HEPATİT DELTA YÖNETİMİ

Mustafa Kemal ÇELEN

Diyarbakır

HDV Virus Yapısı ve Moleküler Özellikleri

RNA Genomu

1.7 kb, dairesel negatif tek iplikli RNA — RNA dünyasının en küçük patojeni

Delta Antijeni (HDAg)

S-HDAg (24 kDa): replikasyon aktivatörü | L-HDAg (27 kDa): replikasyonu inhibe eder, virion farnesilasyonunu tetikler

Zarf Proteini

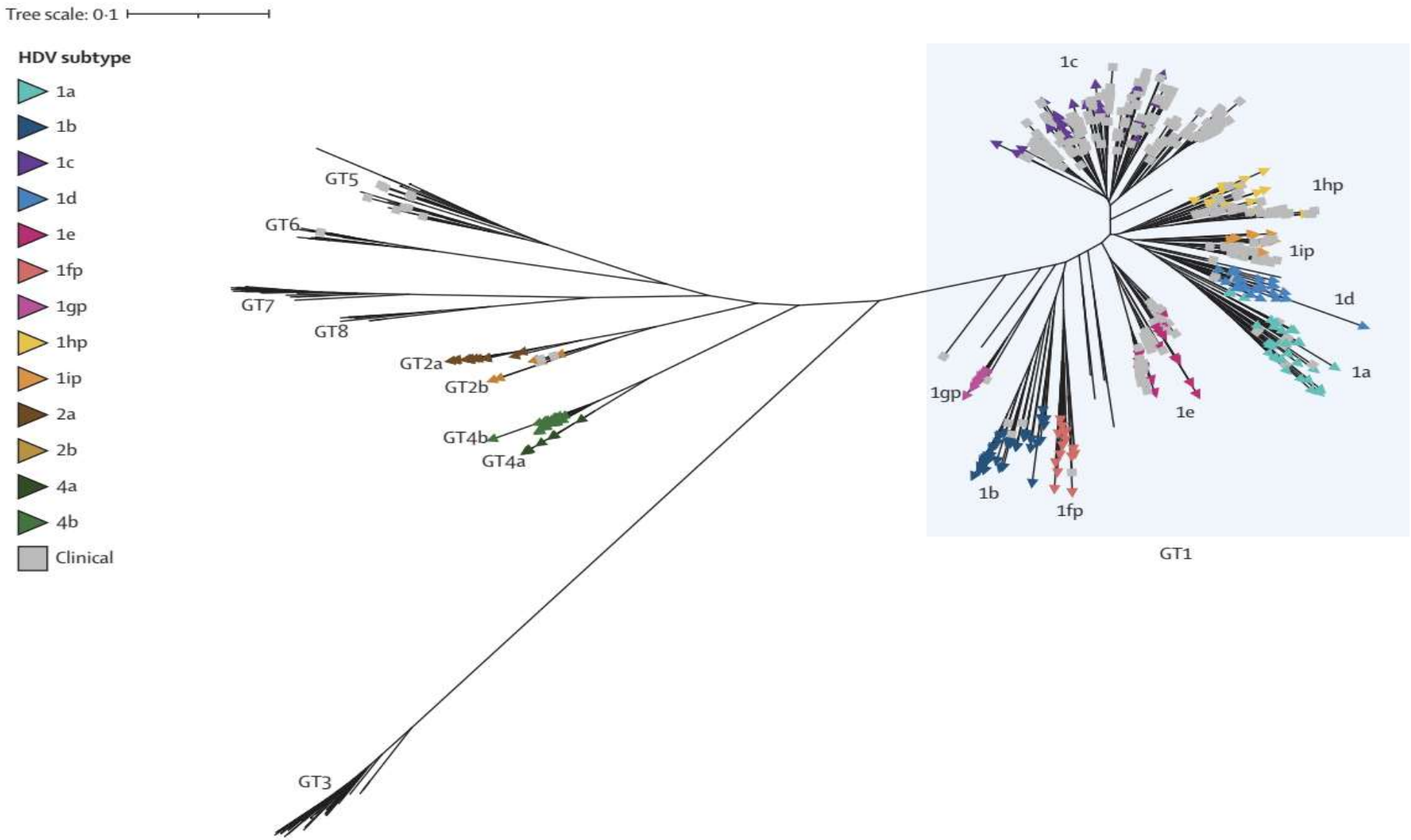
HBV'nin HBsAg proteini kullanılır — HDV kendi zarfını üretemez → HBV bağımlılığı

Ribozim Aktivitesi

Kendi kendini kesen RNA ribozimi — Virozit benzeri yapı (HDAg + RNA)

8 Genotip — Farklı Coğrafya, Farklı Klinik

GT-1	Batı Avrupa, Kuzey Amerika	*Orta şiddet*
GT-2	Japonya, Tayvan, Pasifik	*Hafif seyir*
GT-3	Güney Amerika (Amazon havzası)	*Ağır, hızlı ilerleme*
GT-4	Japonya, Batı Avrupa	*Orta*
GT-5/6	Afrika (Batı & Orta)	*Veriler kısıtlı*
GT-7/8	Afrika (Orta/Doğu)	*Yeni tanımlanan*



Lancet Microbe 2026

Virology
Volume 619, June 2026, 110879

Brief Communication

Hepatitis D Infection: a puzzle still unsolved?

Viral Hepatitlerin en agresif formu

HBsAg pozitif hastaların %5'i

Dünya genelinde 10-20 milyon vaka

HCC gelişimini hızlandırmaktadır

40 yıllık deneyim ancak hala soru işaretleri mevcut

Yeni tedaviler artık umudun ötesinde

Hepatit Delta nedir?

- Bilinen hepatit virüsleri içerisinde prognozu en ağır olanıdır
- Defektif bir virüstür
- Ko-infeksiyon veya süperenfeksiyon
- Vakaların %70-90 şiddetli seyretmektedir
- A.B.D.'lerinde en az 125.000 vaka
- Dünya genelinde 12-60 milyon vaka

NVHR
National Viral Hepatitis Roundtable

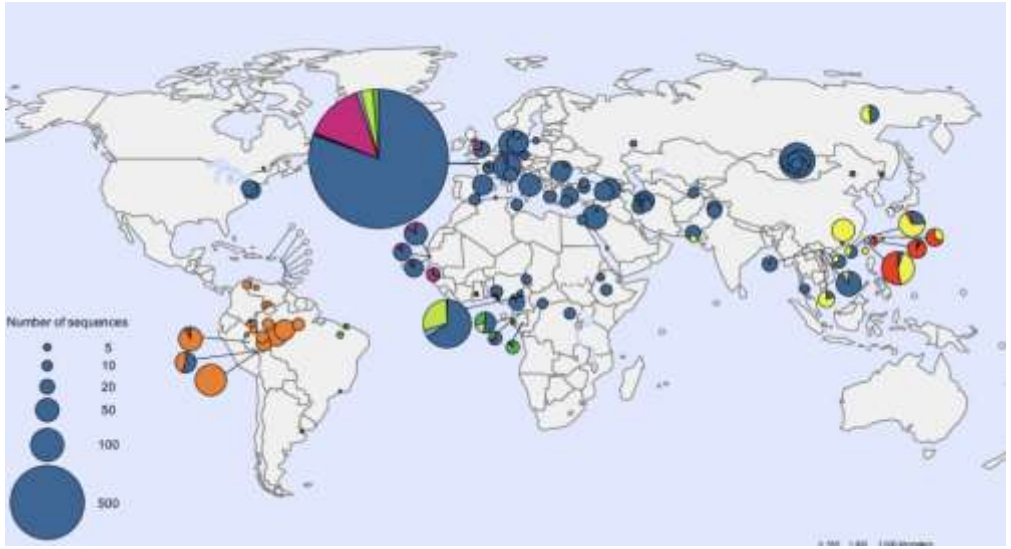
Bulaşma Yolları

- Kan ve diğer vücut sıvılarının teması ile
- Vertikal bulaşı nadir
- HBV ile bulaşı olan herkes risk altındadır
- Uyuşturucu kullananlar, sex işçileri, MSM, HCV ile yaşayanlar ve HIV/HBV'nin yoğun olduğu bölgelerde yaşayanlar risk altındadır

NVHR
National Viral Hepatitis Roundtable

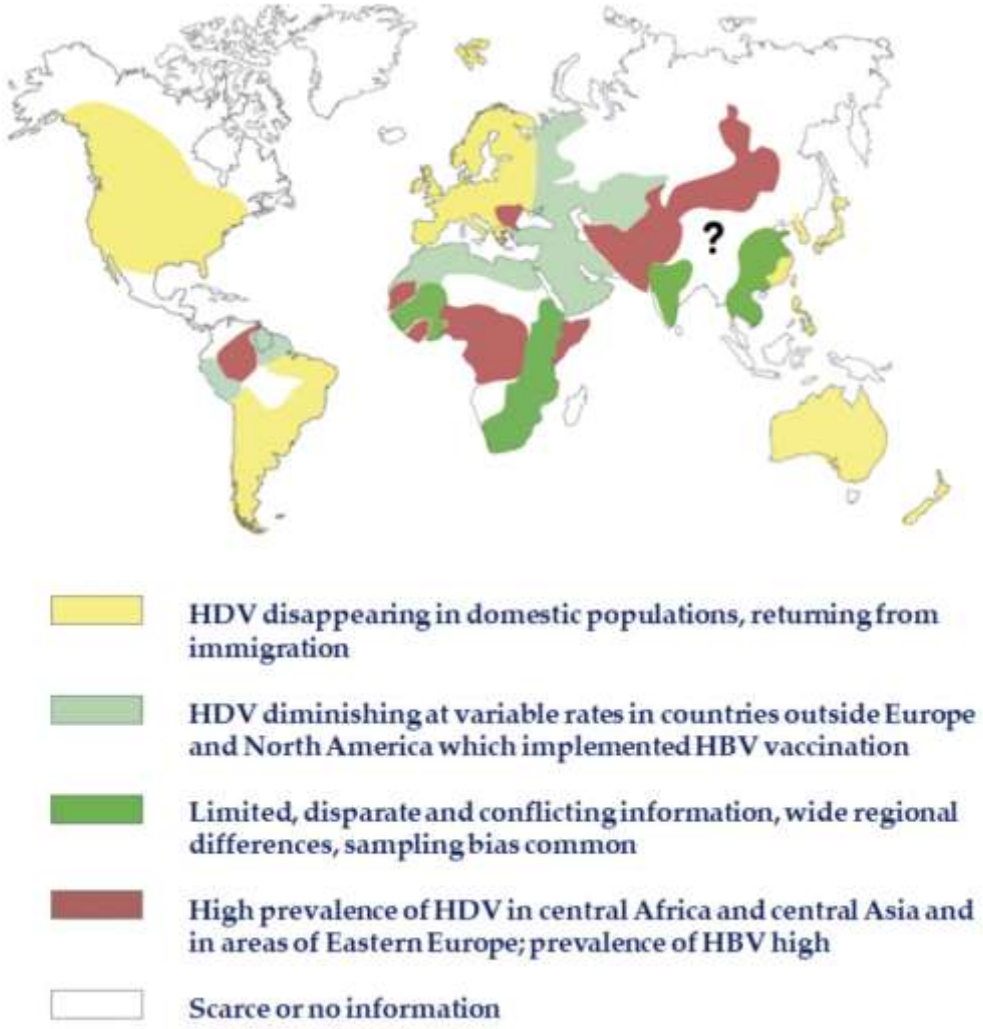
HEPATİT DELTA'DA YENİ GELİŞMELER

- HDV global bir sorundur
- HBV aşısına rağmen 2019 yılında KC-S ve HCC ilişkili 820.000 ölüm
- Gözden kaçan bir hepatit etkeni (CDC)
- Önlenebilir bir hastalıktır



Robinson A. Chronic Hepatitis B Virus and Hepatitis D Virus: New Developments. Clin Liver Dis 2023

HDV Epidemiyolojisi 🤔 🤔



Kabul edilen epidemiyoloji gerçeği yansıtıyor mu?

🤔

Gian PC. A Review of HDV Infection. Viruses 2022.

SITU(HD)VATION TÜRKİYE

GAEP
GÜNEY ANADOLU ENFEKSİYON PLATFORMÜ
ÇEHDER
GÜNİDER

FIND HDV AND DETERMINE ITS STATUS IN TÜRKİYE

NCT06248580 NEW

Find HDV and Determine Its Status in Turkey

Conditions

Chronic Hepatitis D Infection With Hepatitis B Carrier State (Diagnosis) | Cirrhosis, Liver | Fibrosis, Liver | Hepatocellular Carcinoma | Transmission Vertical

αÇG
"Alfa Çalışma Grubu"

Find HDV and Determine Its Status in Türkiye "SITU(HD) VATION TÜRKİYE"

Türkiye'de HDV'yi Bulmak ve Durumunu Belirlemek: SITU(HD)VATION TÜRKİYE

Mustafa Kemal Çelen[1], Çiğdem Mermutluoğlu[1], Yeşim Taşova[2], İsmail Yıldız[3], Yakup Demir[4], Pınar Çakmak[5], Tuba Damar Çakırca[6], Ülkiye Yetim[7], Yaşar Bayındır[8]

DOI: 10.4274/vhd.galenos.2025.2025-9-1
Viral Hepat J 2025;31(3):78-85

ABSTRACT

Objectives: Hepatitis delta virus (HDV) infection is detectable in hepatitis B surface antigen (HBsAg) positive patients and is more significant than other viral hepatitis in terms of the risk of liver cirrhosis/liver cancer. This study aimed to determine the prevalence of HDV and the clinical and histological status of patients with HDV in the southeastern region of Türkiye.

Materials and Methods: A total of 250 family physicians in the provinces of Diyarbakır, Şanlıurfa, Batman, and Mardin were trained on the importance of HDV infection and the follow-up of patients with HBsAg positivity. The importance of HDV was emphasised. For this purpose, the importance of prospectively screening 20,000 HBsAg-positive patients under the care of family physicians for HDV was highlighted. Human immunodeficiency virus (HIV) testing was also conducted in patients who tested positive for anti-delta. Patients who tested positive for HDV were referred to gastroenterology/infectious diseases specialists. Liver stiffness measurement (LSM) and controlled attenuation parameter (CAP) values were measured using Fibroscan® in patients who tested positive for HDV.

Results: A total of 20,000 HBsAg-positive patients were included in the study. The mean age of the patients was 38.2 years; 64.3% of the patients were male. Anti-delta seropositivity was detected in 1,019 (5.1%) of HBsAg-positive patients. Patients with anti-delta positivity were referred to a specialist physician for diagnosis and follow-up. HDV-ribonucleic acid (RNA) >500 copies/mL was detected in 367 patients (36%). Vibration-controlled transient elastography was performed with the M530 Fibroscan® device in 992 HDV-positive patients to assess LSM and CAP. Liver cirrhosis was detected in 5.5% of patients. Among patients with liver cirrhosis, HDV-RNA was positive in 92.8% and alanine aminotransferase levels above the upper limit of normal were detected in 71.4%. The mean LSM in delta patients was 8.7 kPa, compared with 17.2 kPa in cirrhotic HDV-infected patients ($p<0.05$). HIV testing was performed on 1,019 HDV-positive patients, and HIV was detected in 18 patients (1.8%). Of these patients, 38.8% reported a history of intravenous drug use. CAP values were significantly higher in patients with hepatitis B virus+HDV+HIV coinfection. The metabolic dysfunction-associated steatotic liver disease rate was 72.2% in these patients.

Conclusion: Anti-delta positivity was detected in 5.1% of HBsAg-positive patients in the southeastern region of our country. Liver cirrhosis was observed in 5.5% of these patients. HIV positivity was also observed in 1.8% of HDV-positive patients. HDV is a significant problem in our country; therefore, HBsAg-positive patients should be evaluated for HDV. Additionally, HDV/HIV co-infection is a significant issue, particularly among intravenous drug users.

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Conclusion: Anti-delta positivity was detected in 5.1% of HBsAg-positive patients in the southeastern region of our country. Liver cirrhosis was observed in 5.5% of these patients. HIV positivity was also observed in 1.8% of HDV-positive patients. HDV is a significant problem in our country; therefore, HBsAg-positive patients should be evaluated for HDV. Additionally, HDV/HIV co-infection is a significant issue, particularly among intravenous drug users.

Keywords: Chronic hepatitis D, hepatocellular carcinoma, liver cirrhosis, hepatitis B virus (HBV), hepatitis D virus (HDV)

Viral Hepat J 2025; 31(3):78-85

e "SITU(HD)

/ATION TÜRKİYE

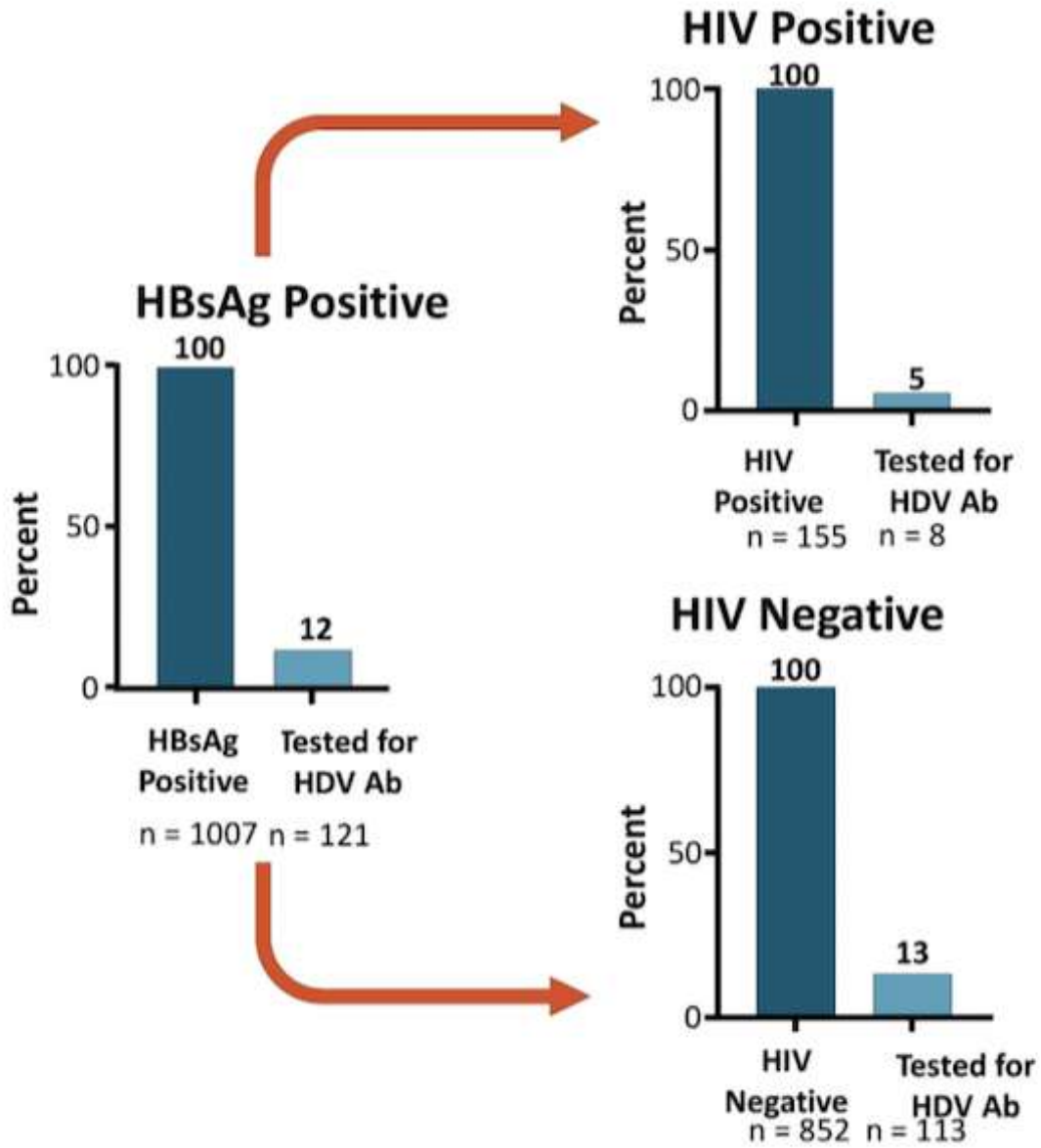
e HDV

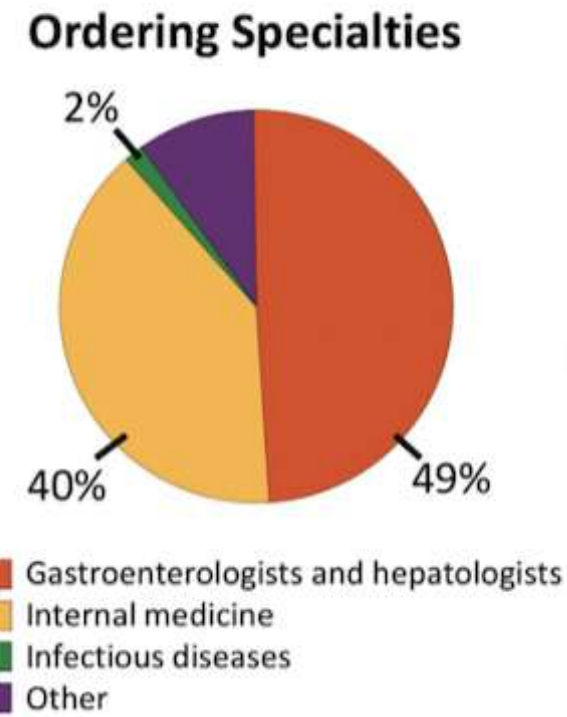
Yıldız[3], Yakup Demir[4],

Curr Opin HIV AIDS 2026, 21:148–154

Linkage to Care: First Step to Care Is Diagnosis

- Study examined patients from University of Cincinnati Medical Center who tested positive for HBsAg from 1994-2004
  - HDV screening very low
  - Significantly lower among people with HIV
  - Vast majority of HDV screening performed by gastroenterologists and internal medicine practitioners





faie. Virus Res. 2018;250:114.

Slide credit: clinicaloptions.com

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DOI: 10.1111/jvh.13797

INVITED REVIEW

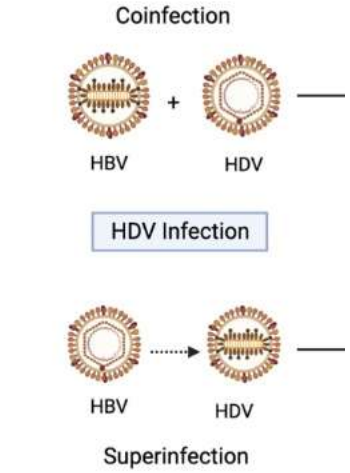
Delta hepatitis epidemiology and t

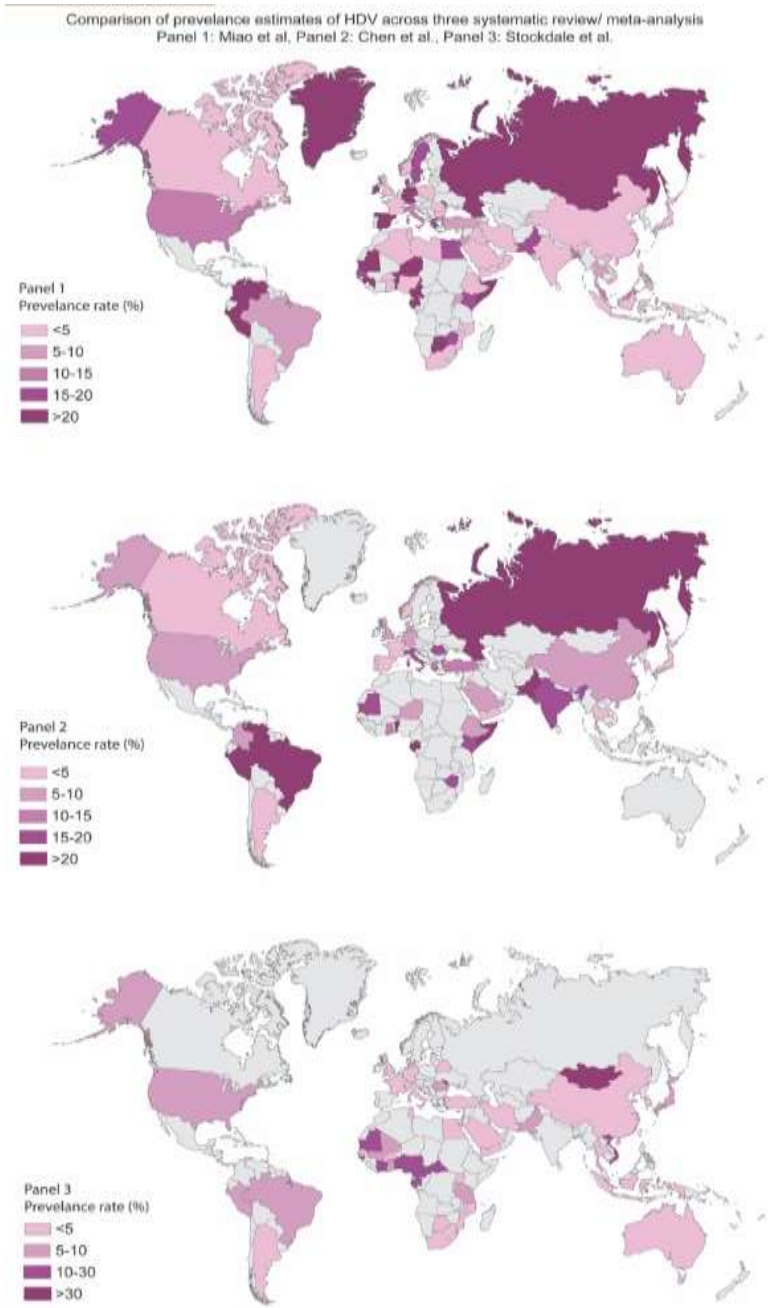
Tatyana Kushner

Division of Liver Diseases, Icahn School of Medicine at Mount Sinai, New York, New York, USA

Correspondence
Tatyana Kushner, Division of Liver Diseases, Icahn School of Medicine at Mount Sinai, One Gustave L Levy Place, Box 1123, New York, NY 10029, USA.
Email: tatyana.kushner@mssm.edu

Abstract





sk factors associated with delta hepatitis.

countries	Low-income countries
; use	HIV infection
rom endemic regions	Sexual transmission
ission	Intrahousehold transmission
	Iatrogenic
	Cultural practices

Kimler HDV açısından taranmalı?

- HBsAg pozitif
- HDV prevalansı yüksek bölgeler
- MSM
- IVDU
- HCV ve HIV öyküsü olanlar
- Çoklu cinsel partneri olanlar
- Düşük HBV-DNA düzeyi olanlar
- KCFT yüksek olanlar

AASLD 2024

Regional Disparities in Hepatitis D Screening and Prevalence Across Turkey:A Multicenter Cohort Study

Number : 3405

Topic: Clinical Science

Sub-Topic: Viral hepatitis B and D: Clinical aspects

Muge Ozari Gulnar[1], Çiğdem Mermutluoğlu[2], Özgür Aktaş[3], Ilker Sen[4], Mehmet Akif Yağlı[5], Erman Mercan[6], Furkan Çakmak[7], Zeynep Melekoğlu Ellik[8], Derya Ari[9], Onur Keskin[7], Meral Akdogan Kayhan[9], Canan Alkim[6], Ramazan Idilman[8], Kendal Yalcin[10], Olga Metİn[4], Sabahattin Kaymakoğlu[5], Mustafa Celen[2], Cihan Yurdaydin[1]

EASL Congress
27-30 May 2026
Barcelona, Spain

Türkiye Genelinde Hepatit D Taraması ve Yaygınlığındaki Bölgesel Farklılıklar: Çok Merkezli Bir Kohort Çalışması

- HDV açısından biz hekimler yeterince farkında mıyız?
- 2016-18 ve 2022-24 dönemleri
- Yeni tanı alan HBsAg pozitif hastalar belirlendi, hangi branş? Süreç?
- GE veya ID ve diğer bölümlerden sevkler
- HDV pozitifliğinin belirleyicilerini belirlemek için tek değişkenli lojistik regresyon ve ardından çok değişkenli analiz kullanıldı
- Model ayrımcılığı AUC ve kalibrasyon ise Hosmer-Lemeshow testi ile değerlendirildi

- 30.546 HBsAg pozitif hastanın %40 tanısı branş dışı alanlarda konmuş
- Covid sonrası HDV taramasında GE'de (%61-67) yükselirken, ID bölümlerinde %74'ten %57'ye düştü
- 15.247 hastanın detaylı analizi, 9.689'unun (%63,5) HDV taramasından geçtiğini ortaya koydu
- Tarama oranları önemli ölçüde farklılık gösterdi:

  GDA %79'a karşı BA %50 ($p<0,001$)
- Anti-HDV pozitif %6,5 bulundu; GDA %7,0 diğer bölgelerde %4,9
- HDV pozitif hastalarda daha yüksek siroz, düşük PLT, GDA kökenli olma
- GDA bölgesinde HDV tarama oranı sırasıyla %63,5 ve %79 olarak saptandı

TEDAVİ...

Published in final edited form as:
Gastroenterology. 2019 January ; 156(2): 461–476.e1. doi:10.1053/j.gastro.2018.09.058.

Pathogenesis of and New Therapies for Hepatitis D

Christopher Koh[1], **Theo Heller**[1], and **Jeffrey S. Glenn, MD**[2]

[1]Liver Diseases Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland, USA;

[2]Division of Gastroenterology and Hepatology, Stanford University School of Medicine, Stanford, California, USA

Abstract

Hepatitis delta virus (HDV) infection of humans was first reported in 1977, and now it is now estimated that 15–20 million people are infected worldwide. Infection with HDV can be an acute or chronic process that occurs only in patients with an HBV infection. Chronic HDV infection commonly results in the most rapidly progressive form of viral hepatitis; it is the chronic viral infection that is most likely to lead to cirrhosis, and it is associated with an increased risk of hepatocellular carcinoma. HDV infection is the only chronic human hepatitis virus infection without a therapy approved by the Food and Drug Administration. Peginterferon alpha is the only recommended therapy, but it produces unsatisfactory results. We review therapeutic agents in development, designed to disrupt the HDV life cycle, that might benefit patients with this devastating disease.

Received: 18 January 2021 | First decision: 27 February 2021 | Accepted: 30 April 2021

DOI: 10.1111/apt.16408

APT Alimentary Pharmacology & Therapeutics WILEY

Uzun süreli PEG-INF ????

Durable virological response and functional cure of chronic hepatitis D after long-term peginterferon therapy

Julian Hercun[1] | Grace E. Kim[1] | Ben L. Da[1] | Yaron Rotman[1] | David E. Kleiner[2] | Richard Chang[3] | Jeffrey S. Glenn[4] | Jay H. Hoofnagle[5] | Christopher Koh[1] | Theo Heller[1]

- Toplamda 12 vaka
- %83 beyaz ırk
- %92'si erkek
- Tedavi: 74 ay Peg-INF
- Takip süresi 104 ay
- SVR oranı %58
- HBsAg kaybı %33

Summary

Background: Hepatitis delta virus (HDV) infection is the most aggressive form of chronic viral hepatitis. Response rates to therapy with 1- to 2-year courses of pegylated interferon alpha (peginterferon) treatment are suboptimal.

Aims: To evaluate the long-term outcomes of patients with chronic hepatitis D after an extended course of peginterferon.

Methods: Patients were followed after completion of trial NCT00023322 and classified based on virological response defined as loss of detectable serum HDV RNA at last follow-up. During extended follow-up, survival and liver-related events were recorded.

Results: All 12 patients who received more than 6 months of peginterferon in the original study were included in this analysis. The cohort was mostly white (83%) and male (92%) and ranged in age from 18 to 58 years (mean = 42.6). Most patients had advanced but compensated liver disease at baseline, a median HBV DNA level of 536 IU per mL and median HDV RNA level of 6.86 $\log_{10}$ genome equivalents per mL. The treatment duration averaged 6.1 years (range 0.8-14.3) with a total follow-up of 8.8 years (range 1.7-17.6). At last follow-up, seven (58%) patients had durable undetectable HDV RNA in serum, and four (33%) cleared HBsAg. Overall, one of seven (14%) responders died or had a liver-related event vs four of five (80%) non-responders.

Conclusions: With further follow-up, an extended course of peginterferon therapy was found to result in sustained clearance of HDV RNA and favourable clinical outcomes in more than half of patients and loss of HBsAg in a third.

Clinical Trial > Lancet Infect Dis. 2019 Mar;19(3):275-286. doi: 10.1016/S1473-3099(18)30663-7.

Peginterferon alfa-2a plus tenofovir disoproxil fumarate for hepatitis D (HIDIT-II): a randomised, placebo controlled, phase 2 trial

Heiner Wedemeyer [1], Cihan Yurdaydin [2], Svenja Hardtke [3], Florin Alexandru Caruntu [4], Manuela G Curescu [5], Kendal Yalcin [6], Ulus S Akarca [7], Selim Gürel [8], Stefan Zeuzem [9], Andreas Erhardt [10], Stefan Lüth [11], George V Papatheodoridis [12], Onur Keskin [13], Kerstin Port [14], Monica Radu [4], Mustafa K Celen [6], Ramazan Idilman [13], Kristina Weber [15], Judith Stift [16], Ulrike Wittkop [17], Benjamin Heidrich [3], Ingmar Mederacke [14], Heiko von der Leyen [18], Hans Peter Dienes [16], Markus Cornberg [14], Armin Koch [15], Michael P Manns [19], HIDIT-II study team

Affiliations + expand

PMID: 30833068 DOI: 10.1016/S1473-3099(18)30663-7

14 merkezli bir çalışma
Randomize plasebo kontrollü
59 hastaya PEG-INF+TDF
61 hastaya PEG-INF+plasebo

944 AO izlendi
SVR açısından fark yok ☹

Kombinasyon tedavileri...???

HDV ve KÜR !?!?

- Hepatit D, karaciğer ilişkili mortalitesi en yüksek olan viral hepatit tipidir.

Prenylation inhibitörleri

Giriş yolu inhibitörleri

Nükleik asid polimeraz blokerleri

- Ciddi yan etkiler ve uzun dönem takiplerde relaps oranı yüksektir
- Acil olarak yeni tedavi seçeneklerine ihtiyaç var.

Wranke A, Wedemeyer H. Antiviral therapy of hepatitis delta virus infection - progress and challenges towards cure. Curr Opin Virol. **2016 Oct 25;20:112-118**.

Pegylated Interferon Lamda (NCT05070364)

- Tıp III interferon reseptör agonisti
- Hepatosite virüslerin girişini bloke etmektedir
- Yan etkileri daha düşük
- Etkinliği daha yüksek
- Faz-2 LIMIT 002 çalışmasında TS sonu viral yanıt %36, SVR ise %19 gibi düşük bir oranda bulundu
- Faz-3 çalışmasında da sonuçlar çok da umut vaade edici olmadı

Pegylated Interferon Lamda (NCT05070364)

DEAR INVESTIGATORS!

This month we celebrate another remarkable success of the **EIG-LMD-002 study** with a total of **147** subjects randomized to date. We are rapidly approaching our randomization goal andthis achievement would not have been possible without your diligence and strong determination. Thank you to all for your unwavering support! Please continue with your outstanding work as we strive to reach more study milestones.
Please contact your CRA for any questions about the study.

ENROLLMENT UPDATES

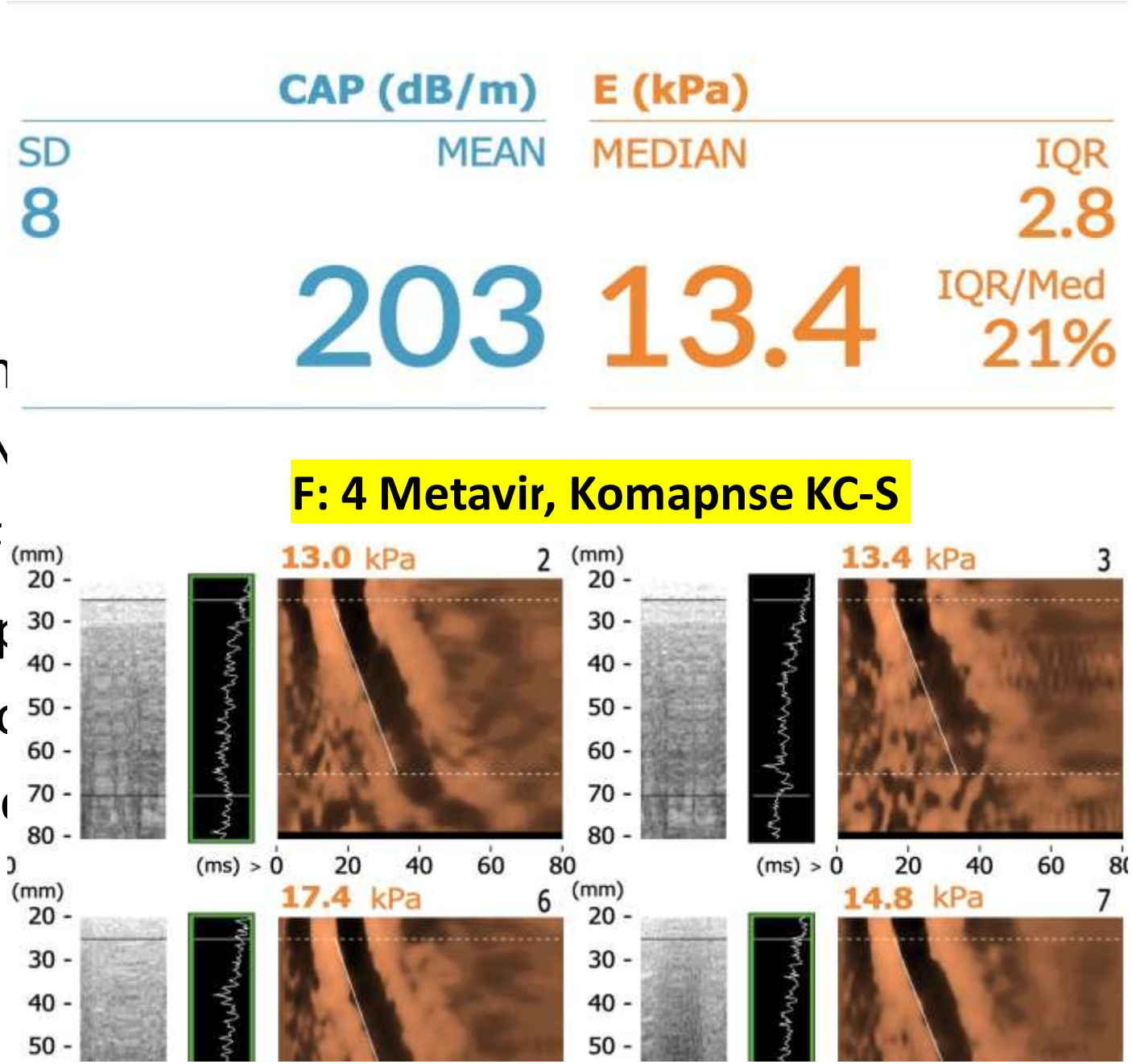
The total number of active sites is **44**. Out of the **273** screened subjects, **147** have been randomized. The top **6** sites with randomized subjects are presented in the table below.

PI	Country	No. of Randomized Subjects
Dr. Elena Laura Iliescu	Romania	25
Dr. Adela Turcanu	Moldova	18
Dr. Mustafa Kemal Celen	Turkey	16
Dr. George Sebastian Gherlan	Romania	14
Dr. Alexandru Florin Caruntu	Romania	13
Dr. Cihan Yurdaydin	Turkey	11

OLGU

- 53 yaş, kadın
- 2011 yılında tan
- ALT 118, HDVRN
- T.Bil normal, AF
- USG; karaciğer p
- Dalak normal bo
- 2014 ve 2017 d

OAV başlandı…



PEG-INF LAMDA 180 mcg/hafta

- Tedavinin 8.haftasında ALT 390, T.Bil 5.1, INR normal
- İdrar rengi koyu, kaşıntı mevcut, iştahsızlık ve kilo kaybı var
- Ne olmuş olabilir? Ne yapmak gerekir?

□ □

SİROTİK HASTAYA PEG-INF LAMDA

Tedavisine ara verildi ve izlendi

- 2 hafta sonra ALT 150, T.Bil 1.1
- Hastaya tedavisi 120 mcg/hafta olarak yeniden başlandı
- TX 16. haftasında HDVRNA 3.400, ALT 91
- TX 48. haftasında HDVRNA negatif ve ALT 32

SVR gelişti... ☺

Editorial

EASL JOURNAL OF HEPATOLOGY

Journal of Hepatology **2016** vol. 65 | 465–466

Myrcludex B, a novel therapy for chronic hepatitis D?

Mario Rizzetto[1,*], Grazia Anna Niro[2]

[1]*Department of Internal Medicine – Gastroenterology, University of Torino, Italy;* [2]*IRCCS "Casa Sollievo Sofferenza" Hospital, Gastroenterology Unit, San Giovanni Rotondo (FG), Italy*

See Articles, pages 483–489 and pages 490–498

The second paper (Treatment of chronic hepatitis D with the entry inhibitor myrcludex B – first results of a Phase Ib/IIa study; Pavel Bogomolov *et al.*) reported the interim results of the use of Myrc in CHD, and aimed to provide a proof of concept of the blocking strategy. The rationale was that the prolonged inhibition of the HDV entry by the HBsAg block should protect uninfected hepatocytes from new HDV infection, ultimately leading to the eradication of the virus.

Myrcludex B 2 mg/gün s.c. 24 hafta

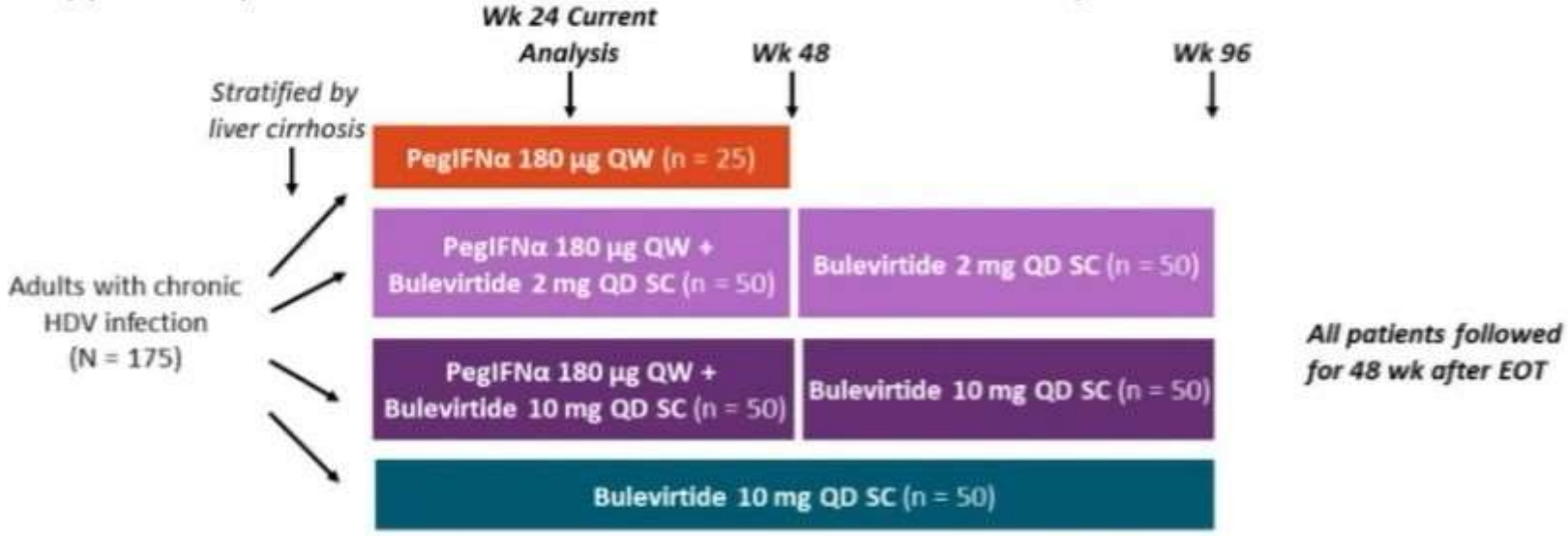
Bulevirtide (Formerly Myrcludex B)

- HBV zarf proteinin Pre-S1 alanından üretilen ve deri altına enjekte edilen sentetik lipopeptittir
- NTCP reseptörüne bağlanarak HBV'nin girişini engeller
- Faz çalışmalarında ALT normalizasyonu
- HDV-RNA kaybı (2 log düşüş)
- Ancak SVR oranı düşük, daha uzun süreli tedavi???
- Bir hastada HBsAg kaybı gelişmiş (PEG-INF+BLV)
- Düşük advers olay

MYR204: FAZ IIB

MYR204: Bulevirtide Alone and Combined With PegIFNα-2a for Chronic HDV Infection: Wk 24 Analysis

- Multicenter, international, open-label, randomized phase IIB trial of bulevirtide, entry inhibitor approved by EMA for use in adults with chronic HDV and compensated cirrhosis

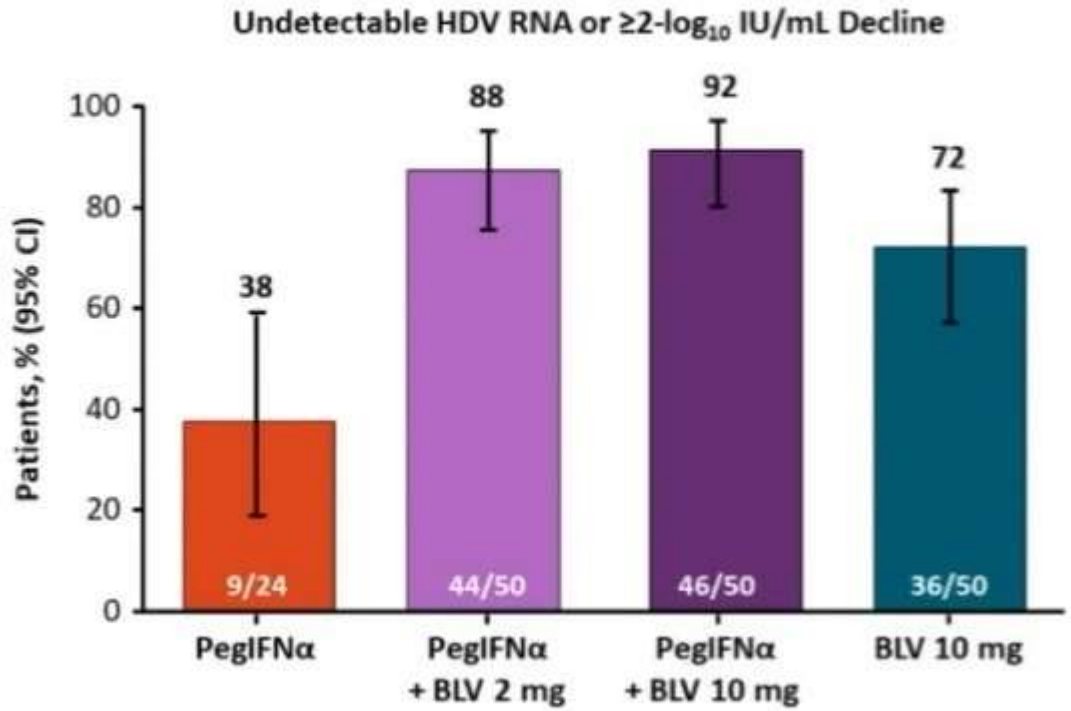


- Primary endpoint: Undetectable HDV RNA (LLD: 6 IU/mL) at Wk 24 after EOT

Asselah. EASL 2020. Abstr 2717.

Slide credit: clinicaloptions.com

MYR204 Interim Wk 24 Analysis: Virologic Response



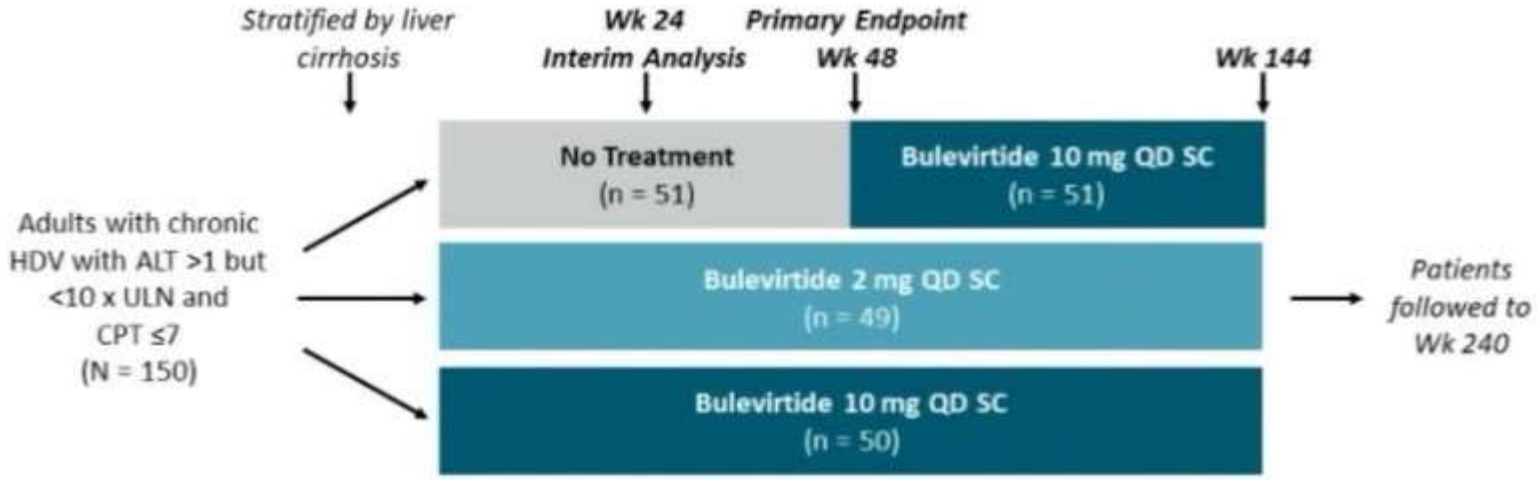
Asselah. EASL 2020. Abstr 2717.

Slide credit: clinicaloptions.com

MYR301: FAZ III

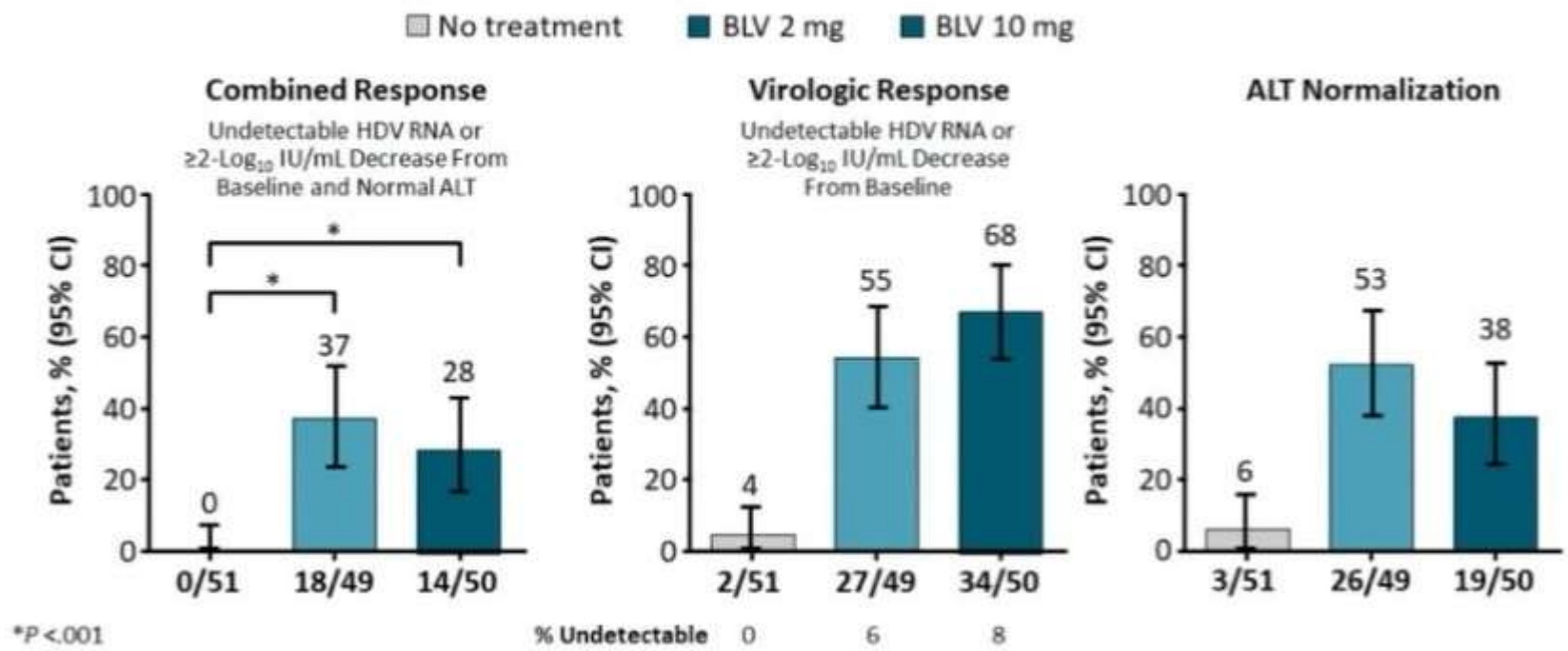
MYR301: High- vs Low-Dose Bulevirtide Monotherapy in Patients With Chronic HDV Infection

- Multicenter, open-label, randomized, phase III trial



- Primary endpoint: Combined response defined by undetectable HDV RNA or decrease by ≥2 $\log_{10}$ IU/mL from baseline + normalized ALT at Wk 48

MYR301 Interim Analysis: Virologic Efficacy at Wk 24



Turkish Real-World Effectiveness and Safety of Bulevirtide in Chronic Hepatitis Delta: A Multicentric Experience with Long-Term Follow Up

Muge Ozari Gulnar
Mustafa Kemal Çelen
Mehmet Akif Yağlı
Özgür Aktaş
Gökhan Kabaçam
Mujdat Zeybel
Yılmaz Çakaloğlu
Murat Akyildiz
Sabahattin Kaymakoğlu
Cihan Yurdaydin

EASL Congress
27-30 May 2026
Barcelona, Spain

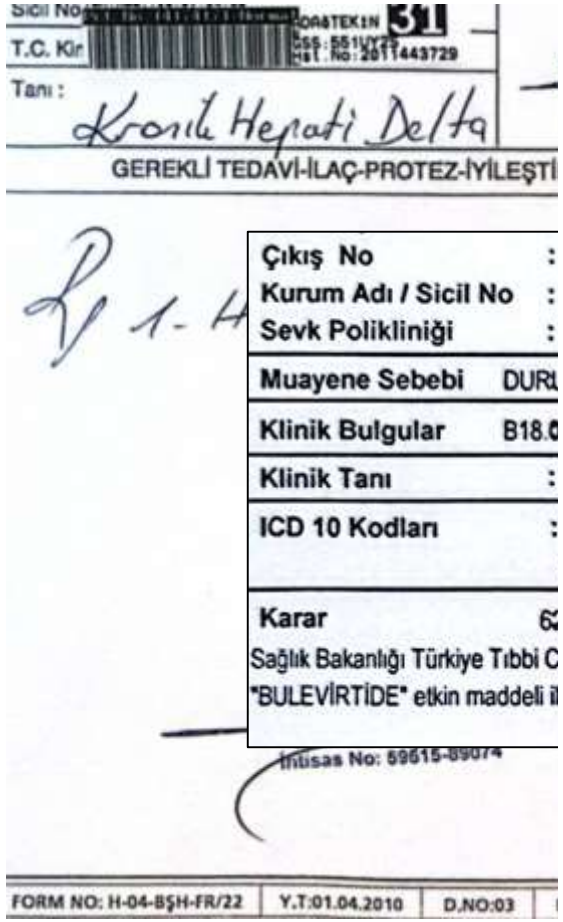
Method:
33 patients with CHD who initiated BLV therapy between 2020-2023 were analyzed. All patients had baseline detectable HDRNA and elevated ALT. Five patients had decompansated cirrhosis all other patients had compensated liver disease. Seven patients used the European label Hepcludex, and remaining 26 patients received Myrcludex from Russia. Primary outcomes were VR (defined as undetectability or > 2 log decrease in HDVRNA) and BR (defined as ALT normalization) at end of on-treatment follow-up (FU). VBr was defined as an increase of HDV RNA > 1log from nadir or HDV RNA becoming detectable after undetectability. Statistical analyses included t and Mann-Whitney U tests for continuous and Fisher's exact and Chi-squared tests for categorical variables.

Results:
Mean (±SD) baseline ALT was 99.6 (± 66.7) U/L and HDVRNA was 4.94 (± 1.11 log) IU/mL. At 12 months, VR was achieved in 74.1% (20/27) of evaluable patients, and BR was 70.4% (19/27). Response rates were sustained through 24 months reaching 61.1% (11/18) with VR and 64.7% (11/17) with BR. VBr occurred in 4 of 26 patients on the Russian BLV (15.4%). Patients with VBr had higher baseline INR (1.22±0.03 vs 1.04 ± 0.14, p=0.033) and a trend toward higher baseline HDVRNA (5.82 ± 0.81 vs 4.82 ± 1.10 log. IU/mL, p=0.091). Two patients with VBr had no on-treatment FU HDVRNA testing. Remaining 2 patients continued therapy and had persistent viremia throughout FU. Mean time to VBr was 18.5 ± 3.87 months (range: 15-24 months). Following VBr, 3 patients experienced ALT elevations. Seven patients (21%) discontinued BLV treatment (21.2%) at median 19 months (range 12-27). Decompensated patients (n=5, 15.2%) demonstrated similar VR rates compared to patients with compensated liver disease, suggesting efficacy across the disease severity spectrum.. BLV was well tolerated.

Conclusion:
In this real-world Turkish cohort, BLV demonstrated VR in 74% of patients at 12 months on-treatment and, maintained VR in the majority throughout 36 months. An unexpected high VBr rate was observed with the Russian BLV. Patients denied non-compliance.

33 Hepatit Delta hastası (5 dekompanse KC-S)
Bluvertide 2 mg
12 aylık tedavinin sonunda SVR %74
Rus BLV VBr %15.4
VBr gelişimi ile baseline da yüksek INR ve HDV-RNA seviyesi

Bluvertide r


T.C. Kir
Tanı : Kronik Hepati Delta
GEREKLİ TEDAVİ-İLAÇ-PROTEZ-İYİLEŞTİ
Çıkış No :
Kurum Adı / Sicil No :
Sevk Polikliniği :
Muayene Sebebi DURL
Klinik Bulgular B18.0
Klinik Tanı :
ICD 10 Kodları :
Karar 6
Sağlık Bakanlığı Türkiye Tıbbi C
"BULEVİRTİDE" etkin maddeli il
İmzası No: 59615-89074
FORM NO: H-04-BŞH-FR/22 Y.T:01.04.2010 D.NO:03

gereğince;

GEREĞİ DÜŞÜNÜLDÜ:

Davacı vekili dava dilekçesinde özetle; davacıya kronik viral hepatit b, delta ajanlı tanısı konulduğunu ve tedavi süresince **"Bulevirtide" etken maddeli "Hepcludex"** isimli ilacı kullanmak zorunda olduğunu, söz konusu ilacı kullanamaması durumunda yaşamının tehlikeye gireceği göz önünde bulundurularak kesinti yapılmaksızın teminatsız olarak ihtiyati tedbir kararı verilmesini, ilaç bedellerinin davalı Kurumtarafından karşılanmasını ve davanın kabulüne karar verilmesini istemiştir.

HMK 389. maddesinde; mevcut durumda meydana gelebilecek bir değişme nedeni ile hakkın elde edilmesinin önemli ölçüde zorlaşacağından yada tamamen imkansız hale geleceğinden veya gecikme sebebi ile bir sakıncanın yahut ciddi bir zararın doğacağından endişe edilmesi halinde uyuşmazlık konusu hakkında ihtiyati tedbir kararı verilebileceği düzenlenmiştir. Dosyaya sunulan delillerden sözkonusu ilacın kullanılmamasının davacının yaşamına, maddi ve manevi bütünlüğüne karşı ciddi bir tehlike oluşturduğu anlaşılmaktadır. Davacının tedavisinin halen devam etmekte oluşu dikkate alındığında davanın tam ispata ulaşılıp karar verilmesinin beklenilmesi ihtimalinde talep sonucu istek karara bağlansa dahi bir anlam ifade etmeyecek olması veya davacının ileride haksız çıkma ihtimalinde de Kurumun ilaç bedelini tahsil imkanının bulunması hususları bir arada gözetilerek ihtiyati tedbir talebinin takdiren teminatsız olarak kabulüne ve davacının tedavisinde kullanılan **"Bulevirtide" etken maddeli "Hepcludex"** isimli ilacın ihtiyati tedbir karar tarihinden itibaren reçetede belirtilen kullanım dozu ile sınırlı olmak üzere **1 yıl süreyle** doz bedelinin kesintisiz olarak davalı Kurumca tedbiren karşılanmasına, karar vermek gerekmiştir.

HÜKÜM:

1-Davacı vekilinin ihtiyati tedbir talebinin **teminatsız olarak KABULÜ** ile; davacının tedavisinde kullanılan **"Bulevirtide" etken maddeli "Hepcludex"** isimli ilacın ihtiyati tedbir karar tarihinden itibaren reçetede belirtilen kullanım dozu ile sınırlı olmak üzere **1 yıl süreyle** doz bedelinin kesintisiz olarak davalı Kurumca tedbiren karşılanmasına,

2-İhtiyati tedbir kararının taraflara tebliğine,

3-Sosyal Güvenlik Kurumu ilgili ünitesine kabul edilen ihtiyati tedbir kararı kapsamında işlem yapılmasının bildirilmesine,

Dair; dosya üzerinde yapılan inceleme sonunda, kararın taraflara tebliğinden itibaren HMK 394/2. maddesi gereğince 1 haftalık süre içinde Mahkememiz nezdinde yapılacak itiraz yolu açık olmak üzere karar verildi.17.04.2026

df

MAL ÇELEN

Alt Tanı	Tanı Tarihi
B18.0	5.08.2025

K. Şekli	Rapor Süresi
Subkutan	1 Yıl

la T.C
en
ranılmıştır.

ındur. "Yurt Dışından İlaç Temini
çileri (SGK bünyesindeki İbn-i Sina Sağlık
Türk Eczacıları Birliği) aracılığı ile
yurtdışından ithalatı uygundur. Tedaviye devam edilmek istenilmesi durumunda başvurunuzu
güncel tetkiklerle birlikte yapabilirsiniz.

Key Questions on Emerging Treatments for Hepatitis Delta

Heiner Wedemeyer, MD

Professor and Chairman
Department of
Gastroenterology, Hepatology
and Endocrinology
Hannover Medical School
Hannover, Germany

?

Bulevirtid kullanımını optimize etmek için cevaplanması gereken sorular var

Kombinasyon tedavisi ve tedavi süresi?

- İnterferon ile kombinasyon tedavisi bir seçenek midir?
- Kombinasyon tedavisinde sinerjik etkiler görüldü, veriler henüz yetersiz
- Hastalarda her iki ilacı da bıraktığında ne olduğunu henüz biliminmemekte
- Devam eden MYR204 çalışma sonuçları beklenmektedir

Yanıtsız hastalar !!!

- Bulevirtid tedavisine yanıt vermeyebilecek hastalar var mı?
- Hangi faktörler tedavi yanıtını etkiler?
- Tedaviyi bıraktıktan sonra nüks?
- Bu vakalardan herhangi biri doğruysa, bulevirtide ek alternatif tedavilere ihtiyacımız olabilir mi?

Lonafarnib

- Farnesil transferaz inhibitörüdür
- Prenilasyonu engelleyerek HDV virion oluşumunu engeller
- Lonafarnib 100 mg ve 200 mg günde iki kez ve 28 gün alındı ve 6 ay takip edildi (faz II)
- Ritonavirli ve ritonavirsiz gruplarda HDV RNA düşüşü görüldü
- PEG-INF ile kombine edildi
- GIS yan etkileri yüksek
- ALT normalizasyonu %52

- Lonafarnib + PEG-INF
- PEG-INF
- Lonafarnib
- 18 hasta dahil edildi
- SVR %30
- AE çok fazla

LMT-2 NEWSLETTER

EIGER BIOPHARMACEUTICALS

biorasi Faster Trials

EIG-LMD-002 | July 2022 | ISSUE #1

SCREENING & ENROLLMENT UPDATES

There are **109 patients screened** in the study and **18 sites activated** in Romania, Moldova, Turkey, Spain, USA, Israel and Germany.

Let us continue working together as we are looking to screen up to 200 more patients.

Congratulations to **Dr. Grambihler** on your site's recent activation! We wish you and your study participants the best of luck!

Site	Country	No. of Patients
Dr. Elena Laura Iliescu	Romania	23
Dr. George Sebastian Gherlan	Romania	20
Dr. Adela Turcanu	Moldova	16
Dr. Mustafa Kemal Celen	Turkey	16
Dr. Alexandru Florin Caruntu	Romania	13
Dr. Liliana Baroiu	Romania	7
Dr. Maria Buti	Spain	7
Dr. Ho Bae	United States	4
Dr. Yana Davidov	Israel	2
Dr. Dieterich	United States	1

Olgu-I

- 40 yaş, erkek, (2019)
- Bursa
- 10 yıl önce tanı almış
- HBV+HDV
- HBVDNA 167 IU/ml
- HDVRNA 40.000
- ALT 89
- İki kez PEG-INF almış

- Non sirotik
- USG de dalak normal
- Anti-HCV negatif
- Steatoz yok
- AST 40
- Trombosit 239.000
- Tedavi almaya istekli

D-LIVER ÇALIŞMASINA DAHİL OLDU…

- Pegasys 180 mcg/haftalık + Lonafarnip
- Tx 10. haftası ALT 399, Trombositler 115.000
- Ne yapmalı??? Ve ne olmuş olabilir??

Tedaviye devam edildi...

- 12. haftada HDV-RNA 2.300 IU/ML
- 16. haftada ALT 33
- 24. haftada HDV-RNA negatif
- 48. haftada HDV-RNA negatif

Advers Olaylar

- Hasta toplamda 9 kg verdi
- 7. ayda antidepresan başlandı
- PEG-INF uyumu %98
- Bulantı, kusma, halsizlik, kas ağrısı, baş ağrısı
- Uykusuzluk

Tedavi Sonu Takipleri

- 6. ay HDVRNA negatif, ALT N
- 12.ay HDVRNA negatif, ALT N
- 24.ay HDVRNA negatif, ALT N

Olgu II

- 41 yaşında erkek hasta
- 15 yıldır HDV+HBV
- 2010 ve 2015 da iki kez Peg INF tedavisi almış
- Nüks
- Non sirotik hasta
- HBV DNA negatif
- HDV RNA 109.000 kp/ml, ALT 71

Faz III çalışamasına dahil oldu

- Lonafarnib+PEG
- Tedavinin 12 haftasında kilo kaybı %4
- Bulantı, kusma ve İshal mevcut
- HDV RNA 1.240 kopya/ml

- Tedavinin 48 haftasında HDV RNA negatif
- ALT normal

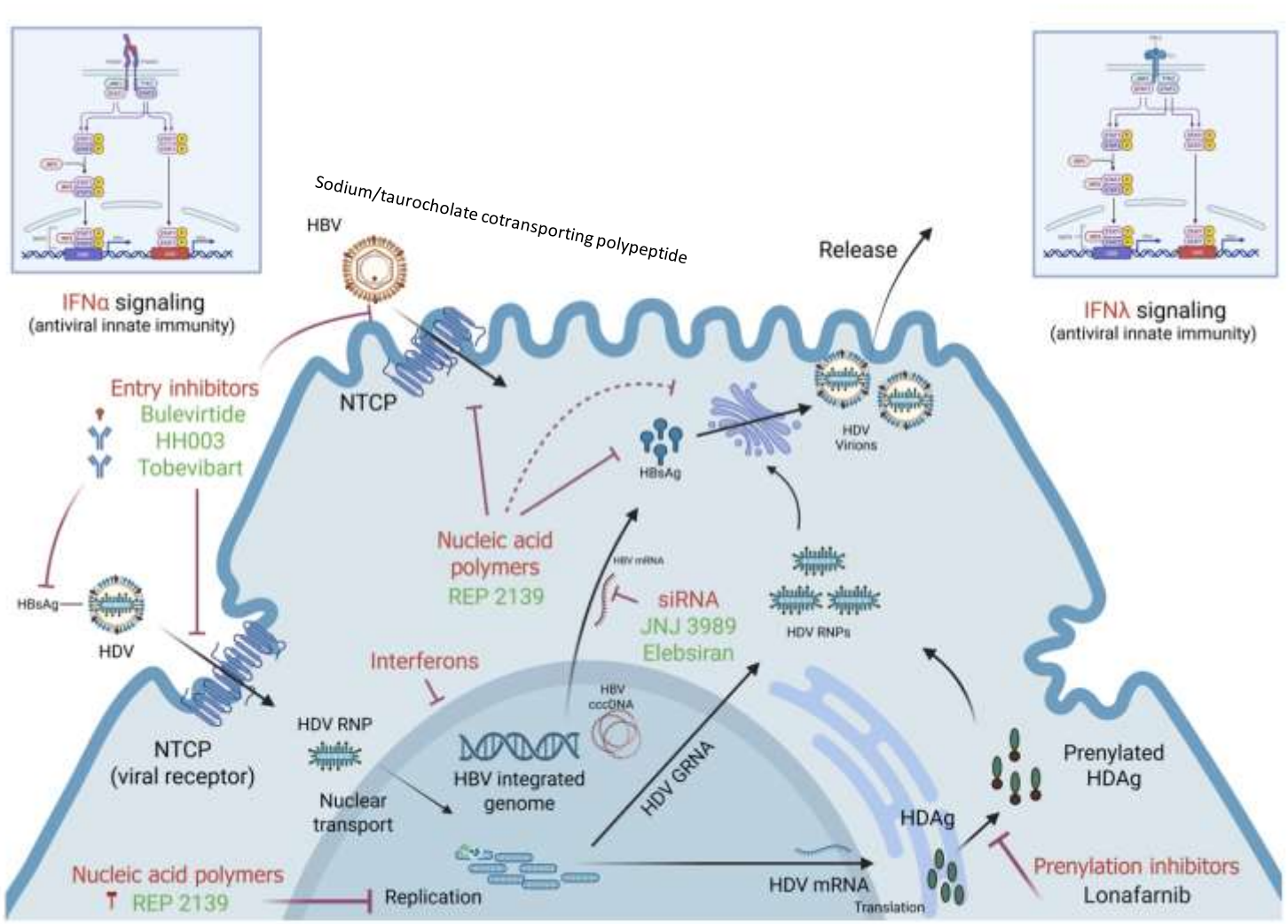
Zor bir tedavi, çok sayıda AO mevcut

TS 6. ay hasta iyi ve HDV RNA negatif ☺

Nucleic Acid Polymers
(NCT02233075, NCT02876419)

- Fosforotiat nükleik asit polimerlerinin (NAP'ler) etki mekanizması henüz açıklığa kavuşturulmamıştır
- Kanıtlar bunların subviral HBsAg partiküllerinin hücresel salınımına müdahale ettiğini göstermektedir
- REP 2055 ve REP 2139 HBeAg pozitif HBV hastalarında HBsAg ve HBVDNA düzeyini azalttığı görüldü. SVR %70 olarak saptandı
- Hastalar tarafından IV uygulanan REP 2139'un tolere edilebildiği görüldü, ancak çalışmada %33 oranında SAE saptandı
- Hastalar 15 hafta boyunca haftada 500 mg REP 2139 IV olarak aldı

HDV Replikasyon Döngüsü ve Terapötik Hedefler



İlaç Hedef Noktaları

Adım 1 — Viral Giriş (NTCP)

Bulevirtide
EMA 2020 / FDA 2023 — 2 mg/gün SC

Tobevibart
Anti-HBsAg mAb — ECLIPSE Faz 3 (NCT06903338)

Brelovitug (BJT-778)
Anti-HBsAg mAb — AZURE Faz 2b/3 (NCT06907290)

Libevitug (HH-003)
Anti-PreS1 mAb — Çin'de onaylı (Ocak 2026) · FDA BTD Kasım 2024 · Faz 2b: %44 kombine yanıt

Adım 3 — RNA Replikasyonu

PEG-IFN alfa
Antiviral + immünomodülatör etki

Adım 4 — Virion Montajı

Lonafarnib + RTV
Farnesyltransferaz inhibitörü — D-LIVR Faz 3

Adım 5 — HBsAg / Salınım

REP-2139-Ca
Nükleik asit polimeri — Faz 2 (NCT02233075)

Elebsiran (VIR-2218)
siRNA — HBV pgRNA hedefi, ECLIPSE Faz 3

JNJ-3989
siRNA — HBV mRNA hedefi, Faz 2

2021 Aralık ☺

Received: 22 December 2021 | Accepted: 3 January 2022

DOI: 10.1111/jvh.13651

INVITED REVIEW

JVH WILEY

Chronic hepatitis D—What is changing?

David Yardeni | Theo Heller | Christopher Koh

Liver Diseases Branch, National Institute of Diabetes & Digestive & Kidney Diseases, National Institutes of Health, Bethesda, Maryland, USA

Correspondence
David Yardeni, National Institute of Diabetes & Digestive & Kidney Diseases, National Institutes of Health, 10 Center Drive, Bldg. 10, Room 4-5722, Bethesda, MD 20892, USA.
Email: David.yardeni@nih.gov

Christopher Koh, National Institute of Diabetes & Digestive & Kidney Diseases, National Institutes of Health, 10 Center Drive, Bldg. 10, Room 5-2740, Bethesda, MD 20892, USA.
Email: christopher.koh@nih.gov

Abstract

Hepatitis D virus (HDV) infection is a chronic viral disease of the liver that is still largely considered to be incurable due to lack of effective treatment options. Without treatment, the risk for the development of advanced liver disease, cirrhosis and hepatocellular carcinoma is significantly high. Currently, new therapeutic options are emerging out of ongoing phase 3 clinical trials, promising a new hope of cure for this devastating liver infection. Recently, bulevirtide, a first in its class HDV entry inhibitor, has received conditional authorization of use from the European Medicines Agency (EMA) and was also submitted for approval in the United States. Other novel therapeutic options in clincal trials include interferon lambda, the prenylation inhibitor lonafarnib and nucleic acidic polymers (NAPs). This review describes all recent advances and ongoing changes to the field of HDV therpaeutics.

KEYWORDS
chronic liver disease, hepatitis D, treatment

Kombinasyon Tedavileri

- PEG-INF LAMDA
- BLUVERTIDE
- LONAFARNIP
- NAP

Digestive Diseases and Sciences
https://doi.org/10.1007/s10620-023-07960-y

REVIEW

Check for updates

Diagnosis and Management of Hepatitis Delta Virus Infection

Calvin Pan[1,2] · Robert Gish[3,4] · Ira M. Jacobson[5] · Ke-Qin Hu[6] · Heiner Wedemeyer[7] · Paul Martin[8]

Received: 8 July 2022 / Accepted: 24 April 2023

Journal of Hepatology, **August 2023**. vol. 79 | 433–460

Clini Digestive Dis
https://doi.or

REVIEW

Received: 25 January 2022 | Revised: 27 May 2022 | Accepted: 8 June 2022

DOI: 10.1111/liv.15338

MINI REVIEW

Liver INTERNATIONAL WILEY

OLOGY

IS☆

Euro

Diagnc Hepatitis delta virus infection prevalence, diagnosis and treatment in the Middle East: A scoping review

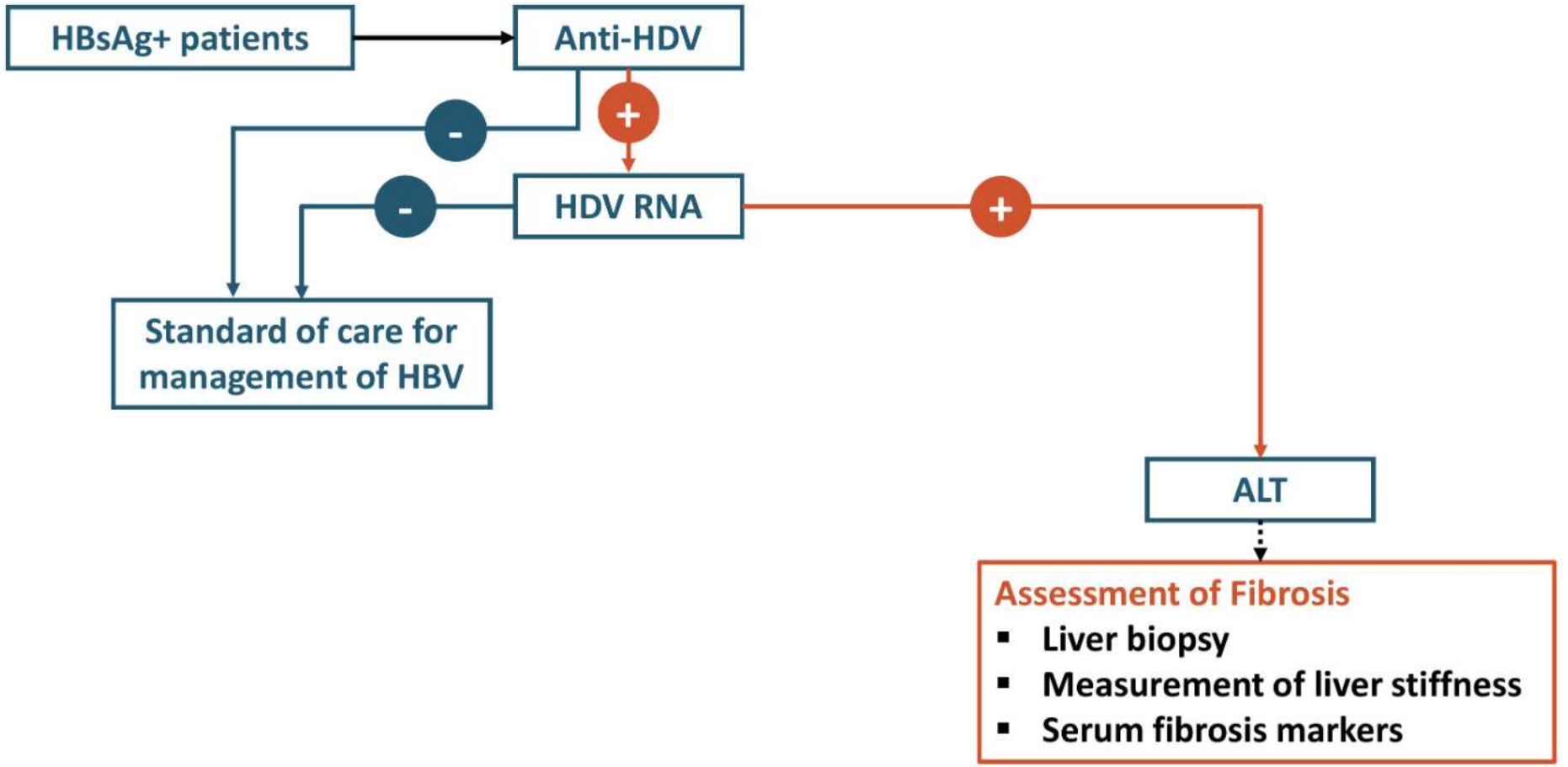
Calvin Par

Jeffrey V. Lazarus[1,2] | Ahmad Al-Rifai[3] | Faisal M. Sanai[4] | Abdullah Saeed Alghamdi[5] | Ala I. Sharara[6] | Motaz Fathy Saad[7] | Lena van Selm[1] | Saleh A. Alqahtani[8,9]

Summary

Hepatitis D virus damage in humans. HDV is responsible for rare acute and chronic liver diseases and is considered the most aggressive hepatitis virus. Acute infection can cause acute liver failure, while persistent infection typically causes a severe form of chronic hepatitis which is associated with rapid and frequent progression to cirrhosis and its end-stage complications, hepatic decompensation and hepatocellular carcinoma. Major diagnostic and therapeutic innovations prompted the EASL Governing Board to commission specific Clinical Practice Guidelines on the identification, virologic and clinical characterisation, prognostic assessment, and appropriate clinical and therapeutic management of HDV-infected individuals.

Algorithm for Evaluation of HDV



Notes

Adapted from: Shah. Gastroenterol Rep (Oxf). 2019;7:396.

Slide credit: clinicaloptions.com

Treatment and Monitoring Recommendations

Elevated ALT	Normal ALT + Fibrosis < F2	Normal or Elevated ALT + Fibrosis ≥ F2
▪ Treat	▪ Monitor – HDV RNA + ALT every 3 mo for first year, then every 6-12 mo if ALT remains normal and no worsening of fibrosis	▪ Treat

ah. Gastroenterol Rep (Oxf). 2019;7:396. Terrault. Hepatology. 2018;67:1560.

Slide credit: clinicaloptions.com

Received: 22 October 2025 | Accepted: 20 January 2026

DOI: 10.1097/HC9.0000000000000915

REVIEW

OPEN

Refining surveillance of hepatocellular carcinoma in chronic hepatitis B through biomarker-based risk stratification

Tai-Chung Tsen[1,2,3] ... Shang-Chin Huang[1,2,4,5] ... Jia-Horng Kao[1,2,3,4]

GALAD SCORE

PAGE-B SCORE

- 6 ay
- Son ... na hassas bir ya...
- HBsAg < 100 IU/mL HCC insidansi %0,2
- Non-siroti... kullanımı ön...
- Sir... nımı

Test Adı	Sonuç	Referans Aralığı
GALAD Skoru (HCC Risk Paneli)		
Kronik karaciğer hastalığı olan hastalarda hepatoselüler karsinomun gelişimi için risk değerlendirmesi:		
AFP	**10.7 ng/mL**	<4.7 ng/mL
AFP-L3	5.1 %	<10 %
DCP	0.17 ng/mL	<7.5 ng/mL

Test Adı	Sonuç	Referans Aralığı
GALAD Skor	< -5.84	
		> -1.93 Yüksek HCC Riski

HDV(+)'lerde HCC ve KC ilişkili AO öngörülebilir mi?

Platelet Count (× 10^3/μL) *

150

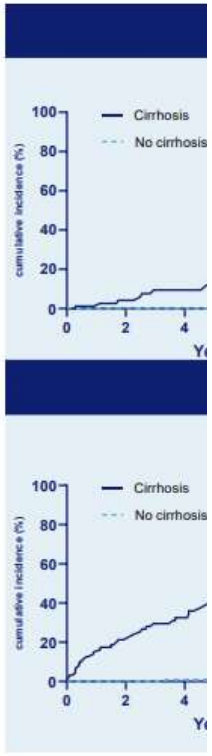
Age (years) *

45

Sex *

Male

Normal range: 150-450 × 10^3/μL



Risk Assessment Results

16

Total Risk Score

Intermediate Risk

Cumulative 5-year HCC incidence rates of 3-4%

Score Breakdown:

Platelet Count: +6 point (100-199)
Age: +4 points (40-49 years)
Sex: +6 point (Male)

Risk Score Interpretation:

≤9 Low Risk

10-17 Intermediate Risk

≥18 High Risk

Clinical Gastroenterology and Hepatology 2025;23:1964–1972

Sonuç Olarak…

Review

HBV/HDV Co-Infection: Epidemiological and Clinical Changes, Recent Knowledge and Future Challenges

Caterina Sagnelli, Evangelista Sagnelli *, Antonio Russo, Mariantonietta Pisaturo, Laura Occhiello and Nicola Coppola

En habis hepatotrop virüs olduğu kesin

Dekompanse Siroz artışı HBV'ye göre 7 kat fazla

HCC gelişimi HBV'ye göre 3 kat fazla

Orta Afrika'dan, Avrupa'ya Genotip 5-8 olan HDV enfeksiyonlarında artış

Pegile-İnterferon da SVR (%20-30)

HBV'de kullanılan OAV tedaviler HDV'de etkin değil

Lonafarnib, Bulevirtide ve Nucleic Acid Polymers daha etkin ancak AO az değil

Kombinasyon Tedavileri