

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 enfeksiyonununun iki önemli sonucu siroz ve HCC, karaciğer ilişkili ölümlere neden oluyor.

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 olgularınının %30,

HCC olgularınının %53'ü

HBV ile ilişkilidir.



Hepatitis B

27 July 2021

DSÖ 2019,

1,5 milyon yeni olgu/yıl

296 milyon kronik hepatit B

820000 ölüm

**İnaktif
taşıyıcılık**

İlerleyici kronik hepatit

**Siroz /
HCC**



Hastalığın spektrumu deęişkenlik 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

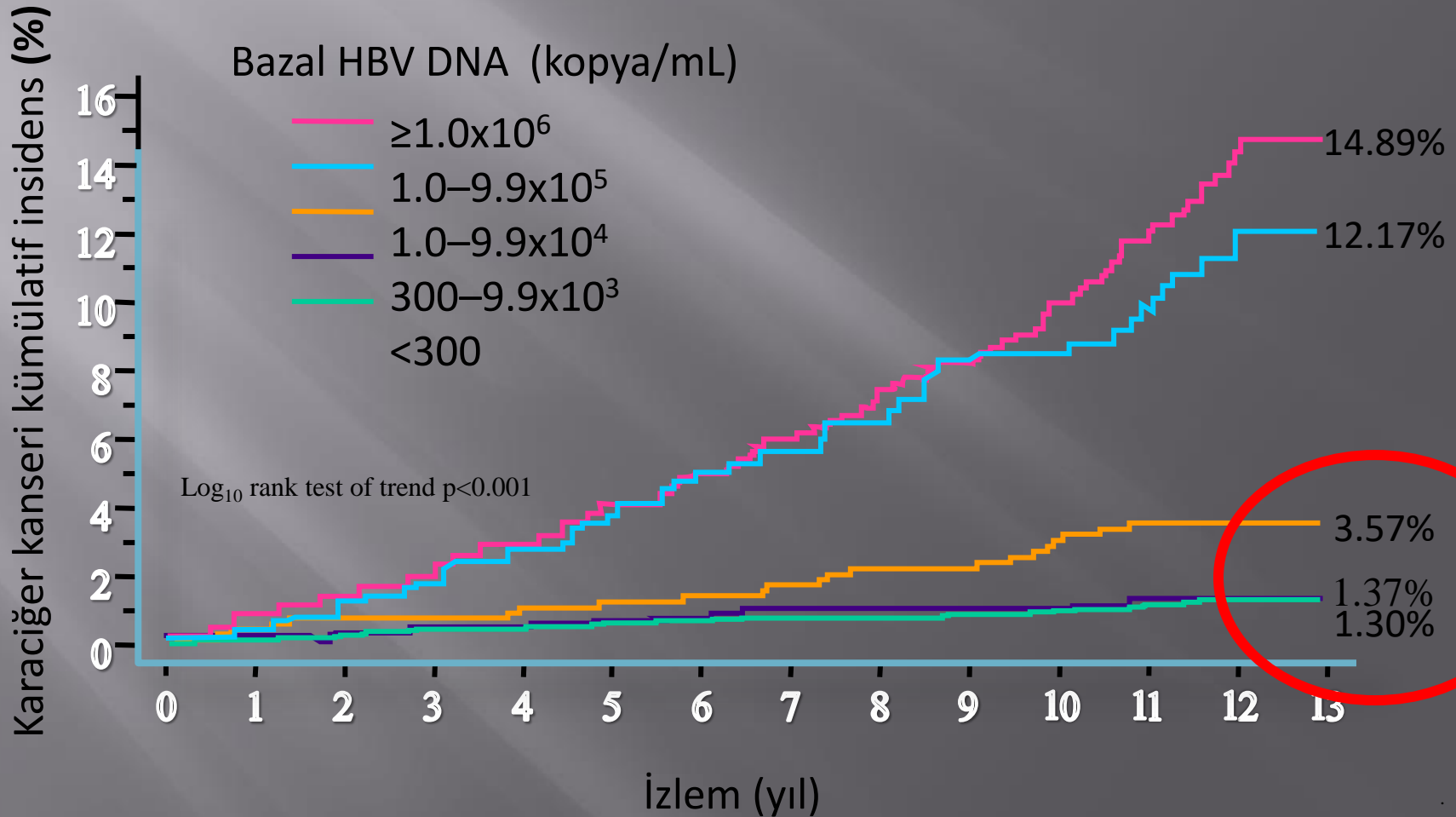
**EASL 2017 Clinical Practice Guidelines on the management
of hepatitis B virus infection[☆]**

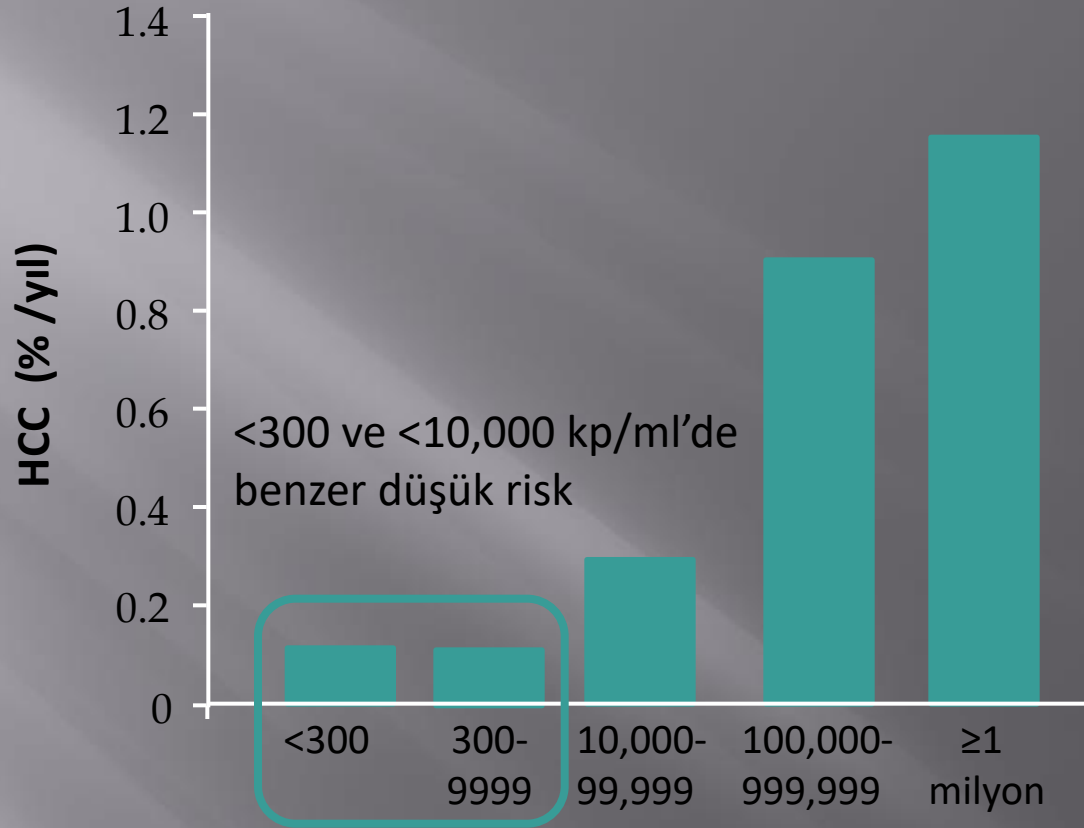
European Association for the Study of the Liver*

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

Yüksek Bazal HBV DNA Düzeyleri ve HCC Gelişimi

REVEAL (n=3,653)

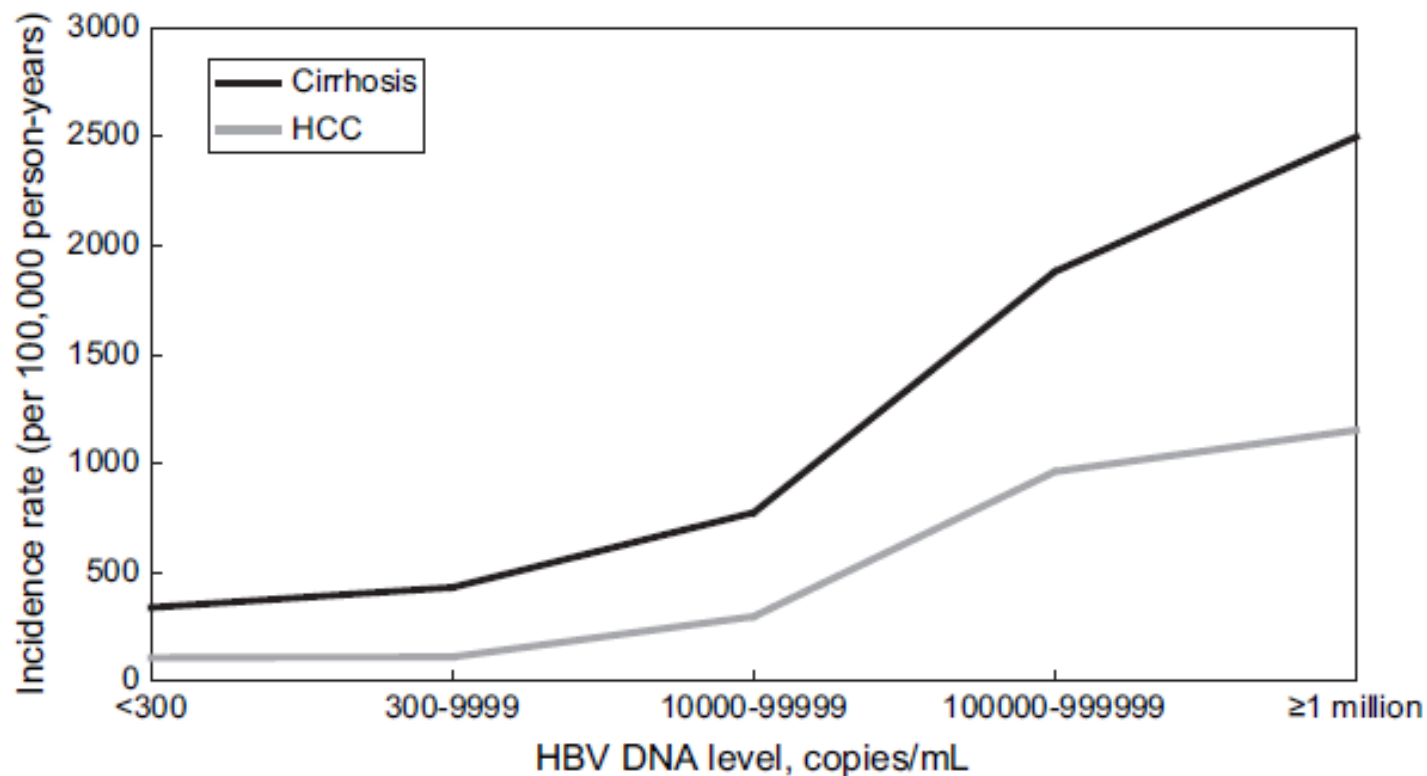




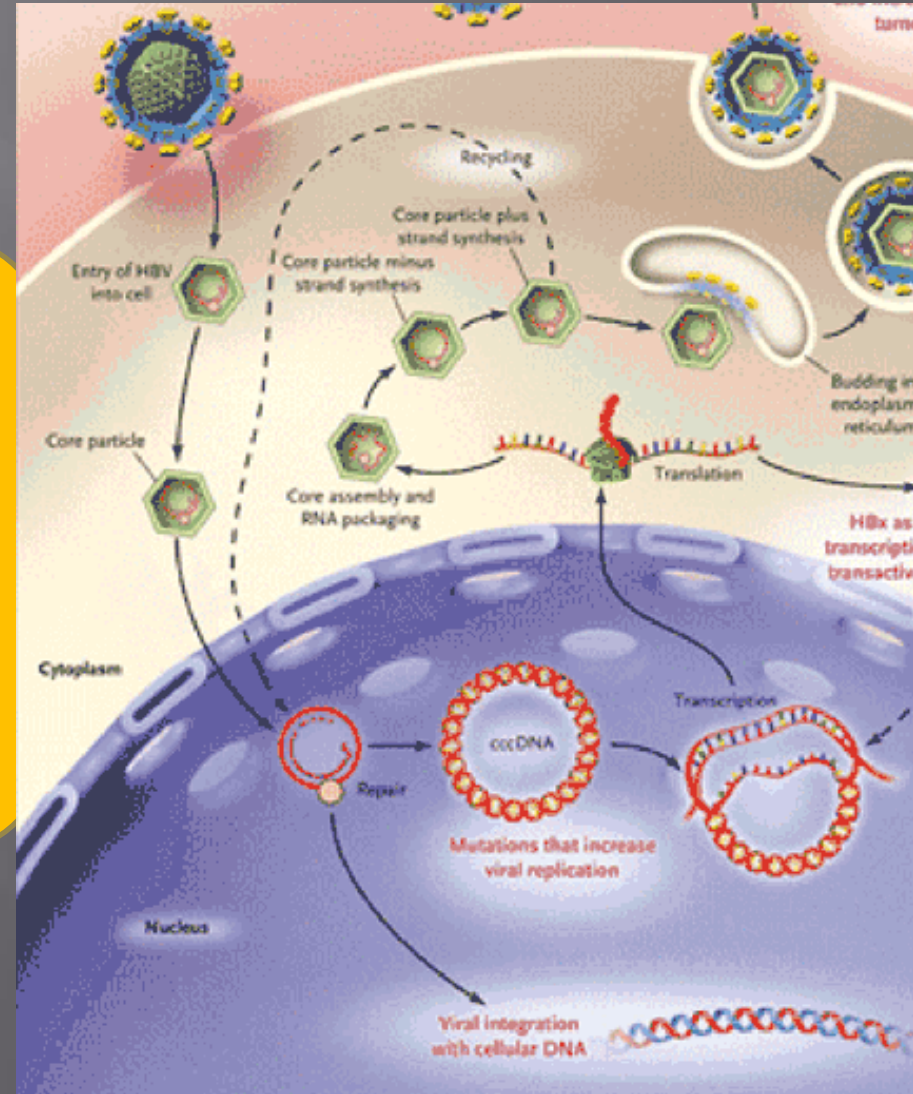
HBV DNA <10,000 kopya/ml olması HCC riskinin düşük olmasıyla ilişkilidir.

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

Chien Jen Chen, ScD^{a,b,*}, Udothen H. Hoque, MD, MPH^c



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



Tedavinin amacı

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*

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

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

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 2017 Clinical Practice Guidelines on the management
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İdeal sonlanım noktası HBsAg kaybı
“Fonksiyonel kür”

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*
<i>HBeAg-positive patients at week 48 or 52</i>							
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
<i>HBeAg-positive patients during extended treatment§</i>							
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)
<i>HBeAg-negative patients at week 48 or 52</i>							
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
<i>HBeAg-negative patients during extended treatment§</i>							
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)

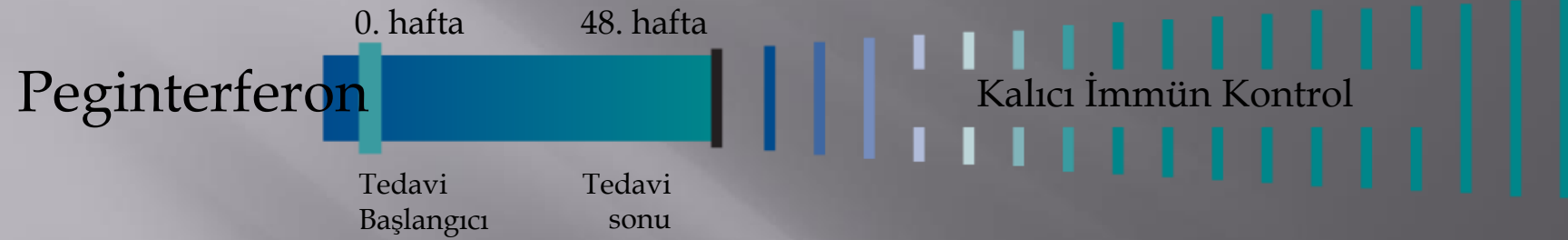
**EASL 2017 Clinical Practice Guidelines on the management
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İdeal sonlanım noktası HBsAg kaybı

Tedavi sonrası kalıcı virolojik yanıt

Tedavi altında sürdürülebilir viral baskılanma



Nükleoz(t)id analogları

Belirsiz tedavi süresi

PEG IFN ya da NA ile süresi belirli tedavi

NA ile uzun süreli tedavi

Update on Prevention, Diagnosis, and Treatment of Chronic Hepatitis B: AASLD 2018 Hepatitis B Guidance

Norah A. Terrault,¹ Anna S.F. Lok,² Brian J. McMahon,³ Kyong-Mi Chang,⁴ Jessica P. Hwang,⁵ Maureen M. Jonas,⁶ Robert S. Brown Jr.,⁷ Natalie H. Bzowej,⁸ and John B. Wong⁹

Kronik hepatit B tedavisinde tercih edilmesi önerilen seçenekler

PEG-IFN, ETV, TDF, TAF

NAs

Etkin viral baskılanma

Optimal direnç profili

Etkinlik/Direnç NAs



ORIGINAL ARTICLE—LIVER, PANCREAS, AND BILIARY TRACT

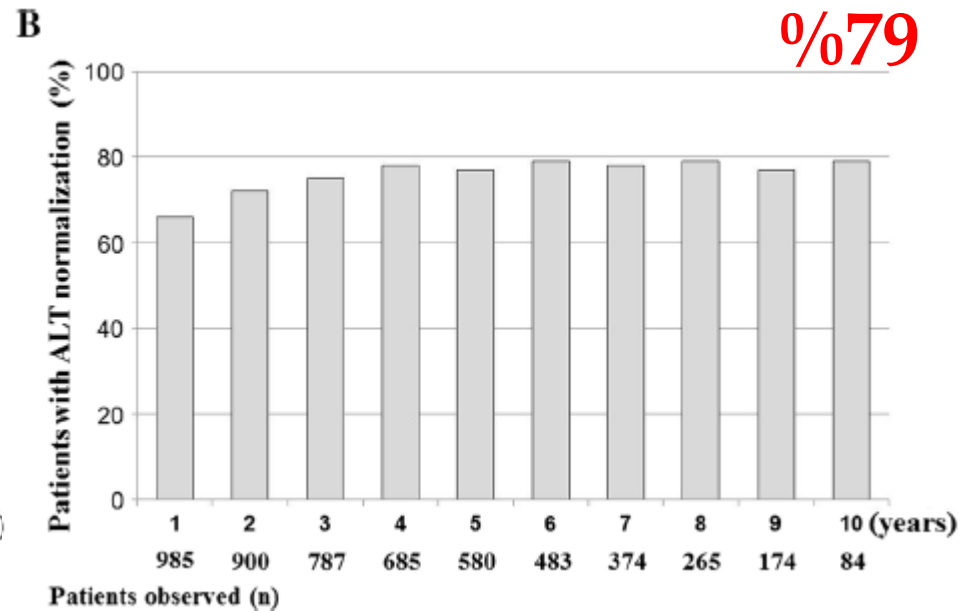
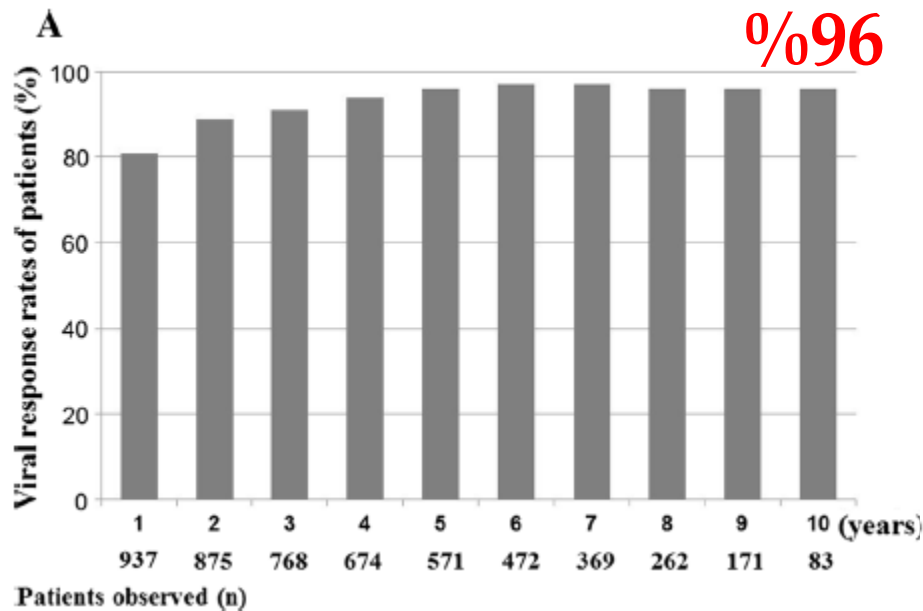
Long-term outcome of entecavir treatment of nucleos(t)ide analogue-naïve chronic hepatitis B patients in Japan

Fumitaka Suzuki^{1,2} · Tetsuya Hosaka¹ · Yoshiyuki Suzuki¹ · Hitomi Sezaki¹ ·
Norio Akuta¹ · Shunichiro Fujiyama¹ · Yusuke Kawamura¹ · Masahiro Kobayashi¹ ·
Satoshi Saitoh¹ · Yasuji Arase¹ · Kenji Ikeda¹ · Mariko Kobayashi³ ·
Rie Mineta³ · Yukiko Suzuki³ · Hiromitsu Kumada¹

1094 naiv KHB hastası, 10 yıllık ETV etkinliği
%42 HBeAg pozitif,
%23 sirotik

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

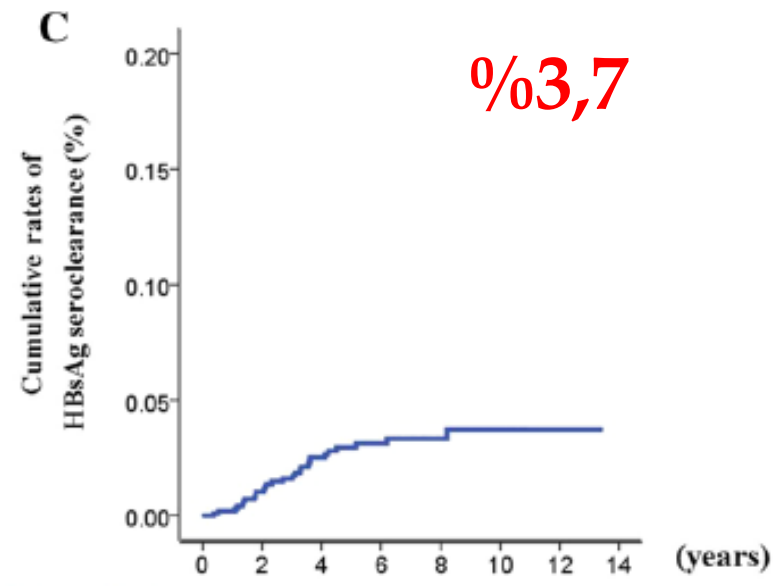
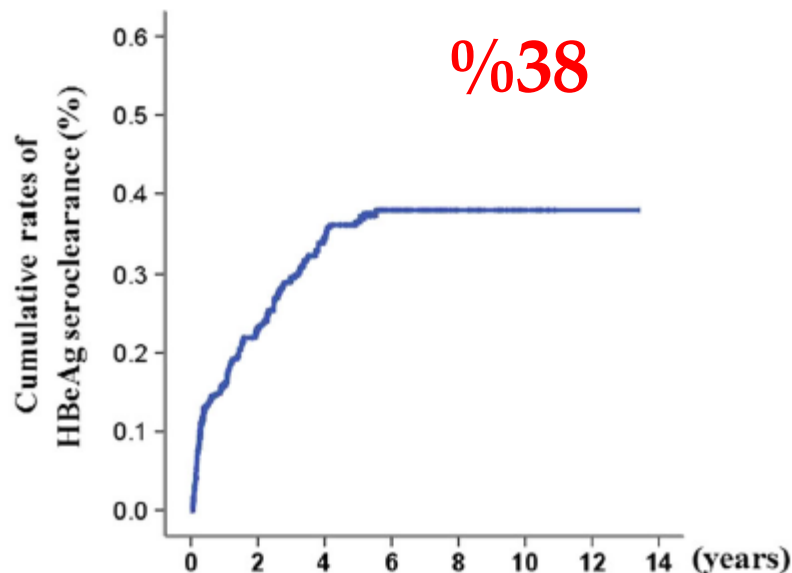
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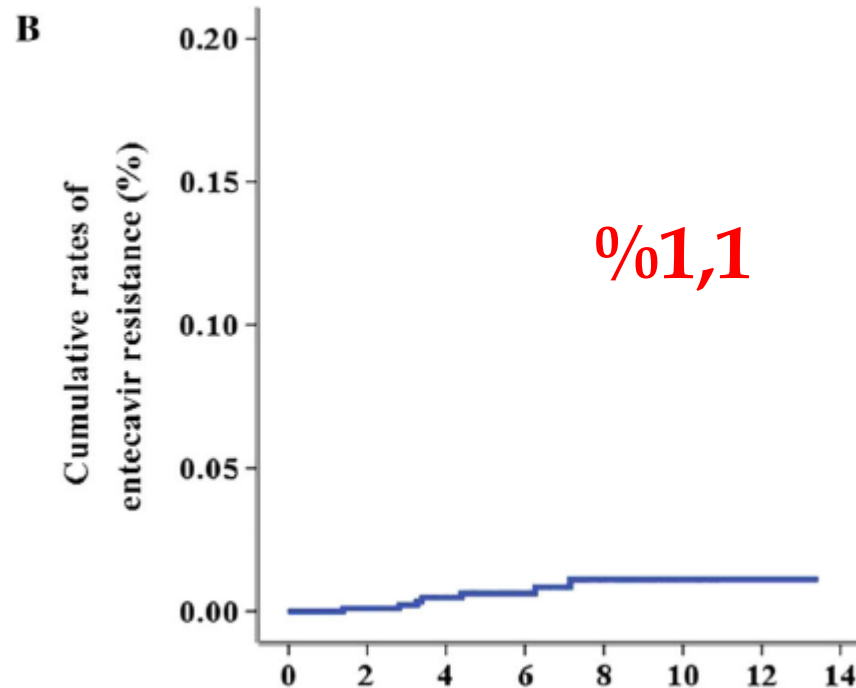
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Ten-year efficacy and safety of tenofovir disoproxil fumarate treatment for chronic hepatitis B virus infection

Patrick Marcellin¹  | David K Wong² | William Sievert³ | Peter Buggisch⁴ |
Jörg Petersen⁴ | Robert Flisiak⁵ | Michael Manns^{6,7} | Kelly Kaita⁸ | Zahari Krastev⁹ |
Samuel S Lee¹⁰ | Andrea L Cathcart¹¹ | Gerald Crans¹¹ | Marjoleine Op den Brouw¹² |
Belinda Jump¹¹ | Anuj Gaggar¹¹ | John Flaherty¹¹ | Maria Buti¹³


641 naiv KHB hastası, 10 yıllık TDF etkinliği
%32 HBeAg pozitif,

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

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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)

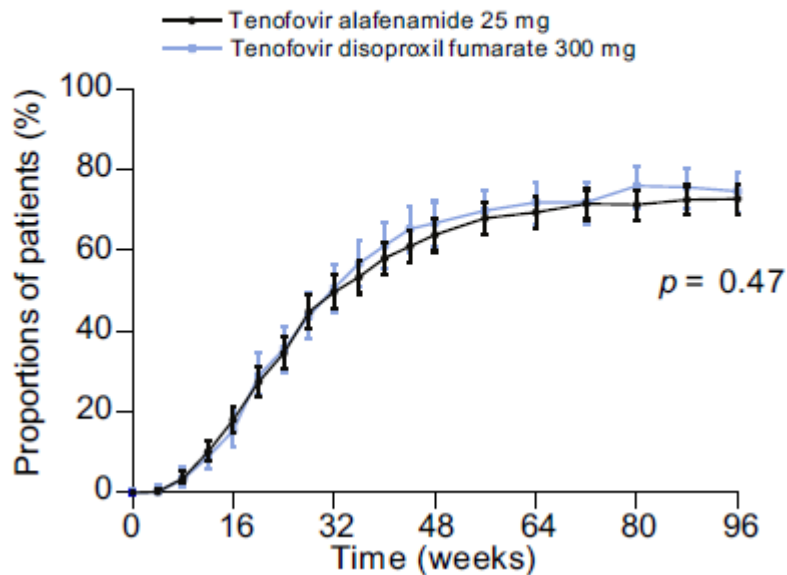
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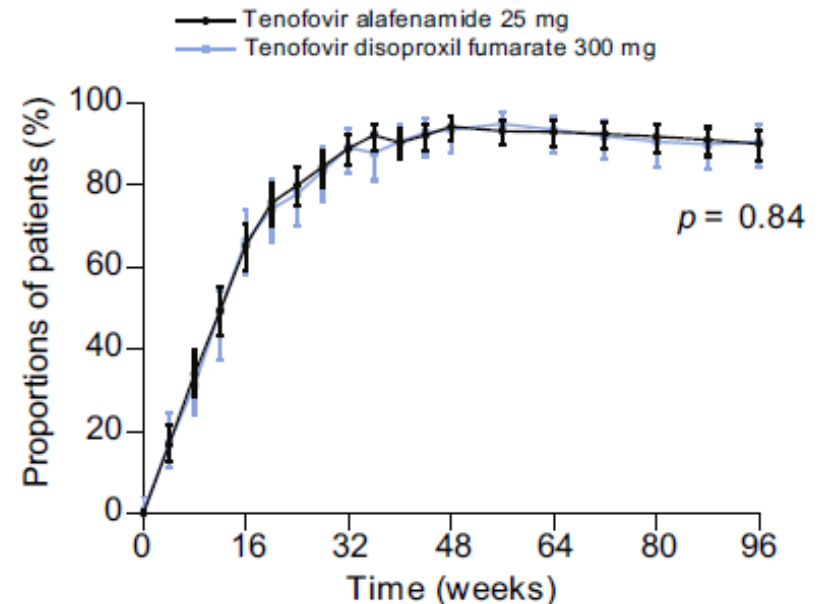
	By initial treatment assignment		
	TDF-TDF n = 389	ADV-TDF n = 196	All n = 585 ^a
Patients who discontinued because of AEs, n (%)	10 (2.6)	1 (0.5)	11 (1.9)
Renal impairment, n (%)			
Serum creatinine increase of 0.5 mg/dL from baseline	9 (2.3)	4 (2.0)	13 (2.2)
Creatinine clearance <50 mL/min	4 (1.0)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

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

Proportion of HBeAg-positive patients with HBV DNA <29 IU/ml by study visit



Proportion of HBeAg-negative patients with HBV DNA <29 IU/ml by study visit



Güvenlik

Safety and efficacy of entecavir for the treatment of chronic hepatitis B



Efficacy and safety of tenofovir disoproxil fumarate in patients with chronic hepatitis B

Andrés Duarte-Rojo and E. Jenny Heathcote

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

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.

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

Weixia Ke¹, Li Liu¹, 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

Histolojik düzelme

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Tedavi

Viral baskılanma

Biyokimyasal iyileşme

Histolojik düzelme

Komplikasyonlar ↓



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.



Journal of Hepatology 38 (2003) S38–S53

Journal of
Hepatology

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Liver fibrosis – from bench to bedside

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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.



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.



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

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

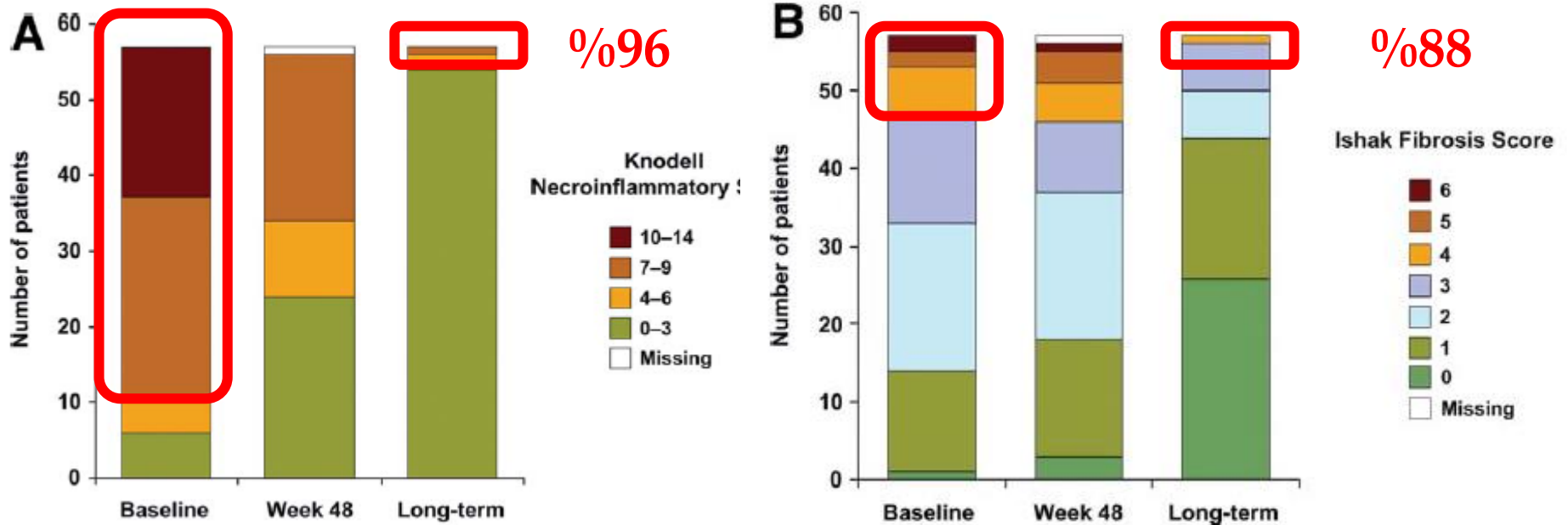
Long-Term Entecavir Therapy Results in the Reversal of Fibrosis/Cirrhosis and Continued Histological Improvement in Patients with Chronic Hepatitis B

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 Hinds,¹² Uchenna Iloeje,¹² Suzanne Beebe,¹² and Bruce Kreter¹²

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

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

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



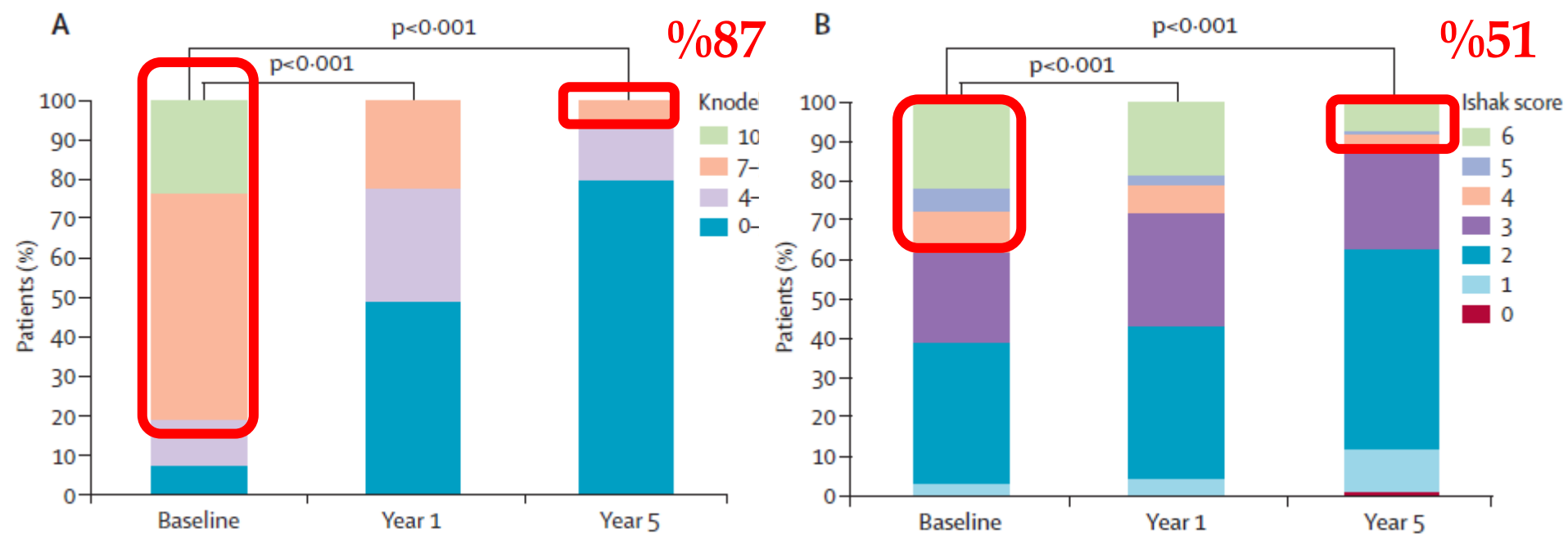
Patrick Marcellin, Edward Gane, Maria Buti, Nezam Afdhal, William Sievert, Ira M Jacobson, Mary Kay Washington, George Germanidis, John F Flaherty, Raul Aguilar Schall, Jeffrey D Bornstein, Kathryn M Kitrinos, G Mani Subramanian, John G McHutchison, E Jenny Heathcote

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



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

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REVIEW

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

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](https://doi.org/10.1002/hep.27723)

707 dekompanse sirotik KHB hastası

5 yıllık transplantasyonsuz sağkalım NA tedavisi alan hastalarda daha yüksek

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

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Affiliations + expand

PMID: 25627342 DOI: [10.1002/hep.27723](https://doi.org/10.1002/hep.27723)

Hastaların %34'ü transplantasyon listesinden çıkartıldı...

HCC risk

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

Review

Does antiviral therapy prevent hepatocellular carcinoma?

Hellan Kwon¹, Anna S Lok^{1}*

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

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

Stuart C. Gordon,* Lois E. Lamerato,* Lorelee 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)

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.

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 Keskin,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 Lampertico¹¹

>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)

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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Sirotik hastalarda

İlk 5 yıl içinde HCC insidansı %3,22

>5 yıl HCC insidansı %1,57 (p=0,039)

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 Keskin,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 Lampertico¹¹

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



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 Sypsa², George Dalekos³, Cihan Yurdaydin⁴, Florian van Boemmel⁵, Maria Buti⁶, John Goulis⁷, Jose Luis Calleja⁸, Heng Chi⁹, Spilios Manolakopoulos¹⁰, Alessandro Loglio¹¹, Spyros Siakavellas¹, Nikolaos Gatselis³, Onur Keskin⁴, Maria Lehretz⁵, Savvoula Savvidou⁷, Juan de la Revilla⁸, Bettina E. Hansen⁹, Anastasia Kourikou¹⁰, Ioannis Vlachogiannakos¹, Kostantinos Galanis³, Ramazan Idilman⁴, Massimo Colombo¹², Rafael Esteban⁶, Harry L.A. Janssen^{9,13}, Thomas Berg⁵, Pietro Lampertico¹¹

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

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 Ip³, Malgorzata Kopaniszen¹, Wai-Kay Seto^{1,2}, James Fung^{1,2}, Fung-Yu Huang¹, Brian Lee⁴, Giuseppe Cullaro⁵, Chun Kong Chong¹, Ringo Wu¹, Charles Cheng¹, John Yuen¹, Vincent Ngai¹, Man-Fung Yuen^{1,2}

En az 5 yıldır viral baskılanmanın sağlandığı
43 hastada kontrol biyopsisi

Medyan tedavi süresi 126 ay



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 Ip³, Malgorzata Kopaniszen¹, Wai-Kay Seto^{1,2}, James Fung^{1,2}, Fung-Yu Huang¹, Brian Lee⁴, Giuseppe Cullaro⁵, Chun Kong Chong¹, Ringo Wu¹, Charles Cheng¹, John Yuen¹, Vincent Ngai¹, Man-Fung Yuen^{1,2}

Uzun süreli antiviral tedavi ile cccDNA düzeyleri belirgin ölçüde gerilemektedir...

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

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.

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

Yongqian Cheng¹, Yingjie Ji¹, Huijuan Duan¹, Yuanyuan Li¹, George Lau^{1,2,*}, Fu-Sheng Wang^{1,*}

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

Reference	Baseline characteristics of patients off-NUCs treatment								Lower limit of HBV DNA	Clinical relapse [n(%)]	Outcomes		
	Total (n)	HBeAg(+) [n(%)]	HBeAg(-) [n(%)]	Cirrhosis [n(%)]	Age in year	Sex, male [n(%)]	Ethnicity	NUCs			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 et 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; (12 IU/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: Tenofovir disoproxil; CLV: Clevudine; HBV DNA: Hepatitis B virus deoxyribonucleic acid.

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, Hippokraton 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

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*

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

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 Chan³

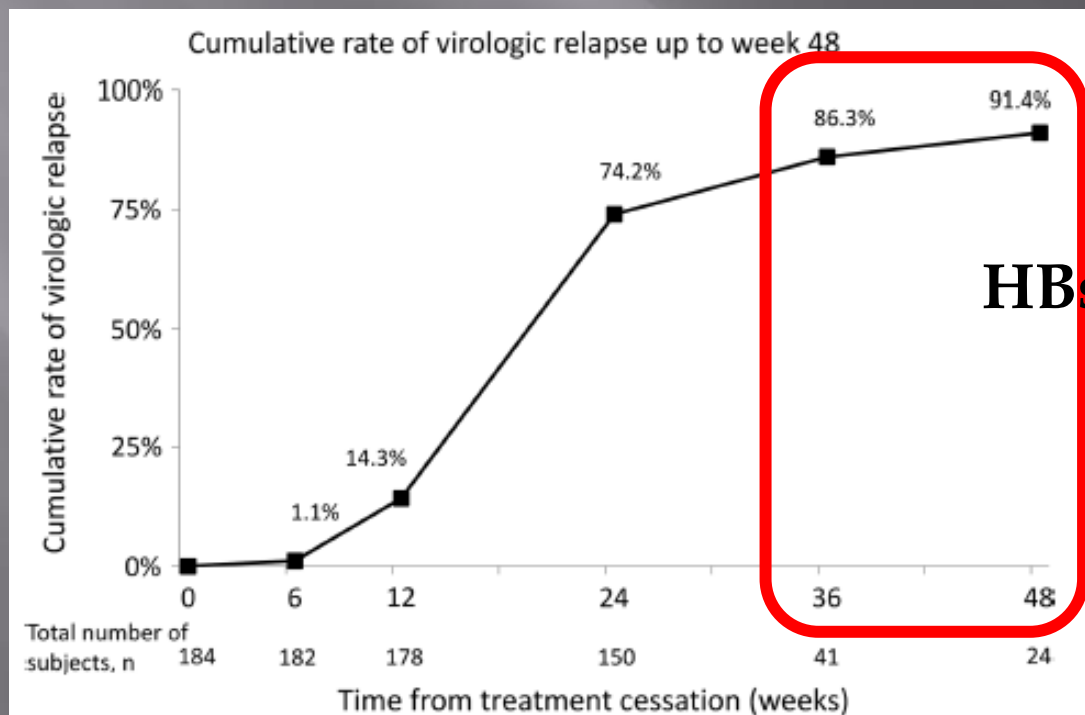
184 HBeAg negatif hasta,
≥2 yıl ETV,
≥ 3 altı ay arayla HBV DNA negatifliği

Virolojik relaps, HBV DNA > 2000 IU/ml

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 Chan³



HBsAg kaybı 0!

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 Chan³

ETV tedavisi alan HBeAg negatif hastalarda tedavinin kesilmesi yüksek oranlarda virolojik relapla 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 Simon², Stefan Mauss³, Eckart Schott⁴, Renate Heyne⁵, Dietmar M. Klass⁶, Christoph Eisenbach⁷, Tania Mara Welzel⁸, Reinhart Zchoval⁹, Gisela Felten¹⁰, Julian Schulze-zur-Wiesch¹¹, Markus Cornberg¹², Marjoleine L. Op den Brouw¹³, Belinda Jump¹⁴, Hans Reiser¹⁴, Lothar Gallo¹⁵, Tobias Warger¹⁵, Jörg Petersen¹⁶, 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

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

Thomas Berg^{1,*}, Karl-Georg Simon², Stefan Mauss³, Eckart Schott⁴, Renate Heyne⁵, Dietmar M. Klass⁶, Christoph Eisenbach⁷, Tania Mara Welzel⁸, Reinhart Zchoval⁹, Gisela Felten¹⁰, Julian Schulze-zur-Wiesch¹¹, Markus Cornberg¹², Marjoleine L. Op den Brouw¹³, Belinda Jump¹⁴, Hans Reiser¹⁴, Lothar Gallo¹⁵, Tobias Warger¹⁵, Jörg Petersen¹⁶, 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)

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

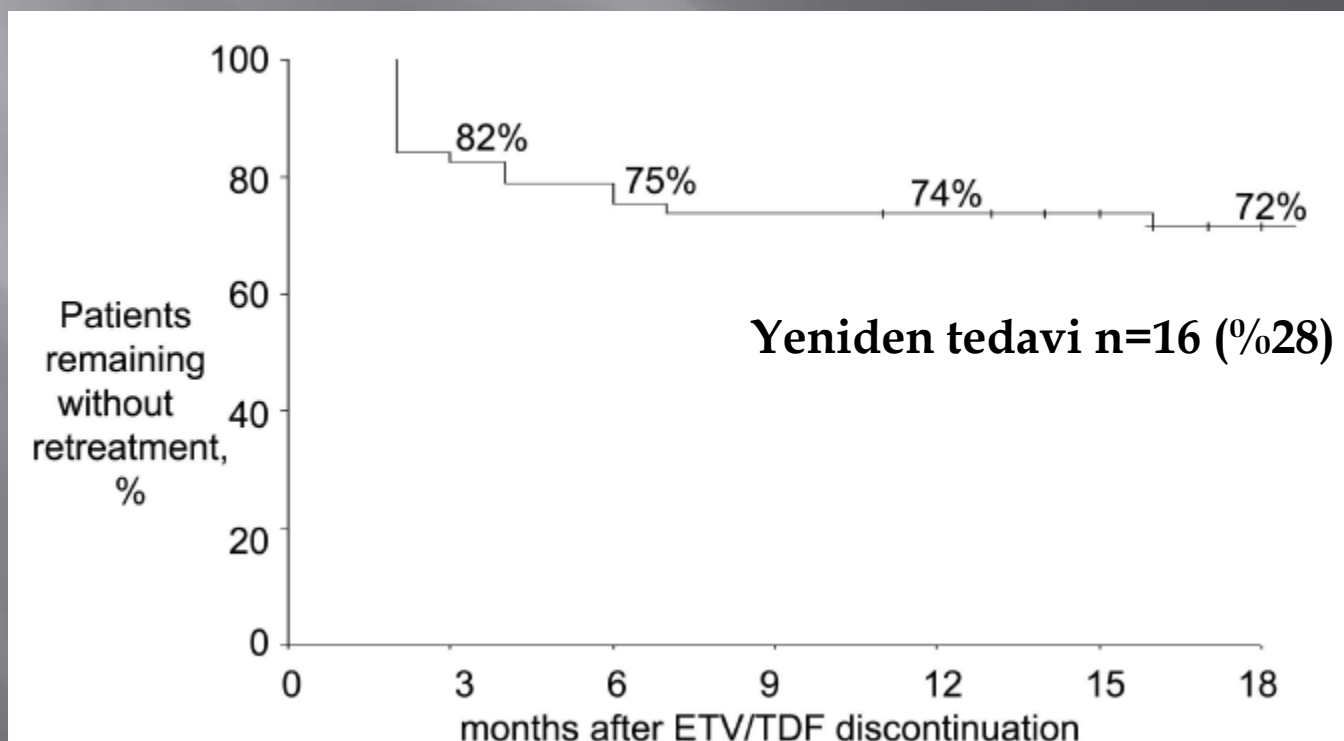
DARING-B: discontinuation of effective entecavir or tenofovir disoproxil fumarate long-term therapy before HBsAg loss in non-cirrhotic HBeAg-negative chronic hepatitis B

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		ALT		HBV DNA, IU/mL	
	>200	>2,000	Any ALT	ALT >ULN	>20,000	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%

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



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

18. ay

HBsAg kaybı n=13 (%25)

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 Nouredin,¹ Jiayun Chen,¹ Jordan J Feld,^{1,3} Bettina E Hansen,^{1,4} Harry L A Janssen¹

Prospektif RCT

>36 ay HBV DNA negatifliği olan KHB

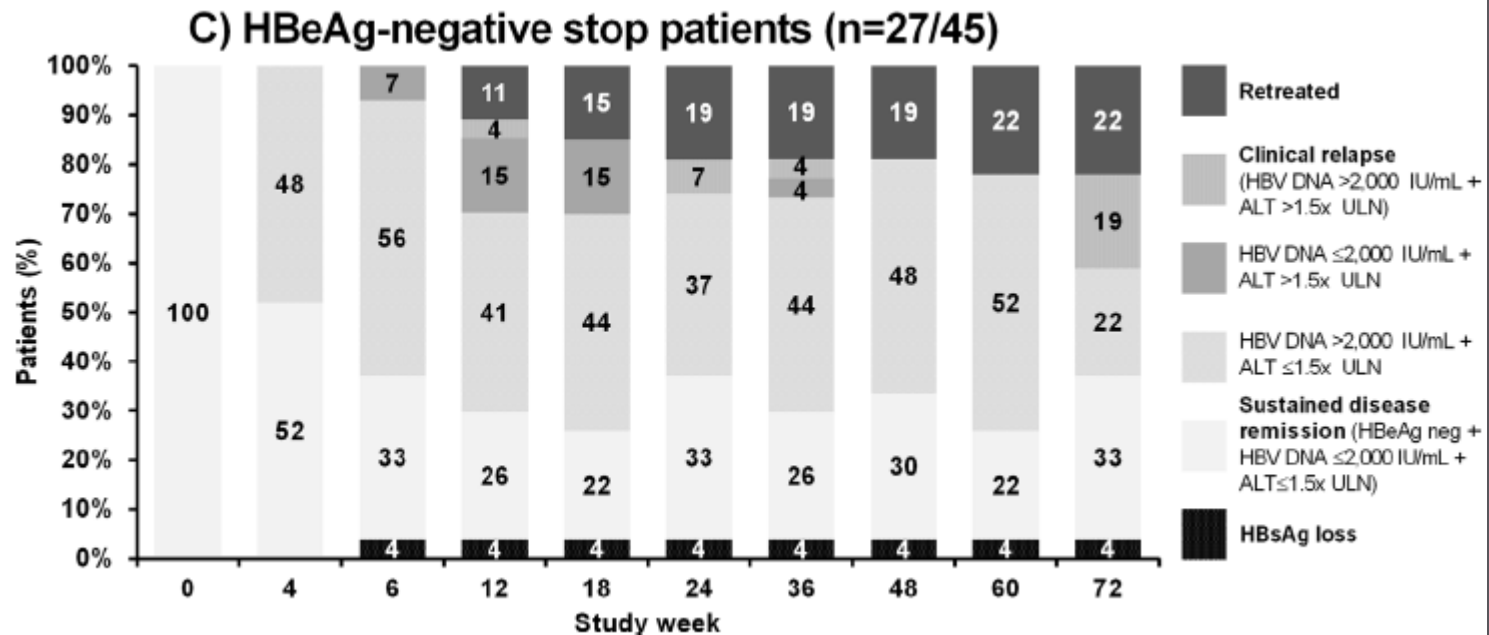
hastaları (n=67),

45 stop, 22 devam

72 hafta izlem

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 Nouredin,¹ Jiayun Chen,¹ Jordan J Feld,^{1,3} Bettina E Hansen,^{1,4} Harry L A Janssen¹



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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)	–	–

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

Florian van Bömmel^{1,*}, Kerstin Stein², Renate Heyne³, Jörg Petersen⁴, Peter Buggisch⁴, Christoph Berg⁵, Stefan Zeuzem⁶, Andreas Stallmach⁷, Martin Sprinzl⁸, Eckart Schott^{9,10}, Anita Pathil-Warth^{6,11}, Ulrike von Arnim¹², Verena Keitel^{12,13}, Jürgen Lohmeyer¹⁴, Karl-Georg Simon¹⁵, Christian Trautwein¹⁶, Andreas Trein¹⁷, Dietrich Hüppe¹⁸, Markus Cornberg^{19,20}, Frank Lammert^{19,21}, Patrick Ingiliz^{22,23}, Reinhart Zachoval²⁴, Holger Hinrichsen²⁵, Alexander Zipprich^{7,26}, Hartmuth Klinker²⁷, Julian Schulze zur Wiesch²⁸, Anett Schmiedeknecht²⁹, 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

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

Florian van Bömmel^{1,*}, Kerstin Stein², Renate Heyne³, Jörg Petersen⁴, Peter Buggisch⁴, Christoph Berg⁵, Stefan Zeuzem⁶, Andreas Stallmach⁷, Martin Sprinzl⁸, Eckart Schott^{9,10}, Anita Pathil-Warth^{6,11}, Ulrike von Arnim¹², Verena Keitel^{12,13}, Jürgen Lohmeyer¹⁴, Karl-Georg Simon¹⁵, Christian Trautwein¹⁶, Andreas Trein¹⁷, Dietrich Hüppe¹⁸, Markus Cornberg^{19,20}, Frank Lammert^{19,21}, Patrick Ingiliz^{22,23}, Reinhart Zachoval²⁴, Holger Hinrichsen²⁵, Alexander Zipprich^{7,26}, Hartmuth Klinker²⁷, Julian Schulze zur Wiesch²⁸, Anett Schmiedeknecht²⁹, 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, 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 Wurstorn,³ Christos Thomadakis,⁴
Giota Touloumi,⁴ and Jörg Petersen³

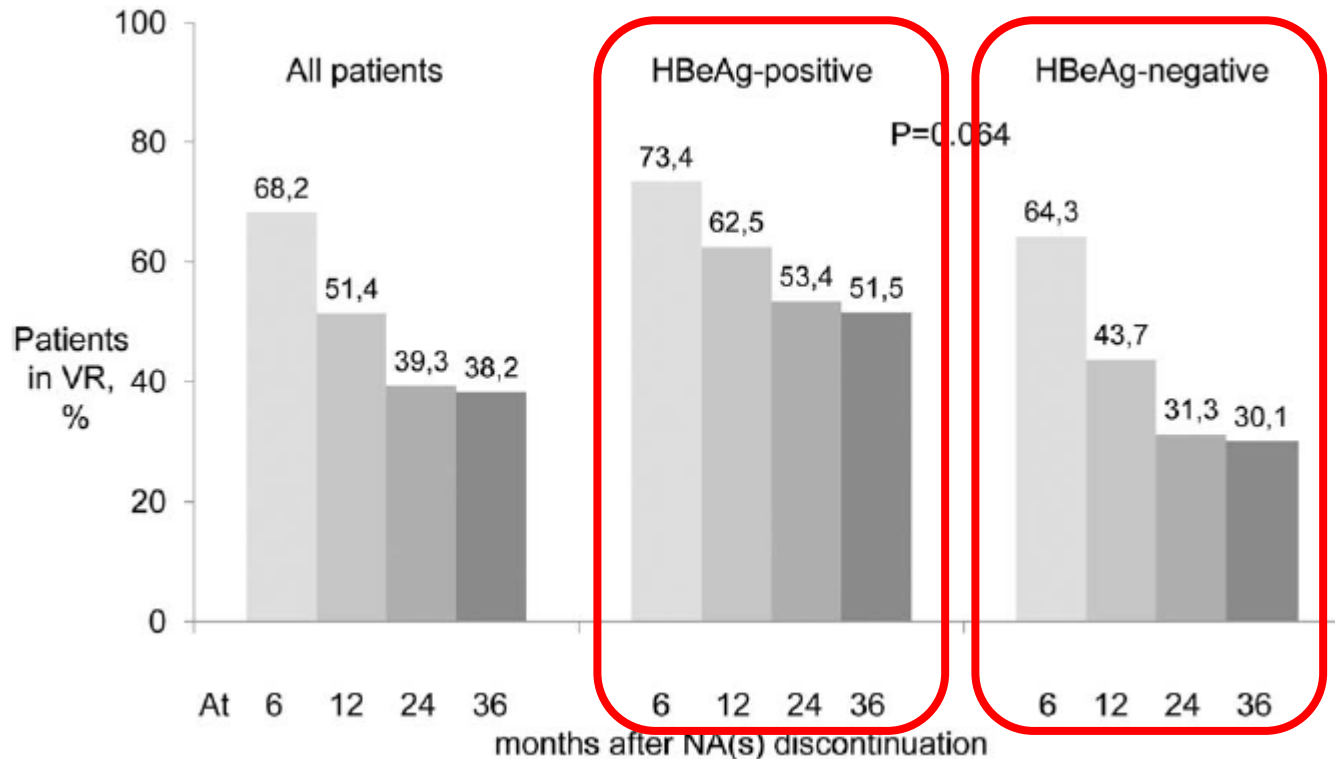
25 çalışma, 1716 hasta

HBeAg pozitif n=733

HBeAg negatif n=967

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

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

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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...

0.513

0.017

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 MD⁶;  Su, Tung-Hung MD, PhD⁷;  Wong, Grace L.H. MD⁸;  Seto, Wai-Kay MD⁹;  d'Almeida, Arno Furquim MSc¹⁰; Papatheodoridi, Margarita MD¹¹; Brakenhoff, Sylvia M. MD¹²;  Lens, Sabela MD¹³;  Choi, Hannah S.J. PhD¹; Chien, Rong-Nan MD¹⁴;  Feld, Jordan J. MD, MPH^{1,2,3}; Forns, Xavier MD¹³;  Sonneveld, Milan J. MD, PhD¹²;  Papatheodoridis, George V. MD¹¹;  Vanwolleghem, Thomas MD, PhD^{10,15};  Yuen, Man-Fung MD, PhD⁹;  Chan, Henry L.Y. MD⁸;  Kao, Jia-Horng MD, PhD⁷; Hsu, Yao-Chun MD, PhD¹⁶;  Cornberg, Markus MD^{17,18};  Jeng, Wen-Juei MD, PhD¹⁴; 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

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,