen.

Table 3
Factors predictive of HBsAg loss for HBeAg-negative patients

Variable	Comparison	Univariate analysis		Multivariate analysis	
		HR (95% CI)	p	HR (95% CI)	p
Age (years)	Increase per year	1.02 (0.99–1.05)	0.19		
Sex	Male vs. female	1.67 (0.64–4.32)	0.29		
ALT (U/L)	Increase per U/L	0.999 (0.999–1.000)	0.17		
Total bilirubin	Increase per mg/dL	0.95 (0.84–1.06)	0.34		
HBV DNA	Increase per log copies/mL	0.81 (0.67–0.99)	0.038		
HBV genotype	C vs. B	1.23 (0.57–2.63)	0.50	3.41 (1.50–7.72)	0.003
Antiviral agents	ETV vs. LAM	0.95 (0.44–2.02)	0.89		
NA-naive status	Yes vs. no	0.35 (0.17–0.75)	0.007		
HBsAg at baseline	Increase per log IU/L	0.52 (0.37–0.74)	<0.001		
HBsAg at 12 months	Increase per log IU/L	0.29 (0.20–0.42)	<0.001		
HBsAg at the end of treatment	Increase per log IU/L	0.28 (0.20–0.38)	<0.001	0.24 (0.17–0.34)	<0.001
HBsAg decline from baseline to end of treatment	Increase per log IU/L	2.27 (1.63–3.15)	<0.001		
Treatment duration	Increase per week	1.006 (0.999–1.012)	0.081		
Consolidation duration	Increase per week	1.006 (0.998–1.011)	0.138		

ALT, alanine aminotransferase; CI, confidence interval; ETV, entecavir; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HR, hazard ratio; LAM, lamivudine; NA, nucleoside analogue.

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The role of hepatitis B virus core-related antigen in predicting hepatitis B virus relapse after cessation of entecavir in hepatitis B e antigen-negative patients

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Affiliations + expand

PMID: 33932245 DOI: 10.1111/jvh.13528

- ETV yanıtlı, tedavi en az 12 ay kesilmiş nonsirotik 301 HBeAg negatif hasta
- APASL 2012 kılavuzunun önerdiği tedavi kesme kriterleri kullanılmış

- Beş yıllık takipe
  - Virolojik relaps %71.6, klinik relaps %57.3, HBsAg kaybı %18.7

- Tedavi kesildiği andaki serum HBsAg düzeyi; relaps ve HBsAg kaybı için en önemli prediktör
  - Optimal eşik değer 150 IU/ml
    - HBsAg <150 ve ≥150 IU/ml olan hastalarda 5 yıllık
      - Virolojik nüks oranları %43.3 ve %82.2 *p<0.001*
      - Klinik nüks oranları %32.3 ve %66.3 *p<0.001*
      - HBsAg kayıp oranları %46.1 ve %5.2 *p<0.001*
- HBcrAg için eşik değer 4 IU/ml ancak HBsAg <150 IU/ml olan hastalar için; ≤4 ve >4 log U/ml olan hastalarda
  - 5 yıllık virolojik relaps %27.9 ve %59.1 *p=0.006* klinik relaps %18 ve %48.1 *p=0.014*

Tedavi kesme kararında işe yarayacak sonuç öngördürücü faktörler

- Yaş, etnik köken ??
- Sirozun olmaması
- Tedavi süresi

- HBV genotipi ??
- HBsAg serum düzeyi
- **HBcrAg serum düzeyi ?**
- **HBV RNA serum ve intrahepatik düzeyi ??**

Tedavi kesildikten sonra alevlenme olursa tedavi ne zaman yeniden başlanmalı?

- En az iki laboratuvar testinde gösterilmiş direkt bilirubin ve ALT yüksekliği bir arada ise
- PT ≥ 2.0 dk ve ALT yüksekliği bir arada ise
- Hasta semptomatik olsun ya da olmasın 10 kattan fazla ALT yüksekliği
- ALT 2-5 kat yüksek ve birlikte HBV-DNA relapsı ≥ 20,000 kopya/mL ve bu yükseklikler ≥ 84 gün (12 hafta) boyunca sebat ediyorsa.
- ALT normalin 5-10 katı yüksek ve bu yükseklik ≥ 28 gün (4 hafta) boyunca sebat ediyorsa

van Bömmel F, Berg T. Hepatol Commun, 2021.

BİZİM HASTALARIMIZ

	cinsiyet	yaş	HBeAg	İlaç	Tedavi süresi (ay)	Takip süresi (ay)	VR (ay)	BR	HBsAg negatifleşmesi
1	K	38	**pozitif**	LAM TDF	50 72	28	3	-	24 ay
2	E	55	negatif	TDF	110	52	6	-	48 ay
3	K	61	negatif	TDF	85	48	3	-	-
4	K	50	negatif	ETV	120	12 - sonrası takipsiz	-	-	-
5	K	50	negatif	ETV	83	18	6	-	-
6	E	43	negatif	ETV	115	24	3	-	18 ay
7	K	46	negatif	TDF	58	12	-	-	12 ay
8	K	40	negatif	TDF	72	36	3	-	-
9	E	32	**pozitif**	TDF	64	48	3	-	-
10	K	52	negatif	LAM	139	48	7	-	40 ay - 44 ayda anti-HBs pozitif

ÖZETLE…

- Uzun süreli virolojik baskılanma sağlanmış NA tedavisi alan KHB hastalarında antiviral tedavi kesilebilir.

- Tedavinin kesilmesi HBsAg serokonversiyon şansını arttırır.

- Ancak hastalar özellikle ilk 6 ay yakından izlenmeli, yeniden tedavi kararı verirken hasta özelinde değerlendirme yapılmalıdır.

TEŞEKKÜR EDERİM