VİRAL HEPATİT YÖNETİMİ

TEDAVİYİ KESEBİLİR MİYİM?

Ediz Tütüncü

12. Türkiye EKMUD Bilimsel Kongresi
18 Mayıs 2024, Antalya

The Natural History of Chronic Hepatitis B Virus Infection

Brian J. McMahon

Kronik hepatit B enfeksiyonunun iki önemli sonucu siroz ve HCC, karaciğer ilişkili ölümlere neden oluyor.

McMahon BJ. Hepatology 2009;49:S45

< Previous Article

Journal of Hepatology
Volume 45, Issue 4, Pages 529–538, October 2006

Next Article >

The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide☆

Joseph F. Perz, Gregory L. Armstrong, Leigh A. Farrington, Yvan J.F. Hutin, Beth P. Bell

Received: January 9, 2006; Received in revised form: May 3, 2006; Accepted: May 16, 2006; Published Online: June 23, 2006

DOI: http://dx.doi.org/10.1016/j.jhep.2006.05.013

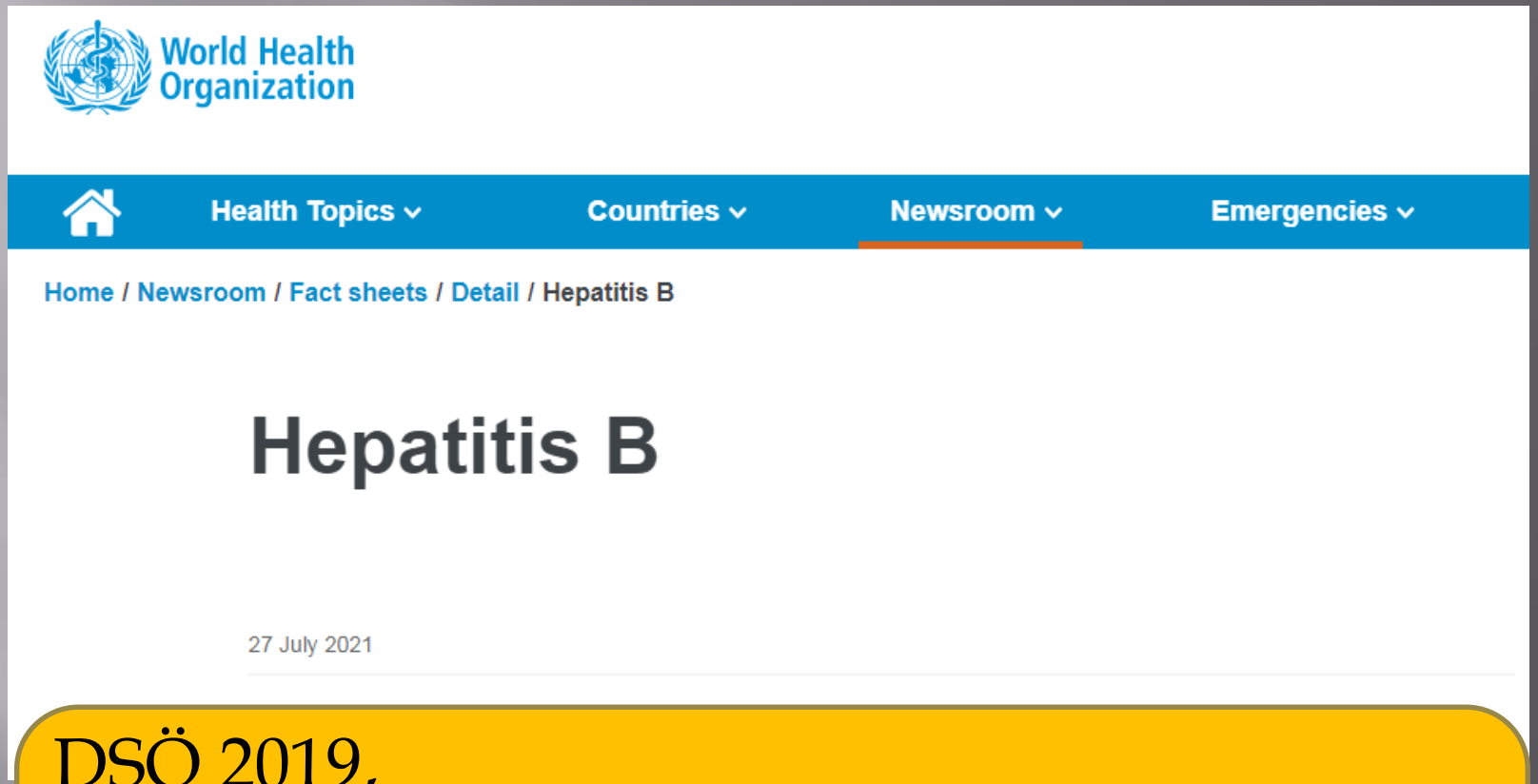
Global olarak,

Siroz olgularının %30,

HCC olgularının %53'ü

HBV ile ilişkilidir.

Perz JF. J Hepatol 2006;45:529



DSÖ 2019,

1,5 milyon yeni olgu/yıl
296 milyon kronik hepatit B
820000 ölüm

https://www.who.int/news-room/fact-sheets/detail/hepatitis-b

Hastalığın spektrumu değişkenlik gösterir

Hastalığın doğal seyri ile ilişkili faktörler

Konak

- erkek cinsiyet,
- ileri yaş,
- sürekli yüksek ALT düzeyleri ya da rekürren alevlenmeler,
- siroz,
- diyabet,
- HCV, HDV, HIV koinfeksiyonları,
- obesite

Viral

- HBeAg varlığı,
- sürekli yüksek HBV DNA varlığı,
- HBV genotipi (C>B),
- core promoter mutasyonları,

Çevresel

- alkol, sigara,
- aflatoksin

Clinical Practice Guidelines

EASL JOURNAL OF HEPATOLOGY

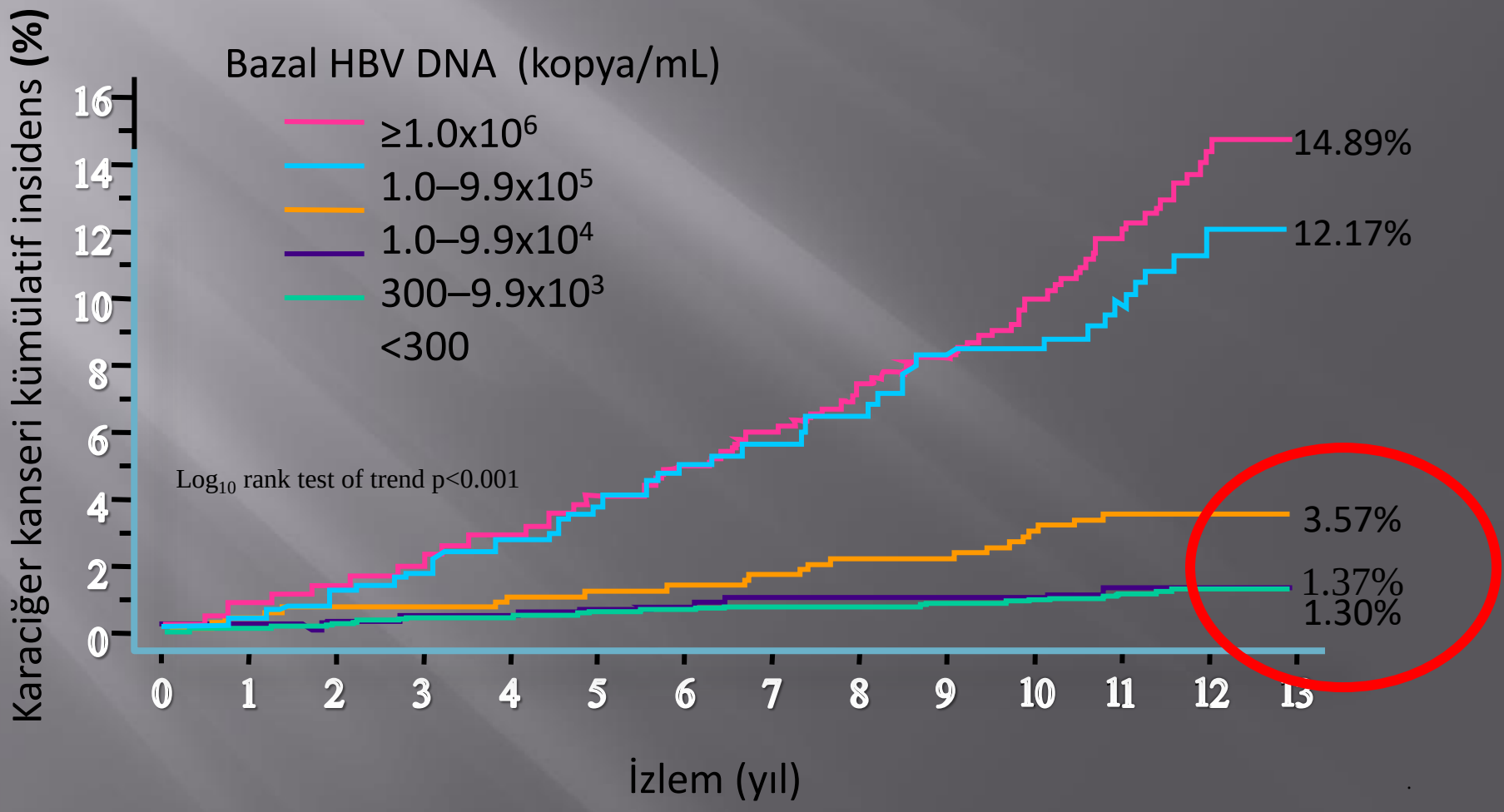
EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection☆

European Association for the Study of the Liver*

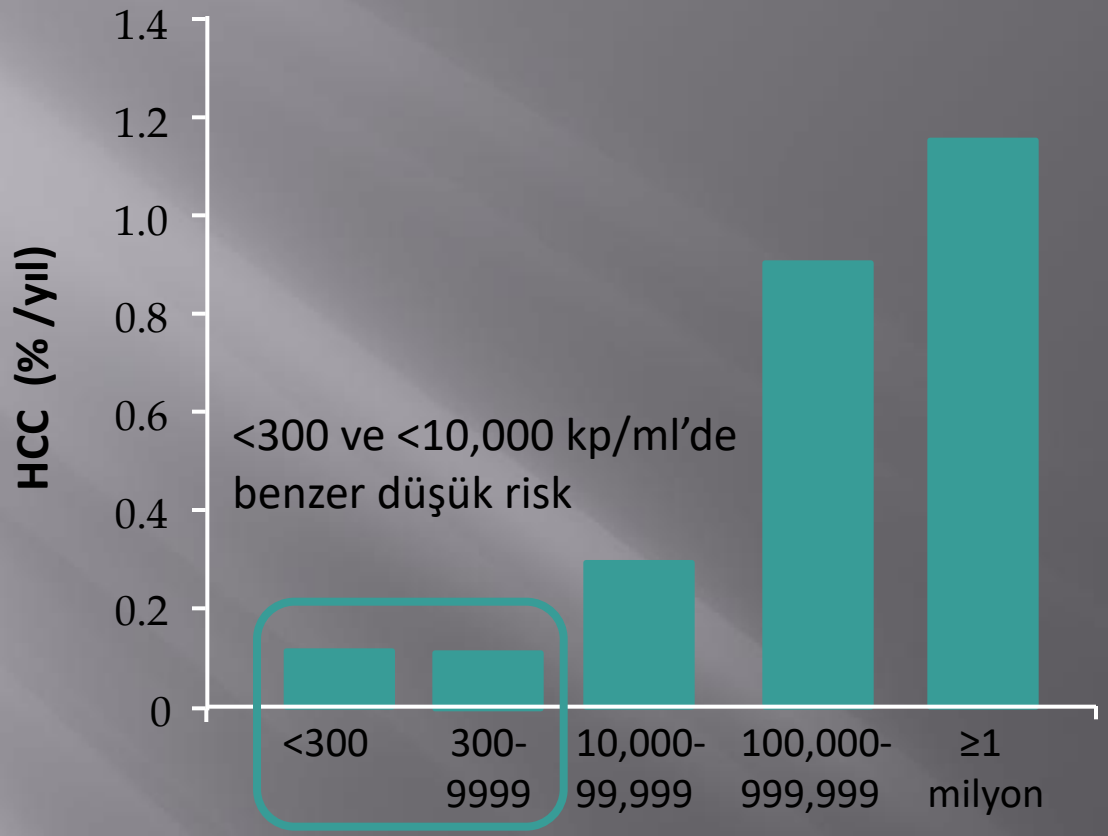
Kronik HBV enfeksiyonun uzun dönem sonuçları ve hastalık progresyonu ile en yakından ilişkili gösterge HBV replikasyonunun düzeyidir.

EASL CPG. J Hepatol 2017;67:370

Yüksek Bazal HBV DNA Düzeyleri ve HCC Gelişimi REVEAL (n=3,653)



Chen CJ et al. JAMA 2006;295:65



HBV DNA <10,000 kopya/ml olması HCC riskinin düşük olmasıyla ilişkilidir.

Chen CJ et al. JAMA 2006;295:65

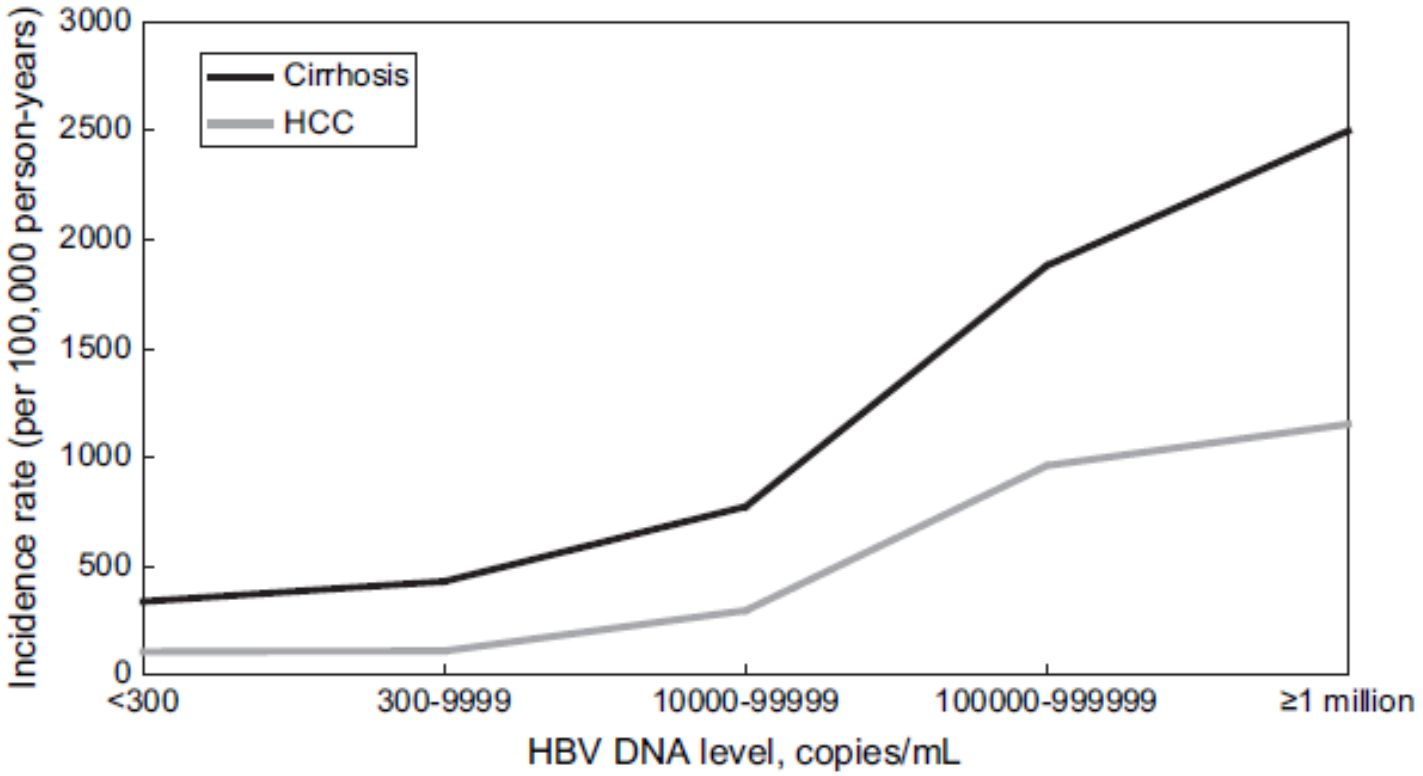
ELSEVIER
SAUNDERS

CLINICS IN
LIVER DISEASE

Clin Liver Dis 11 (2007) 797–816

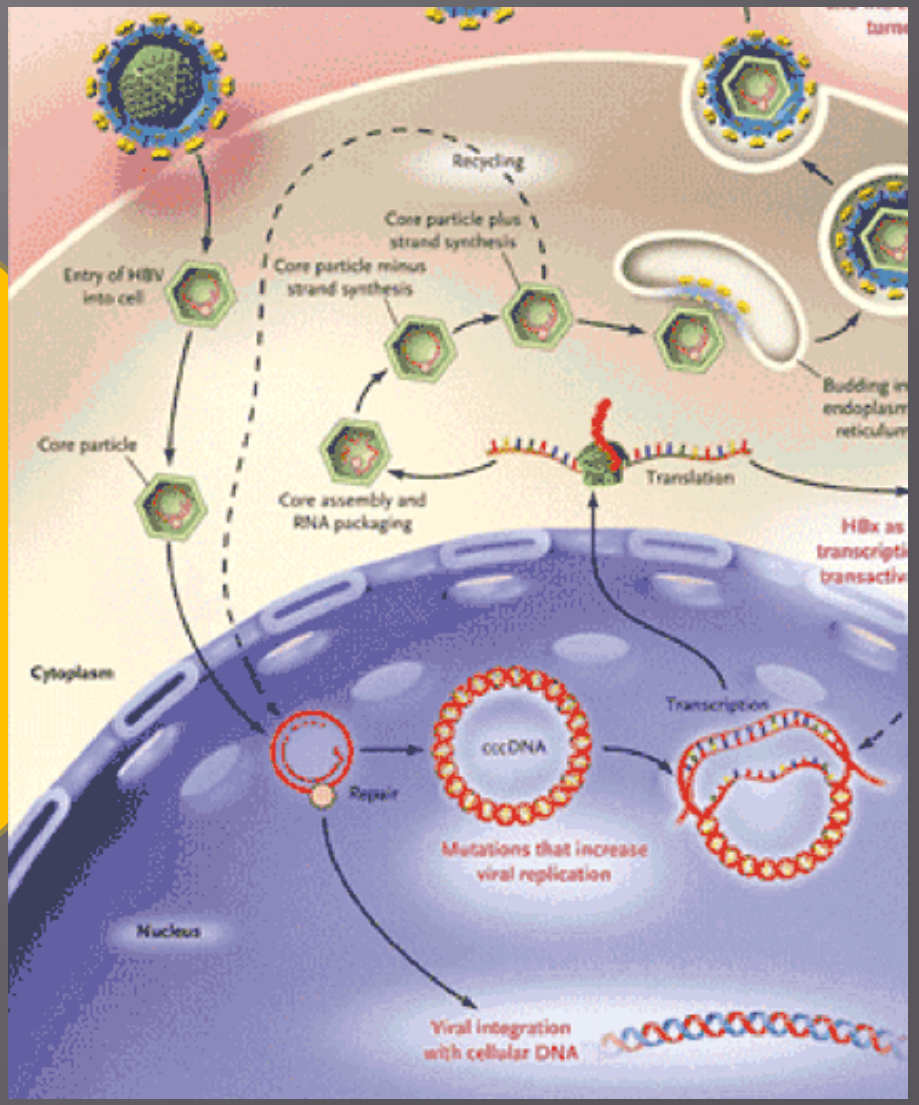
Long-Term Outcomes in Hepatitis B: The REVEAL-HBV Study

Chien-Jen Chen, ScD[a,b,*], Hochenna H. Iloeje, MD, MPH[c]

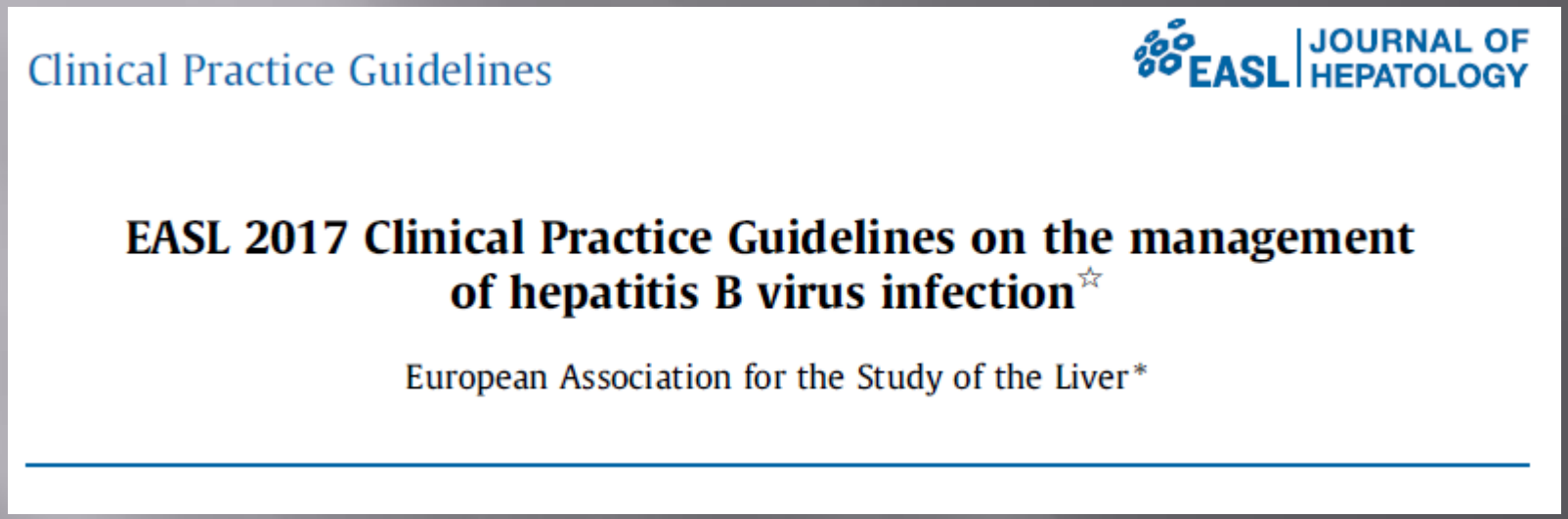


2007;11:797

Enfekte hepatositlerin nükleusundaki cccDNA nedeniyle, HBV enfeksiyonunun tam anlamıyla eradikasyonu olanaklı değildir.



Tedavinin amacı



Hastalığın siroz, dekompanse siroz, son dönem karaciğer yetmezliği, HCC ve ölüme ilerlemesine engel olarak yaşam kalitesini ve sağkalımı arttırmak.

EASL CPG. J Hepatol 2017;67:370

“HBV replikasyonu kalıcı biçimde baskılanabilirse, eşlik eden histolojik aktivitedeki azalma siroz ve HCC riskini azaltacaktır.”

Clinical Practice Guidelines

EASL | JOURNAL OF HEPATOLOGY

EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection☆

European Association for the Study of the Liver*

Tedavi

Viral baskılanma

Biyokimyasal iyileşme

Histolojik düzelme

Komplikasyonlar ↓

EASL CPG. J Hepatol 2017;67:370

Clinical Practice Guidelines

EASL JOURNAL OF HEPATOLOGY

EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection☆

European Association for the Study of the Liver*

İdeal sonlanım noktası HBsAg kaybı
"Fonksiyonel kür"

EASL CPG. J Hepatol 2017;67:370

Table 1 | Response rates (%) to approved therapies for HBeAg-positive and HBeAg-negative chronic hepatitis B

Treatment response parameters	Approved therapies						
	Lamivudine	Adefovir dipivoxil	Entecavir	Telbivudine	Tenofovir disoproxil	PEG-IFN*	PEG-IFN plus lamivudine*
HBeAg-positive patients at week 48 or 52							
Histologic improvement‡	49–62	53–68	72	65	74	38	41
Undetectable HBV DNA	40–44	21	67	60	76	25	69
HBeAg seroconversion	16–21	12	21	22	21	27	24
HBsAg loss	<1	0	2	0	3	3	3
HBeAg-positive patients during extended treatment§							
Undetectable HBV DNA	NA	39(5.0)	94(5.0)	79(4.0)	77(4.0)	13‖ (4.5)	26‖ (4.5)
HBeAg seroconversion	47 (3.0)	48 (5.0)	41 (5.0)	42 (4.0)	31 (3.0)	37‖ (4.5)	36‖ (4.5)
HBsAg loss	0–3 (2.0–3.0)	2(5.0)	5 (2.0)	1 (2.0)	10 (4.0)	8‖ (4.5)	15‖ (4.5)
HBeAg-negative patients at week 48 or 52							
Histologic improvement‡	60–66	64–69	70	67	72	48	38
Undetectable HBV DNA	60–73	51	90	88	93	63	87
HBsAg loss	<1	NA	<1	<1	0	4	3
HBeAg-negative patients during extended treatment§							
Undetectable HBV DNA	6 (4.0)	67 (5.0)	NA	84(4.0)	86(3.0)	18‖ (4.0)	13‖ (4.0)
HBsAg loss	<1 (4.0)	5 (5.0)	NA	<1 (2.0)	0 (4.0)	8‖ (4.0)	8‖ (4.0)

Kwon H et al. Nat Rev Gastroent Hepatol 2011;8:275

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EASL JOURNAL OF HEPATOLOGY

EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection☆

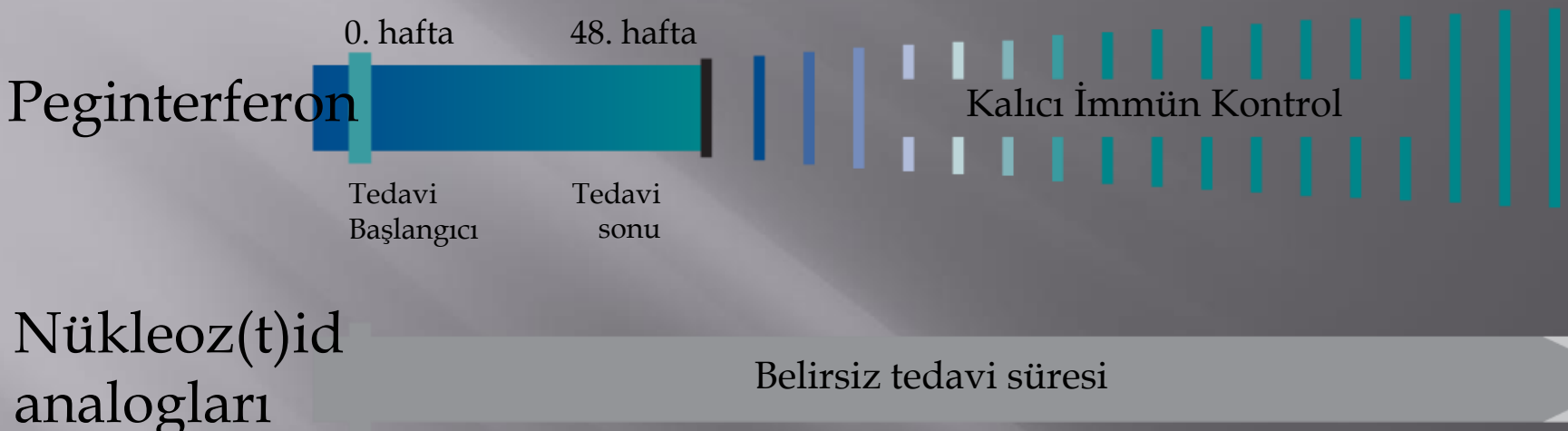
European Association for the Study of the Liver*

İdeal sonlanım noktası HBsAg kaybı

Tedavi sonrası kalıcı virolojik yanıt

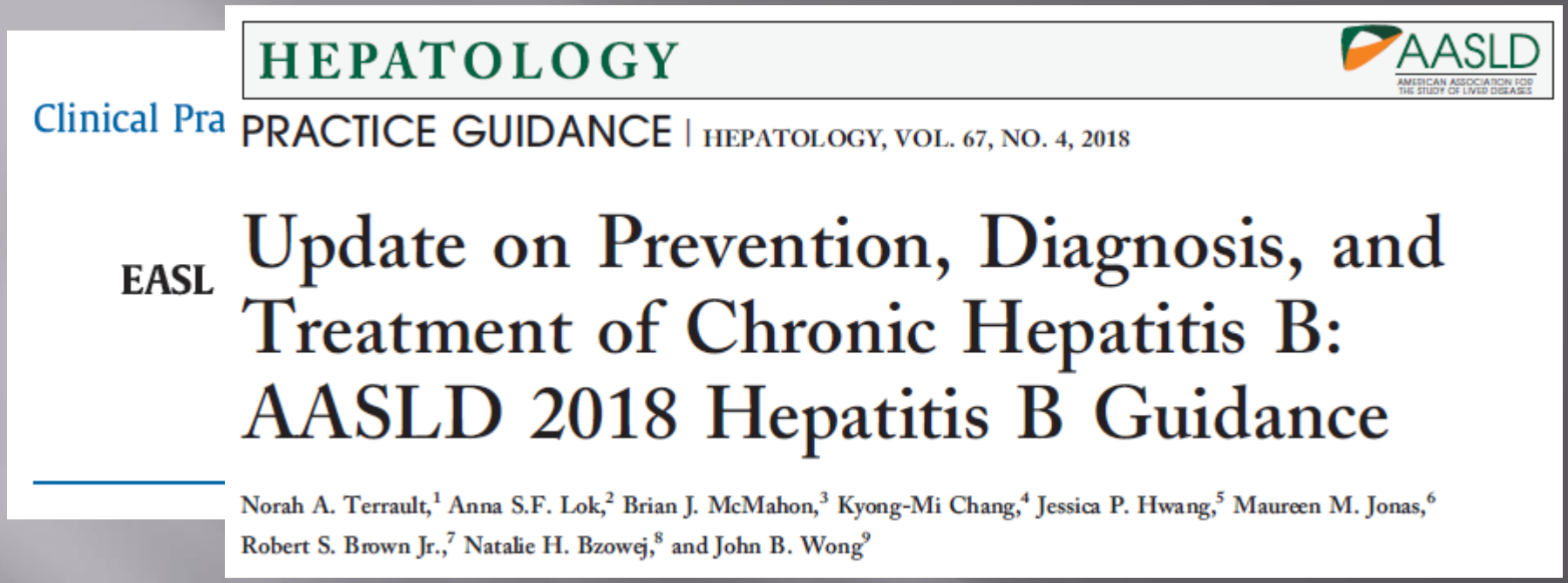
Tedavi altında sürdürülebilir viral baskılanma

EASL CPG. J Hepatol 2017;67:370



PEG IFN ya da NA ile süresi belirli tedavi

NA ile uzun süreli tedavi



Kronik hepatit B tedavisinde tercih edilmesi önerilen seçenekler

PEG-IFN, ETV, TDF, TAF

Terrault NA et al. Hepatology 2018;67:1560

EASL CPG. J Hepatol 2017;67:370

NAs

Etkin viral baskılanma

Optimal direnç profili

Etkinlik/Direnç
NAs

J Gastroenterol (2019) 54:182–193
https://doi.org/10.1007/s00535-018-1502-y

The Japanese Society of Gastroenterology

CrossMark

ORIGINAL ARTICLE—LIVER, PANCREAS, AND BILIARY TRACT

Long-term outcome of entecavir treatment of nucleos(t)ide analogue-naïve chronic hepatitis B patients in Japan

Fumitaka Suzuki[1,2] · Tetsuya Hosaka[1] · Yoshiyuki Suzuki[1] · Hitomi Sezaki[1] · Norio Akuta[1] · Shunichiro Fujiyama[1] · Yusuke Kawamura[1] · Masahiro Kobayashi[1] · Satoshi Saitoh[1] · Yasuji Arase[1] · Kenji Ikeda[1] · Mariko Kobayashi[3] · Rie Mineta[3] · Yukiko Suzuki[3] · Hiromitsu Kumada[1]

1094 naiv KHB hastası, 10 yıllık ETV etkinliği

%42 HBeAg pozitif,

%23 sirotik

Suzuki F et al. J Gastroenterol 2019;54:182

J Gastroenterol (2019) 54:182–193
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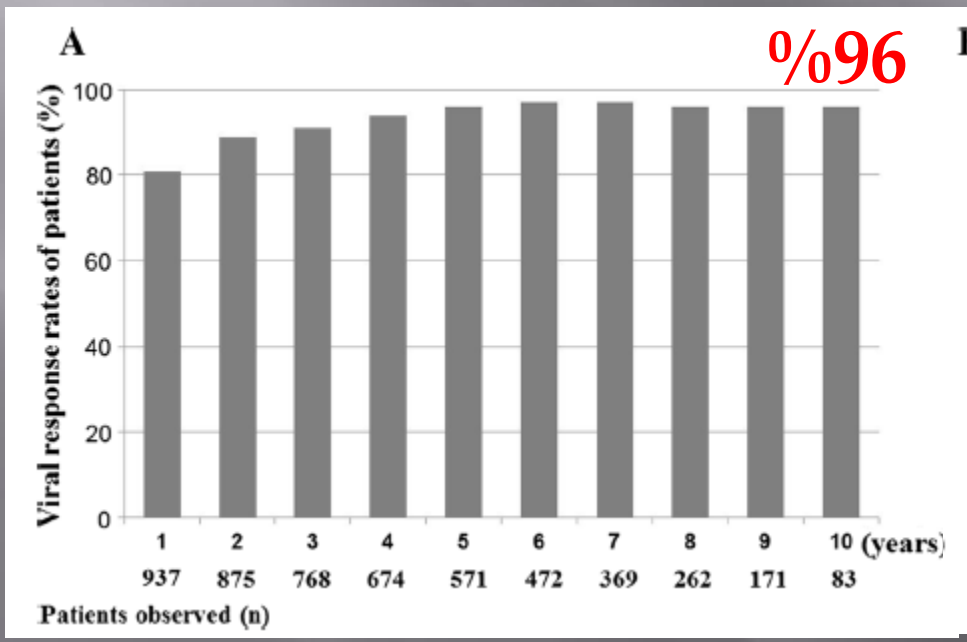

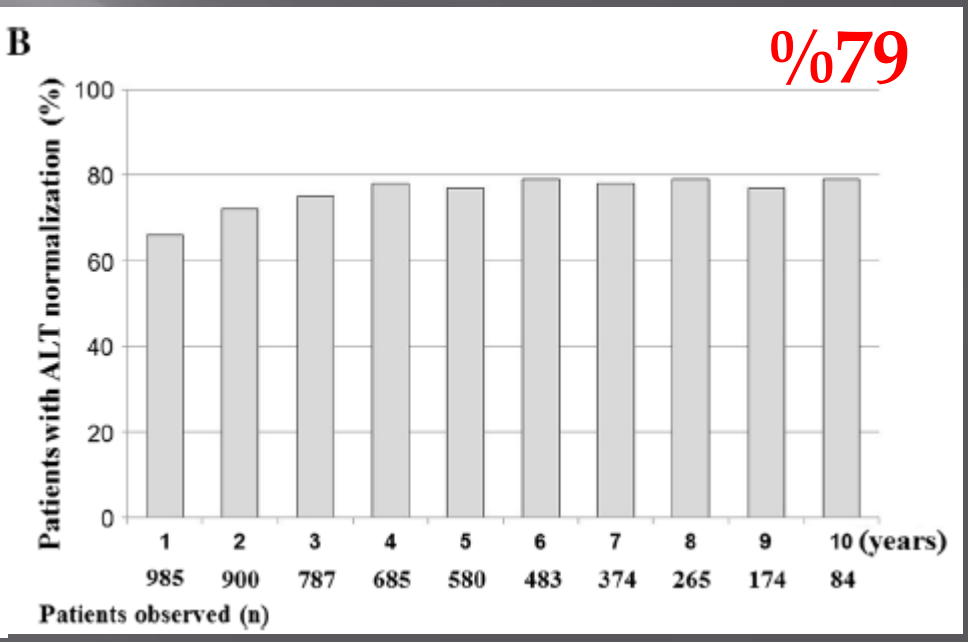

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J Gastroenterol (2019) 54:182–193
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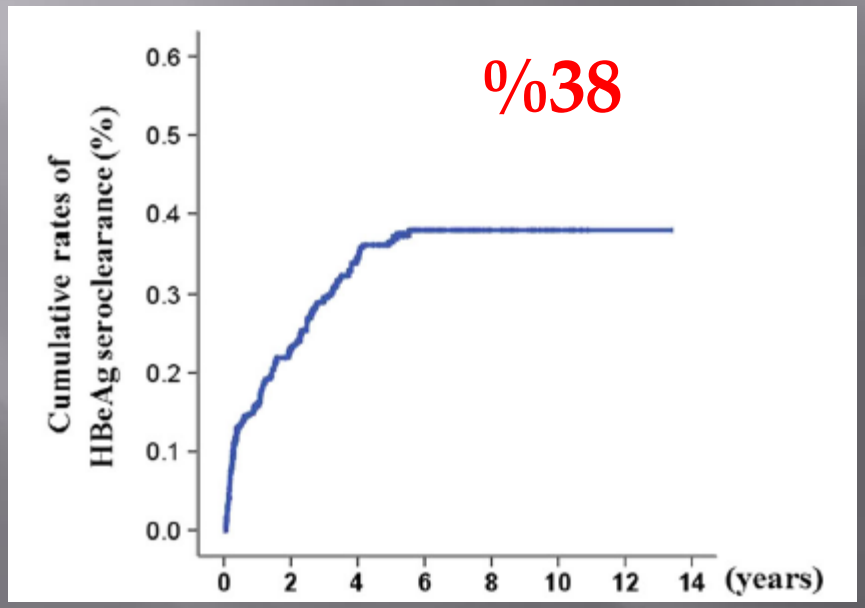

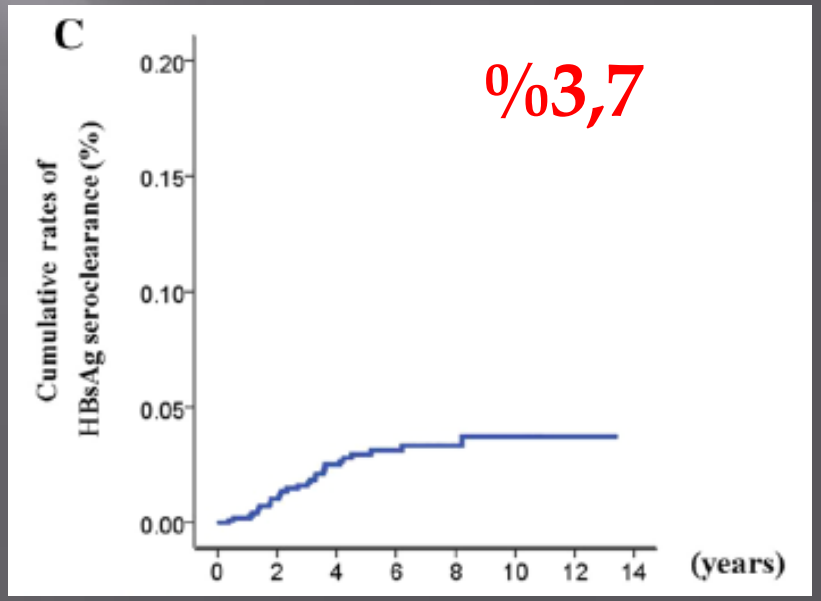

Suzuki F et al. J Gastroenterol 2019;54:182

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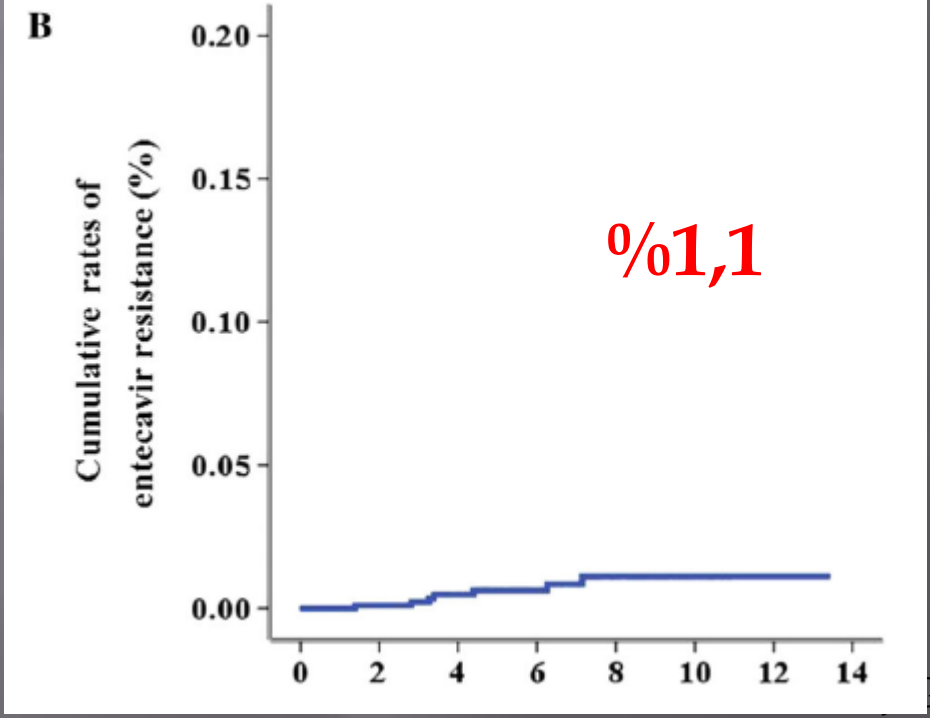

%1,1

Gastroenterol 2019;54:182

VIRAL HEPATITIS

Liver INTERNATIONAL WILEY

Ten-year efficacy and safety of tenofovir disoproxil fumarate treatment for chronic hepatitis B virus infection

Patrick Marcellin[1] | David K Wong[2] | William Sievert[3] | Peter Buggisch[4] | Jörg Petersen[4] | Robert Flisiak[5] | Michael Manns[6,7] | Kelly Kaita[8] | Zahari Krastev[9] | Samuel S Lee[10] | Andrea L Cathcart[11] | Gerald Crans[11] | Marjoleine Op den Brouw[12] | Belinda Jump[11] | Anuj Gaggar[11] | John Flaherty[11] | Maria Buti[13]

641 naiv KHB hastası, 10 yıllık TDF etkinliği

%32 HBeAg pozitif,

Marcellin P et al. Liver Int 2019;39:1868

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	HBeAg status		
	HBeAg-negative[b]	HBeAg-positive[c]	All
HBV DNA <69 IU/mL, % (n/N)	100 (118/118)	97.5 (78/80)	99.0 (196/198)
HBV DNA <29 IU/mL, % (n/N)	100 (118/118)	97.5 (78/80)	99.0 (196/198)
ALT normalisation, % (n/N)	83.0 (88/106)	77.9 (60/77)	80.9 (148/183)
HBeAg loss, % (n/N)	–	52.2 (12/23)	52.2 (12/23)
HBeAg seroconversion, % (n/N)	–	27.3 (6/22)	27.3 (6/22)
HBsAg loss, % (n/N)	3.4 (4/117)	4.9 (4/81)	4.0 (8/198)

Marcellin P et al. Liver Int 2019;39:1868

VIRAL HEPATITIS

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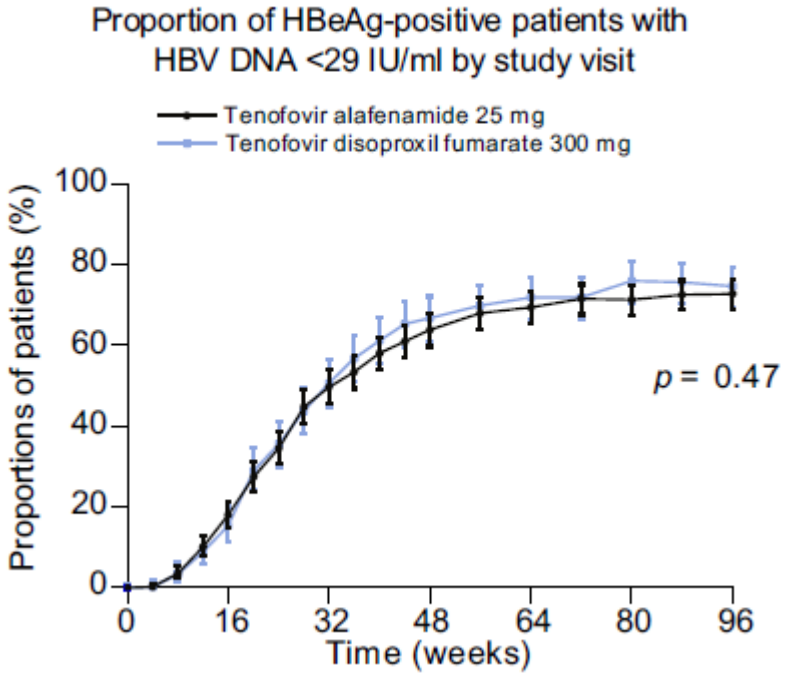
	By initial treatment assignment		
	TDF-TDF n = 389	ADV-TDF n = 196	All n = 585[a]
Patients who discontinued because of AEs, n (%)	10 (2.6)	1 (0.5)	11 (1.9)
Renal impairment, n (%)			
Serum creatinine increase of 0.5 mg/dL from baseline	9 (2.3)	4 (2.0)	13 (2.2)
Creatinine clearance <50 mL/min	4 (1.0)	3 (1.5)	7 (1.2)
Serum phosphate <2 mg/dL	6 (1.5)	4 (2.0)	10 (1.7)

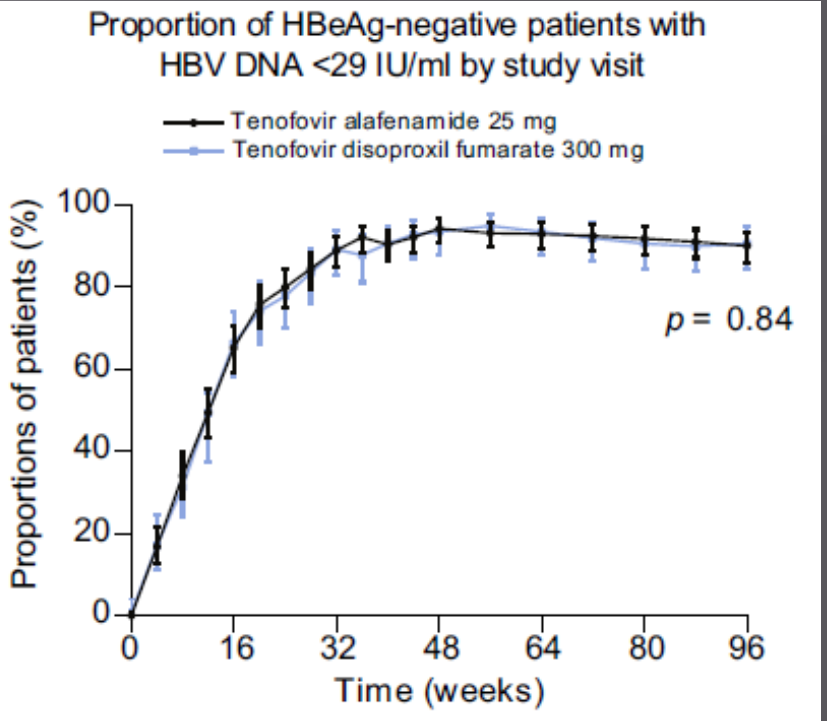
Marcellin P et al. Liver Int 2019;39:1868

Research Article
Viral Hepatitis

JOURNAL
OF HEPATOLOGY

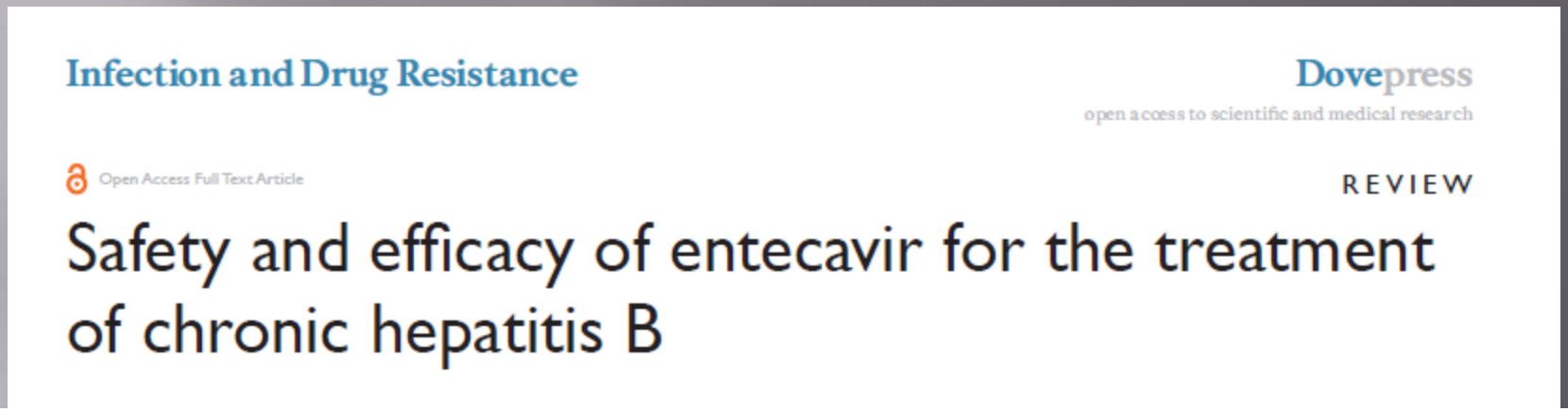
96 weeks treatment of tenofovir alafenamide *vs.* tenofovir disoproxil fumarate for hepatitis B virus infection





Agarwal K et al. J Hepatol 2018;68:672

Güvenlik



Nükleosid/nükleotid analogları ile uzun süreli tedavinin yan etkiler yönünden yönetilebilir olduğu kabul edilmektedir.

Duarte Rojo A et al. Ther Adv Gastroenterol 2010;3:107
Osborn M. Infection and Drug Resistance 2011;4:55

JGH Journal of Gastroenterology and Hepatology

JGHF

doi:10.1111/jgh.12213

REVIEW

Long-term therapy for chronic hepatitis B: Hepatitis B virus DNA suppression leading to cirrhosis reversal

Patrick Marcellin and Tarik Asselah

Service d'Hépatologie, Hôpital Beaujon, University of Paris, Clichy, France

Gerek RCT gerekse de RL çalışmaları, potent NA ile KHB olgularında viral replikasyonun etkin ve güvenli bir biçimde uzun süreli baskılanabileceğini ortaya koymuştur.

Marcellin P et al. J Gastroenterol Hepatol 2013;28:912

OPEN ACCESS Freely available online

PLOS | ONE

Comparison of Efficacy and Safety of Tenofovir and Entecavir in Chronic Hepatitis B Virus Infection: A Systematic Review and Meta-Analysis

Weixia Ke, Li Liu, Chi Zhang, Xiaohua Ye, Yanhui Gao, Shudong Zhou, Yi Yang*

Department of Epidemiology and Biostatistics and Guangdong Key Lab of Molecular Epidemiology, School of Public Health, Guangdong Pharmaceutical University, Guangzhou, Guangdong, China

HBV DNA baskılanması, HBeAg serokonversiyonu, ALT normalizasyonu açısından ETV ile TDF benzer etkinliğe sahip,

ETV ve TDF ile uzun dönemde

>%90 HBV DNA baskılanması

~%30 eAg serokonversiyonu

Ke W et al. PLoS ONE 9(6): e98865

Histolojik düzelme

Clinical Practice Guidelines

EASL | JOURNAL OF HEPATOLOGY

EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection☆

European Association for the Study of the Liver*

Tedavi

Viral baskılanma

Biyokimyasal iyileşme

Histolojik düzelme

Komplikasyonlar ↓

EASL CPG. J Hepatol 2017;67:370

ELSEVIER

Journal of Hepatology 38 (2003) S38–S53

Journal of Hepatology

www.elsevier.com/locate/jhep

Liver fibrosis – from bench to bedside

Scott L. Friedman*

Division of Liver Diseases, P.O. Box 1123, Mount Sinai School of Medicine, 1425 Madison Ave. Room 1170F, New York, NY 10029, USA

Kronik hepatit seyrinde görülen hepatik fibrozis, süregiden karaciğer hasarına karşı gelişen tipik bir yara iyileşmesi sürecidir.

Friedmann SL. J Hepatol 2003;38:S38

ELSEVIER

Journal of Hepatology 38 (2003) S38–S53

Journal of Hepatology

www.elsevier.com/locate/jhep

Liver fibrosis – from bench to bedside

Scott L. Friedman*

Division of Liver Diseases, P.O. Box 1123, Mount Sinai School of Medicine, 1425 Madison Ave. Room 1170F, New York, NY 10029, USA

Karaciğer fibrozisi, subendotelyal boşluktaki ekstrasellüler matrikste, kollajen ve diğer proteinlerin birikimi ve ortadan kaldırılmasının söz konusu olduğu, dinamik ve kompleks sürecin net sonucudur.

Friedmann SL. J Hepatol 2003;38:S38

Pellicoro *et al. Fibrogenesis & Tissue Repair* 2012, **5**(Suppl 1):S26
http://www.fibrogenesis.com/content/5/S1/S26

Fibrogenesis & Tissue Repair

PROCEEDINGS Open Access

Reversibility of liver fibrosis

Antonella Pellicoro*, Prakash Ramachandran, John P Iredale

From Fibroproliferative disorders: from biochemical analysis to targeted therapies
Frauenchiemsee, Germany. 25-30 September 2010

Karaciğer hastalığının geri dönüşümsüz bir süreç olduğuna dair geleneksel görüş geçmişte kalmıştır.

Karaciğerde fibroz gelişimi, dinamik ve iki yönde de ilerleyebilecek bir süreçtir.

Pellicoro A et al. Fibrogenesis Tissue Repair 2012;5(S1):S26

Pellicoro *et al. Fibrogenesis & Tissue Repair* 2012, **5**(Suppl 1):S26
http://www.fibrogenesis.com/content/5/S1/S26

Fibrogenesis & Tissue Repair

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Reversibility of liver fibrosis

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From Fibroproliferative disorders: from biochemical analysis to targeted therapies
Frauenchiemsee, Germany. 25-30 September 2010

Hepatik inflamasyona yol açan kronik ya da tekrarlayan stimulus ortadan kaldırıldığında skar dokusunda resolüsyon izlenmektedir.

Pellicoro A et al. Fibrogenesis Tissue Repair 2012;5(S1):S26

Long-Term Entecavir Therapy Results in the Reversal of Fibrosis/Cirrhosis and Continued Histological Improvement in Patients with Chronic Hepatitis B

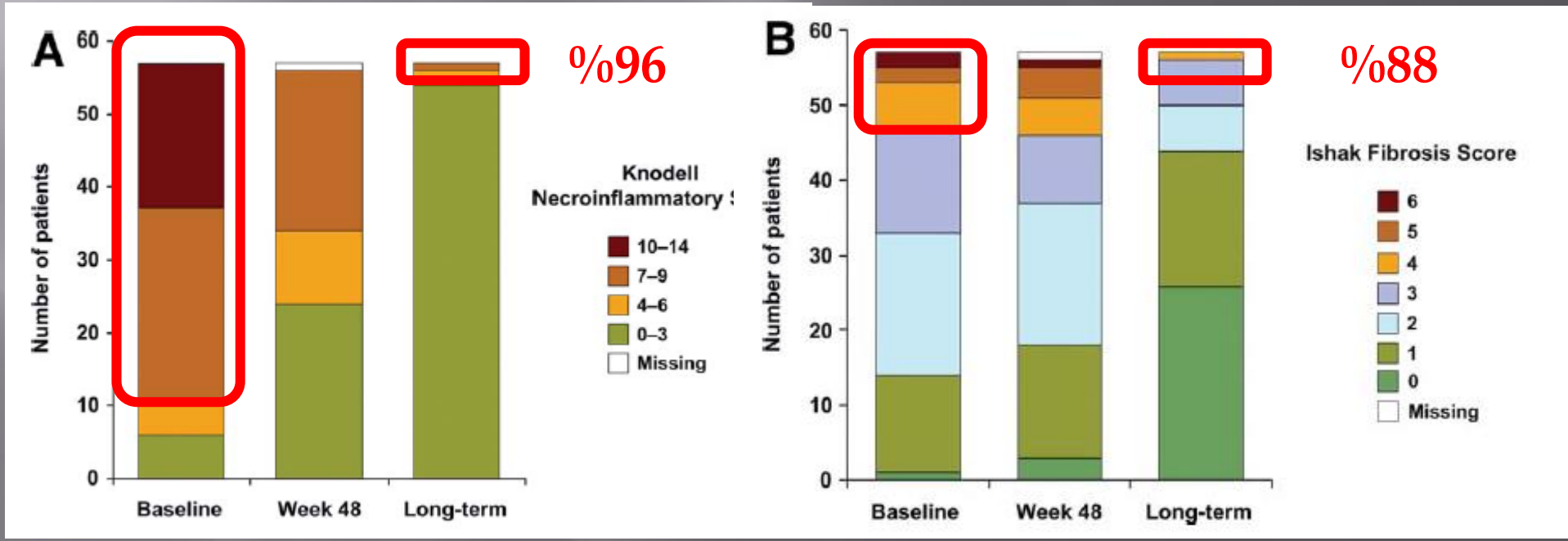
Ting-Tsung Chang,[1] Yun-Fan Liaw,[2] Shun-Sheng Wu,[3] Eugene Schiff,[4] Kwang-Hyub Han,[5] Ching-Lung Lai,[6] Rifaat Safadi,[7] Samuel S. Lee,[8] Waldemar Halota,[9] Zachary Goodman,[10] Yun-Chan Chi,[11] Hui Zhang,[12] Robert Hindes,[12] Uchenna Iloeje,[12] Suzanne Beebe,[12] and Bruce Kreter[12]

57 hasta,
En az 3 yıl ETV tedavisi,
Biyopsi kontrolü medyan 6 yıl

Chang TT et al. Hepatology 2010;52:886

Long-Term Entecavir Therapy Results in the Reversal of Fibrosis/Cirrhosis and Continued Histological Improvement in Patients with Chronic Hepatitis B

Ting-Tsung Chang,[1] Yun-Fan Liaw,[2] Shun-Sheng Wu,[3] Eugene Schiff,[4] Kwang-Hyub Han,[5] Ching-Lung Lai,[6] Rifaat Safadi,[7] Samuel S. Lee,[8] Waldemar Halota,[9] Zachary Goodman,[10] Yun-Chan Chi,[11] Hui Zhang,[12] Robert Hindes,[12] Uchenna Iloeje,[12] Suzanne Beebe,[12] and Bruce Kreter[12]



Chang TT et al. Hepatology 2010;52:886

Regression of cirrhosis during treatment with tenofovir disoproxil fumarate for chronic hepatitis B: a 5-year open-label follow-up study

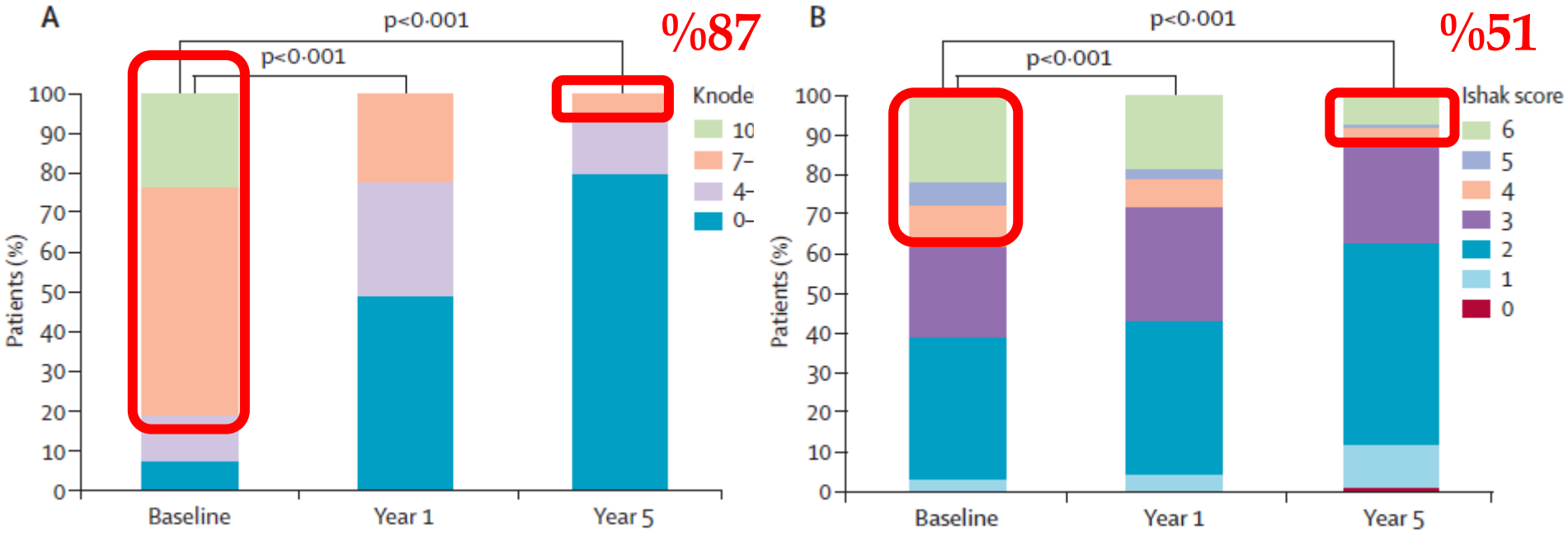
Patrick Marcellin, Edward Gane, Maria Buti, Nezam Afdhal, William Sievert, Ira M Jacobson, Mary Kay Washington, George Germanidis, John F Flaherty, Raul Aguilar Schall, Jeffrey D Bornstein, Kathryn M Kitrinos, G Mani Subramanian, John G McHutchison, E Jenny Heathcote

348 hasta,
TDF tedavisinin 240. haftasını tamamlamış,
Başlangıç, 48. hafta, 240. hafta biyopsi

Marcellin P et al. Lancet 2013;381:468

Regression of cirrhosis during treatment with tenofovir disoproxil fumarate for chronic hepatitis B: a 5-year open-label follow-up study

Patrick Marcellin, Edward Gane, Maria Buti, Nezam Afdhal, William Sievert, Ira M Jacobson, Mary Kay Washington, George Germanidis, John F Flaherty, Raul Aguilar Schall, Jeffrey D Bornstein, Kathryn M Kitrinos, G Mani Subramanian, John G McHutchison, E Jenny Heathcote



Marcellin P et al. Lancet 2013;381:468

Journal of Gastroenterology and Hepatology

JGHF

doi:10.1111/jgh.12213

REVIEW

Long-term therapy for chronic hepatitis B: Hepatitis B virus DNA suppression leading to cirrhosis reversal

Patrick Marcellin and Tarik Asselah

Service d'Hépatologie, Hôpital Beaujon, University of Paris, Clichy, France

Gerek RCT gerekse de RL çalışmaları, potent NA ile KHB olgularında viral replikasyonun etkin ve güvenli bir biçimde uzun süreli baskılanabileceğini ortaya koymuştur.

Bu ajanlarla tedavi hastalığın ilerlemesini engellemekle kalmaz, aynı zamanda seyrini de değiştirir.

;28:912

Observational Study > Hepatology. 2015 Jun;61(6):1809-20. doi: 10.1002/hep.27723. Epub 2015 Mar 18.

Long-term effect of antiviral therapy on disease course after decompensation in patients with hepatitis B virus-related cirrhosis

Jeong Won Jang [1 2], Jong Young Choi [1 2], Young Seok Kim [3 2], Hyun Young Woo [4 2], Sung Kyu Choi [5 2], Chang Hyeong Lee [6 2], Tae Yeob Kim [7 2], Joo Hyun Sohn [7 2], Won Young Tak [8 2], Kwang-Hyub Han [9 2]

Affiliations + expand

PMID: 25627342 DOI: 10.1002/hep.27723

707 dekompanse sirotik KHB hastası

5 yıllık transplantasyonsuz sağkalım NA tedavisi alan hastalarda daha yüksek

Jang JW et al. Hepatology 2015;61:1809

Observational Study > Hepatology. 2015 Jun;61(6):1809-20. doi: 10.1002/hep.27723. Epub 2015 Mar 18.

Long-term effect of antiviral therapy on disease course after decompensation in patients with hepatitis B virus-related cirrhosis

Jeong Won Jang [1 2], Jong Young Choi [1 2], Young Seok Kim [3 2], Hyun Young Woo [4 2], Sung Kyu Choi [5 2], Chang Hyeong Lee [6 2], Tae Yeob Kim [7 2], Joo Hyun Sohn [7 2], Won Young Tak [8 2], Kwang-Hyub Han [9 2]

Affiliations + expand

PMID: 25627342 DOI: 10.1002/hep.27723

Hastaların %34'ü transplantasyon listesinden çıkartıldı…

Jang JW et al. Hepatology 2015;61:1809

HCC riski

Antiviral Therapy 2011; **16**:787–795 (doi: 10.3851/IMP1895)

Review

Does antiviral therapy prevent hepatocellular carcinoma?

Hellan Kwon[1], *Anna S Lok*[1]*

[1]Division of Gastroenterology and Hepatology, University of Michigan, Ann Arbor, MI, USA

Kwon H et al. Antiviral Ther 2011;16:787

Clinical Gastroenterology and Hepatology 2014;12:885–893

Antiviral Therapy for Chronic Hepatitis B Virus Infection and Development of Hepatocellular Carcinoma in a US Population

Stuart C. Gordon,* Lois E. Lamerato,* Loralee B. Rupp,* Jia Li,* Scott D. Holmberg,‡ Anne C. Moorman,‡ Philip R. Spradling,‡ Eyasu H. Teshale,‡ Vinutha Vijayadeva,§ Joseph A. Boscarino,‖ Emily M. Henkle,¶ Nancy Oja–Tebbe,* and Mei Lu,* for the CHeCS Investigators

*Henry Ford Health System, Detroit, Michigan; ‡Division of Viral Hepatitis, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia; §Center for Health Research, Kaiser Permanente Hawaii, Waipahu, Hawaii; ‖Center for Health Research, Geisinger Health System, Danville, Pennsylvania; and ¶Center for Health Research, Kaiser Permanente Northwest, Portland, Oregon

Antiviral tedavi alan hastalarda HCC riski almayanlara göre daha düşüktür. (AHR:0.39)

Gordon SC et al. Clin Gastroenterol Hepatol 2013;12:885

Alimentary Pharmacology & Therapeutics

Meta-analysis: treatment of hepatitis B infection reduces risk of hepatocellular carcinoma

J. J. Y. SUNG, K. K. F. TSOI, V. W. S. WONG, K. C. T. LI & H. L. Y. CHAN

NA tedavisi,
5 çalışma, 2289 hasta

NA tedavisi ile HCC riski %78 azalıyor

HBeAg pozitif hastalarda yarar daha belirgin.

Sung YYK et al. Aliment Pharmaco Ther 2008;28:1067

HEPATOLOGY

HEPATOLOGY, VOL. 66, NO. 5, 2017

The Risk of Hepatocellular Carcinoma Decreases After the First 5 Years of Entecavir or Tenofovir in Caucasians With Chronic Hepatitis B

George V. Papatheodoridis,[1] Ramazan Idilman,[2] George N. Dalekos,[3] Maria Buti,[4] Heng Chi,[5] Florian van Boemmel,[6] Jose Luis Calleja,[7] Vana Sypsa,[8] John Goulis,[9] Spilios Manolakopoulos,[10] Alessandro Loglio,[11] Spyros Siakavellas,[1*] Onur Keskın,[2] Nikolaos Gatselis,[3] Bettina E. Hansen,[5] Maria Lehretz,[6] Juan de la Revilla,[7] Savvoula Savvidou,[9] Anastasia Kourikou,[10] Ioannis Vlachogiannakos,[1] Kostantinos Galanis,[3] Cihan Yurdaydin,[2] Thomas Berg,[6] Massimo Colombo,[12] Rafael Esteban,[4] Harry L.A. Janssen,[5,13] and Pietro Lampertico[11]

>5 yıl TDF/ETV tedavisi alan 1951 KHB hastası

İlk 5 yıl içinde HCC insidansı %1,22
>5 yıl HCC insidansı %0,73 (p=0,05)

Papatheodoridis GV et al. Hepatology 2017;66:1444

HEPATOLOGY

HEPATOLOGY, VOL. 66, NO. 5, 2017

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Sirotik hastalarda

İlk 5 yıl içinde HCC insidansı %3,22
>5 yıl HCC insidansı %1,57 (p=0,039)

Papatheodoridis GV et al. Hepatology 2017;66:1444

HEPATOLOGY

HEPATOLOGY, VOL. 66, NO. 5, 2017

The Risk of Hepatocellular Carcinoma Decreases After the First 5 Years of Entecavir or Tenofovir in Caucasians With Chronic Hepatitis B

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>5 yıl TDF/ETV tedavisi alan Kafkas ırkından KHB hastalarında HCC riski azalmaktadır.

Papatheodoridis GV et al. Hepatology 2017;66:1444

Research Article
Viral Hepatitis

JOURNAL
OF HEPATOLOGY

Eight-year survival in chronic hepatitis B patients under long-term entecavir or tenofovir therapy is similar to the general population☆

George V. Papatheodoridis[1,*], Vana Sypsa[2], George Dalekos[3], Cihan Yurdaydin[4], Florian van Boemmel[5], Maria Buti[6], John Goulis[7], Jose Luis Calleja[8], Heng Chi[9], Spilios Manolakopoulos[10], Alessandro Loglio[11], Spyros Siakavellas[1], Nikolaos Gatselis[3], Onur Keskın[4], Maria Lehretz[5], Savvoula Savvidou[7], Juan de la Revilla[8], Bettina E. Hansen[9], Anastasia Kourikou[10], Ioannis Vlachogiannakos[1], Kostantinos Galanis[3], Ramazan Idilman[4], Massimo Colombo[12], Rafael Esteban[6], Harry L.A. Janssen[9,13], Thomas Berg[5], Pietro Lampertico[11]

Uzun süreli ETV ya da TDF tedavisi alan sirotik/nonsirotik hastalarda 8 yıllık sağkalım genel popülasyondan farklı değildir…

Papatheodoridis GV et al. J Hepatol 2018;68:1129

Research Article

JOURNAL OF HEPATOLOGY

Reduction of covalently closed circular DNA with long-term nucleos(t)ide analogue treatment in chronic hepatitis B

Ching-Lung Lai[1,2,*,†], Danny Wong[1,2,*,†], Philip Ip[3], Malgorzata Kopaniszen[1], Wai-Kay Seto[1,2], James Fung[1,2], Fung-Yu Huang[1], Brian Lee[4], Giuseppe Cullaro[5], Chun Kong Chong[1], Ringo Wu[1], Charles Cheng[1], John Yuen[1], Vincent Ngai[1], Man-Fung Yuen[1,2]

En az 5 yıldır viral baskılanmanın sağlandığı 43 hastada kontrol biyopsisi

Medyan tedavi süresi 126 ay

Lai CL et al. J Hepatol 2017;66:275

Research Article

CrossMark

EASL | JOURNAL OF HEPATOLOGY

Reduction of covalently closed circular DNA with long-term nucleos(t)ide analogue treatment in chronic hepatitis B

Ching-Lung Lai[1,2,*,†], Danny Wong[1,2,*,†], Philip Ip[3], Malgorzata Kopaniszen[1], Wai-Kay Seto[1,2], James Fung[1,2], Fung-Yu Huang[1], Brian Lee[4], Giuseppe Cullaro[5], Chun Kong Chong[1], Ringo Wu[1], Charles Cheng[1], John Yuen[1], Vincent Ngai[1], Man-Fung Yuen[1,2]

Uzun süreli antiviral tedavi ile cccDNA düzeyleri belirgin ölçüde gerilemektedir…

Lai CL et al. J Hepatol 2017;66:275

Hepatol Int (2015) 9:43–51
DOI 10.1007/s12072-014-9593-x

ORIGINAL ARTICLE

Reimbursement policies in the Asia-Pacific for chronic hepatitis B

Seng Gee Lim · Deepak N. Amarapurkar · Henry Lik-Yuen Chan · Darrell H. Crawford · Edward J. Gane · Kwang-Hyub Han · Sang Hoon Ahn · Wasim Jafri · Jidong Jia · Jia-Horng Kao · Laurentius A. Lesmana · C. Rinaldi A. Lesmana · Rosmawati Mohamed · Pham Hoang Phiet · Teerha Piratvisuth · Shiv K. Sarin · Jose D. Sollarno · Yuichiro Eguchi · Mamun-Al Mahtab · Keat Hong Lee

Hepatol Int (2008) 2:263–283
DOI 10.1007/s12072-008-9080-3

OpenAccess

REVIEW ARTICLE

Asian-Pacific consensus statement on the management of chronic hepatitis B: a 2008 update

Yun-Fan Liaw · Nancy Leung · Jia-Horng Kao · Teerha Piratvisuth · Edward Gane · Kwang-Hyub Han · Richard Guan · George K. K. Lau · Stephen Locarnini · for the Chronic Hepatitis B Guideline Working Party of the Asian-Pacific Association for the Study of the Liver

HBeAg negatif hastalarda 6 ay arayla üç kez HBV DNA negatifliği saptanırsa, tedavinin kesilmesi düşünülebilir.

Liaw YF. Hepatol Int 2008;2:263

Review

INFECTIOUS DISEASES & IMMUNITY

OPEN

What Should Be Done to Re-evaluate Cessation of Nucleos(t)ide Analog Therapy for Chronic Hepatitis B Infection?

Yongqian Cheng[1], Yingjie Ji[1], Huijuan Duan[1], Yuanyuan Li[1], George Lau[1,2,*], Fu-Sheng Wang[1,*]

Table 3: Summary of studies on off-therapy virologic relapse and HBsAg seroclearance

	Baseline characteristics of patients off-NUCs treatment									Outcomes			
Reference	Total (*n*)	HBeAg(+) [*n*(%)]	HBeAg(−) [*n*(%)]	Cirrhosis [*n*(%)]	Age in year	Sex, male [*n*(%)]	Ethnicity	NUCs	Lower limit of HBV DNA	Clinical relapse [*n*(%)]	Virologic relapse [*n*(%)]	HBsAg loss [*n*(%)]	Retreatment [*n*(%)]
Liang et al.[40]	84	41 (48.8)	43 (51.2)	3 (3.6)	37	56 (67)	Asian	LMV, ADV, ETV, LMV+ADV	1000 copies/mL	12 (14.3)	37 (44.0)	5 (5.95)	NA
Chanet al.[46]	53	0 (0.0)	53 (100)	18 (34)	56	43 (81)	Asian	LMV	100 copies/mL	NA	37 (69.8)	11 (20.8)	NA
Chaung et al.[43]	39	39 (100)	0 (0.0)	NA	34	24 (62)	Asian	LMV, ADV, ETV	<100 IU/mL	15 (38.5)	35 (89.7)	0 (0.0)	NA
Hadziyannis et al.[37]	33	0 (0.0)	33 (100)	0 (0.0)	53	27 (82)	Caucasian	ADV	<20 IU/mL	25 (75.8)	33 (100)	13 (39.4)	15 (45)
Jeng et al.[47]	95	0 (0.0)	95 (100)	39 (41.1)	52	83 (87)	Asian	ETV	69 copies/mL; (12IU/mL)	43 (45.3)	55 (57.9)	0 (0.0)	34 (35.8)
He et al.[48]	66	0 (0.0)	66 (100)	0 (0.0)	35	50 (76)	Asian	LMV, ADV, ETV, L-dT	<200 IU/mL	NA	19 (28.8)	2 (3.0)	NA
Patwardhan et al.[38]	33	0 (0.0)	33 (100)	0 (0.0)	42	24 (73)	Mixed	LMV, ADV, ETV, TDF	NA	16 (48.0)	21 (63.6)	0 (0.0)	16 (48)
Chen et al.[41]	188	83 (44.1)	105 (55.9)	12 (23.4)	38/49*	143 (76)	Asian	LAM	<60 IU/mL	48 (25.5)	117 (65)	25 (13.9)	NA
Ridruejo et al.[45]	35	33 (94.3)	2 (5.7)	0 (0.0)	NA	NA	Caucasian	ETV	<6 IU/mL	NA	9 (25.7)	18 (51.4)	NA
Sohn et al.[42]	95	41 (43.2)	54 (56.8)	44 (46.3)	47	53	Asian	LMV, ETV, CLV	<60 IU/mL	NA	79 (83.2)	0 (0.0)	65 (68.4)
He et al.[44]	97	97 (100)	0 (0.0)	NA	26	53	Asian	LMV, ADV, ETV, L-dT	<200 IU/mL	1 (1.0)	8 (8.2)	11 (11.3)	NA
Seto et al.[49]	184	0 (0.0)	184 (100)	34 (18.5)	54	125 (67.9)	Asian	ETV	<20 IU/mL	19 (11.7)	169 (91.8)	0 (0.0)	0 (0.0)
Hung et al.[39]	73	0 (0.0)	73 (100)	73 (100)	52	57 (78)	Asian	LMV, ETV, L-dT	<20 IU/mL	NA	40 (54.8)	20 (27.4)	38 (52.1)
Yao et al.[50]	119	0 (0.0)	119 (100)	28 (23.5)	52	94 (79)	Asian	LMV, ETV	<20 IU/mL	29 (24.4)	45 (37.8)	44 (37.0)	NA
Chen et al.[51]	143	39 (27.3)	104 (72.7)	0 (0.0)	40/50*	116 (81)	Asian	TDF	<20 IU/mL	53 (37.1)	71 (49.7)	26 (18.2)	47 (32.9)
Jeng et al.[8]	691	0 (0.0)	691 (100)	308 (44.6)	52	594 (86)	Asian	ETV, TDF	<20 IU/mL	419 (60.6)	547 (79.2)	42 (6.1)	281 (40.7)

* Value indicates age of HBeAg (+) patients/age of HBeAg(−) patients.

HBsAg: Hepatitis B surface antigen; NUCs: Nucleos(t)ide analogs; HBeAg: Hepatitis B e antigen; NA: Not available; LMV: Lamivudine; ADV: Adefovir; ETV: Entecavir; L-dT: Telbivudine; TDF: Tenofovirdisoproxil; CLV: Clevudine; HBV DNA: Hepatitis B virus deoxyribonucleic acid.

GASTROENTEROLOGY 2012;143:629–636

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§

*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

4-5 yıl ADV tedavisi alan
33 HBeAg negatif KHB hastası

Hadziyannis SJ et al. Gastroenterology 2012;143:629

GASTROENTEROLOGY 2012;143:629–636

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

*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

18 hasta (%55) kalıcı virolojik yanıt
(HBV DNA <2000 IU, ALT<ULN)
13 hasta (%39) HBsAg negatif

Hadziyannis SJ et al. Gastroenterology 2012;143:629

ORIGINAL ARTICLE

Treatment cessation of entecavir in Asian patients with hepatitis B e antigen negative chronic hepatitis B: a multicentre prospective study

Wai-Kay Seto,[1] Aric Josun Hui,[2] Vincent Wai-Sun Wong,[3] Grace Lai-Hung Wong,[3] Kevin Sze-Hang Liu,[1] Ching-Lung Lai,[1] Man-Fung Yuen,[1] Henry Lik-Yuen Chan[3]

184 HBeAg negatif hasta,
≥2 yıl ETV,
≥ 3 altı ay arayla HBV DNA negatifliği

Virolojik relaps, HBV DNA>2000 IU/ml

Seto WK et al. Gut 2015;64:667

ORIGINAL ARTICLE

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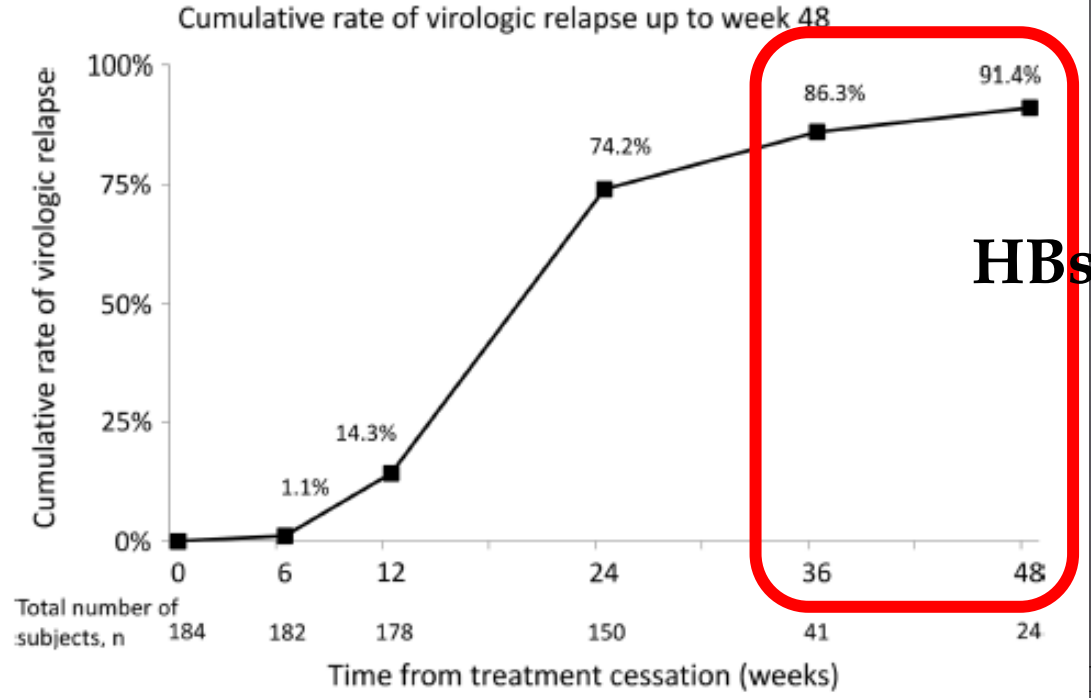

HBsAg kaybı 0!

K et al. Gut 2015;64:667

Hepatology

ORIGINAL ARTICLE

Treatment cessation of entecavir in Asian patients with hepatitis B e antigen negative chronic hepatitis B: a multicentre prospective study

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ETV tedavisi alan HBeAg negatif hastalarda tedavinin kesilmesi yüksek oranlarda virolojik relapsla sonuçlanmaktadır,

Bu hasta grubunda NA tedavisi HBsAg kaybına dek sürdürülmelidir.

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]

≥4 yıl TDF, ≥3,5 yıl DNA süpresyonu
42 HBeAg negatif KHB hastası
21 stop, 21 devam
İzlem 144 hafta

Berg T et al. J Hepatol 2017;67:918

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]

144. hafta
HBsAg kaybı n=4 (%19)
HBV DNA<2000 IU/ml n=9 (%43)
Yeniden tedavi n=8 (%38)

Berg T et al. J Hepatol 2017;67:918

DARING-B: discontinuation of effective entecavir or tenofovir disoproxil fumarate long-term therapy before HBsAg loss in non-cirrhotic HBeAg-negative chronic hepatitis B

George V Papatheodoridis, Eirini I Rigopoulou, Margarita Papatheodoridi, Kalliopi Zachou, Vassilios Xourafas, Nikolaos Gatselis, Emilia Hadziyannis, John Vlachogiannakos, Spilios Manolakopoulos, George N Dalekos

≥4 yıl TDF / ETV,
57 HBeAg negatif KHB hastası
İzlem 18 ay

Papatheodoridis G et al. Antivir Ther 2018;23:677

DARING-B: discontinuation of effective entecavir or tenofovir disoproxil fumarate long-term therapy before HBsAg loss in non-cirrhotic HBeAg-negative chronic hepatitis B

George V Papatheodoridis, Eirini I Rigopoulou, Margarita Papatheodoridi, Kalliopi Zachou, Vassilios Xourafas, Nikolaos Gatselis, Emilia Hadziyannis, John Vlachogiannakos, Spilios Manolakopoulos, George N Dalekos

After NA(s) discontinuation	HBV DNA, IU/mL					
	>200	>2,000			>20,000	
	Any ALT	Any ALT	ALT >ULN	ALT >2x ULN	Any ALT	ALT >ULN
1 month	37%	26%	2%	2%	11%	2%
3 months	65%	56%	35%	28%	25%	20%
6 months	75%	65%	39%	33%	30%	25%
9 months	77%	70%	39%	33%	34%	25%
12 months	79%	70%	39%	33%	38%	25%
18 months	79%	72%	43%	33%	41%	25%

r 2018;23:677

DARING-B: discontinuation of effective entecavir or tenofovir disoproxil fumarate long-term therapy before HBsAg loss in non-cirrhotic HBeAg-negative chronic hepatitis B

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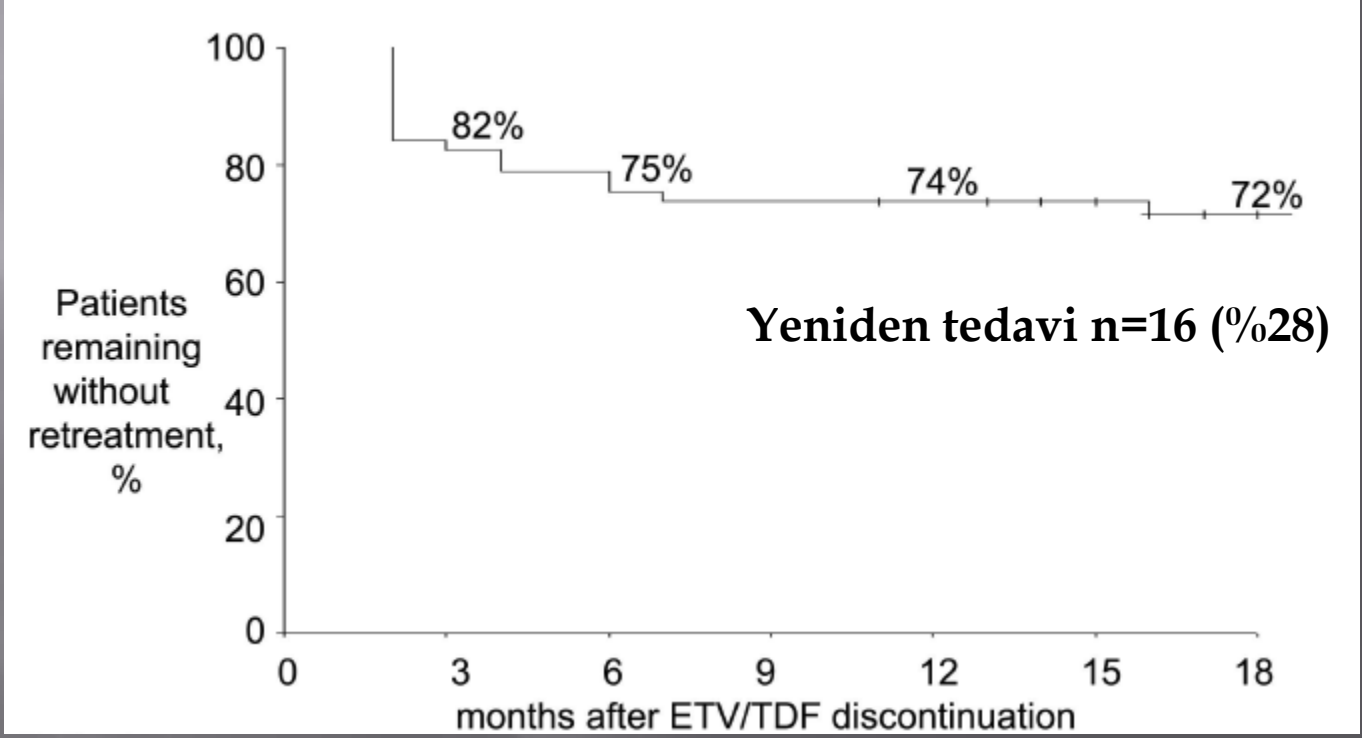

Yeniden tedavi n=16 (%28)

Papatheodoridis G et al. Antivir Ther 2018;23:677

DARING-B: discontinuation of effective entecavir or tenofovir disoproxil fumarate long-term therapy before HBsAg loss in non-cirrhotic HBeAg-negative chronic hepatitis B

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18. ay
HBsAg kaybı n=13 (%25)

Papatheodoridis G et al. Antivir Ther 2018;23:677

ORIGINAL ARTICLE

Limited sustained response after stopping nucleos(t)ide analogues in patients with chronic hepatitis B: results from a randomised controlled trial (Toronto STOP study)

Kin Seng Liem,[1,2] Scott Fung,[1] David K Wong,[1] Colina Yim,[1] Seham Noureldin,[1] Jiayun Chen,[1] Jordan J Feld,[1,3] Bettina E Hansen,[1,4] Harry L A Janssen[1]

Prospektif RCT
>36 ay HBV DNA negatifliği olan KHB hastaları (n=67),
45 stop, 22 devam
72 hafta izlem

Liem KS et al. Gut 2019;68:2206

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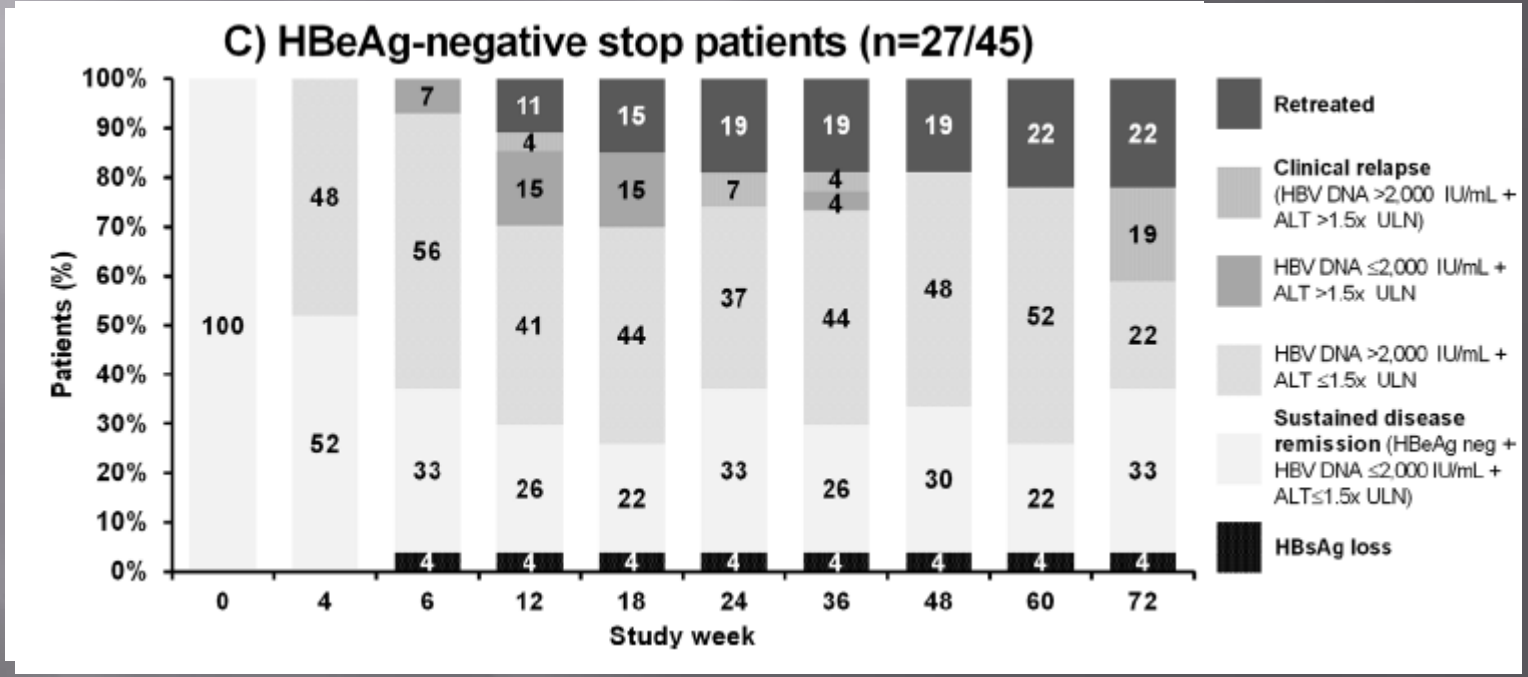

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Table 2 Primary and secondary outcomes at week 24–72 (n=67)

Mean (SD) or n (%)	Week 24			Week 48			Week 72		
	Stop (n=45)	Continue (n=22)	P value	Stop (n=45)	Continue (n=22)	P value	Stop (n=45)	Continue (n=22)	P value
Virological outcome									
HBV DNA <2000 IU/mL	15 (33)	20 (91)	<0.005*	12 (27)	21 (95)	<0.005*	13 (29)	20 (91)	0.04*
HBV DNA <200 IU/mL	9 (20)	20 (91)	<0.005*	7 (16)	21 (95)	<0.005*	5 (11)	20 (91)	<0.005*
Undetectable HBV DNA (<20 IU/mL)	6 (13)	19 (86)	<0.005*	4 (8.9)	21 (95)	<0.005*	1 (2.2)	20 (91)	<0.005*
Serological outcome									
HBeAg seroreversion	0 (0.0)	0 (0.0)	1.00	2 (4.4)	0 (0.0)	1.00	1 (2.2)	0 (0.0)	1.00
HBeAg neg+HBV DNA <2000 IU/mL +ALT ≤ULN	15 (33)	16 (73)	<0.005*	12 (27)	19 (86)	<0.005*	13 (29)	18 (82)	<0.005*
HBsAg loss	1 (2.2)	1 (4.5)	1.00	1 (2.2)	1 (4.5)	1.00	1 (2.2)	1 (4.5)	1.00
HBsAg decline >1 log IU/mL from Wk 0	1 (2.2)	0 (0.0)	1.00	1 (2.2)	0 (0.0)	1.00	4 (8.9)	0 (0.0)	0.29
Biochemical outcome									
ALT normalisation (≤ULN)	28 (62)	16 (73)	0.40	26 (58)	19 (86)	0.03*	21 (47)	18 (82)	0.01*
ALT ≤ULN+HBV DNA <2000 IU/mL	15 (33)	16 (73)	<0.005*	12 (27)	19 (86)	<0.005*	13 (29)	18 (82)	<0.005*
Histological outcome									
LSM (kPa)	–	–	–	5.1 (1.6)	5.1 (2.2)	0.98	5.2 (1.6)	5.3 (1.6)	0.90
LSM change from week 0 (kPa)†	–	–	–	0.2 (–0.7- 1.0)	0.1 (–0.8- 0.7)	0.53	0.0 (–0.9- 1.0)	0.1 (–0.5- 0.9)	0.83
Retreatment									
Retreated	12 (27)	–	–	13 (29)	–	–	17 (38)	–	–

Liem KS et al. Gut 2019;68:2206

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,‡]

RCT, STOP NUC çalışması
>4 yıl HBV DNA negatifliği olan KHB hastaları (n=158),
79 stop, 79 devam
96 hafta izlem

van Bömmel F et al. J Hepatol 2023;;78:926

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,‡]

HBsAg kaybı n=8/79 (%10,1)

HBsAg düzeyi	HBsAg kaybı
<100 IU/ml	5/10 (%50)
>100-<1000 IU/ml	2/15 (%13,3)
>1000 IU/ml	1/54 (%1,9)

HEPATOLOGY

HEPATOLOGY, VOL. 63, NO. 5, 2016

Discontinuation of Oral Antivirals in Chronic Hepatitis B: A Systematic Review

George Papatheodoridis,[1] Ioannis Vlachogiannakos,[1] Evangelos Cholongitas,[2] Karsten Wursthorn,[3] Christos Thomadakis,[4] Giota Touloumi,[4] and Jörg Petersen[3]

25 çalışma, 1716 hasta

HBeAg pozitif n=733

HBeAg negatif n=967

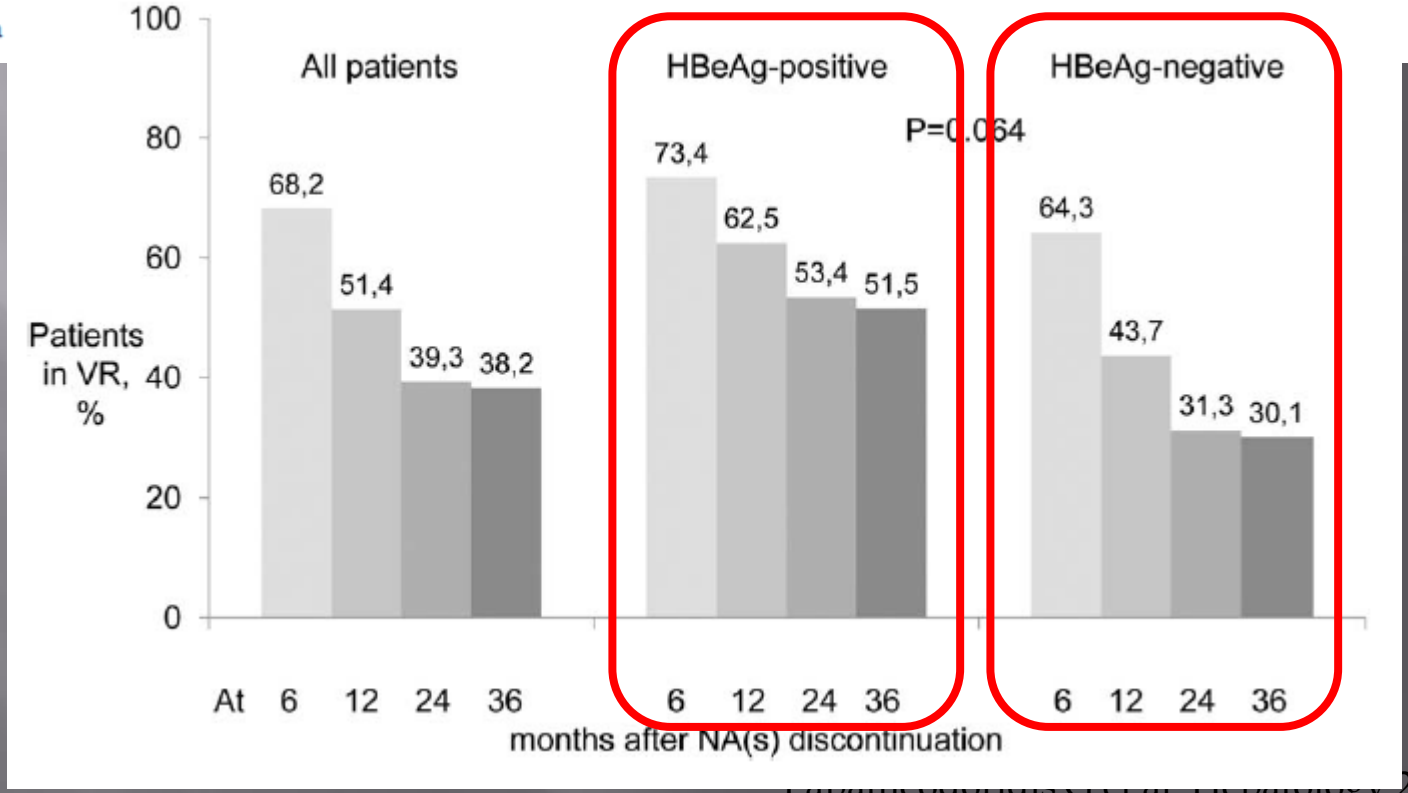
Papatheodoridis G et al. Hepatology 2016;63:1481

HEPATOLOGY

HEPATOLOGY, VOL. 63, NO. 5, 2016

Discontinuation of Oral Antivirals in Chronic Hepatitis B: A Systematic Review

Georg
Giota



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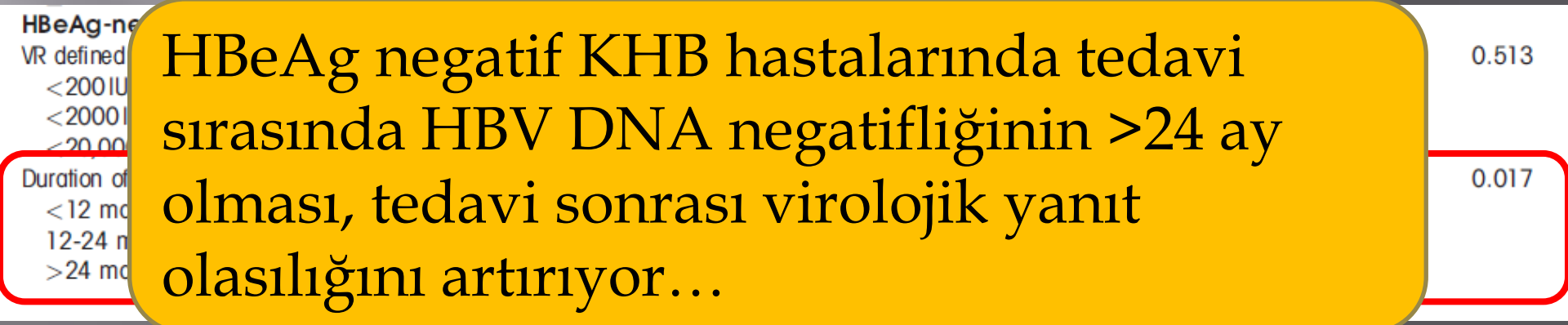
HBsAg kaybı %2

HBeAg negatif KHB hastalarında tedavi sırasında HBV DNA negatifliğinin >24 ay olması, tedavi sonrası virolojik yanıt olasılığını artırıyor…



Papatheodoridis G et al. Hepatology 2016;63:1481

ARTICLE: LIVER

Limited Sustained Remission After Nucleos(t)ide Analog Withdrawal: Results From a Large, Global, Multiethnic Cohort of Patients With Chronic Hepatitis B (RETRACT-B Study)

Hirode, Grishma MSc[1,2,3]; Hansen, Bettina E. MSc, PhD[1,4,5]; Chen, Chien-Hung MD[6]; Su, Tung-Hung MD, PhD[7]; Wong, Grace L.H. MD[8]; Seto, Wai-Kay MD[9]; d'Almeida, Arno Furquim MSc[10]; Papatheodoridi, Margarita MD[11]; Brakenhoff, Sylvia M. MD[12]; Lens, Sabela MD[13]; Choi, Hannah S.J. PhD[1]; Chien, Rong-Nan MD[14]; Feld, Jordan J. MD, MPH[1,2,3]; Forns, Xavier MD[13]; Sonneveld, Milan J. MD, PhD[12]; Papatheodoridis, George V. MD[11]; Vanwolleghem, Thomas MD, PhD[10,15]; Yuen, Man-Fung MD, PhD[9]; Chan, Henry L.Y. MD[8]; Kao, Jia-Horng MD, PhD[7]; Hsu, Yao-Chun MD, PhD[16]; Cornberg, Markus MD[17,18]; Jeng, Wen-Juei MD, PhD[14]; Janssen, Harry L.A. MD, PhD[1,12]; on behalf of the RETRACT-B study group

n=945, 48. ay

- Kalıcı remisyon %29,7
- Virolojik relaps %65,2
- ALT alevlenmesi %15,6
- HBsAg kaybı %9,9
- Yeniden tedavi %34,9

Hirode G et al. Am J Gastroenterol April 22, 2024. | DOI: 10.14309/ajg.0000000000002759

Patient hepatitis status	APASL 2016[5]	EASL 2017[6]	AASLD 2016[4]
HBeAg (+) without liver cirrhosis	At least 12 months of NA therapy, but preferably after 3 years of additional therapy after HBeAg seroconversion with undetectable HBV DNA and persistently normal ALT levels	At least 12 months NA therapy after HBeAg seroconversion, or treat until HBsAg loss	At least 12 months of NA therapy after HBeAg seroconversion with undetectable HBV and persistently normal ALT levels, or treat until HBsAg loss
HBeAg (−) without liver cirrhosis	(i) HBsAg loss, following either anti- HBs seroconversion, or at least 12 months of post-HBsAg clearance consolidation period (ii) After treatment of at least 2 years with undetectable HBV DNA documented on 3 separate occasions, 6 months apart	(i) HBsAg loss (ii) Selected patients who have achieved long-term (≥3 years) virological suppression under NA	Long term treatment with NA until HBsAg loss
Liver cirrhosis	Indefinite treatment with NA regardless of HBV DNA levels and HBeAg status	Indefinite treatment with NA regardless of HBeAg status or HBeAg seroconversion	Indefinite treatment with NA regardless of HBeAg status or HBeAg seroconversion

HBeAg negatif hastalarda en az 2 yıllık tedaviden sonra, 6 ay arayla üç kez HBV DNA negatifliği saptanırsa, tedavinin kesilmesi düşünülebilir.

Siroz olmayan HBeAg negatif hastalarda en az 3 yıllık tedaviden sonra, kesinlikle çok yakın takip sağlanabilecekse, tedavinin kesilmesi düşünülebilir.

HBeAg negatif KHB hastalarında zorunlu bir neden olmadıkça tedavi kesilmeden sürdürülmelidir.

Kronik hepatit B’nin etkin tedavisiyle uzun dönemde

Virolojik, biyokimyasal yanıt elde edilir,

Histolojik düzelme izlenir, fibroz geriler,

Uzun dönem komplikasyonların sıklığı azalır,

Sağkalım artar

Kronik hepatit B tedavisinin kesilmesiyle

HBV DNA reboundu kuraldır,

Çoğu hastada ALT dalgalanmaları ya da flare,

Hastaların yarısında yeniden tedavi,

Hasta uyumu ve yakın izlem gerekliliği,

Sonuçların öngörülemezliği

Kronik hepatit B tedavisinin kesilmesiyle

HBsAg kaybı olasılığı artar,

İnaktif taşıyıcılık olasılığı %20-30,

Maliyet azalır,