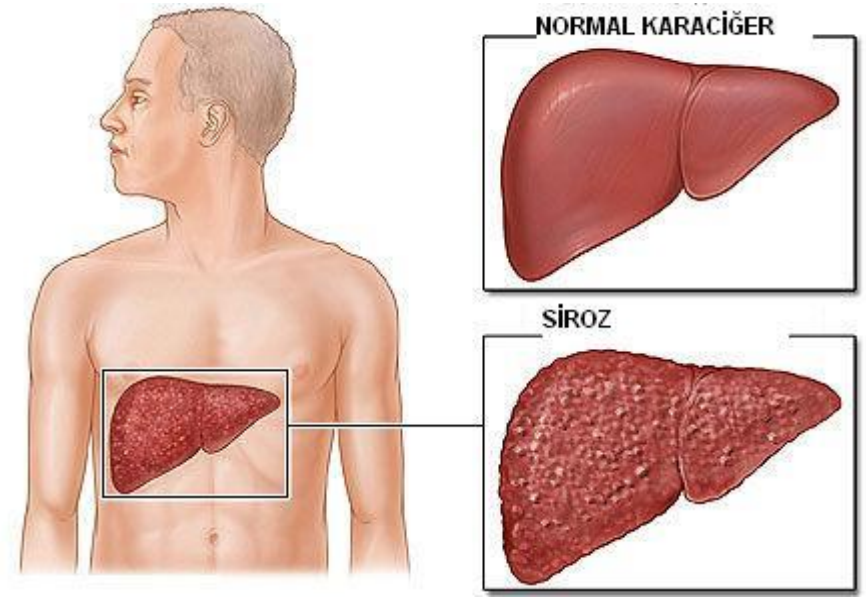

# Potent Antiviralle re Kısmi Yanıtlı Olgular

Fatime Korkmaz

Konya Eğitim Araştırma Hastanesi

# Kr Hepatit B de tedavi amacı

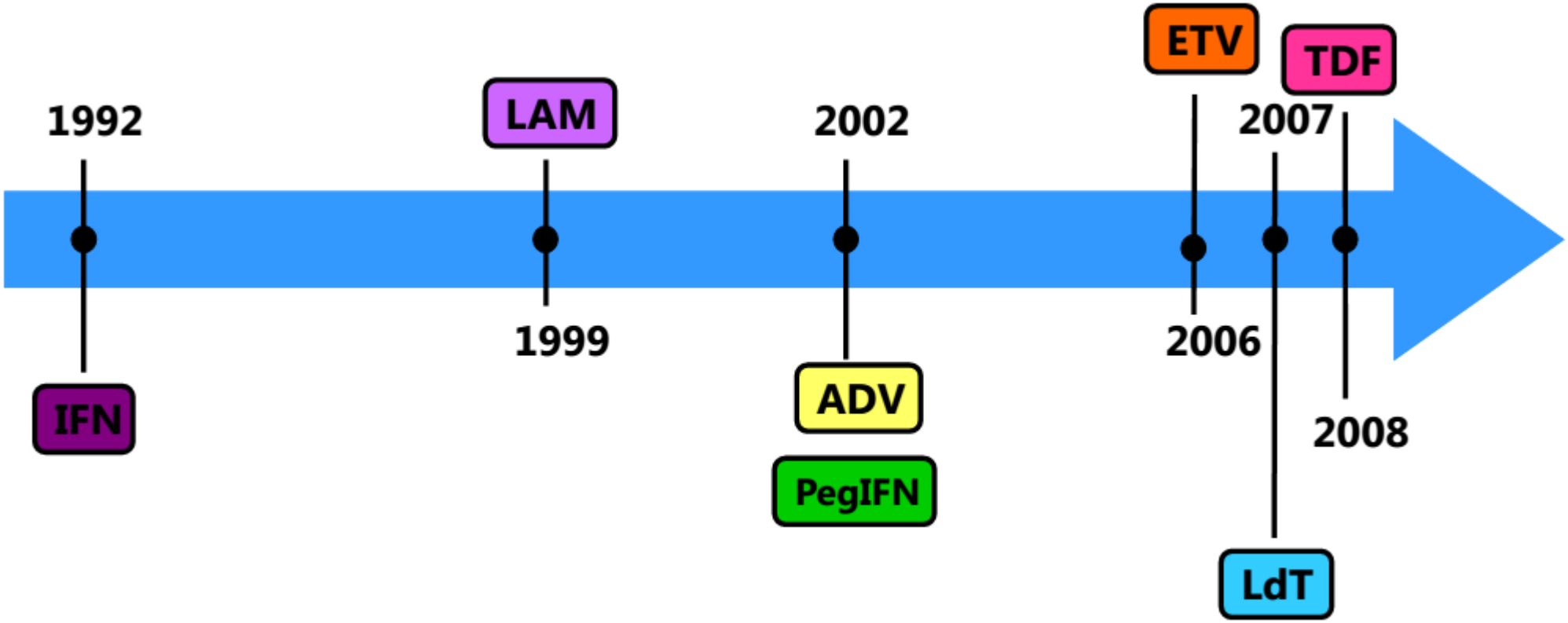
- Siroz, hepatosellüler kanser ve karaciğer yetmezliği gibi uzun dönem komplikasyonları önlemek ve yaşam kalitesini arttırmaktır.
- Karaciğer histolojisinin düzelmesi,
- HBe Ag /Anti HBe serokonversiyonu
- HBs Ag /Anti HBs serokonversiyonu




## TEDAVİNİN BAŞARISI

Kalıcı HBV DNA negatifliğini sağlamak
ALT düzeyinin normal sınırlarda kalması
Virusun tam eradikasyonu? ccDNA kalıcı!

# Tedavideki ilaçlar yıllar içinde….



**Tablo 4. Kronik Hepatit B'de Tedavi Türlerine Göre Virolojik Yanıt Tanımları (89)**

| İnterferon ve Pegile İnterferon Tedavisi |
|---|
| **Virolojik yanıt:** Tedavinin 6. ayında, tedavi bitiminde, tedavi bitiminden 6 ay ve 12 ay sonra HBV DNA<2000 İÜ/ml olması. |
| **Kalıcı virolojik yanıt:** Tedavi bitiminden en az 12 ay sonra HBV DNA<2000 İÜ/ml olması. |
| **Nükleoz(t)id Tedavisi** |
| **Primer yanıtsızlık:** Tedavinin 12. haftasında, HBV DNA düzeyinde <1 log İÜ/ml azalma olması. |
| **Virolojik yanıt:** HBV DNA'nın PCR ile saptanamayacak düzeye inmesi. |
| **Kısmi virolojik yanıt:** Tedavinin 24. haftasında HBV DNA düzeyinde >1 log İÜ/ml azalma olması, fakat RT-PCR ile saptanabilir düzeyde olması. |
| **Histolojik yanıt:** Fibroz skorunda kötüleşme olmaksızın nekroinflamatuar aktivite skorunda en az 2 puan düzelme olması. |
| **Tam yanıt:** Biyokimyasal ve virolojik yanıtla birlikte HBsAg'nin kaybolması. |
| **Tedavi sonu yanıt:** Tedavi bitiminde elde edilen yanıt. |

Akhan S et.al Klimik Dergisi 2014 ,27(özel sayı):2-18

# OLGU 1

**22 yaş, erkek**

Şikayeti/Hikayesi: Halsizlik son 2 aydır

4 yıl önce HBs Ag :pozitif, takip yaptırmamış

3-4 aydır antidepresan kullanıyor (Milnasipran 50 mg)

Aile öyküsü: Anne ve diğer kardeşte HBV

Fizik Muayene: zayıf görünümlü (ağırlık:60 kg boy:172 cm, BKİ= 20.2)

İkteri yok

Karaciğer dalak palpe edilmiyor, traube açık, asit yok

# Laboratuvar Bulguları

- **ALT : 137 U/L**
- **AST:  88 U/L**
- GGT: 35 U/L
- T.bilüribin:1,2 mg/dl
- T.protein:  8.2 mg/dL
- Albümin:  4,8 mg/dL
- Kreatinin:  0.8mg/dL
- PTZ:9.3 sn INR:1
- AFP: 2,3 ng/ml
- Trombosit: 220 000 /*mL*

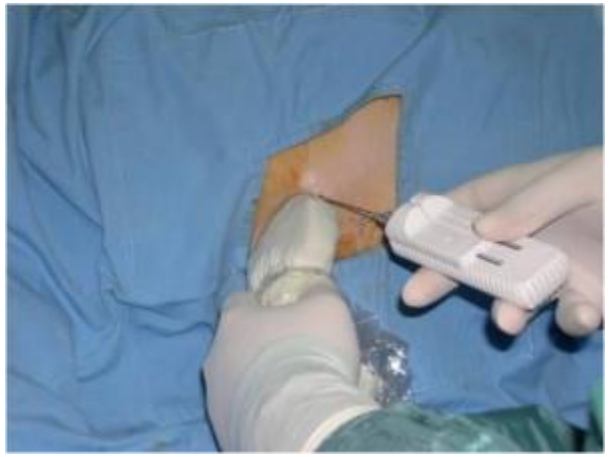
- **HBs Ag:  Pozitif**
- **HBe Ag:  Pozitif**
- Anti HBe:  Negatif
- Anti HBcIgM: Negatif
- Anti HDV:
- Anti HCV:  Negatif
- Anti HIV:
- Anti HAV IgG:  Pozitif

**HBV DNA: 1 250 000 000 IU/ml**

a

## ÜST BATIN USG

Normal bulgular



## KC BİYOPSİ (Modifiye ISHAK)

- Periportal alanda orta şiddete%50 den az piecemal nekroz (3)
- Fokal konfluent nekroz (1)
- İntralobüler alanda 2-4 fokal litik nekroz,fokal inflamasyon (2)
- Portal alanda orta derecede inflamasyon (2)
- Portal alanda fibrozis (2)

**HAİ:8 E:2**

# Tedavi seçenekleri rehberler

| | | EASL 2012 | APASL 2012 | AASLD 2009 | VHSD 2011 | KLİMİK – VHÇG 2014 |
|---|---|---|---|---|---|---|
| HBe Ag ( + ) | HBV DNA IU/ml | ≥ 20 000 | ≥ 20000 | ≥ 20 000 | > 2000 | > 2000-20000 |
| | ALT U/L | > 2 kat | > 2-5 kat | > 2 kat | > normal | > 2 kat |
| | KC BİYOPSİ | >2000 biyopsi ile ≥ A2- ≥ F2 >20000 biyopsi olmadan da | ? Orta/şiddetli İnflamasyon | Opsiyonlu Orta/şiddetli İnflamasyon Belirgin fibrozis | HAİ≥4 E ≥ 2 | Biyopsi önerilir |
| | ÖNERİ | Tedavi et | 3 - 6 ay ara ile ALT, HBe Ag izlemi | 1-3 ay ara ile ALT, HBe Ag izlemi | Tedavi et | Tedavi et |

# Tedavi seçimi : Entekavir 0.5 mg / gün ile....

- DNA polimerazın potent inhibitörlerinden
- Nükleozid analoğu
- Genetik bariyeri yüksek
- Yan etki yönünden rahat

JOURNAL OF VIRAL HEPATITIS
JVH

*Journal of Viral Hepatitis*, 2012, **19**, 377–386 doi:10.1111/j.1365-2893.2012.01602.x

REVIEW

# First-line treatment of chronic hepatitis B with entecavir or tenofovir in 'real-life' settings: from clinical trials to clinical practice

S. Pol[1] and P. Lampertico[2] [1]*Unité d'Hépatologie, Hôpital Cochin, Université Paris Descartes, APHP, INSERM U.1016, Paris, France; and* [2]*First Gastroenterology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico Università di Milano, Milan, Italy*

**Table 2** Summary of efficacy results from real-life studies of entecavir in NUC-naïve patients

| Study [ref] | Median follow-up (range) | No. patients | Cut-off (assay limit) (IU/mL) | HBV DNA undetectable, % (*n*/N*) | ALT normalization, % (*n*/N*)† | HBeAg seroconversion, % (*n*/N*)‡ | HBsAg loss, % (*n*/N*) |
|---|---|---|---|---|---|---|---|
| ORIENTE [22] | 52 weeks (46–53) | 190 | 50 | 83 (150/181) | 82 (115/141) | 21 (12/57) | 1 (2/190) |
| VIRGIL [23] | 19 months (3–45) | 243 | 80 | 86 (208/243) | 74 (126/171) | 15 (13/86) | 1 (3/243) |
| Argentinean cohort [25] | 110 weeks (56–164) | 69 | 6 | 88 (61/69) | 98 (63/64) | 44 (19/43) | 10 (7/69) |
| King's College cohort [26] | 28 months (NR) | 154 | 12 | 76 (NR) | NR | 8 (NR) | 1 (NR) |
| Italian cohort [27] | 42 months (2–53) | 418 | 12 | 99 (66/67) | 88 (60/68) | 56§ (27 patients) | 21§ (12 patients) |
| Hong Kong cohort [28] | 3 years (12–60 months) | 222 | 12 | 96 (67/70) | 90 (51/57) | 53 (16/30) | 0.5 (1/222)§ |

ALT, alanine transaminase; HBeAg, e antigen; HBsAg, surface antigen; HBV, hepatitis B virus; NR, not reported; NUC, nucleos(t)ide analogue; VIRGIL, Vigilance against Viral Resistance.

*N = number of patients on treatment, unless stated otherwise. †Among those with elevated ALT at baseline. ‡Among those HBeAg(+) at baseline. §Kaplan–Meier estimate.

# EASL 2012

**Table 2. Results of main studies for the treatment of HBeAg-positive chronic hepatitis B at 6 months following 12 months (48 or 52 weeks) of pegylated interferon alpha (PEG-IFN) and at 12 months (48 or 52 weeks) of nucleos(t)ide analogue therapy.**

| | PEG-IFN | | Nucleoside analogues | | | Nucleotide analogues | |
|---|---|---|---|---|---|---|---|
| | PEG-IFN-2a | PEG-IFN-2b | Lamivudine | Telbivudine | Entecavir | Adefovir | Tenofovir |
| Dose* | 180 µg | 100 µg | 100 mg | 600 mg | 0.5 mg | 10 mg | 245 mg |
| [Ref.] | [63] | [64] | [63, 65-68] | [68] | [67] | [69, 70] | [70] |
| Anti-HBe seroconversion (%) | 32 | 29 | 16-18 | 22 | 21 | 12-18 | 21 |
| HBV DNA <60-80 IU/ml (%) | 14 | 7 | 36-44 | 60 | 67 | 13-21 | 76 |
| ALT normalisation# (%) | 41 | 32 | 41-72 | 77 | 68 | 48-54 | 68 |
| HBsAg loss (%) | 3 | 7 | 0-1 | 0.5 | 2 | 0 | 3 |

*PEG-IFN were given as percutaneous injections once weekly and nucleos(t)ide analogues as oral tablets once daily.

#The definition of ALT normalisation varied among different trials (i.e. decrease of ALT to ⩽1.25-times the upper limit of normal (ULN) in the entecavir or ⩽1.3-times the ULN in the telbivudine trial).

# EASL KAYNAKLARI


[63] Lau GK, Piratvisuth T, Luo KX, Marcellin P, Thongsawat S, Cooksley G, et al. Peginterferon Alfa-2a, lamivudine, and the combination for HBeAg-positive chronic hepatitis B. N Engl J Med 2005;352:2682–2695.

[64] Janssen HL, van ZM, Senturk H, Zeuzem S, Akarca US, Cakaloglu Y, et al. Pegylated interferon alfa-2b alone or in combination with lamivudine for HBeAg-positive chronic hepatitis B: a randomised trial. Lancet 2005;365:123–129.

[65] Lai CL, Chien RN, Leung NW, Chang TT, Guan R, Tai DI, et al. A one-year trial of lamivudine for chronic hepatitis B. Asia Hepatitis Lamivudine Study Group. N Engl J Med 1998;339:61–68.

[66] Dienstag JL, Schiff ER, Wright TL, Perrillo RP, Hann HW, Goodman Z, et al. Lamivudine as initial treatment for chronic hepatitis B in the United States. N Engl J Med 1999;341:1256–1263.

[67] Chang TT, Gish RG, de Man R, Gadano A, Sollano J, Chao YC, et al. A comparison of entecavir and lamivudine for HBeAg-positive chronic hepatitis B. N Engl J Med 2006;354:1001–1010.

[68] Lai CL, Gane E, Liaw YF, Hsu CW, Thongsawat S, Wang Y, et al. Telbivudine versus lamivudine in patients with chronic hepatitis B. N Engl J Med 2007;357:2576–2588.

[69] Marcellin P, Chang TT, Lim SG, Tong MJ, Sievert W, Shiffman ML, et al. Adefovir dipivoxil for the treatment of hepatitis B antigen-positive chronic hepatitis B. N Engl J Med 2003;348:808–816.

[70] Marcellin P, Heathcote EJ, Buti M, Gane E, de Man RA, Krastev Z, et al. Tenofovir disoproxil fumarate versus adefovir dipivoxil for chronic hepatitis B. N Engl J Med 2008;359:2442–2455.

# EVALUATION OF 3 YEARS TREATMENT RESULTS OF ENTECAVIR NAIVE CHRONIC HEPATITIS B PATIENTS

*Fatma KACAR, Nazlım AKTUĞ DEMİR, Halil KARATAŞ, Mehmet ÖZCAN, Fatime KORKMAZ*
*Konya Meram Research and Education Hospital*

| **HBV DNA** | **1.Year** | **2. Year** | **3. Year** |
|---|---|---|---|
| **HBeAg (+) n:15** | 13 (%86.6) | 15(%100.0) | 15(%100.0) |
| **HBeAg (-) n:36** | 25 (% 69.4) | 33 (%91.6) | 35 (%97.2) |

APASL 2013 POSTER

# EVALUATION OF 3 YEARS TREATMENT RESULTS OF ENTECAVIR NAIVE CHRONIC HEPATITIS B PATIENTS

**Fatma KACAR, Nazlım AKTUĞ DEMİR, Halil KARATAŞ, Mehmet ÖZCAN, Fatime KORKMAZ**

**Konya Meram Research and Education Hospital**

**Purpose:** In this study 3 years treatment results of 51 chronic hepatitis B patients treated with 0.5 mg/day entacavir.

**Method:** This study included 51 patients admitted to Infectious Diseases clinic of Konya Research and Education Hospital between January 2008 and September 20121. Data were recorded to SPSS 16.0 package program and chi-square test was used for statistical evaluation of cathegorical variables. $p<0.05$ was considered as statistically significant.

**Findings**: Thirty three (64.7%) patients were males, 18 (35.3%) were females and mean age was 41 ± 16.8. HBeAg was positive in 15 (29.5%) patients and Anti-HBe was positive in 36 (70.5%) patients. Median HBV DNA value was 86424000 (21000-19937832620) IU/Ml, and median alanine aminotransferase (ALT) value was 97(28-468) u/l. Three years treatment responses of patients are given in Table 1.

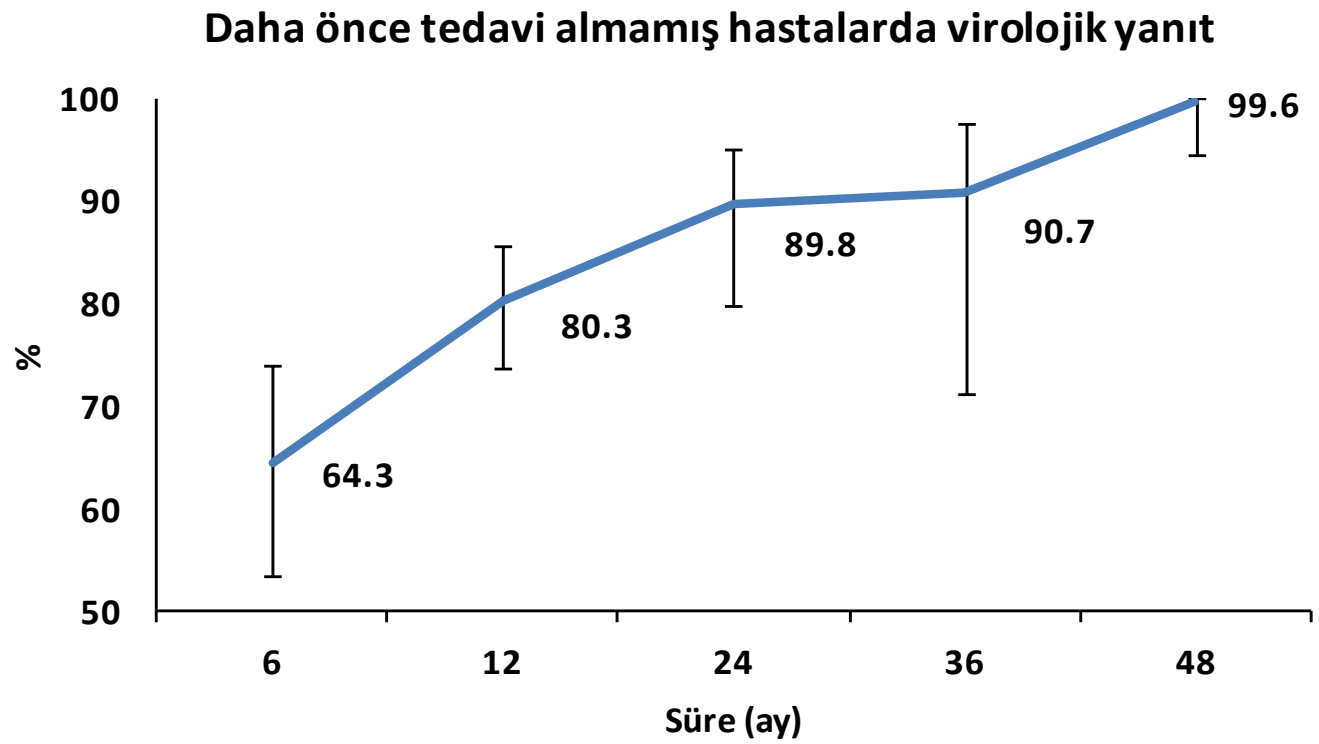
**Table 1**. Treatment Responses of Patients Versus Years

| | **1.Year** | **2.Year** | **3.Year** |
|---|---|---|---|
| **HBV DNA (IU/ml)** | 38(%74.5) | 48(%94.1) | 50(%98) |
| **ALT(U/L)** | 40(78.4) | 49(%96) | 50(%98) |

Rate of turning of HBV DNA test to negative and rate of ALT normalisation in HBeAg positive, Anti-Hbe positive patients are shown in Table 2 and Table 3.

**Table 2.** Rate of Turning of HBV DNA Test to Negative in HBeAg positive and Anti-Hbe Positive Patients

# Kronik B Hepatitinde Entekavir Kullanımının Etkinliği ile İlgili Türkiye Kaynaklı Çalışmaların Meta-Analizi




Akarca US ve ark.

# TEDAVİ SEYRİ

| AY - HAFTA | ALT U/ L | HBV DNA İU/ml |
|---|---|---|
| 0 - | 137 | 1 250 000 000 |
| 3 (12) | 60 | |
| 6 (24) | 43 | 44600 |
| 9 (36) | 32 | 33659 |

Biyokimyasal yanıt : 6. ay

Kısmi virolojik yanıt !

# EASL 2012 :KISMİ VİROLOJİK YANIT YÖNETİMİ

The optimal management of patients with partial virological response under entecavir or tenofovir (highly potent drugs with a high genetic barrier to resistance) is currently debatable. In such patients with a partial virological response at week 48, the HBV DNA levels at week 48 and their kinetics must be taken into account. Patients with declining serum HBV DNA levels may continue treatment with the same agent (entecavir or tenofovir) given the rise in rates of virological response over time and the very low risk of resistance with long-term monotherapy with both these agents [137] (**B1**). Some experts would suggest adding the other drug in order to prevent resistance in the long term, particularly in the rare patients without further HBV DNA decline despite drug compliance (**C2**).

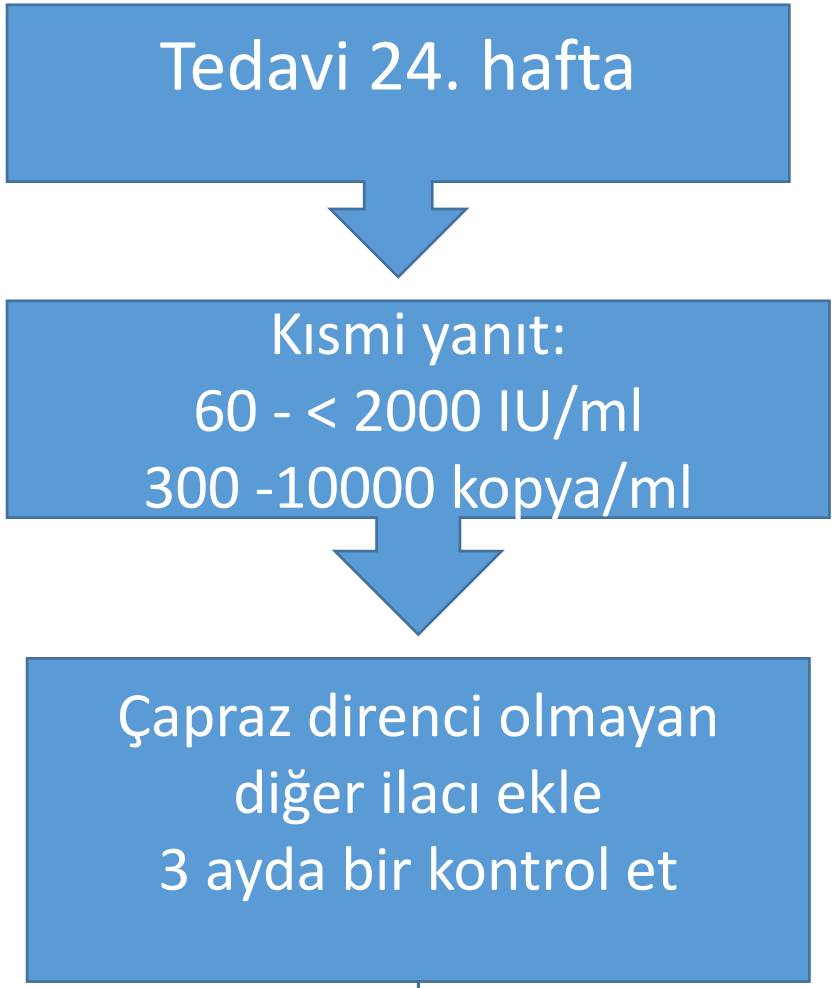
[137] Zoutendijk R, Reijnders JG, Brown A, Zoulim F, Mutimer D, Deterding K, et al. Entecavir treatment for chronic hepatitis B: adaptation is not needed for the majority of naive patients with a partial virological response. Hepatology 2011;54:443–451.

- Yönetim tartışmalı.
- 48. Haftada HBV DNA düşme eğilimde ise aynı ajanla devam edilebilir :

  (ETV ya da TDF) (B1)

- 2 ‘li tedavi (C2)

# 24. Haftaya göre kısmi viral yanıtta yol haritası




Keeff et al.Clinical Gastroenterology and hepatology 2007: 5 s:890-97

# VİRAL YÜKÜ YÜKSEK HBE AG(+) HASTADA ENTEKAVİR SEÇİMİ UYGUN MU?

*Efficacy of entecavir treatment for up to 96 weeks in nucleoside-naive HBeAg-positive chronic hepatitis B patients with high viral load.*

| TEDAVİ HAFTASI | VİROLOJİK YANIT HBV DNA > 10 log 9 kopya/ml | VİROLOJİK YANIT HBV DNA < 10 log 9 kopya/ml | p |
|---|---|---|---|
| 48 | % 42 | % 67.34 | 0.006 |
| 72 | % 62 | % 85.71 | 0.007 |
| 96 | % 68 | % 85.71 | 0.037 |

- 99 HBe Ag(+) hasta,naif
- 50'si yüksek viral yük:

  > 10 log 9 kopya/ml
- 49 'u yüksek olmayan VY

  < 10 log 9 kopya/ ml
- Virolojik yanıt : <300 kopya/ml

SONUÇ: Başlangıçtaki viral yükün yüksek Olması virolojik yanıt için negatif bir belirteç

Yan LB et al.Clin Res Hepatol Gastroenterol. 2014

# Partial virological response to three different nucleotide analogues in naive patients with chronic hepatitis B

Ender G Yegin and Osman Cavit Ozdogan

*Istanbul, Turkey*

Viral yük : ≥ 7 log IU/ml

Viral yük : < 7 log IU/ml

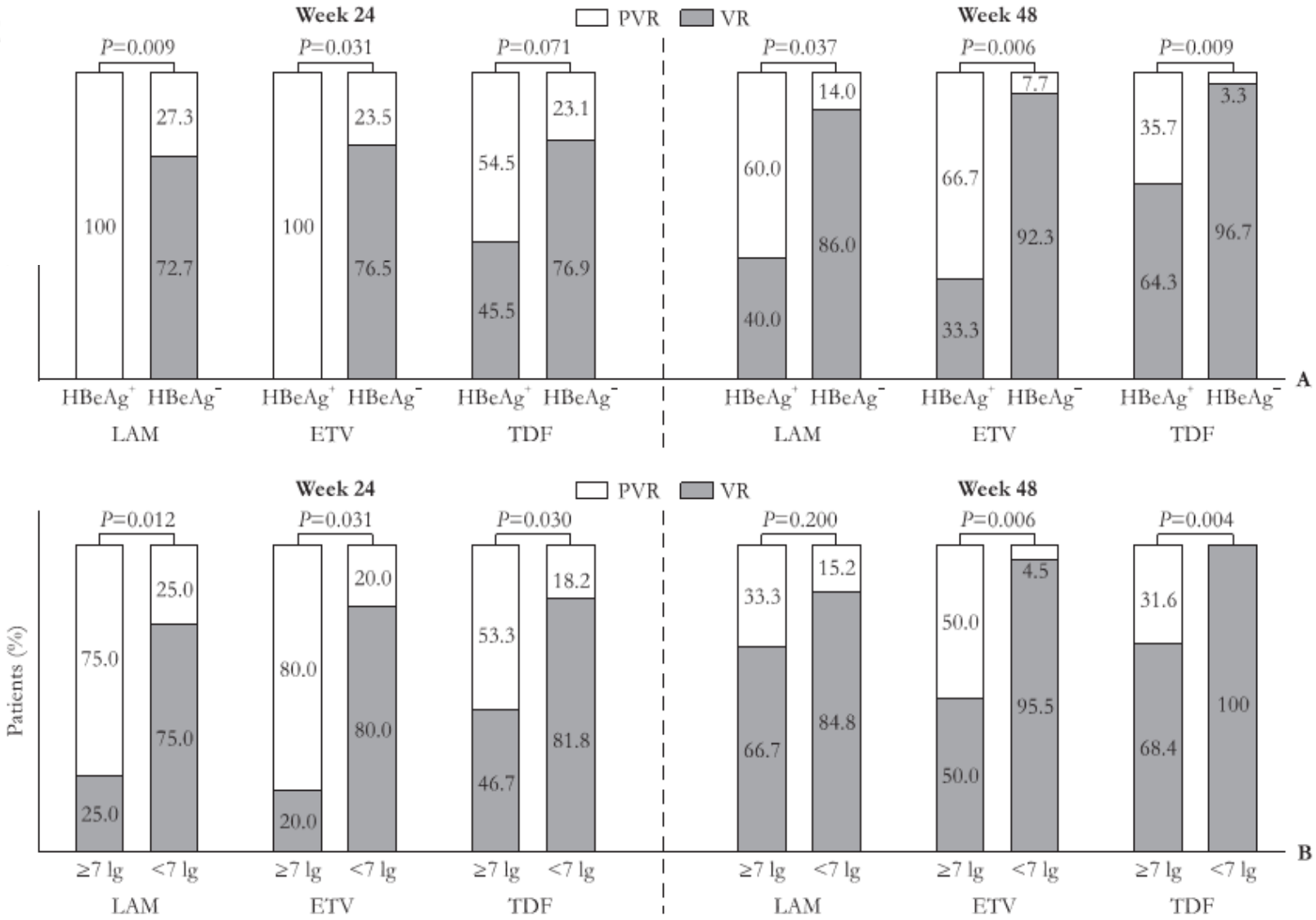



**Fig. 1.** The distribution of patients with PVR and VR at week 24 and 48 for three NA groups; lamivudine, entecavir and tenofovir according to, (**A**) Baseline HBeAg status, (**B**) High (≥7 lg IU/mL) and low (<7 lg IU/mL) baseline HBV DNA level. LAM: lamivudine; ETV: entecavir; TDF: tenofovir.

**150 NA naif hasta,**
**LAM:69, ETV:35 TDF:46**

# Tedaviye TDF eklendi……

| AYLAR | 0<br>ETV | 3<br>ETV | 6<br>ETV | 9<br>ETV+TDF | 12<br>ETV+ TDF |
|---|---|---|---|---|---|
| ALT U/L | 137 | 60 | 43 | 32 | 26 |
| HBV DNA IU/ml | 1 250 000 000 | | 44600 | 33659 | 773 |

# 2’li tedavi süresi ?
# …… Sonra monoterapi?

- KESİN VERİ YOK DENEYİMLER GENELLİKLE 24-48 HAFTADA

(ÇOĞUL İLAÇ DİRENCİ YOKSA) VİRAL SÜPRESYON SAĞLANIP MONOTERAPİ YÖNÜNDE,

DİRENÇLİ VİUSTA DEVAM…

# 2 li sonrası TDF monoterapisi?

- Eur J Gastroenterol Hepatol. 2015 Apr 21. [Epub ahead of print]
- **Tenofovir monotherapy after achieving complete viral suppression on entecavir plus tenofovir combination therapy.**
- Kim LH[1], Chaung KT, Ha NB, Kin KC, Vu VD, Trinh HN, Nguyen HA, Nguyen MH.
- **Author information**
- **Abstract**
- **OBJECTIVES:**
- It is unclear whether patients with chronic hepatitis B with partial response to entecavir (ETV) who have achieved complete viral suppression (CVS) with ETV plus tenofovir (TDF) combination therapy maintain CVS if switched to TDF or ETV. Our goal was to examine virologic outcomes in such patients.
- **METHODS:**
- This is a retrospective cohort study of 57 ETV partial responders with chronic hepatitis B who showed CVS on ETV+TDF combination therapy, who were switched back to monotherapy with either ETV (n=16) or TDF (n=18), or continued on combination therapy (n=23). The majority of patients were Asian (91%) and male (65%), with a mean age of 41±12 years.
- **RESULTS:**
- The patients switched back to ETV had significantly higher rates of virologic breakthrough by 6 months after the switch compared with their TDF counterparts (88 vs. 39%, P=0.004). Patients who remained on ETV+TDF also had virologic breakthrough, due to either confirmed or suspected nonadherence. On multivariate analysis inclusive of age, sex, and hepatitis B virus DNA levels at initiation of combination therapy, ETV (compared with TDF) was found to be an independent predictor for virologic breakthrough (odds ratio 112.7, P=0.03), as well as duration of CVS of less than 12 months while on ETV+TDF (odds ratio 60.2, P=0.03).
- **CONCLUSION:**
- TDF monotherapy, especially in those who have had CVS for at least 12 months on combination therapy, may be considered for some ETV partial responders who have achieved CVS with combination therapy, given the financial advantage and convenience of monotherapy.

# Olgu 2

**43 yaş, erkek, işçi**

Şikayeti/Hikayesi: Yakınması yok, Tarama sırasında HBs Ag(+)

Aile öyküsü : Özellik yok

Fizik Muayene : İkteri yok

Karaciğer dalak palpe edilmiyor, traube açık, asit yok

# LABORATUVAR BULGULARI (Mart 2008)

- **ALT : 75 - 282 U/L**
- **AST: 51 - 161 U/L**
- GGT: 55 U/L
- T.bilüribin: 0.6 mg/dl
- T.protein: 7,8 mg/dL
- Albümin: 4 mg/dL
- Kreatinin: 1.1 mg/dl
- PTZ: 12,9 sn INR:1,03
- AFP: 6,2 ng/ml
- Trombosit: 182 000 /*mL*

- **HBs Ag : Pozitif**
- **Anti HBe: Pozitif**
- HBe Ag : Negatif

- Anti HDV:
- Anti HCV: → Negatif
- Anti HIV:
- Anti HAV IgG: Pozitif

**HBV DNA: > 100 000 000 kopya/ml**

# İlk Takipte ALT artışı???

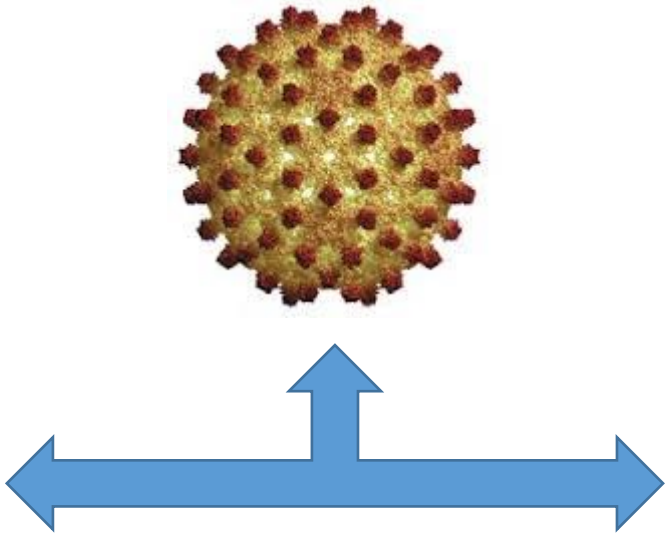
- Anti HBc IgM :Negatif
- CMV ,EBV, HSV koinf yok
- Demir, bakır depo hst yok
- İmmün marker (ANA,AMA)
- Negatif

| | Mart | Nisan Biyopsi | mayıs | Haziran Tedavi başlandı |
|---|---|---|---|---|
| ALT U/L | 75 | 282 | 464 - 190 | 182 |
| AST U/ml | 51 | 161 | 269- 77 | 75 |

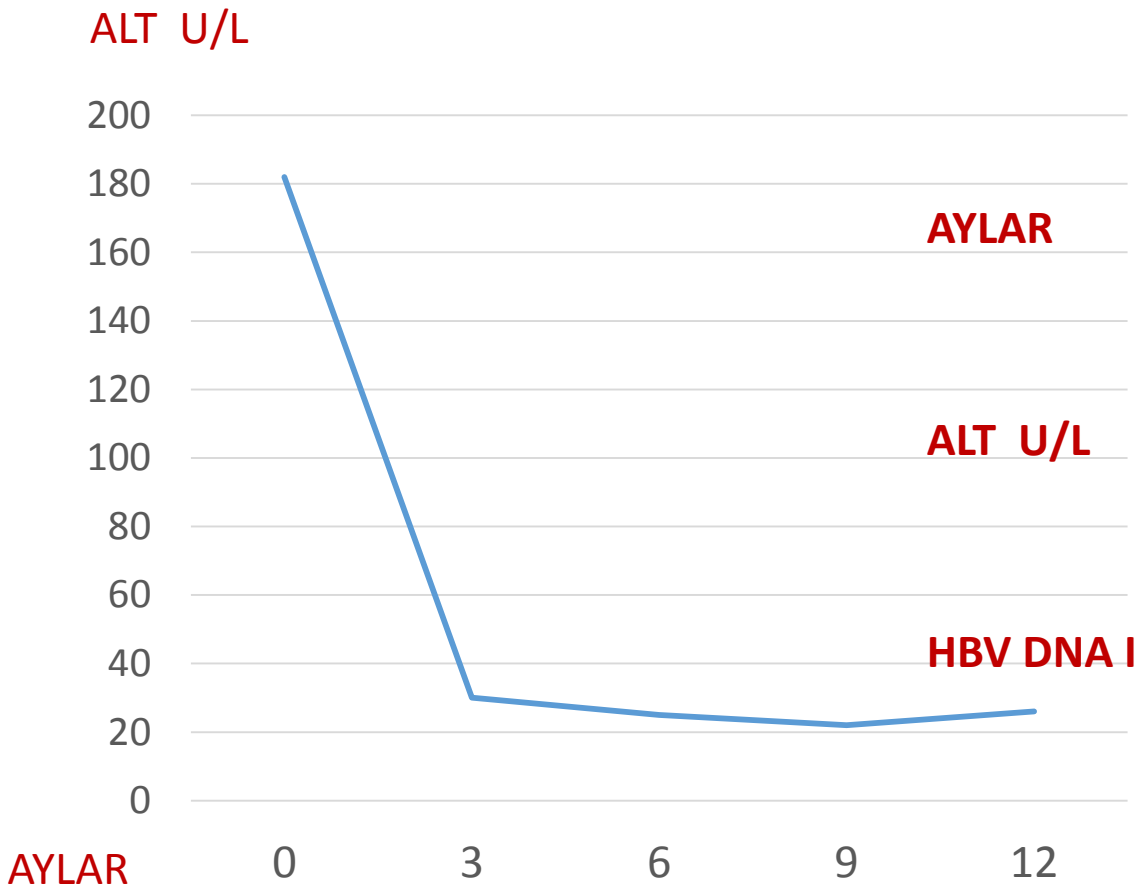
# TEDAVİ SEÇENEĞİ?

- **USG. Normal bulgular**
- **KARACİĞER BİYOPSİ (Mod ISHAK)**
- **HAİ :10 E:1**

# TEDAVİ KARARI : Tenofovir disoproxil 245 mg (Haziran 2008)

# TDF TEDAVİ İZLEMİ: 3. ay biyokimyasal yanıt
# 6.ay kısmi VY
# 12.ay VY




| AYLAR | 0 | 3 | 6 | 9 | 12 |
|---|---|---|---|---|---|
| ALT U/L | 182 | 30 | 25 | 22 | 26 |
| HBV DNA IU/ml | 100000000 kopya | | 2000 kopya | | 35 IU/ml |

# ANCAK HASTA MUTSUZ-GİS YAN ETKİ

## Tenofovir yan etkiler:

- Nadiren laktik asidoz bulguları
- Sarılık
- Nadir bulantı, kusma, mide ağrısı, gaz-şişkinlik
- Uyku problemi, baş dönmesi
- Kaşıntı
- Uzun süreli kullanımda renal fonksiyon bozukluğu
- « « osteopeni-poroz

# GASTRİK YAKINMALAR İÇİN ENDOSKOPİ

- ÖZEFAJİT
- LES DİSFONKSİYONU
- PANGASTRİT

- PPI
- ANTİASİT

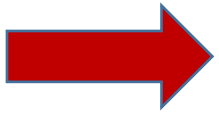
- TEDAVİ 48. HF (1 YIL) HASTA İSTEĞİ İLE İLAÇ DEĞİŞİMİ

- ENTEKAVİR

# TDF→ ETV tedavi seyiri

•

- **viral kırılma**
- **ilaç uyumu ?**



| AYLAR | ALT U/L | HBV DNA IU/ml |
|---|---|---|
| 0 | 26 | 35 |
| 3 | 28 | |
| 6 | 38 | < 10 |
| 12 | 33 | < 10 |
| 18 | 40 | |
| 24 | 115 | 259 000 |
| | | |

# Viral kırılmada EASL 2012 önerisi

- LAM,LdT ,ADV→İlaca uyum varsa direnç düşünülmeli
- Potent ilaçlarda hasta uyumsuzluğu ?
- Çok düşük ihtimal entekavir direnci?
- Entecavir direncinde TDF değişim/ekleme

# HASTAMIZDA DURUM?

- Hastanın ağabeyi vefat etmiş,
- ETV ‘i aksatmış ama kesmemiş!!!
- ETV direnci baktırmadık (2011)

- ETV ‘ye TDF EKLENEREK DEVAM……

# ETV+ TDF 6 AYLIK SEYİR

ALT :115 → 55 U/L

HBV DNA → 240 IU/ml

YENİDEN TENOF0VİR MONOTERAPİ

# TENOFOVİRLE DEVAM

| AYLAR | ALT U/L | HBV DNA IU/ml |
|---|---|---|
| 0 (42) | 55 | 240 |
| 6 (48) | 32 | 192 |
| 12 (54) | 24 | NEGATİF |
| 18 (60) | 18 | 507 |

**VİRAL KIRILMA**

# VHÇG
# ULUSAL HBV İLAÇ DİRENCİ PROJESİ

Doç.Dr.Murat SAYAN
Kocaeli Üniversitesi Hastanesi
Merkez Laboratuvarı, PCR Ünitesi

| Sequence Information | |
|---|---|
| **Identifier:** | **Konya EAH, N A HBV** |
| **Genotype:** | **D** |
| **Dual Infection:** | **No indication of dual infection was found (100% confidence)** |
| **Subgenotype:** | **D1 (similarity to subgenotype profile = 98.65%)** |
| **Included *RT* domain codons:** | **82 - 243 (similarity to reference = 98.15%)** |
| **Included *SHB* protein codons:** | **74 - 227 (similarity to reference = 98.05%)** |
| **Mutations *RT* domain:** | **H124Y, Y135S, Q215S (LAM ve ADV ile ilişkili kompansatuvar - viral replikasyonu onarıcı/arttırıcı-mutasyon)** |
| **Mutations *SHB* protein:** | **T127P, S207R, I208T** |
| **Escape mutations *SHB* protein:** | |

| Drug Resistance | | | |
|---|---|---|---|
| **Drugs** | **Scored mutations** | **Resistance analysis** | |
| Lamivudine, Zeffix® | **none** | **susceptible** | |
| Adefovir, Hepsera® | **none** | **susceptible** | |
| Entecavir, Baraclude® | **none** | **susceptible** | |
| Tenofovir DF | **none** | **susceptible** | |
| Telbivudine, Tyzeka®, Sebivo® | **none** | **susceptible** | |

# TENOFOVİRE DEVAM…
# VE NİHAYET …. 2013 - 2015

| AYLAR | ALT U/L | HBV DNA IU/ml |
|---|---|---|
| 18 (60) | 18 | 507 |
| 21 (63) | 17 | 20 |
| 24 (66) | 18 | NEGATİF |
| 30 (72) | 20 | NEGATİF |
| 36 (78) | 19 | NEGATİF |

- HBs Ag .Pozitif
- Anti HBs :Negatif
- HBe Ag : Negatif
- Anti HBe :Pozitif

- ÜRE :42
- Kreatinin. 1.11
- AFP: 3
- Plt :280 000
- USG : Normal
- Kemik dansitometre patolojiksınırda değil


TEŞEKKÜR EDERİM