



Güncel Rehberler Işığında Antiretroviral Tedavi

Dr. Birgül Mete

**İ.Ü. Cerrahpaşa Tıp Fakültesi Enfeksiyon
Hastalıkları ve Klinik Mikrobiyoloji A.D.**



Rehberler



- ✓ **DHHS** (Departement of Human and Health Services)
- ✓ **EACS** (European AIDS Clinical Society)
- ✓ **IAS** (International AIDS Society)
- ✓ **WHO** (World Health Organization; DSÖ)
- ✓ **BHIVA** (British HIV Association)
- ✓ **Türkiye HIV/AIDS Tanı Tedavi Rehberi**



Tedaviye başlama zamanı





Ne zaman başlamalı?





İdeal tedavi zamanıyla ilgili yıllar içinde deęişen görüřler

Yeni, basit, daha az toksik ajanlar, kontrolsüz HIV replikasyonu sonucu gelişen komorbiditeler

Yan etkiler, tedavi uyum problemleri, direnç, eradike edilememesi

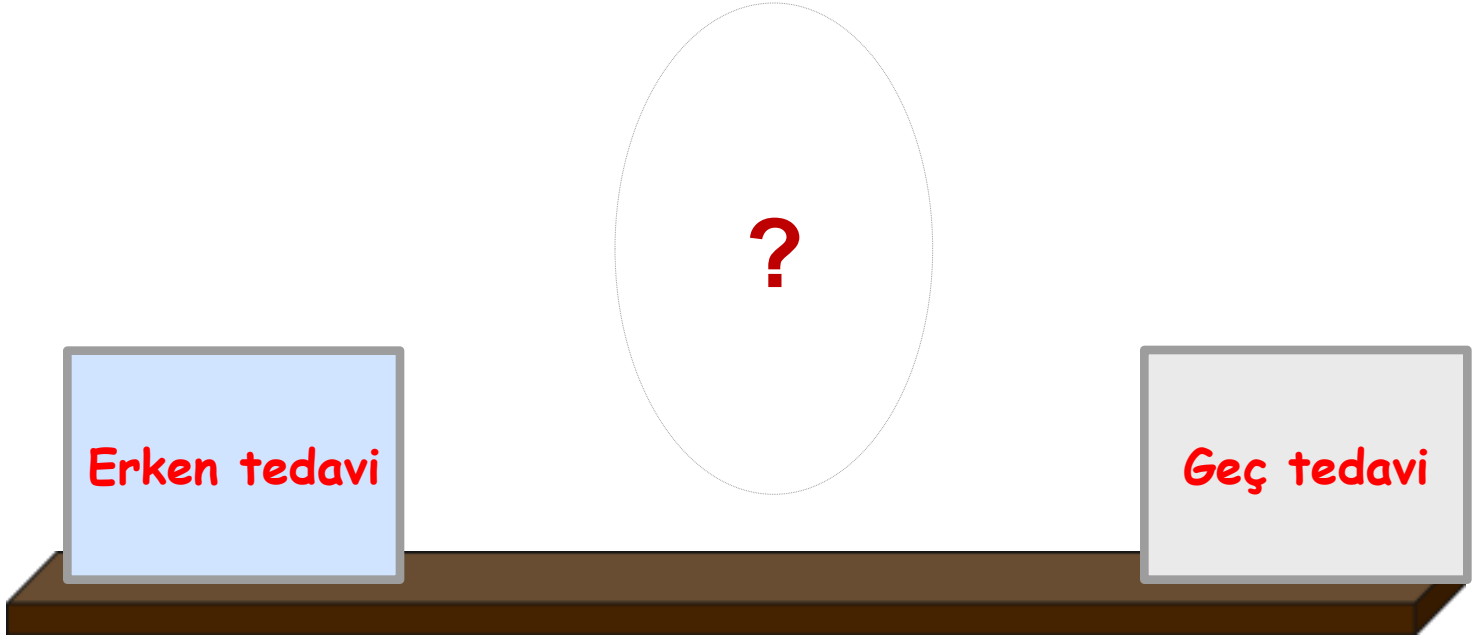
ART'nin keşfi yüksek beklenti

1996

Herkese tedavi

Ertelenen tedavi

Herkese tedavi





Erken?

- ✓ **HIV ile ilişkili morbidite ve mortalite**
 - HIV ile ilişkili immün yetmezlik
 - virüsün doğrudan organlarda oluşturduğu hasar
 - kronik enflamasyonun organlardaki dolaylı etkisine bağlı
- ✓ Tedavi edilmeyen **HIV enfeksiyonu veya viremi sonucunda AIDS ile ilişkili olmayan** hastalıkların gelişimi ve sonucunda ölüm

1-O'Brien WA, et al. N Engl J Med. 1996;334:426-431.

2- Garcia F, et al. J Acquir Immune Defic Syndr. 2004;36:702-713.



Erken?

- ✓ Sürekli virolojik supresyon ile immün fonksiyonlarda iyileşme ve kaliteli bir yaşam
Geç dönemde başlanan tedavi erken dönemde viral replikasyona bağlı organlarda gelişen hasarı iyileştirmeyebilir
- ✓ **Bulaşın engellenmesi**
- ✓ Daha çok tedavi seçeneği
etkin
kullanımı kolay
yan etki profili düşük
direnç bariyeri yüksek

1-Study Group on Death Rates at High CDCiANP, Lodwick RK, et al. Lancet. 2010;376:340-345.

2-Cohen MS, et al. N Engl J Med.2011;365:493-505.



Ertelenmeli?

- ✓ Uzun süreli tedavi
- ✓ Uyum ve direnç sorunu
- ✓ Kümülatif kullanıma bağlı bilinmeyen yan etkiler
- ✓ Maliyet

1- Friis-Moller N, et al. N Engl J Med.2007;356:1723-1735.

2- Horberg M, et al. J Acquir Immune Defic Syndr. 2010;53:62-69.



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection

The INSIGHT START Study Group*

ABSTRACT



The NEW ENGLAND JOURNAL *of* MEDICINE

ORIGINAL ARTICLE

A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa

The TEMPRANO ANRS 12136 Study Group*



- ✓ **CD4 düzeyi 500/mm³'ün üzerinde olan hastalarda ART'ye başlanması tedaviyi ertelemeye üstün**
- ✓ **Erken tedavi grubunda AIDS ile ilişkili ya da ilişkili olmayan ciddi durumlar anlamlı oranda daha düşük**



Önerilerde Değişiklikler





DHHS

Klinik

Öneri

AIDS tanımlayıcı hastalık öyküsü (AI)
Gebe hasta (AI)
HIV ile ilişkili nefropatili hasta (AII)
HBV tedavi endikasyonu olan
HBV ko-enfeksiyonlu hasta (AIII)
HCV ko-enfeksiyonu (BII)
HIV ile ilişkili demans (AI)

ART başla



Klinik

Öneri

Bulaşı engellemek

- Perinatal (AI)
- Heteroseksüel (AI)
- Diğer risk grupları (AIII)

ART başla

Diğer

- Erken HIV enfeksiyonu (BII)
- > 50 yaş (BIII)



DHHS

Asemptomatik hasta	Öneri
CD4 < 350/mm ³ (AI) CD4 350-500/mm ³ (AII) CD4 > 500/mm ³ (BIII)	ART başla



DHHS

Statement by the HHS Panel on Antiretroviral Guidelines for Adults and Adolescents Regarding Results from the START and TEMPRANO Trials Date: July 28, 2015

Source: AIDSinfo

Results for two pivotal randomized controlled trials (START1 and TEMPRANO2) were recently published, both demonstrating that the clinical benefits of antiretroviral therapy (ART) are greater when ART is started early, with pre-treatment CD4 T lymphocyte (CD4) counts >500 cells/mm³, than when initiated at a lower CD4 cell count threshold. The Panel already recommends ART for all HIV-infected patients to reduce the risk of disease progression. However, until the results of these two studies became available, the Panel's recommendations for starting ART in patients with CD4 cell counts 350 to 500 cells/mm³ (AII)^a and >500 cells/mm³ (BIII)^a were primarily based on data from observational cohort studies and expert opinion.

With the availability of the START and TEMPRANO trial results, the Panel's overall recommendation remains the same:

ART is recommended for all HIV-infected patients regardless of pre-treatment CD4 count. However, the strength of the recommendation will be changed to **A_{Ia} (strong recommendation based on data from randomized controlled trials) for all patients.**



DHHS

Asemptomatik hasta

Öneri

CD4 >500/mm³(AIa)

ART başla



Acil tedavi gerektiren durumlar

- ✓ AIDS göstergesi hastalık öyküsü (HIV ilişkili demans dahil) (AI)
- ✓ Gebelik (AI)
- ✓ Akut fırsatçı enfeksiyonlar
- ✓ CD4 $<200/\text{mm}^3$ (AI)
- ✓ Yüksek viral yük (>100.000 kopya/ml) (BII)
- ✓ HIV-ilşkili nefropatili hasta (AII)
- ✓ HIV/HBV ko-enfeksiyonlu hasta (AII)
- ✓ HIV/HCV ko-enfeksiyonlu hasta (BII)
- ✓ CD4 sayısında hızlı düşüş ($>100/\text{yıl}$) (AIII)
- ✓ Akut/erken HIV enfeksiyonu (BII)





© 2015 British HIV Association

British HIV Association guidelines for the treatment of HIV-1-positive adults with antiretroviral therapy 2015



BHIVA

Kronik enfeksiyon

- $CD4 \leq 350/mm^3$ (1A)
- AIDS (CD4 sayısından bağımsız) (1A)
- HIV ilişkili komorbidite varlığı (CD4 sayısından bağımsız) (HIV ilişkili nefropati, idiyopatik trombositopenik purpura, semptomatik HIV ilişkili nörokognitif bozukluklar) (1C)
- Geb
- Kro **CD4 sayısından bağımsız (1A)** (1B)
- Kro **BHIVA;2015** (1C)
- İmmunsupressif kemoterapi ya da radyoterapi gerektiren AIDS tanımlayıcı olmayan maliniteler (1C)
- Kronik hepatit B ko-enfeksiyonlu hastada $CD4 > 500/mm^3$ ise ve hepatit B tedavi endikasyonu var ise (2B)



BHIVA

AIDS veya majör enfeksiyon ile başvuran hasta

- AIDS tanımlayıcı enfeksiyon veya ciddi bakteriyel enfeksiyon ile başvuran ve $CD4 < 200/mm^3$ olan hastada özgül antibiyoterapi başlandıktan sonra ilk 2 hafta içinde ART başlanması önerilir (1B)

Primer HIV enfeksiyonu (aşağıdaki kriterlerden herhangi biri varlığı)

- Nötrofil sayısının $< 1500/mm^3$ olması (1A)
- AIDS tanımlayıcı hastalık (1A)
- Kanıtlanmış $CD4 < 350/mm^3$ (1C)
- Negatif seroloji sonucundan sonra 12 hafta içinde gelişen primer HIV enfeksiyonu (1C)

Bulaş riskini azaltmak için ART başlanması

- CD4 sayısının $< 500/mm^3$ baş

Bulaş riskini azaltmak için ART herkese önerilmeli (1A)

BHIVA;2015

A; 2013



DSÖ

Ciddi/ileri HIV enfeksiyonu
(DSÖ klinik evre 3 veya 4)

CD4 sayısından bağımsız olarak ART başlanır

DSÖ klinik evre 1 ve 2

CD4 sayısı $< 500/\text{mm}^3$ olan hastalara

anlar

GUIDELINES



Tüberküloz

ırak ART

DSÖ klinik evre ve CD4 sayısına bakılmaksızın tüm hastalara ART başlanmalıdır

--- Ağır ve ilerlemiş HIV enfeksiyonu (DSÖ klinik evre 3 ve 4) ve CD4 sayısı $\leq 350/\text{mm}^3$ olanlar öncelikli

DSÖ;2015

HIV serolojisi

SEPTEMBER 2015

ırak ART

Gebe ve emziren hastalar

başlanır

ırak ART



EACS

Semptomatik hasta	Aseptomatik hasta	
CD4 sayısından bağımsız	CD4 < 350/mm ³	CD4 ≥ 350/mm ³
ART (güçlü öneri)	ART (güçlü öneri)	ART (öneri)



- ✓ Antiretroviral tedavi başlanacak hastanın tedaviye **istekli ve hazır olması**, tedavinin yarar ve riskleri ve **ilaç uyumunun önemi** hakkında bilgilendirilmesi gerekmektedir (**AIII**).
- ✓ Hasta tedaviyi **ertelemek isteyebilir** ya da olgu bazında klinik ve/veya psikososyal faktörler nedeniyle hekimler **ART'yi erteleyebilir**.





Erteleme

- ✓ İmmun rekonstitüsyon sendromu: TB, PCP
- ✓ İlaç etkileşimleri (kronik HCV)
- ✓ Operasyon



Antiretroviral tedavi



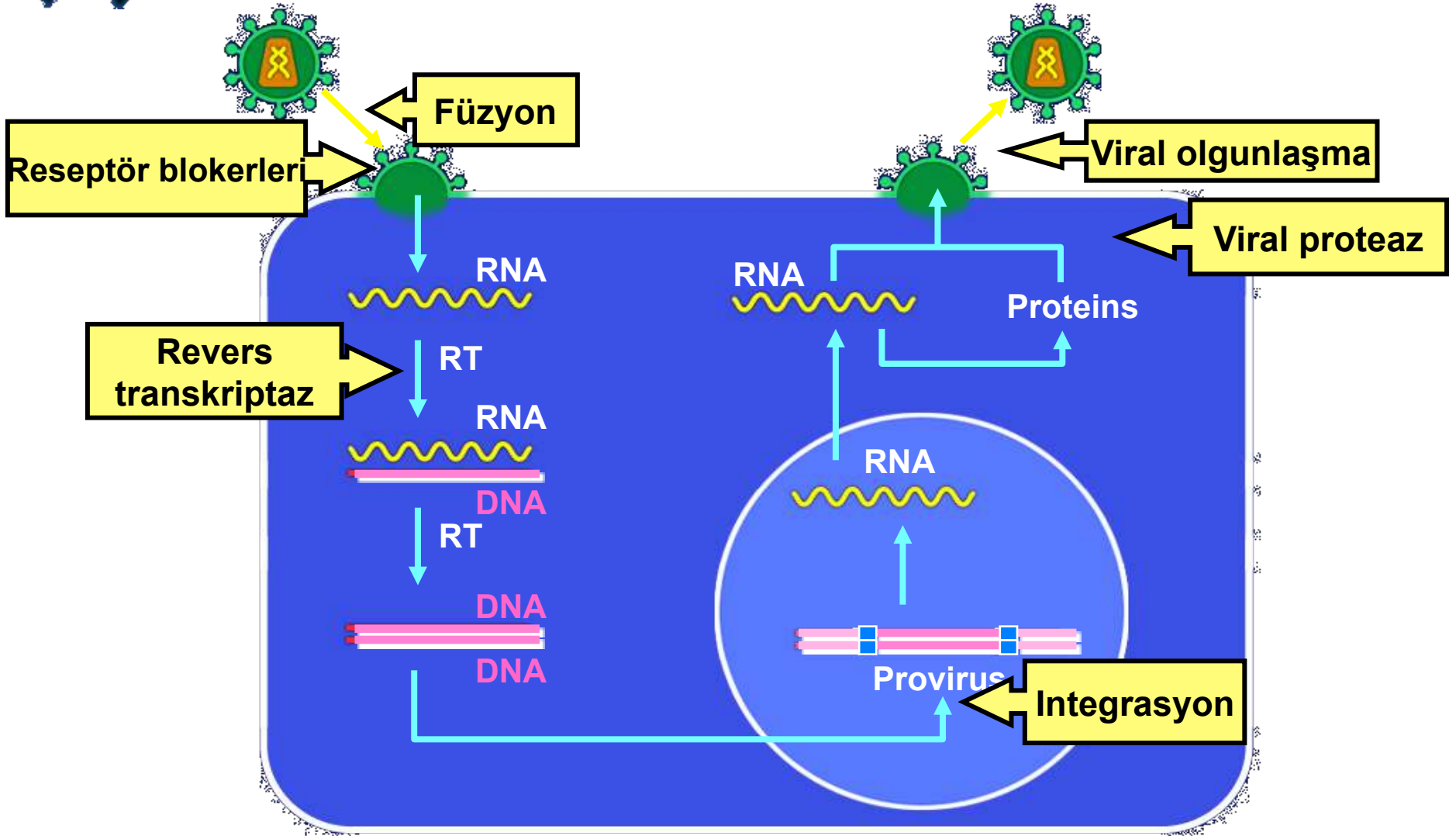


Tedavi hedefleri

- ✓ Viral yükü maksimum düzeyde ve uzun süreli baskılamak
- ✓ İmmünolojik fonksiyonları korumak ve iyileştirmek
- ✓ Yaşam kalitesini arttırmak
- ✓ HIV'e bağlı morbidite ve mortaliteyi azaltmak
- ✓ Bulaşı engellemek



Antiretroviral ilaçların hedefleri





Antiretroviral ilaç grupları

- 1-Nükleozid veya nükleotid revers transkriptaz inhibitörleri (NRTİ)
- 2-Non-nükleozid revers transkriptaz inhibitörleri (NNRTİ)
- 3-Proteaz inhibitörleri (PI)
- 4-Giriş inhibitörleri (ko-reseptör antagonistleri) (GI)
- 5-Füzyon inhibitörleri (FI)
- 6-İntegraz inhibitörleri (İNİ)



Antiretroviral ilaçlar



Nükleozid veya nükleotid revers transkriptaz inhibitörleri (NRTİ)

Tenofovir (TDF)
Emtrisitabin (FTC)
Abakavir (ABC)
Lamivudin (3TC)
Zidovudin (AZT)
Zalsitabin (ddC)
Didanozin (ddI)
Stavudin (d4T)

Non-nükleozid revers transkriptaz inhibitörleri (NNRTİ)

Efavirenz (EFV)
Nevirapin (NVP)
Rilpivirin (RPV)
Etravirin (ETV)
Delavirdin (DLV)



Antiretroviral ilaçlar



Proteaz inhibitörleri (Pİ)

Tipranavir (TPV)

İndinavir (IDV)

Sakinavir (SQV)

Darunavir (DRV)

Atazanavir (ATV)

Lopinavir (LPV)

Ritonavir (RTV)

Amprenavir (APV)

Fosamprenavir (FPV)

Nelfinavir (NFV)

Giriş inhibitörleri (Gİ)

Maravirok (MVC)

Füzyon inhibitörleri (Fİ)

Enfuvirtid (T-20)

İntegrasyon inhibitörleri (İNİ)

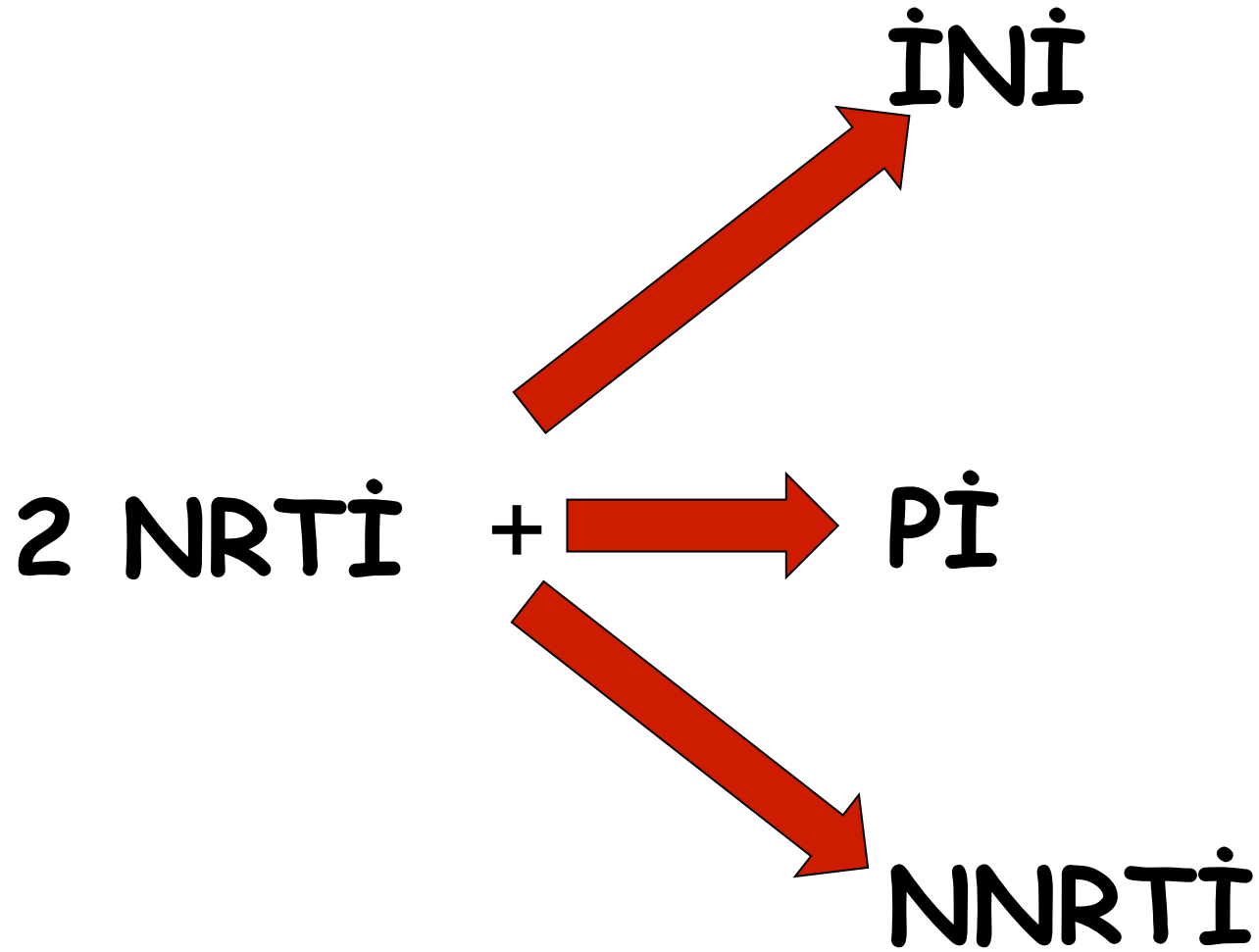
Raltegravir (RAL)

Dolutegravir (DTG)

Elvitegravir/kobisistat (EVG/cobi)



Tedavide 2 ya da daha fazla sınıftan en az 2 tercihen 3 ilaçlı kombinasyonlar kullanılmalı



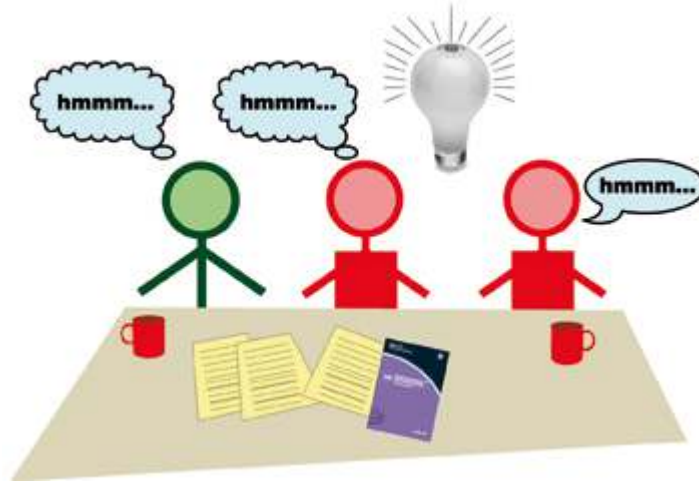


Neden kombinasyon?

- Viral replikasyonun baskılanması daha fazla
- Sinerjistik veya additif etki
- HIV yaşam siklusunun farklı noktalarına etki
- Virusun farklı hücre rezervuarlarına etki
 - Santral sinir sistemi, lenfoid doku
- Dirençli mutant seçiminin azalması



Öneriler





Önerilen Tedaviler

İNİ temelli

- DTG + ABC/3TC (AI)

(sadece HLA-B*5701

negatif olan hastalar)

- DTG + TDF/FTC (AI)

- EVG/cobi/TDF/FTC

(AI)

(sadece KrKl ≥ 70 mL/dak

olan hastalar)

- RAL + TDF/FTC (AI)

PI temelli

- DRV/r + TDF/FTC

(AI)

Alternatif Tedaviler

NNRTI temelli

- EFV/TDF/FTC (BI)

- RPV/TDF/FTC (BI)

(sadece tedavi öncesi viral yükü < 100.00

kopya/ml ve CD4 sayısı $> 200/\text{mm}^3$ olan

hastalar)

PI temelli

- ATV/c + TDF/FTC (BI)

(sadece KrKl ≥ 70 mL/dak olan hastalar)

- ATV/r + TDF/FTC (BI)

- DRV/c veya DRV/r+ABC/3TC (DRV/r
BII;DRV/c BIII)

(sadece HLA-B*5701 negatif olan hastalar)

- DRV/c+TDF/FTC (BII)

(sadece KrKl ≥ 70 mL/dak olan hastalar)



Diğer Tedaviler

İNİ temelli

- RAL+ABC/3TC (CII)
(sadece HLA-B*5701 negatif olan hastalar)

NNRTİ temelli

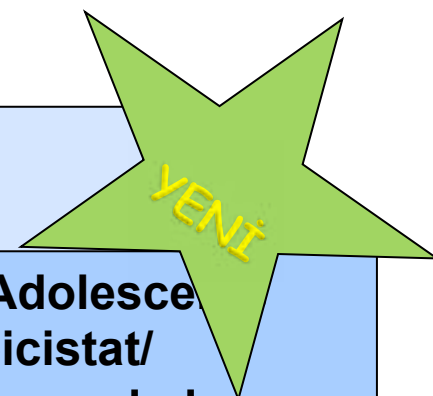
- EFV+ABC/3TC (CI)
(sadece HLA-B*5701 negatif olan ve tedavi öncesi viral yükü <100.00 kopya/ml olan hastalar)

PI temelli

- ATC/c veya ATV/r + ABC/3TC (ATV/r CI, ATV/c CII)
(sadece HLA-B*5701 negatif olan ve tedavi öncesi viral yükü <100.00 kopya/ml olan hastalar)
- LPV/r (günde bir kez ya da iki kez) + ABC/3TC (CI)
(sadece HLA-B*5701 negatif olan hastalar)
- LPV/r (günde bir kez ya da iki kez) + TDF/FTC (CI)

TDF veya ABC kullanılmadığında diğer seçenekler

- DRV/r+RAL (CI)
(sadece tedavi öncesi viral yükü <100.00 kopya/ml ve CD4 sayısı >200/mm³ olan hastalar)
- LPV/r+3TC (CI)



Tenofovir alafenamid (TAF)

HHS Panel on Antiretroviral Guidelines for Adults and Adolescents Includes a Fixed-Dose Combination of Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide Among the Recommended Regimens for Antiretroviral Treatment-Naive Individuals with HIV-1 Infection

Date: November 18, 2015

Source: *AIDSinfo*

Panel's Recommendation

Based on efficacy and safety data from phase 3 randomized clinical trials, EVG/c/FTC/TAF will be added as one of the Recommended Initial Regimens for ART-naive adults and adolescents with estimated creatinine clearance ≥ 30 mL/min (AI).



Önerilmeyen rejimler

	Rationale	Exception
Antiretroviral Regimens <u>Not</u> Recommended		
Monotherapy with NRTI (All)	<ul style="list-style-type: none">• Rapid development of resistance• Inferior ARV activity when compared with combination of three or more ARV agents	<ul style="list-style-type: none">• No exception
Dual-NRTI regimens (AI)	<ul style="list-style-type: none">• Rapid development of resistance• Inferior ARV activity when compared with combination of three or more ARV agents	<ul style="list-style-type: none">• No exception
Triple-NRTI regimens (AI) except for ABC/ZDV/3TC (BI) or possibly TDF + ZDV/3TC (BII)	<ul style="list-style-type: none">• High rate of early virologic nonresponse seen when triple-NRTI combinations, including ABC/TDF/3TC and TDF/ddI/3TC, were used as initial regimen in ART-naive patients.• Other triple-NRTI regimens have not been evaluated.	<ul style="list-style-type: none">• ABC/ZDV/3TC (BI) and possibly TDF + ZDV/3TC (BII) in patients in whom other combinations are not desirable



ATV + IDV (AIII)	<ul style="list-style-type: none">• Potential additive hyperbilirubinemia	<ul style="list-style-type: none">• No exception
ddl + d4T (All)	<ul style="list-style-type: none">• High incidence of toxicities: peripheral neuropathy, pancreatitis, and hyperlactatemia• Reports of serious, even fatal, cases of lactic acidosis with hepatic steatosis with or without pancreatitis in pregnant women	<ul style="list-style-type: none">• No exception
ddl + TDF (All)	<ul style="list-style-type: none">• Increased ddl concentrations and serious ddl-associated toxicities• Potential for immunologic nonresponse and/or CD4 cell count decline• High rate of early virologic failure• Rapid selection of resistance mutations at failure	<ul style="list-style-type: none">• Clinicians caring for patients who are clinically stable on regimens containing TDF + ddl should consider altering the NRTIs to avoid this combination.
2-NNRTI combination (AI)	<ul style="list-style-type: none">• When EFV combined with NVP, higher incidence of clinical adverse events seen when compared with either EFV- or NVP-based regimen.• Both EFV and NVP may induce metabolism and may lead to reductions in ETR exposure; thus, they should not be used in combination with ETR.	<ul style="list-style-type: none">• No exception
EFV in first trimester of pregnancy or in women with significant childbearing potential (AIII)	<ul style="list-style-type: none">• Teratogenic in nonhuman primates	<ul style="list-style-type: none">• When no other ARV options are available and potential benefits outweigh the risks (BIII)
FTC + 3TC (AIII)	<ul style="list-style-type: none">• Similar resistance profiles• No potential benefit	<ul style="list-style-type: none">• No exception



	Rationale	Exception
NVP in ARV-naive women with CD4 count >250 cells/mm³ or men with CD4 count >400 cells/mm³ (BI)	<ul style="list-style-type: none">• High incidence of symptomatic hepatotoxicity	<ul style="list-style-type: none">• If no other ARV option available; if used, patient should be closely monitored
d4T + ZDV (All)	<ul style="list-style-type: none">• Antagonistic effect on HIV-1	<ul style="list-style-type: none">• No exception
Unboosted DRV, SQV, or TPV (All)	<ul style="list-style-type: none">• Inadequate bioavailability	<ul style="list-style-type: none">• No exception
ETR + unboosted PI (All)	<ul style="list-style-type: none">• ETR may induce metabolism of these PIs; appropriate doses not yet established	<ul style="list-style-type: none">• No exception
ETR + RTV-boosted ATV or FPV (All)	<ul style="list-style-type: none">• ETR may alter the concentrations of these PIs; appropriate doses not yet established	<ul style="list-style-type: none">• No exception
ETR + RTV-boosted TPV (All)	<ul style="list-style-type: none">• ETR concentration may be significantly reduced by RTV-boosted TPV	<ul style="list-style-type: none">• No exception



İlk seçenekler

İNİ

- DTG/ABC/3TC
- DTG+TDF/FTC
- EVG/cobi/TDF/FTC
- RAL+TDF/FTC

NNRTİ

- **RPV/TDF/FTC**

(viral yük < 100.000 kopya/ml ve CD4 hücre sayısı > 200/mm³)

PI

- DRV/r+TDF/FTC

Alternatif seçenekler

İNİ

- RAL+ABC/3TC

NNRTİ

- EFV+(TDF/FTC veya ABC/3TC)

PI

- (ATV/c veya ATV/r)+ (TDF/FTC veya ABC/3TC)
- DRV/r + (TDF/FTC veya ABC/3TC)
- DRV/c+ TDF/FTC
- **LPV/r+TDF/FTC**



TDF veya ABC kullanılmadığında diğer seçenekler

- DRV/r+RAL

(sadece tedavi öncesi viral yükü <100.00 kopya/ml ve CD4 sayısı $> 200/\text{mm}^3$ olan hastalar)

- LPV/r+3TC



	İlk tercih	Alternatif
NRTİ belkemiği	TDF/FTC	ABC/3TC (HLA-B 5701 negatif)
3. ilaç	ATV/r DRV/r DTG EVG/cobi (KrKl \geq 70 mL/dak olan hastalar) RAL RPV (viral yük < 100000 kopya/ml)	EFV



	Tercih edilen tedavi	Alternatif tedavi
NNRTİ+2 NRTİ	EFV/TDF/FTC (A1a) EFV+ABC/3TC (A1a) RPV/TDF/FTC (A1a)	NVP+2 NRTİ (B1a) RPV+ABC/3TC (A1a)
PI/r+2 NRTİ	DRV/r+TDF/FTC (A1a) ATV/r+TDF/FTC (A1a) ATV/r+ABC/3TC (A1a)	ATV/cobi+2 NRTİ (B1a) DRV/cobi+2 NRTİ (BIII) DRV/r+ABC/3TC (B1b) LPV/r +2 NRTİ (B1a)
İNİ+2 NRTİ	DTG+TDF/FTC (A1a) DTG+ABC/3TC (A1a) EVG/cobi/TDF/FTC (A1a) RAL+TDF/FTC (A1a)	RAL+ ABC/3TC (B1a)
NRTİ içermeyen rejim		DRV/r+RAL (B1b) LPV/r+3TC (B1a) LPV/r+RAL (B1a)

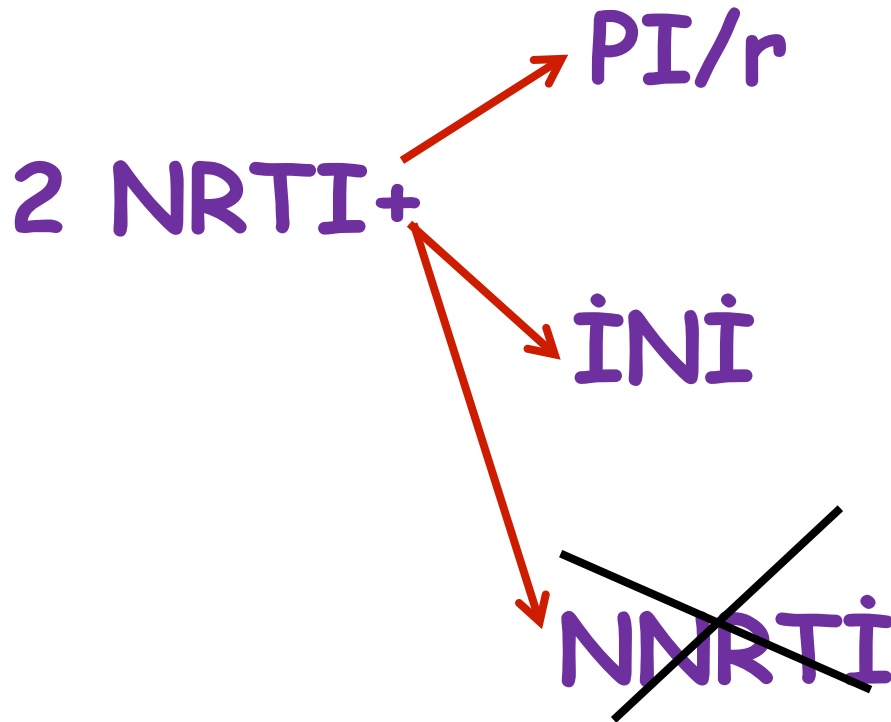


Tercih edilen tedaviler	TDF+3TC (veya FTC)+ EFV
Alternatif tedaviler	AZT+3TC+EFV (veya NVP) TDF+3TC (veya FTC)+DTG TDF+3TC (veya FTC)+EFV ₄₀₀ TDF+3TC (veya FTC)+ NVP
Özel durumlar	ABC ve güçlendirilmiş Pİ içeren rejimler



HIV-2

- ✓ NNRTI'lere ve enfuvirtid'e intrinsik direnç
- ✓ NRTI'ler, PI'ler ve İNI'ler etkili





antiretroviral drug chart

Drugs listed in the 2019 WHO Guidelines – February 2022

Generic name	Trade name	Formulation	Treatment adult dose	PIR score	Major side effects	Food restriction
Zidovudine (ZDV) zidovudine (ZDV) only (ZDV)						
Zidovudine	Zidovudine	Tablets 250mg	300mg twice daily with meals	1	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Myelosuppression	Can be taken with food
Abacavir	Abacavir	Tablets 300mg	300mg twice daily	2	Common: Headache, nausea, vomiting, diarrhoea Rare: Hypersensitivity reaction	Can be taken with food
ATC combination	Abacavir/Zidovudine	Tablets 150mg/150mg	150mg twice daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Myelosuppression	Can be taken with food
3TC combination	Abacavir/3TC	Tablets 150mg/150mg	150mg twice daily	2	Common: Headache, nausea, vomiting, diarrhoea Rare: Hypersensitivity reaction	Can be taken with food
3TC combination	Abacavir/3TC/Zidovudine	Tablets 150mg/150mg/150mg	150mg twice daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Myelosuppression	Can be taken with food
3TC combination	Abacavir/3TC/Raltegravir	Tablets 150mg/150mg/250mg	150mg twice daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Myelosuppression	Can be taken with food
3TC combination	Abacavir/3TC/Raltegravir/Zidovudine	Tablets 150mg/150mg/250mg/150mg	150mg twice daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Myelosuppression	Can be taken with food
Emtricitabine (FTC) emtricitabine (FTC) only (FTC)						
Emtricitabine	Emtricitabine	Tablets 200mg	200mg twice daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Hypersensitivity reaction	Can be taken with food
FTC combination	Emtricitabine/Raltegravir	Tablets 200mg/250mg	200mg twice daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Hypersensitivity reaction	Can be taken with food
FTC combination	Emtricitabine/Raltegravir/Zidovudine	Tablets 200mg/250mg/150mg	200mg twice daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Myelosuppression	Can be taken with food
FTC combination	Emtricitabine/Raltegravir/Zidovudine/3TC	Tablets 200mg/250mg/150mg/150mg	200mg twice daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Myelosuppression	Can be taken with food
Dolutegravir (DTG) dolutegravir (DTG) only (DTG)						
Dolutegravir	Dolutegravir	Tablets 50mg	50mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Hypersensitivity reaction	Can be taken with food
DTG combination	Dolutegravir/3TC	Tablets 50mg/150mg	50mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Hypersensitivity reaction	Can be taken with food
DTG combination	Dolutegravir/3TC/Zidovudine	Tablets 50mg/150mg/150mg	50mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Myelosuppression	Can be taken with food
DTG combination	Dolutegravir/3TC/Raltegravir	Tablets 50mg/150mg/250mg	50mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Hypersensitivity reaction	Can be taken with food
DTG combination	Dolutegravir/3TC/Raltegravir/Zidovudine	Tablets 50mg/150mg/250mg/150mg	50mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Myelosuppression	Can be taken with food
Dolutegravir (DTG) dolutegravir (DTG) only (DTG)						
Dolutegravir	Dolutegravir	Tablets 50mg	50mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Hypersensitivity reaction	Can be taken with food
DTG combination	Dolutegravir/3TC	Tablets 50mg/150mg	50mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Hypersensitivity reaction	Can be taken with food
DTG combination	Dolutegravir/3TC/Zidovudine	Tablets 50mg/150mg/150mg	50mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Myelosuppression	Can be taken with food
DTG combination	Dolutegravir/3TC/Raltegravir	Tablets 50mg/150mg/250mg	50mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Hypersensitivity reaction	Can be taken with food
DTG combination	Dolutegravir/3TC/Raltegravir/Zidovudine	Tablets 50mg/150mg/250mg/150mg	50mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Myelosuppression	Can be taken with food
Bictegravir (BIC) bictegravir (BIC) only (BIC)						
Bictegravir	Bictegravir	Tablets 50mg	50mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Hypersensitivity reaction	Can be taken with food
BIC combination	Bictegravir/3TC	Tablets 50mg/150mg	50mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Hypersensitivity reaction	Can be taken with food
BIC combination	Bictegravir/3TC/Zidovudine	Tablets 50mg/150mg/150mg	50mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Myelosuppression	Can be taken with food
BIC combination	Bictegravir/3TC/Raltegravir	Tablets 50mg/150mg/250mg	50mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Hypersensitivity reaction	Can be taken with food
BIC combination	Bictegravir/3TC/Raltegravir/Zidovudine	Tablets 50mg/150mg/250mg/150mg	50mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Myelosuppression	Can be taken with food
Cobicistat (CBI) cobicistat (CBI) only (CBI)						
Cobicistat	Cobicistat	Tablets 150mg	150mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Hypersensitivity reaction	Can be taken with food
CBI combination	Cobicistat/3TC	Tablets 150mg/150mg	150mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Hypersensitivity reaction	Can be taken with food
CBI combination	Cobicistat/3TC/Zidovudine	Tablets 150mg/150mg/150mg	150mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Myelosuppression	Can be taken with food
CBI combination	Cobicistat/3TC/Raltegravir	Tablets 150mg/150mg/250mg	150mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Hypersensitivity reaction	Can be taken with food
CBI combination	Cobicistat/3TC/Raltegravir/Zidovudine	Tablets 150mg/150mg/250mg/150mg	150mg once daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Myelosuppression	Can be taken with food
Raltegravir (RAL) raltegravir (RAL) only (RAL)						
Raltegravir	Raltegravir	Tablets 400mg	400mg twice daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Hypersensitivity reaction	Can be taken with food
RAL combination	Raltegravir/3TC	Tablets 400mg/150mg	400mg twice daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Hypersensitivity reaction	Can be taken with food
RAL combination	Raltegravir/3TC/Zidovudine	Tablets 400mg/150mg/150mg	400mg twice daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Myelosuppression	Can be taken with food
RAL combination	Raltegravir/3TC/Raltegravir	Tablets 400mg/150mg/250mg	400mg twice daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Hypersensitivity reaction	Can be taken with food
RAL combination	Raltegravir/3TC/Raltegravir/Zidovudine	Tablets 400mg/150mg/250mg/150mg	400mg twice daily	2	Common: Headache, dizziness, nausea, vomiting, diarrhoea, weight loss Rare: Myelosuppression	Can be taken with food

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WHO Guidelines for ART (2019), WHO (2019), WHO (2020)







İlaç seçiminde göz önünde bulundurulanan faktörler

- Direnç
- Tedavi öncesi HIV RNA ve CD4 düzeyi
- İlaçların genetik bariyer direnci
- Yan etki
- İlaç etkileşimi
- Gebelik ya da gebelik potansiyeli
- HLA-B*5701
- Komorbidite varlığı (kardiyovasküler hastalık, kronik hepatit B, kronik hepatit C, karaciğer ya da renal hastalık, tüberküloz, psikiyatrik bozukluk, bağımlılık)
- Hastanın tercihi ve uyum potansiyeli
- Kullanım kolaylığı (ilaç yükü, doz aralığı, tek tablet...)
- Maliyet



Klinik durum	Öneriler
CD4 <200 hücre/mm ³	RPV temelli rejimler DRV/r +RAL kullanılmamalı
HIVRNA >100.000 kopya/ml	RPV temelli rejimler DRV/r +RAL ABC/3TC + EFV veya ATV/r kullanılmamalı
HLA-B*5701 pozitif	ABC temelli rejimler kullanılmamalı
HIV direnç sonuçları olmadan ART başlanan durumlar	NNRTI içeren rejimlerden kaçınılmalı



Klinik durum	Öneriler
e-GFR < 60 ml/dak	<p>TDF'den kaçınılmalı e-GFR is > 70 mL/dak</p> <ul style="list-style-type: none">• EVG/c/TDF/FTC veya• ATV/c + TDF/FTC veya• DRV/c + TDF/FTC <p>KBY'li hastada tercihler: HLA-B*5701 negatif ise ABC/3TC kullanılmalı</p> <ul style="list-style-type: none">• HIV RNA >100,000 kopya/ ise ABC/3TC + EFV veya ATV/r kullanılmamalı <p>• KrKl <50 mL/dak, ABC/3TC temelli rejimler kullanılmamalı (3TC doz ayarı)</p> <p>Diğer tercihler:</p> <ul style="list-style-type: none">• DRV/r + RAL (HIV RNA <100,000 kopya/mL ve CD4 >200/mm³) veya• LPV/r + 3TC veya• TDF dozunu değiştirmek gerekir



Klinik durum	Öneriler
Psikiyatrik hastalık	EFV temelli rejimlerden kaçınılmalı
HIV ilişkili demans	EFV temelli rejimlerden kaçınılmalı DRV veya DTG temelli rejimler tercih edilmeli
Osteoporoz	TDF'den kaçınılmalı HLA-B*5701 negatif ise ABC/3TC kullanılmalı



Klinik durum	Öneriler
Narkotik replasman tedavisi	Hasta metadon kullanıyorsa EFV temelli rejimlerden kaçınılmalı EFV kullanılıyorsa metadon dozunun arttırılması gerekebilir
Yüksek kardiyak risk	ABC veya LPV/r temelli rejimlerden kaçınılmalı
Hiperlipidemi	Lipid düzeyleri üzerine olumsuz etkileri olan rejimler: <ul style="list-style-type: none">• PI/r• ABC• EFV• EVG/c (TDF ABC'ye kıyasla tercih)
Gebelik, tüberküloz, kronik HBV/HCV	Etkileşim



İlaç-ilaç etkileşimleri

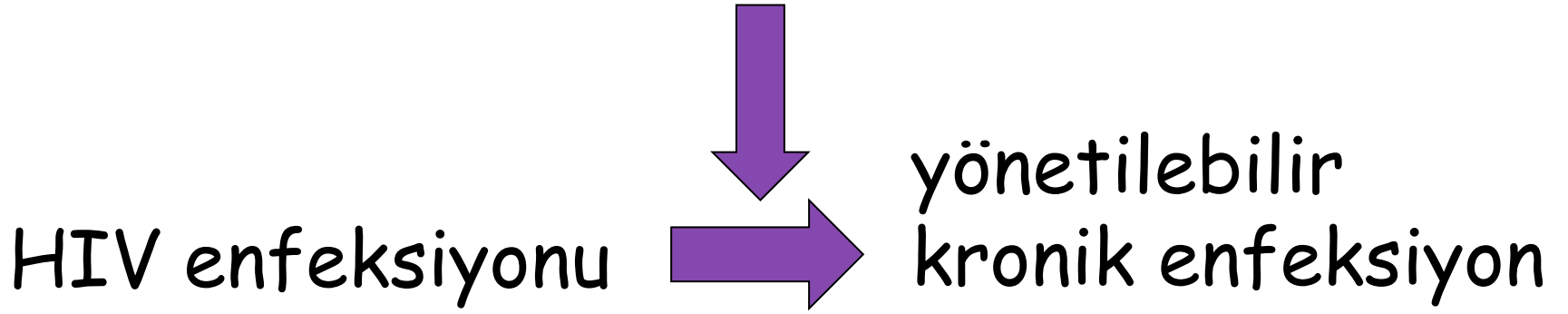
- ✓ DHHS
- ✓ EACS
- ✓ UpToDate
- ✓ <http://www.hiv-druginteractions.org>
- ✓ ...



Sonuç



Akılcı kombine antiretroviral tedavi





Sonuç



	DHHS	EACS	DSÖ	BHIVA	Türkiye
CD4 <350/ mm ³	Evet	Evet	Evet	Evet	Evet
CD4 350-500/ mm ³	Evet	Evet	Evet	Evet	Düşünülür
CD4 > 500/ mm ³	Evet	Evet	Evet	Evet	Düşünülür



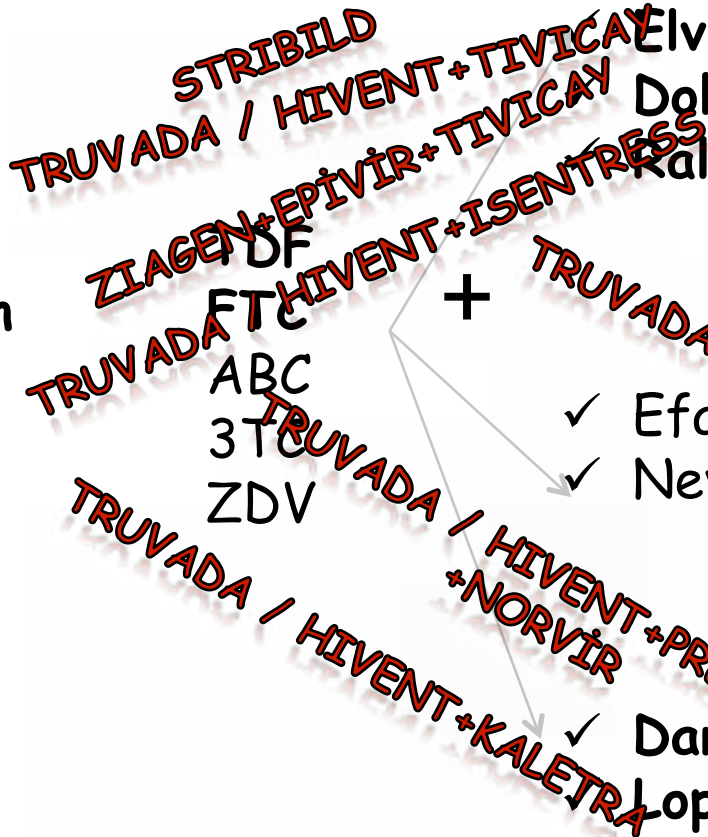
NRTI

INI

EVG/cobi
DTG
RAL

Elvitegravir/kobisistat
Dolutegravir
Raltegravir

- ✓ Tenofovir
- ✓ Emtricitabin
- ✓ Abakavir
- ✓ Lamivudin
- ✓ Zidovudin



NNRTI

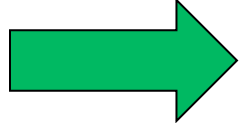
EFV
NVP

- ✓ Efavirenz
- ✓ Nevirapin

PI

DRV/r
LPV/r

Darunavir/ritonavir
Lopinavir/ritonavir





**Günde tek tablet
tercihi**

- DTG/ABC/3TC
- EFV/TDF/FTC
- **EVG/c/TDF/FTC**
- RPV/TDF/FTC

(HIV RNA <100,000 kopya/mL ve CD4 >200/mm³)



GETTING TO ZERO

END AIDS BY 2030

WORLD AIDS
DAY 2015



World Health
Organization



16 MILLION
PEOPLE

are now receiving
antiretroviral treatment;
21 million are not yet



7.8 MILLION

HIV-related deaths
have been averted in
the last 15 years

WITH A **DROP** IN:

DEATHS 42%

Since
2004

NEW INFECTIONS 35%

Since
2000

**FAST-TRACK NOW TO
END AIDS WITHIN
A GENERATION**



**STEP UP
PREVENTION**



**OFFER TESTING TO
EVERYONE AT RISK**

46% of people living
with HIV don't know it



**TREAT ALL
LIVING
WITH HIV**



Kaynaklar

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TEŞEKKÜR EDERİM...