HIV/AIDS ve HEPATİT B

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24.03.2017

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GLOBAL STATISTICS

36.7 MILLION
people worldwide are currently living with HIV/AIDS.

1.8 MILLION CHILDREN
worldwide are living with HIV. Most of these children were infected by their HIV-positive mothers during pregnancy, childbirth or breastfeeding.

The vast majority of people living with HIV are in low- to middle-income countries, particularly in Sub-Saharan Africa.

400 milyon HBV

37 milyon HIV

World Health Organization

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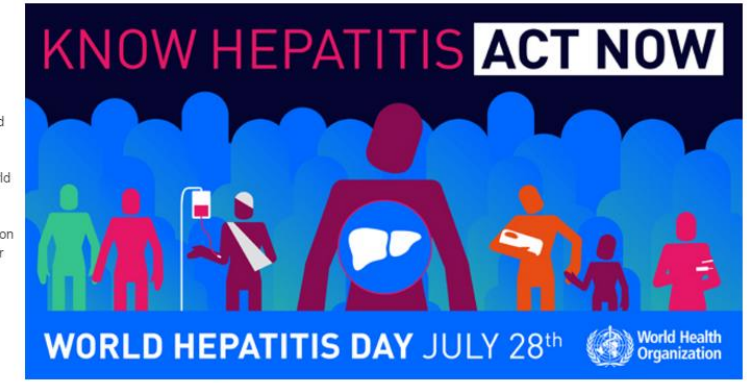
World Hepatitis Day, 28 July 2016

WHO encourages countries to act now to reduce deaths from viral hepatitis

25 July 2016 -- WHO urges countries to take rapid action to improve knowledge about hepatitis, and to increase access to testing and treatment services. Today, only 1 in 20 people with hepatitis know they have it. And just 1 in 100 with the disease is being treated. "The world has ignored hepatitis at its peril," said Dr Margaret Chan, WHO Director-General. "It is time to mobilize a global response to hepatitis on the scale similar to that generated to fight other like HIV/AIDS and tuberculosis."

Read the press release
Read the story on hepatitis testing



400 million
Viral hepatitis affects 400 million people globally. Every year 6–10 million people are newly infected.

95%
An estimated 95% of people with hepatitis do not know there are infected.

90%
Over 90% of people with hepatitis C can be completely cured within 3–6 months.

HIV ve HBV Bulaş yolları

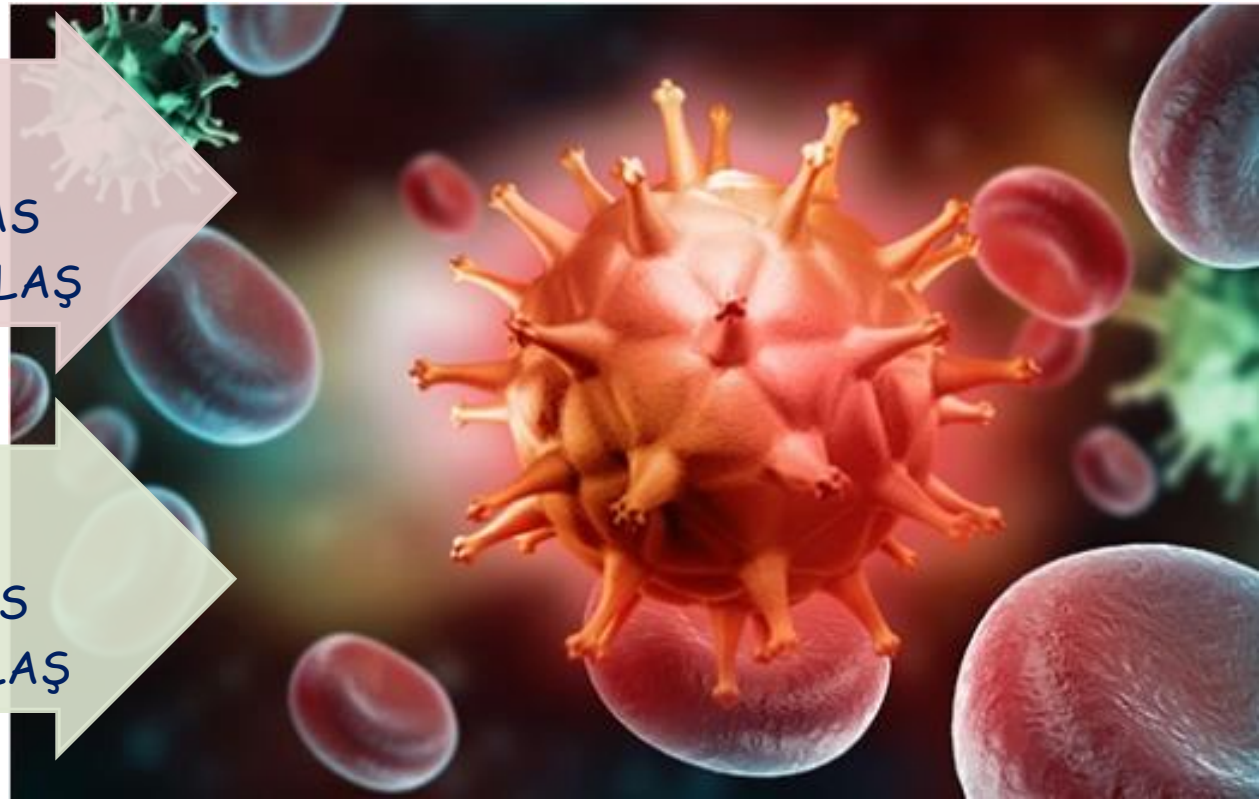
HBV- HIV Koenfeksiyonu

HIV

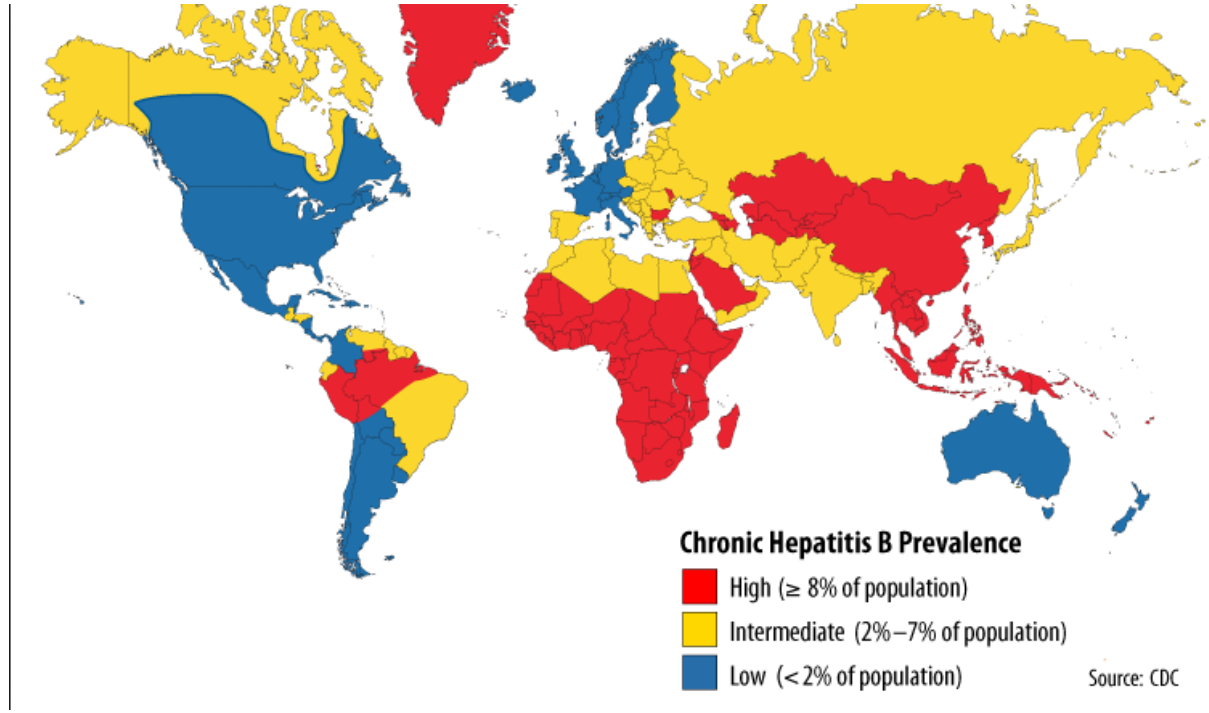
- KAN
- CİNSEL TEMAS
- VERTİKAL BULAŞ

HEPATİT B

- KAN
- CİNSEL TEMAS
- VERTİKAL BULAŞ



HIV-HBV Koenfeksiyonu Riski HBV Prevalansı ile Bağlantılı



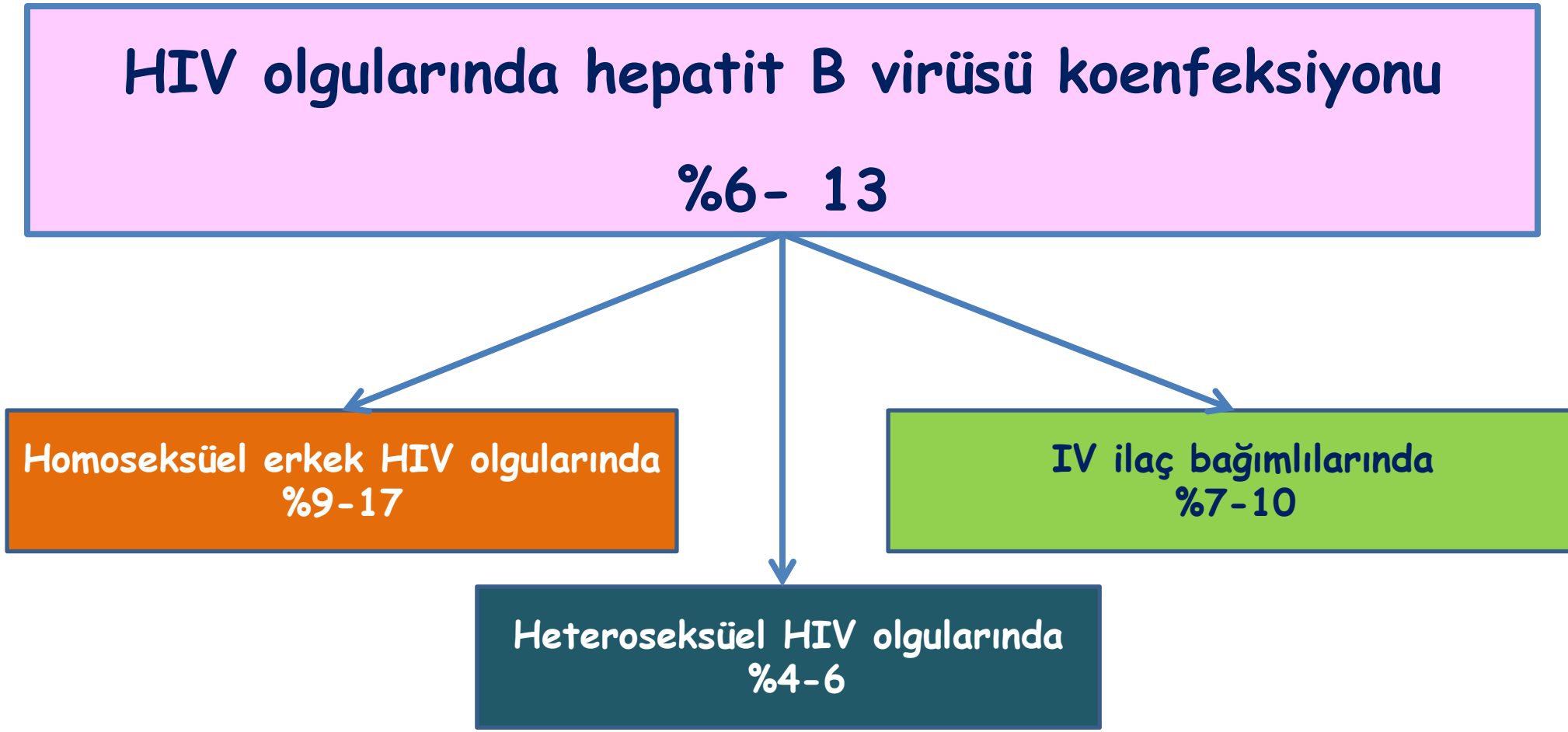
- HBV prevalansı düşük olan ülkelerde

  ko-infeksiyon oranı %5 - 7

- HBV prevalansı yüksek olan ülkelerde

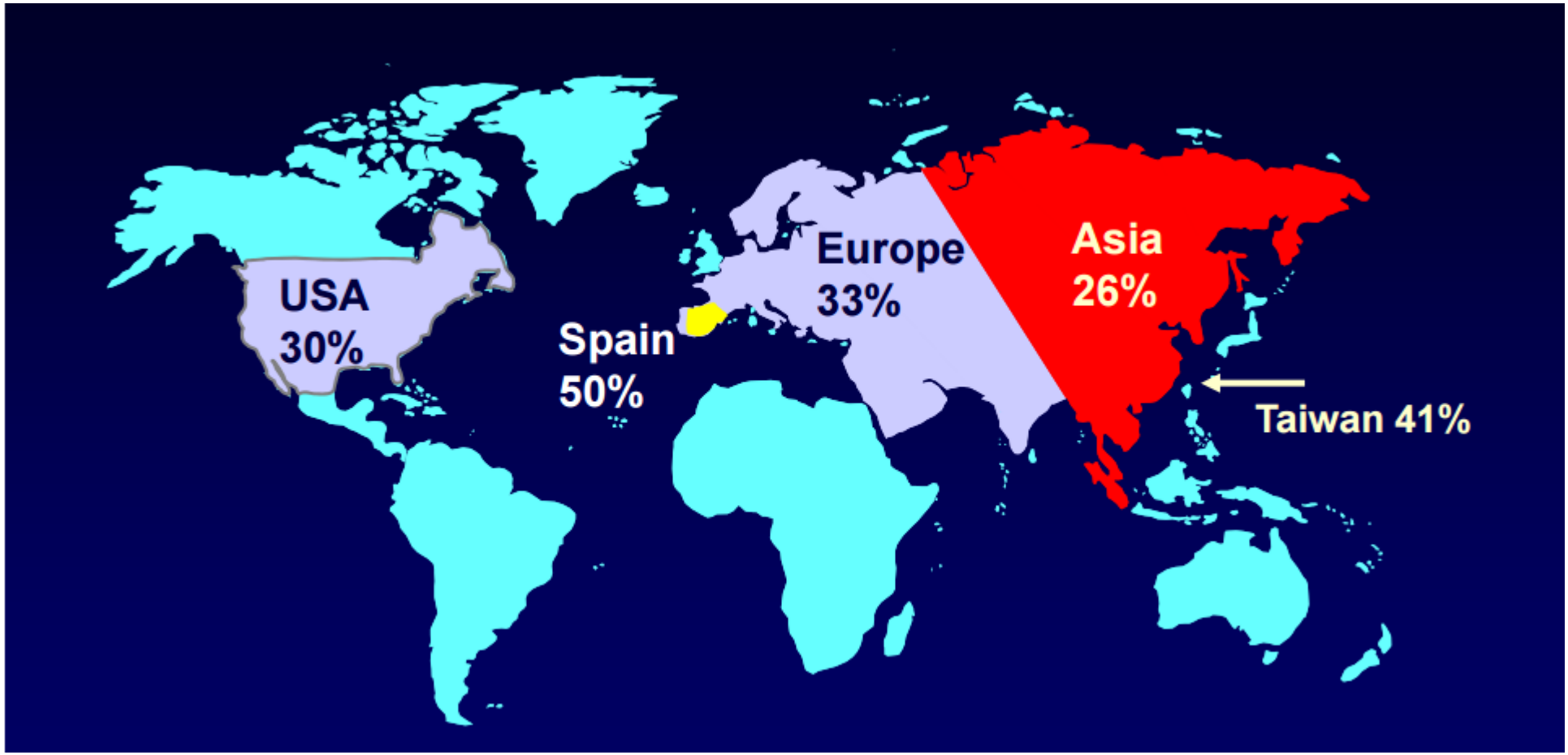
  ko- infeksiyon oranı %10 – 20

HIV/ HBV Koenfeksiyonu



Sun HY. World J Gastroenterol. 2014: 28;20(40):14598-614

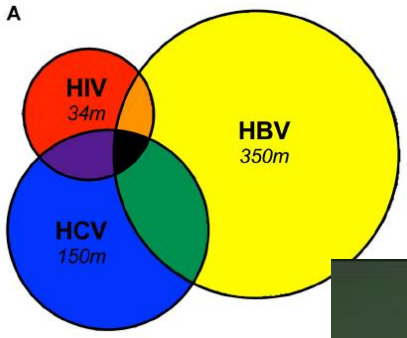
HIV-HBV Koenfeksiyonu Prevalansı



HIV olgularında hepatit B virüsü koenfeksiyonu sık (%6- 13) görülmektedir

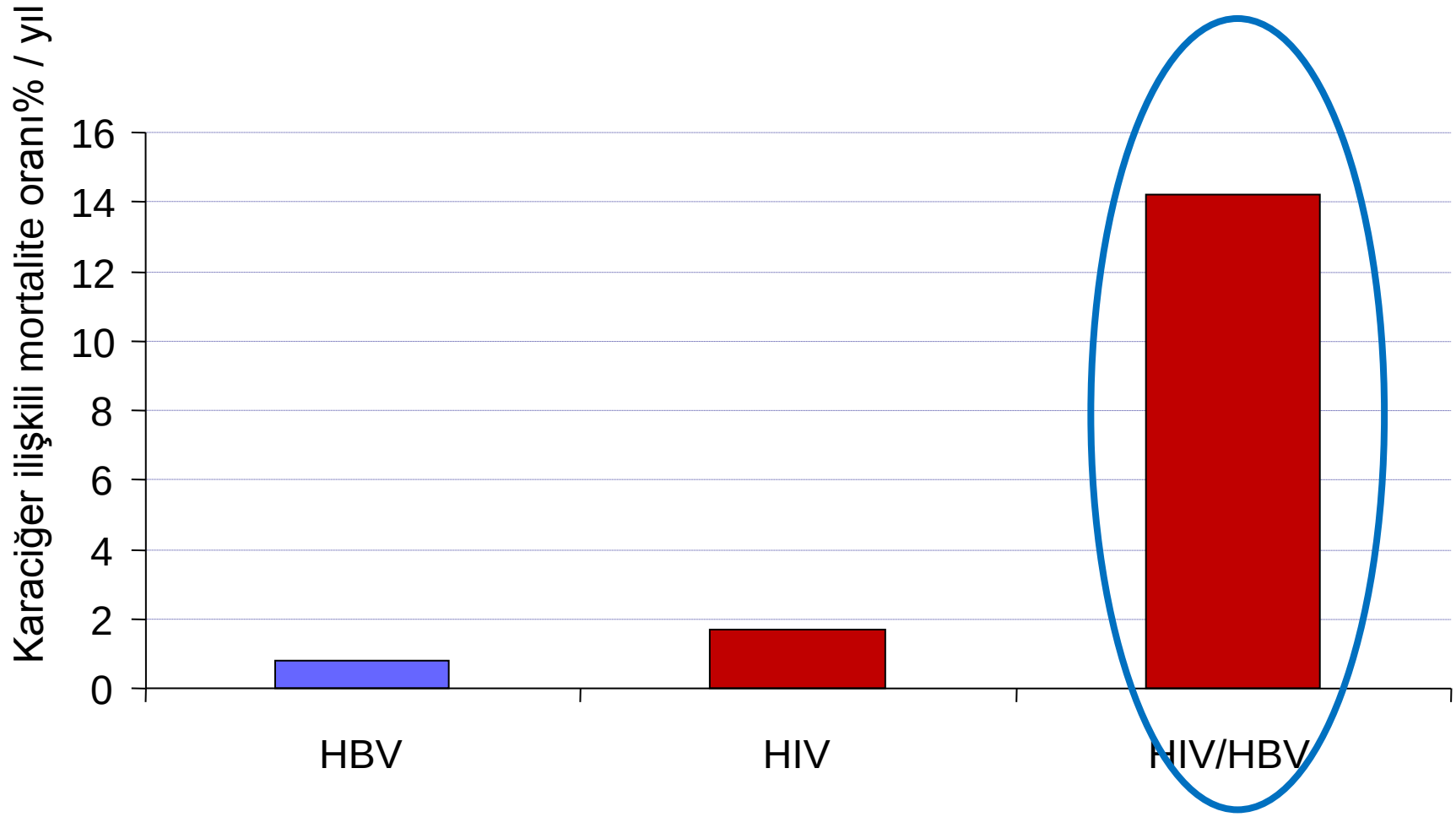
ANEAH'de takip edilen HIV olgularında HBV koenfeksiyonu % 5

Sun HY, Am J Gastroenterol 2009



KO ENFEKSİYON

HAART Öncesi Dönemde HIV/HBV Koenfeksiyonunda Karaciğer Patolojisine Bağlı Mortalite



Thio CL, Lancet 2002;360:1921–6

HBV'nin HIV Üzerine Etkisi

MAJOR ARTICLE HIV/AIDS

CID 2009:48 (15 June) • HIV/AIDS

Impact of Hepatitis B Virus Infection on the Progression of AIDS and Mortality in HIV-Infected Individuals: A Cohort Study and Meta-Analysis

Georgios K. Nikolopoulos, Dimitrios Paraskevis, Eleni Hatzitheodorou, Zissis Moschidis, Vana Sypsa, Xenophon Zavitsanos, Victoria Kalapothaki, and Angelos Hatzakis

- HBV, CD4 hücrelerinde azalmaya yol açar
- HBV X proteini HIV replikasyonunu arttırır
- Hepatit HAART tolerabilitesini bozar
- HARRT yanıtı açısından fark yok*

MAJOR ARTICLE

Hepatitis B Virus Coinfection Negatively Impacts HIV Outcomes in HIV Seroconverters

Helen M. Chun,[1,5] Mollie P. Roediger,[1,7] Katherine Huppler Hullsiek,[1,7] Chloe L. Thio,[3] Brian K. Agan,[1] William P. Bradley,[1] Sheila A. Peel,[1,4] Linda L. Jagodzinski,[1,4] Amy C. Weintrob,[1,8] Anuradha Ganesan,[1,2] Glenn Wortmann,[1,8] Nancy F. Crum-Cianflone,[1,6] Jason D. Maguire,[1,9] Michael L. Landrum,[1,10] and the Infectious Dis

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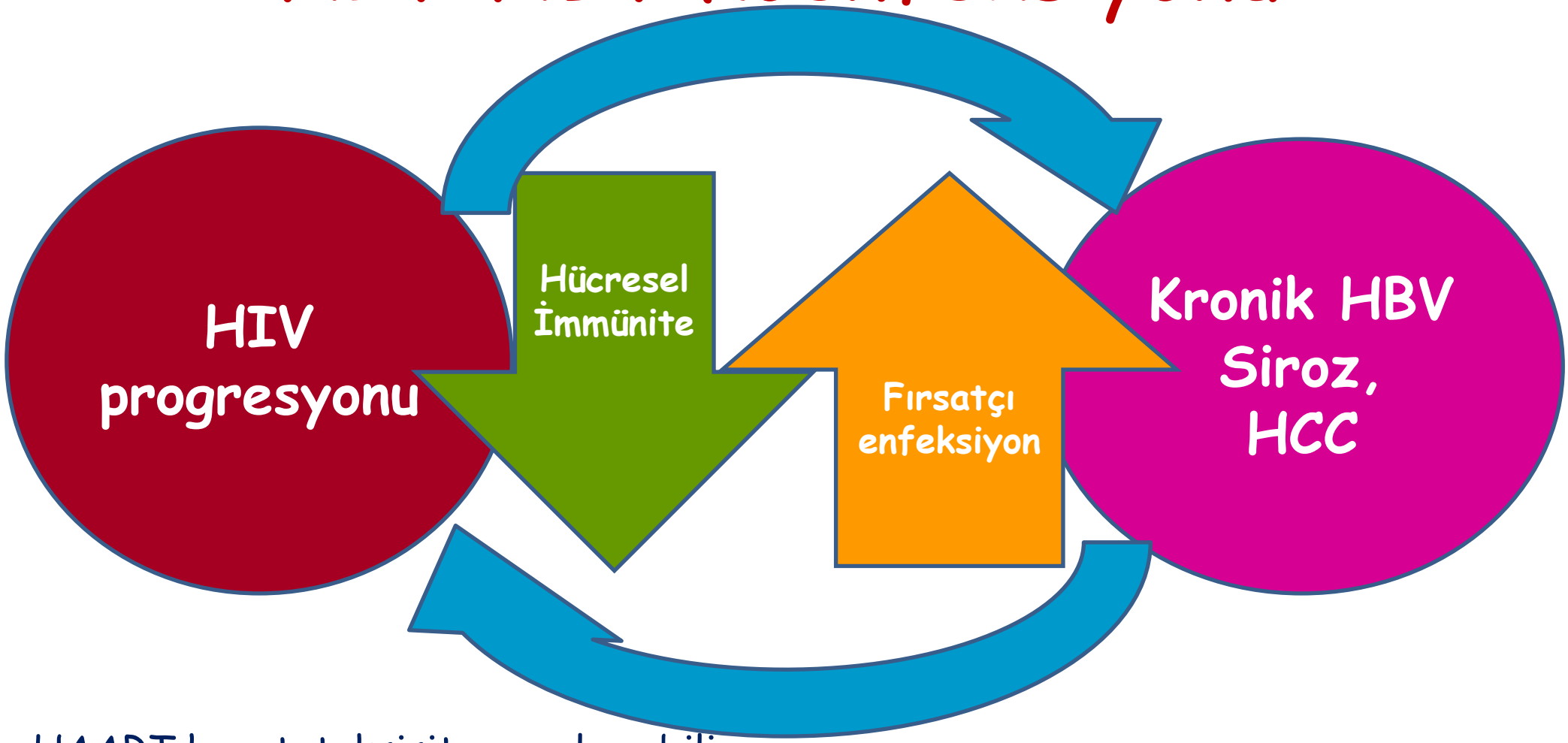
HIV'in HBV Üzerine Etkisi

- HIV doğal olarak hepatotropik bir virüs değil
- Karaciğer hücreleri üzerinde doğrudan sitopatik etkisi var
- Pro-inflamatuvar yanıtta bozukluk ve apoptozda artış
- HBV/HIV koinfekte hastalarda siroz, son dönem karaciğer hastalığı ve HCC daha sık
- İleri HIV enfeksiyonu, anti HBs pozitif olan bir olguda bile HBV aktivasyonuna yol açabilir

Chun HM. J İnfect Dis 2012: 185-93
Sun HY. World J Gastroenterol. 2014: 28;20(40):14598-614

HIV-HBV Koenfeksiyonu



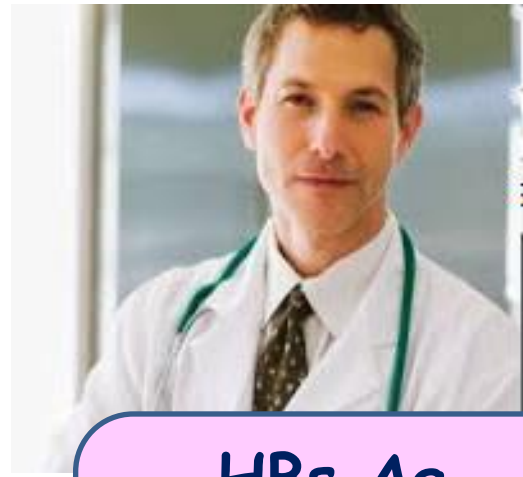
HAART hepatotoksisiteye yol açabilir

Hepatitle ilişkili karaciğer hasarı HAART kullanımını güçleştirir

Colin JFHepatology 1999;29:1306-10
Thio CL, Lancet 2002;360:1921-6
Sulkowski MS,. JAMA. 2000;283(1):74- 80.

Yeni Tesbit HIV Pozitif Olguya Yaklaşım

HIV +



HBs Ag

Anti HBc

Anti HBs

HBs Ag +

HBV DNA

Anti Delta

HBV Serolojisi Taraması

HEDEF

Seroloji negatif

Seroloji pozitif

TEMASIN ve BULAŞIN ÖNLENMESİ

HASTALIĞIN ÖNLENMESİ

HEMEN KOENFEKSİYON TEDAVİSİ BAŞLANMAK

HBV Serolojisi Negatif HIV olguları

HBV bulaşı açısından riskli davranışlar ve bulaşı önleme yolları anlatılmalı

- Cinsel temas sırasında alınması gereken önlemler
- IV uyuşturucu bağımlılarının enjektör paylaşımının önlenmesi
- Dövme ve piersingden kaçınma

AIDSinfo

A Service of the U.S. Department of Health and Human Services

Recommended Immunizations for HIV Positive Adults

Immunization Name	Associated Disease	Dosage	Comments and Warnings
Recommended for All HIV Positive Adults			
Hepatitis B virus (HBV)	Hepatitis B	3 shots over a 6-month period	Recommended unless there is evidence of immunity or active hepatitis. Blood test to check for HBV antibody levels should be done after completion of immunization series. Additional shots may be necessary if antibody levels are too low.
Influenza	Flu	1 shot	Must be given every year. Only injectable flu vaccine should be given to those who are HIV positive. The nasal spray vaccine (FluMist/LAIV) should not be used in this population.
Polysaccharide pneumococcal	Pneumonia	1 or 2 shots	Should be given soon after HIV diagnosis, unless vaccinated within the previous 5 years. If CD4 count is < 200 cells/mm^3 when the vaccine is given, immunization should be repeated when CD4 count is ≥ 200 cells/mm^3. Repeat one time after 5 years.
Tetanus and Diphtheria Toxoid (Td)	1. Lockjaw 2. Diphtheria	1 shot	Repeat every 10 years.
Tetanus, Diphtheria, and Pertussis (Tdap)	1. Lockjaw 2. Diphtheria 3. Pertussis	1 shot	Recommended for adults 64 years of age or younger and should be given in place of next Td booster. Can be given as soon as 2 years after last Td for persons in close contact with babies under 12 months and health care workers.

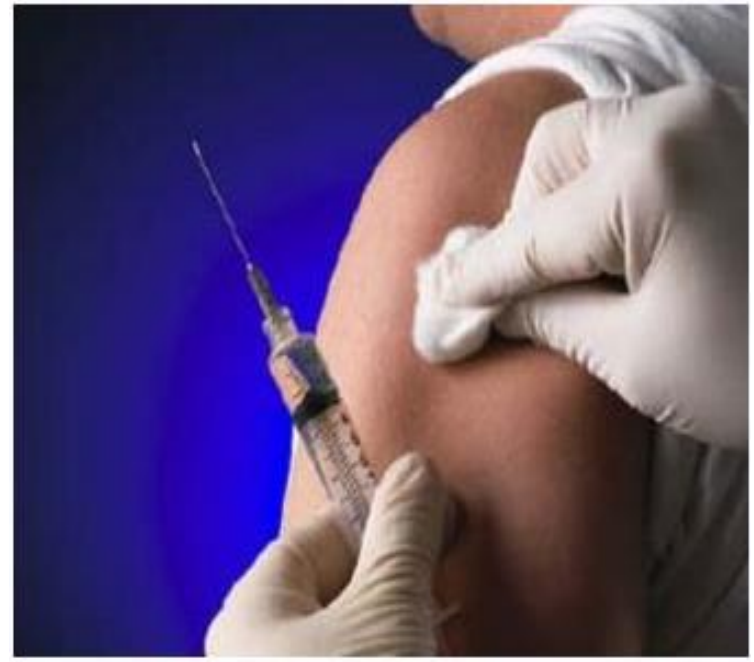
HBV Serolojisi Negatif HIV olguları

CD4 düzeyine bakılmaksızın ilk vizitte aşılanmalı

- İzole Anti HBc pozitifliği olup

  HBV DNA negatif olanlara

  3 doz hepatit B aşısı yapılmalıdır



HBV Serolojisi Negatif HIV olguları

HIV pozitif olgularda hepatit aşının immünijenitesi oldukça düşüktür

- CD4 sayısı düşük olan,
- HIV RNA'sı saptanabilir düzeyde olan,
- HCV enfeksiyonu da bulunan olgularda

aşıya yanıt oranı düşüktür.

CD4 sayısı 200 altında olduğunda cevap oranı %25 civarındadır

Original Article

Immune Response to Standard Hepati

Amitis Ramezani[1], Minoo Mohraz[2], Mohammad Banif

1 Department of Clinical Resear
2 Iranian Research Cer
3 Iranian Society for Support of Pa

Accepte

Abstract

Introduction: Due to their similar routes of transmis
virus (HBV) co-infection occurs considerably. HBV
Therefore, HBV vaccination of all non-immune HIV
infected subjects have suboptimal responses to HBV
responses to standard HBV vaccination in HIV-infe
lacked evidence of either prior HBV infection or in
intramuscular injections of the standard dose (20 µg)
B surface antibody (anti-HBs) titers were checked
antibody response was defined as an anti-HBs titer
56.6% of HIV-infected patients. There was no
seroprotection regarding age, sex, possible route of
(and its duration) and HCV infection. **Conclusion:** O
have a lower response rate to the standard HBV vac
are needed to improve the HBV vaccine response rate

Keywords: Human Immunodeficiency Virus(HIV), I

Table. 1. Studies comparing seroprotection rates of standard Hepatitis B vaccination in HIV-positive patients.

Publications	Seroprotection Rates
Collier *et al.* (1988) [24]	CD4 >500 : 87.5% CD4 <500: 33.2%
Hess *et al.* (1989) [23]	0%
Rey *et al.* (2000) [15]	CD4 >500: 87.5% CD4 200-500: 33.3%
Wilson *et al.* (2001) [22]	37.1%
Alaei *et al.*(2003) [29]	29.1%
Tedaldi *et al.* (2004) [19]	37.2%
Gandhi *et al.* (2005) [18]	62.3%
Overton *et al.* (2005) [16]	17.5%
Fonseca *et al.*(2005) [13]	34%
Cornejo-Juárez *et al.* (2006) [26]	60.7%
Janbakhsh *et al.* (2006) [30]	52.7%
Veiga *et al.* (2006) [31]	59%
Ungulkraiwit *et al.* (2007) [32]	46%
Bailey *et al.*(2008) [27]	47%
Paitoonpong *et al.*(2008) [28]	71.4%
Landrum *et al.* (2009) [33]	35%
Psevdos *et al.* (2010) [34]	34.7%
Launay *et al.*(2011) [35]	65%
Kaech *et al.* (2012) [36]	22%

World Journal of Gastroenterology

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DOI: 10.3748/wjg.v20.i46.17360

World J Gastroenterol 2014 December 14; 20(46): 17360-17367
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

REVIEW

Hepatitis B and human immunodeficiency virus co-infection

Bao-Chau Phung, Philippe Sogni, Odile Launay

4 doz

Table 1 Immunogenicity of 4 intramuscular double doses and 4 intradermal low doses vs standard hepatitis B vaccine regimen in adults with human immunodeficiency virus[53]

n = 426	IM 20 μg x 3 *n* = 141	IM 40 μg x 4 *n* = 145	ID 4 μg x 4 *n* = 140
Response rates At week 28 (Anti-HBs > 10 mIU/mL)	65% 95%CI: 56%-72%	82% 95%CI: 77%-88% *P* < 0.001 *vs* IM 20 × 3	77% 95%CI: 69%-84% *P* = 0.02 *vs* IM 20 × 3
High responders rates (Anti-HBs > 100 mIU/mL)	41% 95%CI: 33%-50%	74% 95%CI: 66%-81% *P* < 0.001 *vs* IM 20 × 3	53% 95%CI: 44%-61% *P* = 0.06 *vs* IM 20 × 3

Anti-HBs: Antibody to hepatitis B antigen.

Vaccine. 2005 Apr 22;23(22):2902-8.

Randomized trial of recombinant hepatitis B vaccine in HIV-infected adult patients comparing a standard dose to a double dose.

Fonseca MO[1], Pang LW, de Paula Cavalheiro N, Barone AA, Heloisa Lopes M.

Standart doza yanıt % 34,

yanıt alınamayanlara çift doz aşı uygulanması durumunda

yanıt % 47 bulunmuş

Published in final edited form as:
Lancet Infect Dis. 2012 December ; 12(12): 966–976. doi:10.1016/S1473-3099(12)70243-8.

Strategies to increase responsiv... in adults with HIV-1

Jennifer A Whitaker, Nadine G Rouphael, Sril... Mulligan
Division of Infectious Diseases, Emory University... Emory Vaccine Center, Decatur, GA, USA (J A W... MD, L Lai MD, Prof M J Mulligan MD); and Mayo...

✓Çift doz aşı
✓4 doz intradermal aşı (0,1,6,12. ay)
✓Hepatit A aşısı ile kombine aşı
✓Adjuvan eklemesi ile güçlendirilmiş aşı

HBs Ag Pozitifliğinin Değerlendirilmesi

Tablo 1 Kronik HBV İnfeksiyonunun Laboratuvara Dayalı Sınıflandırılması

	HBsAg	Anti-HBs	Anti-HBc	HBeAg	Anti-HBe	HBV DNA
Kronik aktif HBV						
Hbe pozitif	+	–	+	+	–	+
Hbe negatif	+	–	+	–	+	+
Ocult HBV	–	–	+	–	+/–	+[b]
İnaktif HBV taşıyıcılığı	+	–	+	–	+	–

- Anti HBc ve Anti HBs pozitifliği olan olgularda % 6.6 – 58.6 Anti HBs kaybı
- İzole Anti HBc pozitifliğinde HBV viremi insidansı % 1-36

Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention

Olgu 1

25.10.2016

- 30 yaşında erkek, marangoz
- Bulantı, kusma, idrar renginde koyulaşma ikter ve ateş şikayeti ile başvurdu. Uykuya meyilli. Koopere oryante
- 5 yıl önce bir kez HBsAg pozitifliği olduğu söylenmiş.

Korunmasız cinsel temas

IV ilaç kullanım öyküsü

Olgu 1

BK: 6800

Parçalı: % 51

Lenfosit: % 27

Monosit: % 17

Trombosit :**113000**

CRP: 38 mg/L

- AKŞ: 90 mg/dl
- Üre: 33mg/dl
- Kreatinin: 0.7mg/dl
- **ALT: 2393 U/L**
- **AST: 1858 U/L**
- GGT: 77 U/L
- ALP: 136 IU/L
- Amilaz 54 IU/L
- LDH 582 U/L
- CPK 27 U/L
- T. Protein:7.7 g/dl
- **Albumin: 2.7 g/dl**
- **T. Bil: 11 mg/dl**
- **İ. Bil: 6 mg/dl**

- PT: 21 sn
- INR: 1.89
- Fib: 184
- **HBs Ag+,Anti HBc total+**

  Anti Hbe+
- **HBV DNA: 262 000 IU/ml**
- Delta Ag ve Anti Delta -
- Anti HAV Ig G+
- TORCH Ig M -

  Ig G ler+
- VDRL: -

Olgu 1

Entekavir 0.5 mg tab

- Kültürler negatif

- **Ultrasonografi:**

  Karaciğer boyutları artmış olup sağ lob kraniokauda

  Yüzeyi düzgündür. Parankim eko şiddeti artmıştır

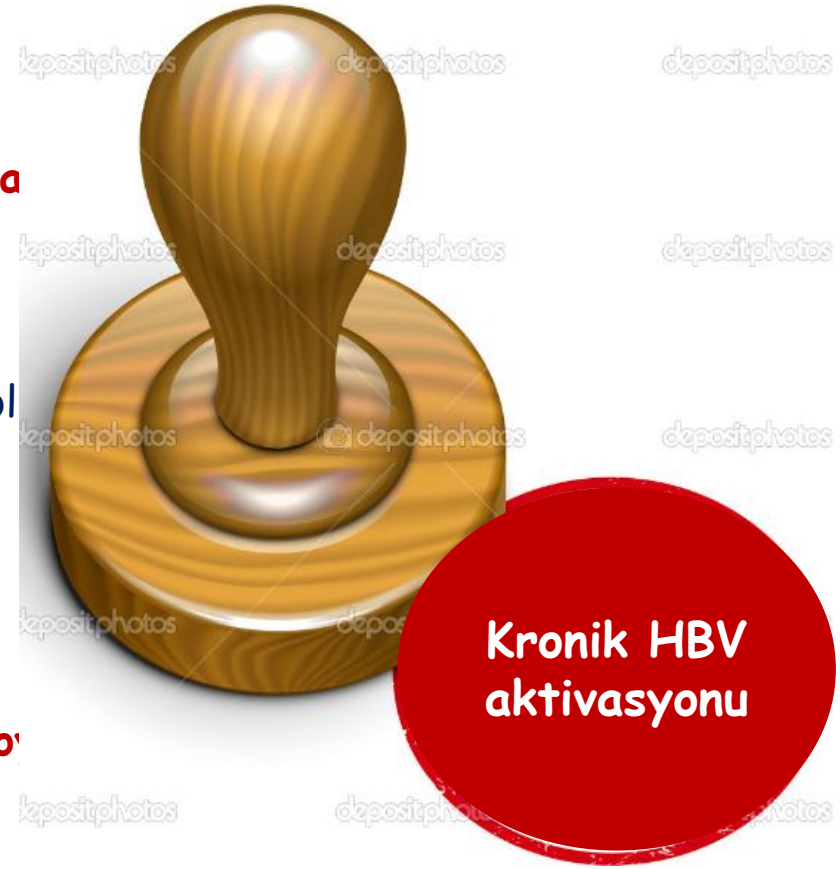
  Portal ve hepatik venöz sistem, intrahepatik safra yol

  genişliktedir

  Safra kesesi, koledok ve pankreas normal

  Dalak boyutları hafif artmış olup kraniokaudal bo

  eko paterni homojen



Olgu 1

- Anti HIV pozitif
- HIV RNA: 176000000 kopya /ml
- CD4: 133,
- CD8: 618,
- CD4/CD8:0.2

HIV+ HBV koenfeksiyonu

Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

Initiation of Antiretroviral Therapy

(Last updated: January 28, 2016; last reviewed: January 28, 2016)

- Section Only PDF (270 KB)
- Full Guideline PDF (1.21 MB)
- Recommendations Only PDF (88.9 KB)
- Tables Only PDF (563 KB)

Panel's Recommendations for Initiating Antiretroviral Therapy in Treatment-Naive Patients

Panel's Recommendations
• Antiretroviral therapy (ART) is recommended for all HIV-infected individuals, regardless of CD4 T lymphocyte cell count, to reduce the morbidity and mortality associated with HIV infection **(AI)**. • ART is also recommended for HIV-infected individuals to prevent HIV transmission **(AI)**. • When initiating ART, it is important to educate patients regarding the benefits and considerations regarding ART, and to address strategies to optimize adherence. On a case-by-case basis, ART may be deferred because of clinical and/or psychosocial factors, but therapy should be initiated as soon as possible.
Rating of Recommendations: *A = Strong; B = Moderate; C = Optional* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Box 1. The START study

The interim results of the Strategic Timing of Antiretroviral Treatment (START) trial were reviewed as a complementary assessment of the evidence. This study enrolled 4685 people at 215 sites in 35 countries. Twenty-seven percent of the participants were women, and approximately half were gay men. The study examined the rates of AIDS and serious AIDS-defining illness or death among people who were randomized to receive immediate ART versus deferring ART until their CD4 count dropped below 350 cells/mm^3. The median baseline CD4 count was 651 cells/mm^3 in the intervention group. In the deferred group, the median CD4 count at ART initiation was 408 cells/mm^3. Follow-up lasted for a mean of three years. A total of 86 events (death, AIDS and serious non-AIDS events) occurred among those with later treatment initiation, whereas 41 events occurred among those starting ART immediately, representing a 57% reduction in negative outcomes among those treated early. In both groups, most events occurred when CD4 counts were higher than 500 cells/mm^3. The study also showed that immediate ART reduced both AIDS-related and non-AIDS-related events, but the benefit was greater for AIDS-related events. Tuberculosis (TB), Kaposi sarcoma and lymphoma — the most common AIDS-related events — all occurred less frequently in the immediate ART group. Serious non-AIDS events (cardiovascular disease, malignancies) were lower in the immediate ART group. Adverse events and deaths were similar between groups. These effects were consistent across CD4 levels and across geographical regions.

2.1 When to start antiretroviral therapy

2.1.1 When to start ART among adults (>19 years old)

NEW

Recommendation

- ART should be initiated among all adults with HIV regardless of WHO clinical stage and at any CD4 cell count *(strong recommendation, moderate-quality evidence).*
  - As a priority, ART should be initiated among all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with CD4 count ≤350 cells/mm^3 *(strong recommendation, moderate-quality evidence).*

HIV-HBV Koenfeksiyonu

International Journal of Infectious Diseases 28 (2014) 29–34

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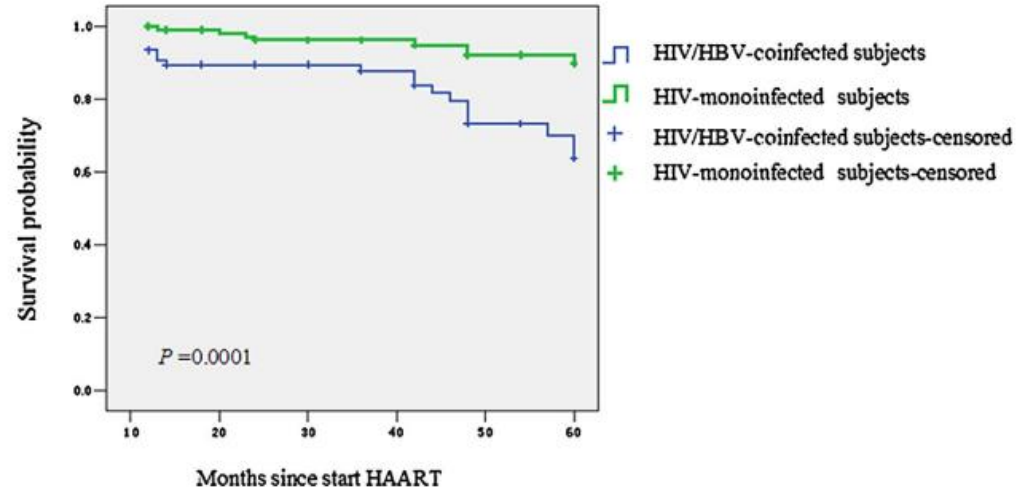
journal homepage: www.elsevier.com/locate/ijid

Impact of hepatitis B virus infection on HIV response to antiretroviral therapy in a Chinese antiretroviral therapy center

Rongrong Yang, Xien Gui *, Yong Xiong, Shi-cheng Gao, Yajun Yan

Department of Infectious Diseases, Zhongnan Hospital of Wuhan University, 169 Donghu Road, Wuhan 430071, China



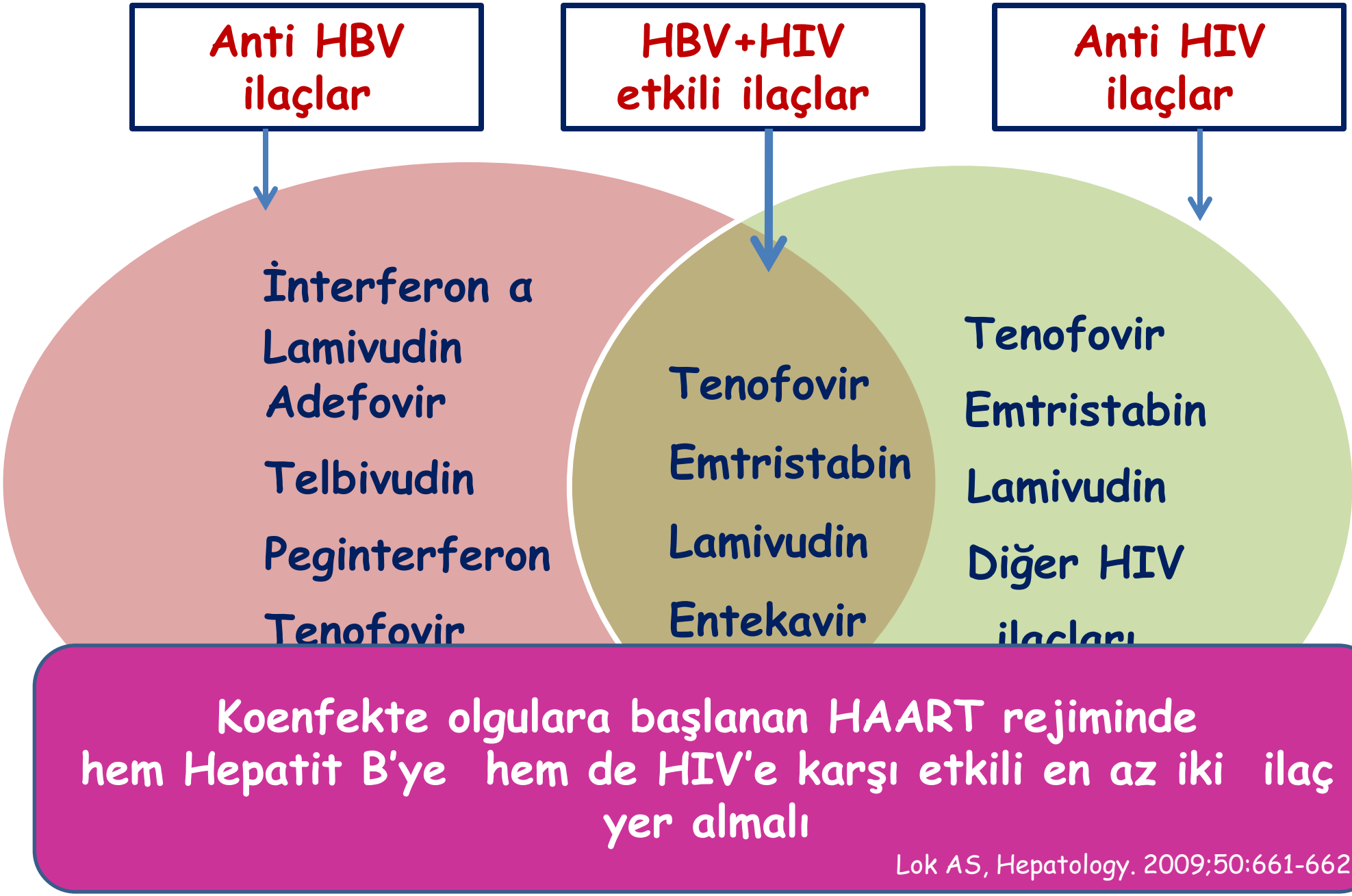
Erken ART

- HIV viremisini baskılar
- İRİS ve ile ilişkili karaciğer fibrozisi ilerlemesini engeller
- HAART yanıtı daha düşük

HIV/HBV Koenfekte Olgulara Yaklaşım

- HIV/HBV koenfekte olgularda her iki virüsün eş zamanlı tedavisine odaklanılmalı
- Karaciğer fibrozisinin değerlendirilmesinde noninvaziv metodlar (Fibroscan elastometri) öncelenmeli
- Karaciğer biyopsisi de gerekebilir

Miailhes P, Proficiency of transient elastography compared to liver biopsy for the assessment of fibrosis in HIV/HBV-coinfected patients. *J Viral Hepat. 2011;18(1):61-69.*



Koenfekte olgulara başlanan HAART rejiminde hem Hepatit B'ye hem de HIV'e karşı etkili en az iki ilaç yer almalı

Lok AS, Hepatology. 2009;50:661-662

HAART

2 NRTI

- 1 İntegraz inhibitörü
- 1 Proteaz inhibitörü
- 1 NNRTI
- 1 Reseptör Antagonisti
- 1 Füzyon inhibitörü

Naive Hastalara Önerilen ART Rejimleri

Regimen	DHHS[1]	IAS-USA[2]	BHIVA[3]	EACS[4]	GeSIDA[5]
DTG/3TC/ABC	Önerilen	Önerilen	Alternatif	Önerilen	Önerilen
DTG + FTC/TDF	Önerilen	Alternatif	Önerilen	Önerilen	Önerilen
DTG + FTC/TAF	Önerilen	Önerilen	Önerilen	Önerilen	Eklenmemiş
EVG/COBI/FTC/TDF	Önerilen	Alternatif	Önerilen	Önerilen	Alternatif
EVG/COBI/FTC/TAF	Önerilen	Önerilen	Önerilen	Önerilen	Önerilen
RAL + FTC/TDF	Önerilen	Alternatif	Önerilen	Önerilen	Önerilen
RAL + FTC/TAF	Önerilen	Önerilen	Önerilen	Önerilen	Eklenmemiş
ATV/RTV + FTC/TDF	Alternatif	Eklenmemiş	Önerilen	Alternatif	Alternatif
ATV/RTV + FTC/TAF	Alternatif	Eklenmemiş	Önerilen	Alternatif	Alternatif
DRV/RTV* + FTC/TDF	Önerilen	Alternatif	Önerilen	Önerilen	Alternatif
DRV/RTV* + FTC/TAF	Önerilen	Alternatif	Önerilen	Önerilen	Eklenmemiş
RPV/FTC/TDF	Alternatif	Alternatif	Önerilen	Önerilen	Alternatif
RPV/FTC/TAF	Alternatif	Alternatif	Önerilen	Önerilen	Eklenmemiş

Önerilen Alternatif Eklenmemiş

References in slidenotes.

Slide credit: clinicaloptions.com

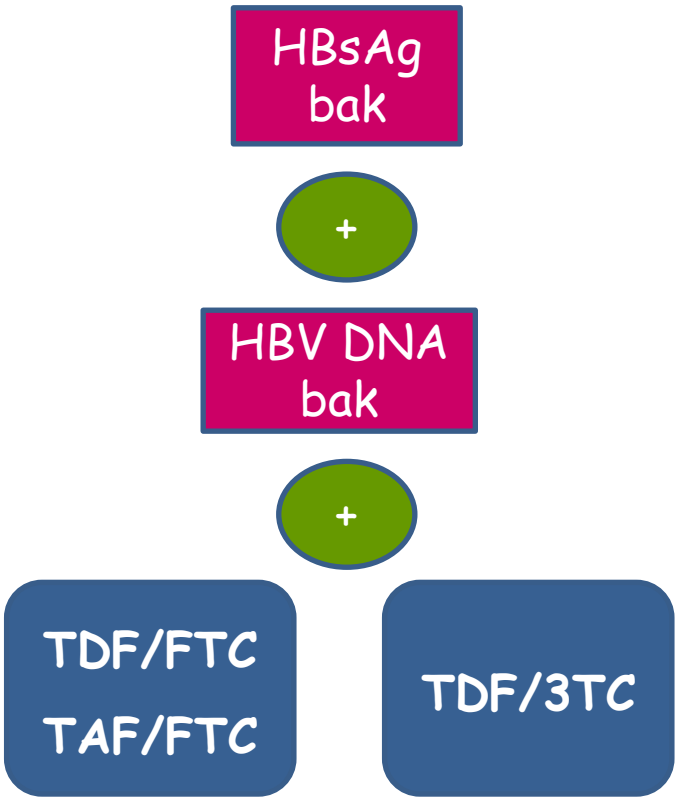
Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

Considerations for Antiretroviral Use in Patients with Coinfections

Hepatitis B (HBV)/HIV Coinfection

(Last updated: July 14, 2016; last reviewed: July 14, 2016)

ART Başlamadan Önce



Panel's Recommendations Regarding Hepatitis B (HBV) / HIV Coinfection

Panel's Recommendations
• Before initiation of antiretroviral therapy (ART), all patients who test positive for hepatitis B surface antigen (HBsAg) should be tested for hepatitis B virus (HBV) DNA using a quantitative assay to determine the level of HBV replication **(AIII)**. • Because emtricitabine (FTC), lamivudine (3TC), tenofovir disoproxil fumarate (TDF) and tenofovir alafenamide (TAF) have activity against both HIV and HBV, for patients coinfected with HIV and HBV, ART should be initiated with the fixed-dose combination of TDF/FTC or TAF/FTC, or the individual drug combinations of TDF plus 3TC as the nucleoside reverse transcriptase inhibitor (NRTI) backbone of a fully suppressive antiretroviral (ARV) regimen **(AI)**.

Neden HBV ye etkili iki ilaç

1. Her iki virüste gelişebilecek direnç sorununu
2. HBV ye karşı IRIS gelişme riskini azaltır

• If ART needs to be modified due to HIV virologic failure and the patient has adequate HBV suppression, the ARV drugs active against HBV should be continued for HBV treatment in combination with other suitable ARV agents to achieve HIV suppression **(AIII)**.

Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*

Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Immune Reconstitution İnflammatory Syndrome (IRIS)

IRIS: ART sonrası immün sistemin toparlanmasından sonra HBV ile ilişkili karaciğer hastalığının alevlenmesi

- ART başlanmasından 6-12. haftadan sonra CD4 sayısındaki yükselmenin başlaması ile birlikte ALT nin yükselmesi şeklinde görülür
- Semptomlar ve bulgular akut hepatit B deki gibidir

Immune Reconstitution İnflammatory Syndrome (IRIS)

- Özellikle sirotik olgularda alevlenme ağır seyreder
- IRIS'in ART ilişkili hepatotoksisite ve diğer viral enfeksiyonlardan ayırt edilmesi zordur
- Bu nedenle ART başlandıktan sonra 6 ve 12 haftalarda ALT nin bakılması önerilmektedir. ALT yüksekliği ile birlikte karaciğer sentez fonksiyonlarında (INR ve albumin) bozukluk gelişebilir

Olgu 1

- Anti HIV pozitif
- HIV RNA: 176000000 kopya /ml
- CD4: 133,
- CD8: 618,
- CD4/CD8:0.2

HIV+ HBV koenfeksiyonu

2 NRTI + 1 integraz inhibitörü

TRUVADA veya HIVEND (Tenofovir emtristabin) + TİVİCAY (dolutegravir)

HIV+ HBV

Entekavir 0.5 mg'a bir ay daha devam edildi.

DRUG RECORD

DOLUTEGRAVIR

Hepatotoxicity

In large clinical trials, therapy with dolutegravir was associated with alanine aminotransferase (ALT) elevations of greater than 3 times the upper limit of normal (ULN) in 2% to 5% of patients, but these rates were similar to those in comparator groups receiving matched background optimized antiretroviral therapy without dolutegravir. These elevations were not associated with clinical symptoms and generally did not require dose modification. A few instances of acute liver injury with jaundice were described in the registration trials for dolutegravir which occurred in association with hypersensitivity reactions and resolved with drug discontinuation. The clinical features of these cases were not provided and their association with dolutegravir as opposed to the concurrent antiretroviral agents was not fully established. The product label for dolutegravir mentions hepatitis and hepatic failure as potential adverse reactions and states that patients with hepatitis B or C coinfection are susceptible to worsening or flares of hepatitis with initiation of dolutegravir therapy, perhaps as a consequence of immune reconstitution syndrome.

Olgu 1

03.01.2017

- BK: 7000
  Trombosit :145 000
- ALT: 53 U/L
- AST: 139 U/L
- GGT: 65 U/L
- ALP: 123 IU/L
- T. Protein:7.7 g/dl
- Albumin: 2.9 g/dl
- T. Bil 2 mg/dl
- İ. Bil: 1.2 mg/dl
- PT: 19 sn
- INR: 1.5

- CD4: 297
- CD8: 1670
- CD4/CD8:0.18
- HIV RNA: 65 kopya/ml
- HBV DNA: 144 IU/ml

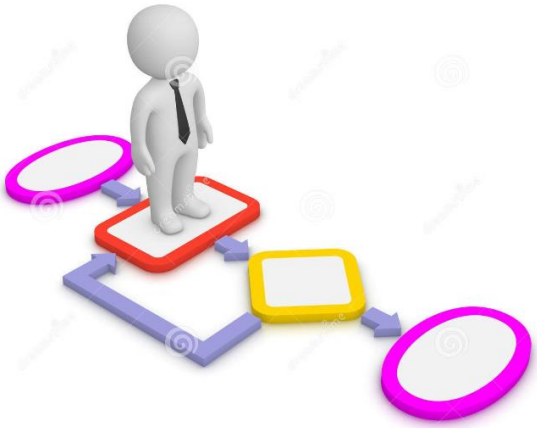
Başlangıçtaki ART Rejimini Seçerken Dikkat Edilmesi Gereken Faktörler

Hasta spesifik	Rejim spesifik
Bazel HIV-1 RNA	Uzun süreli tolerabilite ve güvenlik
Kronik HBV veya HCV koenfeksiyonu	Basitlik
Renal fonksiyonlar	Yiyecekle alım gereksinimleri (ve beslenme alışkanlıkları)
Hamile olma arzusu	**ART nin eşlik eden ilaçlarla etkileşimi ve hayat tarzı**
Yasadışı uyuşturucu kullanımı	**ART'nin dirence karşı genetik bariyeri**
HLA-B*5701 durumu	
Komorbiditeler ve komedikasyonlar	
Genotipik ilaç direnç testi sonuçları	
Beklenen uyum	

DHHS Guidelines. July 2016.

Olgu 2

- HIV pozitif +
- Doğrulama testi +
- CD4:920 hücre/ml
- CD8 :1380 hücre/ml
- CD4/CD8: 0.7
- HIV RNA: 10 000 kopya/ml
- GFR: 55
- HBs Ag ve HBe Ag pozitif, AST:70, ALT 65
- HBV DNA: 5700 IU/ml



Yanıtlar

Koenfeksiyon

Hemen HAART başlanması gerekiyor

HBV etkili iki ilaç tedavide yer alacak

TDF /FTC
Truvada
Hivend

GFR 55
Yakın takip
Gereğinde doz ayarı

ABC / 3TC
Epzicom

HLA B 5701 negatif

Entekavir ekle

Appendix B, Table 7. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency

ARVs Generic Name (Abbreviation) *Trade Name*	Usual Daily Dose[a]	Dosing in Renal Insufficiency[b]	Dosing in Hepatic Impairment
NRTIs Stribild should not be initiated in patients with CrCl <70 mL/min. Use of the following fixed-dose combinations is not recommended in patients with CrCl <50 mL/min: Atripla, Combivir, Complera, Epzicom, Stribild, Triumeq, or Trizivir. Use of Truvada is not recommended in patients with CrCl <30 mL/min.			
Tenofovir Disoproxil Fumarate/Emtricitabine (TDF/FTC) *Truvada*	• 1 tablet PO once daily	CrCl (mL/min) / Dose 30–49 / 1 tablet q48h <30 or on HD / Not recommended	No dosage recommendation

<table>
<tr>
<td>Emtricitabine
(FTC)
Emtriva</td>
<td>• 200 mg oral capsule once daily, or
• 240 mg (24 mL) oral solution once daily</td>
<td>
<table>
<tr><th colspan="3">Dose</th></tr>
<tr><th>CrCL (mL/min)</th><th>Capsule</th><th>Solution</th></tr>
<tr><td>30–49</td><td>200 mg q48h</td><td>120 mg q24h</td></tr>
<tr><td>15–29</td><td>200 mg q72h</td><td>80 mg q24h</td></tr>
<tr><td><15 or on HD[c]</td><td>200 mg q96h</td><td>60 mg q24h</td></tr>
</table>
</td>
<td>No dosage recommendation</td>
</tr>
</table>

Emtristabin doz ayarı ile kullanılabilecek bir ilaç

<table>
<tr>
<td>Abacavir
(ABC)
Ziagen</td>
<td>• 300 mg PO BID</td>
<td>No dosage adjustment necessary</td>
<td><u>Child-Pugh Class A</u>:
• 200 mg PO BID (use oral solution)

<u>Child-Pugh Class B or C</u>:
• Contraindicated</td>
</tr>
<tr>
<td>Lamivudine
(3TC)
Epivir</td>
<td>• 300 mg PO once dail, or
• 150 mg PO BID</td>
<td>
<table>
<tr><th>CrCl (mL/min)</th><th>Dose</th></tr>
<tr><td>30–49</td><td>150 mg q24h</td></tr>
<tr><td>15–29</td><td>1 x 150 mg, then 100 mg q24h</td></tr>
<tr><td>5–14</td><td>1 x 150 mg, then 50 mg q24h</td></tr>
<tr><td><5 or on HD[c]</td><td>1 x 50 mg, then 25 mg q24h</td></tr>
</table>
</td>
<td>No dosage adjustment necessary</td>
</tr>
</table>

Truvada yerine ilk tercih edilecek bel kemiği tedavi Abacavir + lamivudin olabilir
Abacavirde doz ayarı yok. Lamivudin ise doz ayarı ile kullanılabilir

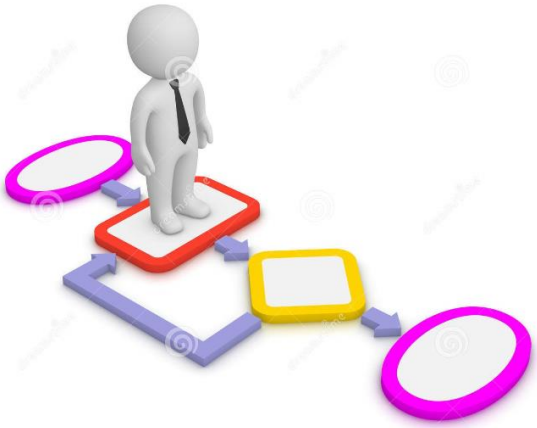
Entekavir Renal Doz

Günlük doz 0.5 mg.

CrCl ≥ 50 ml/d doz ayarı gerekmez

CrCl 30- 49 ml/d 0.25 mg/ g veya 0. 5 mg 48 saatte bir

CrCl< 10 ml/d, hemodiyaliz veya CAPD 0.05 mg/g veya 0.5 mg 7 günde bir



Yanıtlar

Koenfeksiyon

Hemen HAART başlanması gerekiyor

HBV etkili iki ilaç tedavide yer alacak

TDF /FTC
Truvada
Hivend

GFR 50
Yakın takip
Gereğinde doz ayarı

ABC / 3TC
Epzicom

HLA B 5701 pozitif

Entekavir ekle

Antiviral Research 125 (2016) 63–70

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Review

Tenofovir alafenamide: A novel prodrug of tenofovir for the treatment of Human Immunodeficiency Virus

Adrian S. Ray*, Marshall W. Fordyce, Michael J.M. Hitchcock

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ABSTRACT

Despite substantial progress in the development of antiretroviral regimens that durably suppress Human Immunodeficiency Virus (HIV) infection, new agents that maintain high efficacy while further optimizing the safety of lifelong, chronic therapy are needed. Tenofovir alafenamide (TAF; formerly known as GS-7340) is a novel prodrug of the antiviral acyclic nucleoside phosphonate tenofovir (TFV) with improved properties relative to tenofovir disoproxil fumarate (TDF). Although potent and generally well tolerated, TDF therapy has been associated with changes in markers of renal function, decreases in bone mineral density and a rare occurrence of serious renal adverse events, including Fanconi's Syndrome. The renal and bone toxicity observed with TDF is associated with high circulating plasma levels of TFV. TAF was discovered to be a more efficient prodrug able to further refine HIV therapy and better address life-long therapy in an older and increasingly comorbid HIV infected population. By enhancing stability in biological matrices while being rapidly activated in cells, TAF produces higher levels of intracellular TFV diphosphate, the pharmacologically active metabolite, in HIV-target cells at substantially reduced oral doses of TFV equivalents. All TFV released in the body is eventually eliminated renally; therefore, lowering the TFV equivalents administered reduces off-target kidney exposure. Effective therapy is thus achieved at approximately 90% lower systemic exposure to TFV, translating to statistically and clinically significant improvement in safety parameters associated with bone mineral density and markers of renal function.

Appendix B, Table 7. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency

ARVs Generic Name (Abbreviation) *Trade Name*	Usual Daily Dose[a]	Dosing in Renal Insufficiency[b]	Dosing in Hepatic Impairment
NRTIs Stribild should not be initiated in patients with CrCl <70 mL/min. Use of the following fixed-dose combinations is not recommended in patients with CrCl <50 mL/min: Atripla, Combivir, Complera, Epzicom, Stribild, Triumeq, or Trizivir. Use of Truvada is not recommended in patients with CrCl <30 mL/min.			
Tenofovir Alafenamide/Emtricitabine (TAF/FTC) *Descovy*	TAF only available as a component of fixed-dose combinations (i.e., *Descovy*, *Genvoya*, and *Odefsey*) • TAF 10 mg PO daily with EVG/c (*Genvoya*), *or* • TAF 25 mg PO daily in other FDCs	**CrCl (mL/min)** / **Dose** <30 or on HD[c] / Not recommended	Child-Pugh Class A or B: • No dosage adjustment Child-Pugh Class C: • No dosage recommendation

Tenofovir alafenamide
GFR <30 veya hemodiyalizde kullanılmaz

Olgu 3

- HIV pozitif +
- Doğrulama testi +
- CD4:920 hücre/ml
- CD8 :1380 hücre/ml
- HIV RNA: 975 kopya/ml
- HBs Ag pozitif anti HBe ag pozitif
- GFR: 55

CD4/CD8: 0.7

Long-term-nonprogressors elite-controllers

Hasta HAART kullanmayı reddediyor

Değerlendirme

- AST: 75 U/L, ALT: 55 U/L
- T.protein: 4.8 g/dl, Albumin:3.1 g/dl
- Hbe Ag: +, Anti HB e:-
- HBV DNA: 5700 IU/ml
- Trombosit 160 000
- INR 1.5
- Batın US: Hepatomegali,karaciğer parankimi heterojen

•Noninvaziv yöntemlerle karaciğer değerlendirmesi- fibroscan

•Biyopsi:Direkt HAART tedavisi başlanmıyorsa Karaciğer sirozu bulguları yoksa

HIV/HBV Tedavi Seçenekleri

İlaç	HBV	HIV
Lamivudin/ Emtristabin	++	++
Tenofovir	+++	+++
Adefovir	++	?
Entecavir	+++	+
Telbivudine	+++	-/+
IFN / Peg-IFN	+++	+

Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

Considerations for Antiretroviral Use in Patients with Coinfections

Hepatitis B (HBV)/HIV Coinfection

(Last updated: July 14, 2016; last reviewed: July 14, 2016)

Panel's Recommendations Regarding Hepatitis B (HBV) / HIV Coinfection

Panel's Recommendations
• Before initiation of antiretroviral therapy (ART), all patients who test positive for hepatitis B surface antigen (HBsAg) should be tested for hepatitis B virus (HBV) DNA using a quantitative assay to determine the level of HBV replication **(AIII)**. • Because emtricitabine (FTC), lamivudine (3TC), tenofovir disoproxil fumarate (TDF) and tenofovir alafenamide (TAF) have activity against both HIV and HBV, for patients coinfected with HIV and HBV, ART should be initiated with the fixed-dose combination of TDF/FTC or TAF/FTC, or the individual drug combinations of TDF plus 3TC as the nucleoside reverse transcriptase inhibitor (NRTI) backbone • Entekavirin tek başına HBV tedavisinde kullanılması M184V mutasyonunun seçilmesine neden olarak HIV tedavisinde etkili lamivudin ve emtristabin direncine yol açabileceği için önerilmez monitored during interruptions in HBV treatment **(AII)**. • If ART needs to be modified due to HIV virologic failure and the patient has adequate HBV suppression, the ARV drugs active against HBV should be continued for HBV treatment in combination with other suitable ARV agents to achieve HIV suppression **(AIII)**.

Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*

Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Koenfekte Olgularda HBV Monoterapisinde Seçilebilecek Ajan

- İnterferon: Hbe Ag pozitif, ALT ve HBV DNA düzeyi yüksek olan olgularda etkili, HIV'e karşı etkinliği düşük
- HIV açısından direnç gelişme sorunu olmayan bir ajan bu nedenle HAART vermediğimiz olguların HBV tedavisinde tercih edilebilir

GASTROENTEROLOGY 2002;123:1812–1822

CLINICAL–LIVER, PANCREAS, AND BILIARY TRACT

Influence of HIV Infection on the Response to Interferon Therapy and the Long-term Outcome of Chronic Hepatitis B

VINCENT DI MARTINO,* THIERRY THEVENOT,* JEAN–FRANÇOIS COLIN,* NATHALIE BOYER,* MICHÈLE MARTINOT,* FRANÇOISE DEGOS,* JEAN–PIERRE COULAUD,† JEAN–LOUIS VILDE,† FRANÇOIS VACHON,† CLAUDE DEGOTT,§ DOMINIQUE VALLA,* and PATRICK MARCELLIN*

- HIV + kronik HBV: interferon yanıtı % 28
  HIV - kronik HBV: interferon yanıtı % 51
  } (P 0.06)
  IFN tedavisine kısa süreli yanıtta fark yok
- CD4 düşükse yanıt daha kötü (P 0.038)
- Reaktivasyon HIV pozitiflerde daha yüksek (P 0.033)
- HIV pozitifler CD4<200 olanlarda siroz riski daha yüksek

Olgu 4

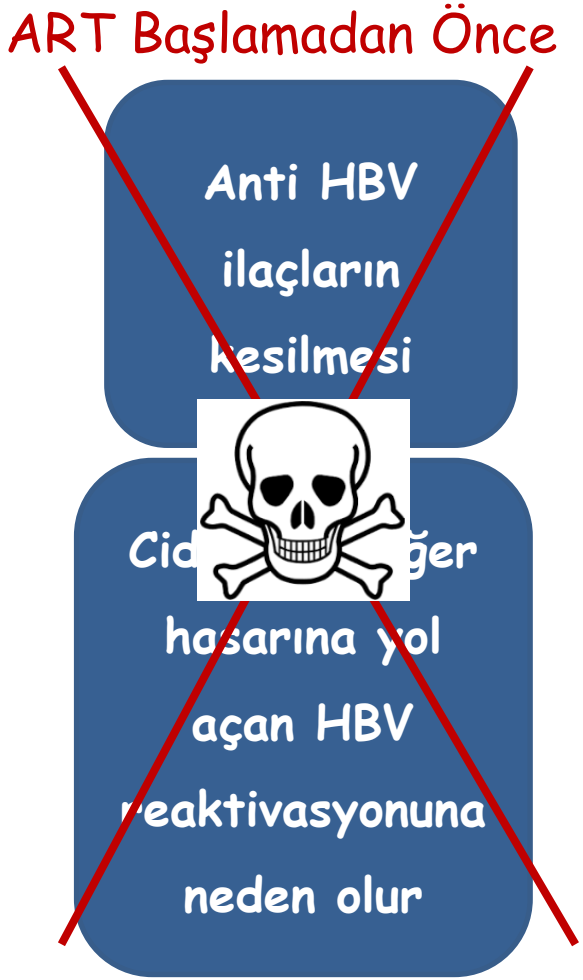
- 28 yaşında kadın hasta
- Kronik hepatit B tanısı ile 5 yıldır lamivudin kullanıyor
- HBV DNA 65 IU/ml
- 3 ay önce eşinde Anti HIV pozitif saptanmış
- ELISA anti HIV: + Doğrulama testi: +
- HIV RNA 345 000 k/ml
- CD4:245, CD8:318

Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

Considerations for Antiretroviral Use in Patients with Coinfections

Hepatitis B (HBV)/HIV Coinfection

(Last updated: July 14, 2016; last reviewed: July 14, 2016)



Panel's Recommendations Regarding Hepatitis B (HBV) / HIV Coinfection

Panel's Recommendations
• Before initiation of antiretroviral therapy (ART), all patients who test positive for hepatitis B surface antigen (HBsAg) should be tested for hepatitis B virus (HBV) DNA using a quantitative assay to determine the level of HBV replication **(AIII)**. • Because emtricitabine (FTC), lamivudine (3TC), tenofovir disoproxil fumarate (TDF) and tenofovir alafenamide (TAF) have activity against both HIV and HBV, for patients coinfected with HIV and HBV, ART should be initiated with the fixed-dose combination of TDF/FTC or TAF/FTC, or the individual drug combinations of TDF plus 3TC as the nucleoside reverse transcriptase inhibitor (NRTI) backbone of a fully suppressive antiretroviral (ARV) regimen **(AI)**. • If TDF or TAF cannot safely be used, the alternative recommended HBV therapy is entecavir in addition to a fully suppressive ARV regimen **(BI)**. Entecavir has activity against HIV; its use for HBV treatment without ART in patients with dual infection may result in the selection of the M184V mutation that confers HIV resistance to 3TC and FTC. Therefore, entecavir must be used in addition to a fully suppressive ARV regimen when used in HBV/HIV-coinfected patients **(AII)**. Peginterferon alfa monotherapy may also be considered in certain patients **(CII)**. • Other HBV treatment regimens including adefovir alone or in combination with 3TC or FTC and telbivudine are not recommended for HBV/HIV coinfected patients **(CII)**. • Discontinuation of agents with anti-HBV activity may cause serious hepatocellular damage resulting from reactivation of HBV; patients should be advised against stopping these medications and carefully monitored during interruptions in HBV treatment **(AII)**. • If ART needs to be modified due to HIV virologic failure and the patient has adequate HBV suppression, the ARV drugs active against HBV should be continued for HBV treatment in combination with other suitable ARV agents to achieve HIV suppression **(AIII)**.

Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*

Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Olgu 4

- HIV-ile enfekte bireyler HBV için lamivudin veya emtristabin monoterapisi alıyorlarsa
- 3TC'ye ve FTC'ye karşı rtM204 de YMDD direnç mutasyonu gelişme riski yüksektir
- Bu direnç sonucunda, telbivudinde HBV'ye karşı aktivitesini yitirecek, entekavirin ise etkinliği azalacaktır.

Olgu 4

Bu olguda lamivudini kesmemek ancak tedaviye hem HIV'e hem de HBV ye etkili bir ilacı daha içerek HAART tedavisi başlamak gerekir

Koenfekte Son Dönem Karaciğer Hastaları

- Bu olgularda monoenfekte olgularda olduğu gibi interferon kontrendike ancak nükleozid analogları güvenlidir
- Olgular hepatolog ile konsülte edilmeli
- Gereğinde transplantasyona hazırlanmalıdır

June 10, 2009

Liver Transplant in HBV/HIV Coinfected Patients Successful

People coinfected with both the hepatitis B virus (HBV) and HIV have excellent survival rates following a liver transplant, according to a study published in the June 1 issue of AIDS.

HBV can become a chronic disease in roughly 25 percent of people who are also infected with HIV. When this occurs, people are at increased risk of liver failure and liver cancer, usually many years after first becoming infected. HBV disease, however, progresses more rapidly in coinfected people than in people not infected with HIV.

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FDA Approves New Single-Tablet HIV Regimen, Triumeq

Life Expectancy for Young People With HIV Is Nearly Normal

A 15-Year Jump in Life Expectancy for People With HIV

Scientists Devise Method of Snipping HIV From Immune Cells

Monkey HIV Vaccine Success Opens Door for Human Trials

HIV Combo Pill Less Toxic

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World Journal of Gastroenterology

Submit a Manuscript: http://www.wjgnet.com/esps/
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World J Gastroenterol 2015 November 21; 21(43): 12311-12321
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

TOPIC HIGHLIGHT

2015 Advances in Liver Transplantation

Role of liver transplantation in human immunodeficiency virus positive patients

Deepak Joshi, Kosh Agarwal

Tablo 2. HIV Pozitif Bireylerde Karaciğer Transplantasyonu için Kriterler

Transplant adayı olguların karşılaması gereken kriterler
CD4 > 100 h/μL (daha önce fırsatçı enfeksiyon öyküsü olan hastada CD4 >200 h/μL)
HIV viral yük <50 kopya/mL (ultrasensitif Amplicor Monitor PCR assay)
AIDS tanımlayıcı hastalığının olmaması
IRIS tablosunun bulunmaması
Progressif multifokal lökoensefalopati, kronik intestinal kriptosporidiozis (> 1ay) veya primer SSS lenfoması olmaması

Published in final edited form as:
Infect Dis Clin North Am. 2013 June ; 27(2): 459–471. doi:10.1016/j.idc.2013.02.010.

Perspectives on Liver and Kidney Transplantation in the HIV-Infected Patient

Peter Chin-Hong, MD, **George Beatty, MD, MPH**, and **Peter Stock, MD, PhD***

- HIV-HBV koenfekte olgularda karaciğer transplantasyonu yüz güldürücü
- 2001-2007 yılları arasında nakil yapılan 22 koenfekte hasta ile 20 HBV monoinfekte hasta prospektif olarak karşılaştırmıştır
- 4 yıllık hasta sağkalım oranı
  - HIV / HBV grubunda % 85
  - HBV'de% 100

- HBV-HIV koenfekte karaciğer transplant hastalarında Hepatit B yönetimi, transplant sonrası HBV'nin tedavisi ile aynı olup hepatit B immün globulin (HBIG) ve ek olarak HBV aktif ajanları içeren antiretrovirallerin kullanması şeklindedir
- Bu strateji HBV nüksünü önleme ve graft ömrü açısından önemlidir

Published in final edited form as:
Infect Dis Clin North Am. 2013 June ; 27(2): 459–471. doi:10.1016/j.idc.2013.02.010.

- HAART' ta integraz inhibitörlerinin yer alması

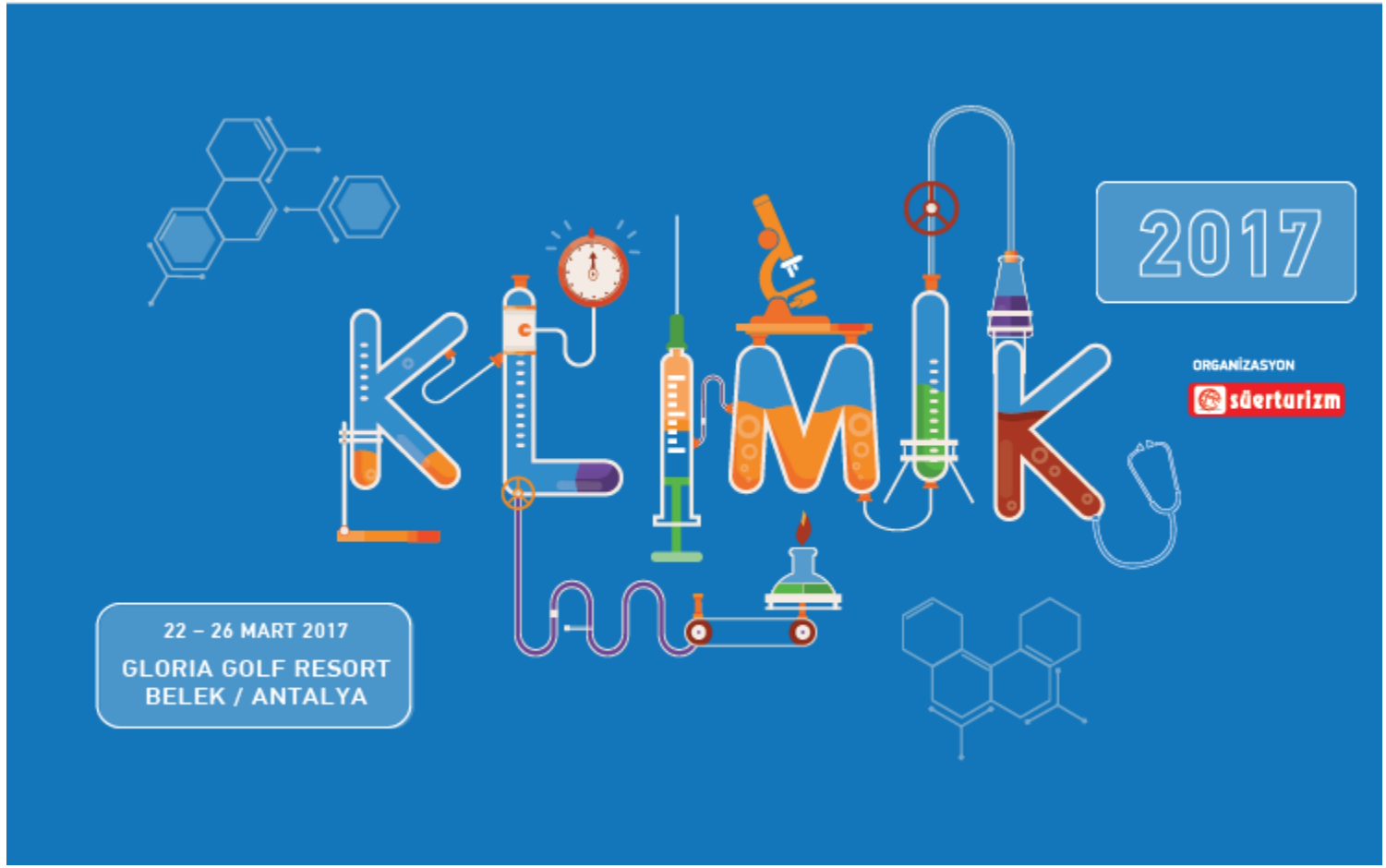
ilaç etkileşimlerinin daha az olması nedeniyle posttransplant dönemde tedavi yönetimini basitleştirebilir, organ reddini azaltabilir

Sonuç

- HIV pozitifliği saptanan tüm olgular HBV koenfeksiyonu açısından araştırılmalıdır
- Olgularda HAV, HCV ve Delta virüs serolojisine bakılmalı,
- HBV serolojik göstergeleri negatif olan olgular hepatit B aşısı ile bağışıklanmalıdır
- Seronegatif olgulara HAV aşısı yapılmalıdır

Sonuç Olarak

- Tedavi gerektiren kronik HBV enfeksiyonu olan HIV olgularında CD4 düzeyine bakılmaksızın hemen HAART başlanmalı
- Başlanacak olan HAART rejimi HBV 'ye etkili en az iki ilaç içermelidir



İLGİNİZ İÇİN TEŞEKKÜR EDİYORUM