Rehberler Eşliğinde ART

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Ankara Numune Eğitim ve Araştırma Hastanesi
16.12.2017

HIV ve HAART

- Bu gün ki bilgilerimizle HIV ömür boyu süren kronik bir hastalık
- HAART ömür boyu sürecek kompleks bir tedavi gerekli
- Sürekli yeni ilaçlar geliştirilmekte

https://www.cdc.gov/hiv/library/dcl/dcl/092717.html

HIV Enfeksiyonu Tedavisinde Kullanımda Olan Antiretroviral Ajanlar

Nükleozid RTI (NRTI)

- Zidovudin (ZDV)
- Didanosin (ddI)
- Zalsitabin (ddC)
- Stavudin (d4T)
- Lamivudin (3TC)
- Abakavir (ABC)
- Emtrisitabin (FTC)
- Tenofovir DF (TDF)
- Tenofovir alafenamid (TAF)

Nonnükleoz(t)ide RTI (NNRTI)

- Nevirapin (NVP)
- Delavirdin (DLV)
- Efavirenz (EFV)
- Etravirin (ETR)
- Rilpivirin

İntegraz İnhibitörleri

- Raltegravir (RAL)
- *Dolutegravir**
- *Elvitegravir**

Proteaz İnhibitörleri (PI)

- Saquinavir (SQV)
- Ritonavir (RTV)
- Indinavir (IDV)
- Nelfinavir (NFV)
- Amprenavir (APV)
- Lopinavir/r (LPV/r)
- Atazanavir (ATV)
- Fosamprenavir (Fos-APV)
- Tipranavir (TPV)
- Darunavir (DRV)

Fusion İnhibitörleri

- Enfuvirtid (T-20)

CCR5 Antagonist

- Maravirok (MVC)

Boosterler

- Ritonavir (RTV)
- *Cobicistat* (cobi)*

2 NRTI

+

İntegraz İnhibitörü

veya

Proteaz İnhibitörü

veya

NNRTI

HAART

HAART

Geçmiş

3 farklı ilaç 20 ye yakın tablet

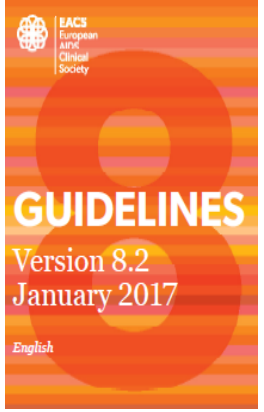
Tedavi uyumu çok önemli

Günümüzde

Tek tablet

Rehberler

- DHHS: Department of Human and Health Services
- EACS: European AIDS Clinical Society
- WHO: World Health Organization (DSÖ)
- BHIVA: British HIV Association
- Ulusal HIV/AIDS Tanı Tedavi Rehberi



World Health Organization

British HIV Association
BHIVA

Hızla ART Başlanması Gereken Durumlar

- Akut/erken infeksiyon (akut retroviral sendrom)
- Gebelik
- HIV/hepatitis B–C koinfeksiyonu
- AIDS tanımlayıcı hastalık, HIV-ilişikili demans ve AIDS-ilişkili malignite
- Fırsatçı infeksiyonlar
- Düşük CD4 sayısı (<200 /mm^3)
- HIV ilişkili nefropati (HIVAN)

http://www.eacsociety.org/files/guidelines_8.2-english.pdf
https://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf

Tedavi Ne Zaman Başlayalım?

- Hastalığın evresi?
- CD4 sayısı?
  - 200 h/mm^3
  - 350 h/mm^3
  - 500 h/mm^3
- Viral yük?

Initiating Antiretroviral Therapy in Treatment-Naive Patients (Last updated May 1, 2014; last reviewed May 1, 2014)

Panel's Recommendations

• Antiretroviral therapy (ART) is recommended for all HIV-infected individuals to reduce the risk of disease progression.
  ◦ The strength of and evidence for this recommendation vary by pretreatment CD4 T lymphocyte (CD4) cell count: CD4 count <350 cells/mm^3 **(AI)**; CD4 count 350 to 500 cells/mm^3 **(AII)**; CD4 count >500 cells/mm^3 **(BIII)**.
• ART is also recommended for HIV-infected individuals to prevent of transmission of HIV.
  ◦ The strength of and evidence for this recommendation vary by transmission risks: perinatal transmission **(AI)**; heterosexual transmission **(AI)**; other transmission risk groups **(AIII)**.
• Patients starting ART should be willing and able to commit to treatment and understand the benefits and risks of therapy and the importance of adherence **(AIII)**. Patients may choose to postpone therapy, and providers, on a case-by-case basis, may elect to defer therapy on the basis of clinical and/or psychosocial factors.

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*

Tempering the enthusiasm to treat all patients regardless of CD4 count is the absence of randomized trial data that demonstrate a definitive clinical benefit of ART in patients with higher CD4 counts (e.g., >350 cells/ mm^3) and mixed results from observational cohort studies as to the definitive benefits of early ART (i.e., when CD4 count >500 cells/mm^3). For some asymptomatic patients, the potential risks of short- or long-term drug-related complications and non-adherence to long-term therapy may offset possible benefits of earlier initiation of therapy. An ongoing randomized controlled trial evaluating the role of immediate versus delayed ART in patients with CD4 counts >500 cells/mm^3 (see Strategic Timing of Antiretroviral Treatment (START); ClinicalTrials.gov identifier NCT00867048) should help to further define the role of ART in this patient population.

The known and potential benefits and limitations of ART in general, and in different patient populations are discussed below.

Tedavi Ne Zaman Başlayalım?
2015

- START ve TEMPRANO çalışmaları
- Tedavi başlama önerileri değişti
- Saptadığın anda tedavi ver

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

More recently, preliminary results of the START study have been presented and published [17]. This study enrolled 4685 adults with CD4 cell counts above 500 cells/μL (median CD4 cell count 651 cells/μL) in 35 countries, and randomised them to start ART immediately or to defer ART until the CD4 count fell below 350 cells/μL. The risk of developing AIDS, a serious non-AIDS event or of death (combined as the primary endpoint) was reduced by 57% in those who were randomised to start earlier, after a median follow-up period of 3 years. The results were similar in high-income when compared to low- and middle-income countries and driven mainly by a difference in rates of AIDS events, particularly TB and cancers. Immediate ART was not associated with higher risk of grade 4 events or unscheduled hospital admissions.

BHIVA

4.0 When to start

4.1 Chronic infection

4.1.1 Recommendations

- We recommend people with HIV start ART (1A).

4.1.2 Auditable outcomes

- Proportion of diagnosed PLWH on ART.
- Proportion of PLWH not on ART where the rationale for this, and a discussion of the benefits of ART, has been documented at least annually.

World Health Organization

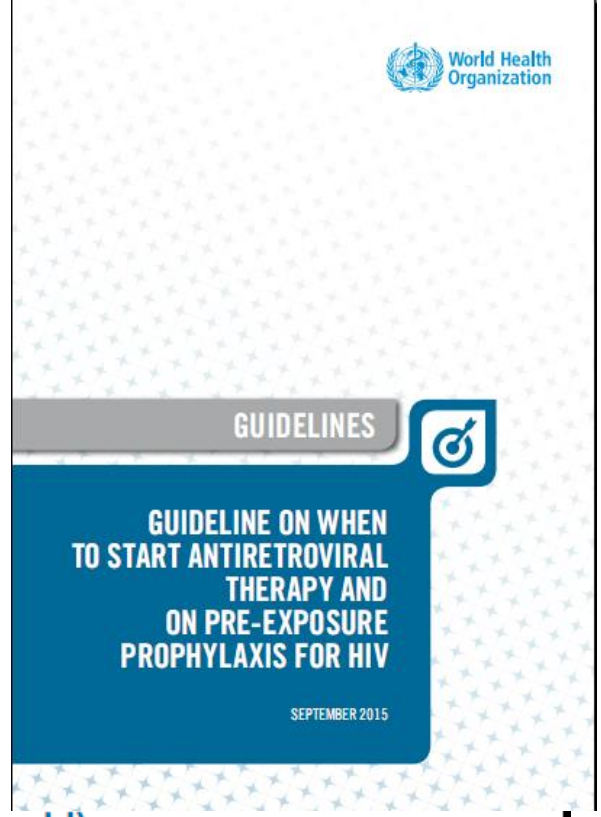
GUIDELINES

GUIDELINE ON WHEN TO START ANTIRETROVIRAL THERAPY AND ON PRE-EXPOSURE PROPHYLAXIS FOR HIV

SEPTEMBER 2015

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/mm³. The median baseline CD4 count was 651 cells/mm³ in the intervention group. In the deferred group, the median CD4 count at ART initiation was 408 cells/mm³. 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/mm³. 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 g
malignancies) were lower in the imme
were similar between groups. These e
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/mm³ *(strong recommendation, moderate-quality evidence).*

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

Developed by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents – A Working Group of the Office of AIDS Research Advisory Council (OARAC)

Immediate Antiretroviral Therapy Initiation on the Day of HIV Diagnosis

Since many individuals may fail to engage in care during the delay between initial HIV diagnosis (or first clinic visit) and the time ART is prescribed, some groups have proposed rapid ART initiation on the same day of HIV diagnosis as a strategy to increase engagement in care and increase the proportion of individuals who achieve and maintain ART-mediated viral suppression. This strategy was recently tested in a randomized controlled trial of 377 individuals in South Afr
immediate ART on the day of diagn
(three to five additional visits with a
suppressed at 10 months (64% vs. 5
in care achieving viral suppression a
controlled trial of same-day ART in
health care systems, structural barri
Africa and Haiti that limit the gener
that same-day initiation of ART may
randomized controlled trials have b
San Francisco suggested that initiat
to achieving viral suppression.[55] It s
diagnosis is resource-intensive, requ
coordinate the patient transportation
intake laboratory testing, and systen
available in all settings and the long
the United States, this approach ren

Initiation of Antiretroviral Therapy (Last updated October 17, 2017; last reviewed October 17, 2017)

Panel's Recommendations
• Antiretroviral therapy (ART) is recommended for all individuals with HIV, regardless of CD4 T lymphocyte cell count, to reduce the morbidity and mortality associated with HIV infection (**AI**).
• ART is also recommended for individuals with HIV to prevent HIV transmission (**AI**).
• When initiating ART, it is important to educate patients regarding the benefits and considerations of 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*

Erken Dönemde Başlanan HAART

- İmmunolojik fonksiyonları korumak ve iyileştirmek
- AIDS'e ilerlemeyi geçiktirmek ve ömürü uzatmak
- Viral yükü baskılamak
- HIV bulaşını azaltmak

- Erken dönemde ilaç yan etkileri nedeniyle yaşam kalitesinin bozulması
- Tedavilerin tahmin edilemeyen uzun süreli toksisiteleri
- Bazı ilaç /rejimlerin etkinlik sürelerinin belirsizliği
- İlaç etkileşimleri
- Uyum olmazsa direnç gelişimi ve gelecekteki ilaç seçeneklerinin azalması
- İlaç dirençli suşların bulaştırılması

Tedaviye Başlama Kararı

Klinik muayene
Bazal tetkikler

Değerlendir

Acil başlamayı gerektiren bir durum var mı?

EVET

Tedavi başla

HAYIR

- **Hasta ile tedavinin yarar ve riskleri, ilaç uyumunun önemi hakkında konuşulmalı**
- **Tedaviye hazır ve istekli mi?değerlendirilmeli**

http://www.eacsociety.org/files/guidelines_8.2-english.pdf
https://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf

Part II ART of HIV-positive Persons

Assessing HIV-positive Persons' Readiness to Start and Maintain ART[x]

Goal: to help persons start and/or maintain ART	
Successful ART requires a person's readiness to start and adhere to the regimen over time. The trajectory from problem awareness to maintenance on ART can be divided into five stages. Knowing a person's stage, health	Identify the person's stage of readiness using WEMS[i] techniques, and start discussion with an open question/invitation: "I would like to talk about HIV medicines." <wait> "What do you think about

ART Başlamaya Karar verme ve Başlanan Tedavinin Devamlılığını Sağlayabilmek İçin

Aile desteği
Sosyal destek
Alkol ve uyuşturucu kullanımı
Depresyon durumu
Kognitif fonksiyonları
Meslek
Sağlık güvencesi

http://www.eacsociety.org/files/guidelines_8.2-english.pdf
https://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf

EACS 2017-İlk Seçenekte Önerilen Tedaviler

Initial Combination Regimen for ART-naïve Adult HIV-positive Persons

A) Recommended regimens (one of the following to be selected)[*,**]

Regimen	Dosing	Food requirement	Caution
2 NRTIs + INSTI			
ABC/3TC/DTG[(I, II)]	ABC/3TC/DTG 600/300/50 Triumeg	None	Al/Ca/Mg-containing antacids or multivitamins should be taken well separated in time (minimum 2h after or 6h before). DTG 50 mg bid with rifampicin.
TAF/FTC[(II)] or TDF/FTC[(iv, v)] + DTG	TAF/FTC 25/200 mg, 1 tablet qd or TDF/FTC 300/200 mg, 1 tablet qd + DTG 50 mg, 1 tablet qd	None	
TAF/FTC/EVG/c[(II)] or TDF/FTC/EVG/c[(iv, vi)]	TAF/FTC/EVG/c 10/200/150/150 mg, 1 tablet qd or TDF/FTC/EVG/c 300/200/150/150 mg, 1 tablet qd	With food	Al/Ca/Mg-containing antacids or multivitamins should be taken well separated in time (minimum 2h after or 6h before).
TAF/FTC[(II)] or TDF/FTC[(iv, v)] + RAL	TAF/FTC 25/200 mg, 1 tablet qd or TDF/FTC 300/200 mg, 1 tablet qd + RAL 400 mg, 1 tablet bid	None	Co-administration of antacids containing Al or Mg not recommended. RAL 400 or 800 mg bid with rifampicin.
2 NRTIs + NNRTI			
TAF/FTC/RPV or TDF/FTC/RPV	TAF/FTC/RPV 25/200/25 mg, 1 tablet qd or TDF/FTC/RPV 300/200/25 mg, 1 tablet qd	With food	Only if CD4 count > 200 cells/µL and HIV-VL < 100,000 copies/mL. PPI contra-indicated; H2 antagonists to be taken 12h before or 4h after RPV.
2 NRTIs + PI/r or PI			
TAF/FTC[(II)] or TDF/FTC[(iv, v)] + DRV/c or + DRV/r	TAF/FTC 10/200 mg, 1 tablet qd or TDF/FTC 300/200 mg, 1 tablet qd DRV/c 800/150 mg, 1 tablet qd or + DRV 800 mg, 1 tablet qd + RTV 100 mg, 1 tablet qd	With food	Monitor in persons with a known sulfonamide allergy.

DTG (tivicay)

TAF/FTC TDF/FTC (Truvada; Hivend)

RAL (isentress)

TAF/FTC TDF/FTC EVG © Genvoya Stribild

EACS 2017-İlk Seçenekte Önerilen Tedaviler

Initial Combination Regimen for ART-naïve Adult HIV-positive Persons

A) Recommended regimens (one of the following to be selected)[*,**]

Regimen	Dosing	Food requirement	Caution
2 NRTIs + INSTI			
ABC/3TC/DTG[(I, II)]	ABC/3TC/DTG 600/300/50 mg, 1 tablet qd	None	Al/Ca/Mg-containing antacids or multivitamins should be taken well separated in time (minimum 2h after or 6h before). DTG 50 mg bid with rifampicin.
TAF/FTC[(III)] or TDF/FTC[(IV, V)] + DTG	TAF/FTC 25/200 mg, 1 tablet qd or TDF/FTC 300/200 mg, 1 tablet qd + DTG 50 mg, 1 tablet qd	None	
TAF/FTC/EVG/c[(III)] or TDF/FTC/EVG/c[(IV, VI)]	TAF/FTC/EVG/c 10/200/150/150 mg, 1 tablet qd or TDF/FTC/EVG/c 300/200/150/150 mg, 1 tablet qd	With food	Al/Ca/Mg-containing antacids or multivitamins should be taken well separated in time (minimum 2h after or 6h before).
+ RAL	AF/FTC 25/200 mg, 1 tablet qd or DF/FTC 300/200 mg, 1 tablet qd + RAL 400 mg, 1 tablet bid	None	Co-administration of antacids containing Al or Mg not recommended. RAL 400 or 800 mg bid with rifampicin.
2 NRTIs + NNRTI			
	FTC/RPV 25/200/25 mg, 1 tablet qd or FTC/RPV 300/200/25 mg, 1 tablet qd	With food (min 390 Kcal required)	Only if CD4 count > 200 cells/µL and HIV-VL < 100,000 copies/mL. PPI contra-indicated; H2 antagonists to be taken 12h before or 4h after RPV.
2 NRTIs + PI/r or PI/c			
	et qd + RI , 1 tablet qd	With food	Monitor in persons with a known sulfonamide allergy.

RPV

TAF/FTC
TDF/FTC

DRV®

TAF/FTC
TDF/FTC

DRV©

EACS 2017-Alternatif Tedaviler

B) Alternative regimens (to be used when none of the preferred regimens are feasible or available, whatever the reason)

Regimen	Dosing	Food requirement	Caution
2 NRTIs + INSTI			
	600/300 mg, 1 tablet qd + RAL 400 mg, 1 tablet bid	None	Co-administration of antacids containing Al or Mg not recommended. RAL 400 or 800 mg bid with rifampicin.
2 NRTIs + NNRTI			
	1 tablet qd	At bed time or 2 hours before dinner	Only if HIV-VL < 100,000 copies/mL
2 NRTIs + PI/r or PI/c			
ABC/3TC[(i, ii)] + ATV/c or	1 tablet qd	With food	Only if HIV-VL < 100,000 copies/mL
TAF/FTC[(iii)] or TDF/FTC[(iv, v)] + LPV/r	TAF/FTC 10/200 mg 1 tablet qd + DRV 800 mg, 1 tablet qd + RTV/c 100 mg, 1 tablet qd	With food	Use with caution in persons with

ABC/3TC+RAL

ABC/3TC+EFV

TDF/FTC/EFV

ATV®

DRV ©

ABC/3TC

ATV©

HIV RNA <100000

ATV®

TAF/FTC TDF/FTC

ATV©

DRV ®

LOP®

EACS 2017-Diğer Tedaviler

ABC
TDF
TAF
kullanılamıyorsa

3TC+LPV ®

3TC[f] + LPV/r	3TC 300 mg, 1 tablet qd + LPV 200 mg, 2 tablets bid + RTV 50 mg, 2 tablets bid	With food	
RAL[f] + DRV/c or + DRV/r	RAL 400 mg, 1 tablet bid + DRV/c 800/150 mg, 1 tablet qd or + DRV 800 m	With food	Only if CD4 count > 200 cells/µL and HIV-VL < 100,000 copies/mL. Co-administration of antacids containing Al or Mg not recommended.

RAL+DRV®

RAL+DRV ©

HIV RNA
<100000
CD4>200

DHHS-Temmuz 2016-Önerilen Tedaviler

Panel's Recommendations

- An antiretroviral (ARV) regimen [İntegraz inhibitörlü kombinasyonlar] (NRTIs) in combination with a t]), a non-nucleoside reverse transcriptase inhibitor (NNRTI), or a protease inhibitor (PI) with a pharmacokinetic (PK) enhancer (booster) (cobicistat or ritonavir).
- The Panel on Antiretroviral Guidelines for Adults s as Recommended regimens for antiretroviral therapy (ART)-naive p

ABC/3TC/DTG

Integrase Strand Transfer Inhibitor-Based Regimens:

- Dolutegravir/abacavir/lamivudine[a]—**only** for patients who are HLA-B*5701 negative (**AI**)
- Dolutegravir plus either tenofovir disoproxil fumarate/emtricitabine[a] (**AI**) or tenofovir alafenamide/emtricitabine (**AII**)

Recommended Regimen Options

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use.

INSTI plus 2-NRTI Regimen:

- DTG/ABC/3TC[a] (**AI**)—**if HLA** 1 negative
- DTG plus either TDF/FTC[a] (A F/FT
- EVG/c/TAF/FTC (**AI**) or EVG
- RAL plus either TDF/FTC[a] (A F/FT

DTG

TAF/FTC
TDF/FTC

EVG©

RAL

Boosted PI plus 2 NRTIs:

- DRV/r plus either TDF/FTC[a] TAF/FTC[b] (A

Proteaz inhibitörlü kombinasyon

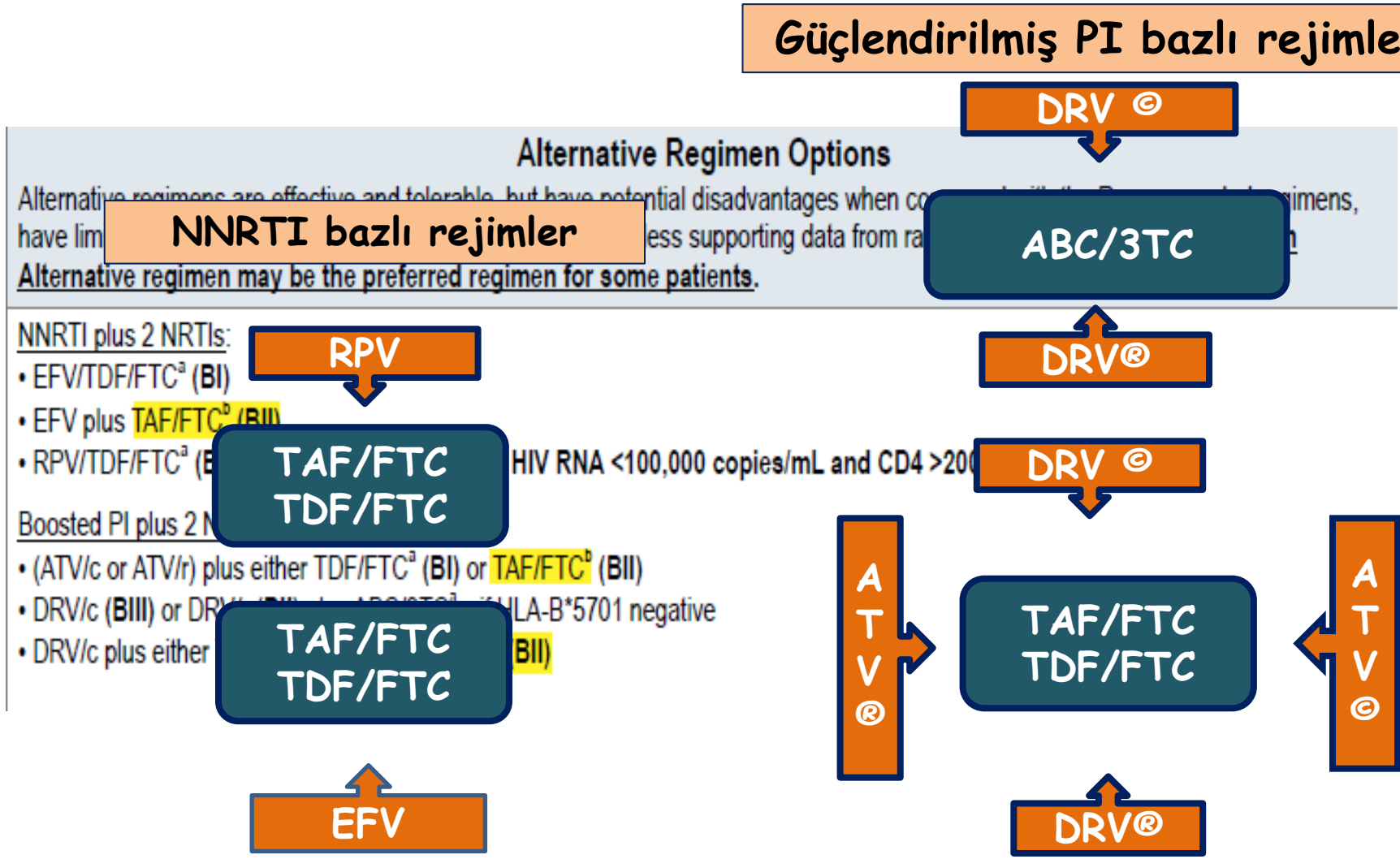
DRV/r

TAF/FTC
TDF/FTC

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, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion*

DHHS-Alternatif Tedaviler



DHHS-Diğer Tedaviler

Table 6. Recommended, Alternative, and Other Antiretroviral Regimen Options for Treatment-Naive Patients (page 2 of 2)

Other Regimen Options

When compared with Recommended and Alternative regimens, Other regimens may have reduced virologic activity, limited supporting data from large comparative clinical trials, or other factors such as greater toxicities, higher pill burden, drug interaction potential, or limitations for use in certain patient populations.

If HIV RNA <100,000 copie… HLA-B*5701 Negative:

• ATV/c (CIII) or ATV/r (CI) …/3TC

• …(CI)

…Consid… …AF, TDF, or ABC Cannot be Used:

• DRV/r plus RAL (BID) (CI… …RNA <100,000 copies/mL and CD4 >200 cells/mm³

• LPV/r plus 3TC[a] (BID) (CI…

…, or vice versa, if a non-fixed dose NRTI combination is desire…

…gimen is based on relative bioavailability data coupled with data from randomized, controlled switch trials …icacy of TAF-containing regimens.

…as coformulated products: ABC/3TC, ATV/c, DRV/c, DTG/AB… EVG/c/TDF/FTC, LPV/r, RPV/TAF/FTC, RPV/TDF/FTC, TAF/FTC, and TDF/FTC.

…ine; ABC = abacavir; ATV/c = atazanavir/cobicistat; ATV/r = ata… …/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; E… …; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside …L = raltegravir; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

ATV®

ABC/3TC

ATV©

3TC+LPV ®

ABC/3TC+RAL

RAL+DRV®

ABC/3TC+EFV

Başlangıç Rejimine Karar Verirken

Eşlik Eden Hastalıklar
Diyabet,
Kalp hastalığı,
Hepatit,
Hiperlipidemi
Böbrek patolojisi
Gebelik
Depresyon
Alkol veya uyuşturucu

Fırsatçı enfeksiyonlar

Başlangıç HAART Rejimi

Günlük yaşam
İlaç adedi
Doz aralığı

Viral yük
Genetik yapı
İlaç direnci
Tropizm

http://www.eacsociety.org/files/guidelines_8.2-english.pdf
https://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf

Yan Etkiler-NRTI

NRTI	Yan etki
Tenofovir dipivosil fumarat	**Böbrek Etkisi** •Serum kreatinin↑ •Proteinüri •Hipofosfatemi •Glikozüri •Hipokalemi •Fanconi sendromu **Kemik Etkisi** •Proximal renal tubulopati-osteomalazi •Kemik mineral yoğunluğu **Lipid profili üzerine etkisi** .TAF ve abacavire göre daha iyi
Tenofovir alafenamide fumarate	Böbrek ve kemik yan etkileri daha
Abacavir	HLA B 5701 ile ilişkili allerjik yan etki

Yan Etkiler-NRTI

INSTI	Yan etki
Dolutegravir-DTG	• ≥%2 uykusuzluk, başağrısı • İntihar düşüncesi-nadir • Rifampisin DTG düzeyini düşürür • DTG Metformin düzeyini 2 kat artırır • Antiasitler ve laksatifler
Raltegravir-RAL	• Hipersensitivite reaksiyonu • CPK↑, kas güçsüzlüğü, rabdomiyoliz • Depresyon, İntihar düşüncesi-nadir
Elvitegravir-EVG	• Depresyon • İntihar düşüncesi-nadir • TG↑,LDL↑,HDL↑ • Bulantı-İshal • Antiasitler ve laksatifler

Yan Etkiler-NNRVI

NNRTI	Yan etkiler
Efavirenz	SSS yan etkileri •Depresyon •Kötü rüyalar •Baş ağrısı •Baş dönmesi •İntihar eğiliminde artış Nöral tüp defekti Deri döküntüsü TG↑,LDL↑,Kolesterol↑
Rilpivirin HIVRNA >100 000 CD4<200 Ortak yan etkiler efavirenze göre daha az	SSS yan etkileri •Depresyon •Kötü rüyalar •Baş ağrısı •Baş dönmesi •İntihar eğiliminde artış •TG↑,LDL↑, •Kolesterol↑ •**QT uzaması**

Yan Etkiler-PI

PI	Yan etkiler
•Darunavir/Ritonovir -DRV/r •Darunavir/kobisistat - DRV /c	GİS yan etkileri •Bulantı-kusma, ishal •Transaminaz yüksekliği Lipid paneli •TG↑,LDL↑, Kolesterol↑ Deri döküntüsü, Ateş,
Lopinovir/Ritonovir (LPV/r)	**GİS yan etkileri** • **Bulantı-kusma, ishal** •Transaminaz yüksekliği **Lipid paneli** •**TG↑,LDL↑, Kolesterol↑** Deri döküntüsü, Ateş, Uzun süreli kullanımda QT uzaması (MI riski) İnsülin direnci
Atazanavir/Ritonovir ATV/r Atazanavir/kobisistat ATV/c	**GİS yan etkileri** • Bulantı, İshal • Sarılık, Kolelitiazis, • İndirekt hiperbilirubinemi, Nefrotoksisite, Nefrolitiazis, Deri döküntüsü,

Rehberlerde ilk seçenek tedaviler
2NRTI + İntegraz İnhibitörü

	TAF/FTC TDF/FTC EVG ©	ABC/3TC/DTG	TAF/FTC TDF/FTC+RAL
Endikasyon	12 yaş ve üzeri vücut ağırlığı en az 35 kg olan HIV-1 ile enfekte, içeriğinde bulunan ajanlara karşı bilinen dirençle ilişkili mutasyonu bulunmayan erişkin ve adolesanların tedavisinde endikedir.	12 yaş ve üzeri vücut ağırlığı en az 40 kg üzeri HIV 1 ile enfekte içeriğinde bulunan ajanlara karşı bilinen dirençle ilişkili mutasyonu bulunmayan erişkin ve adolesanların tedavisinde endikedir.	16 yaşın altındaki hastalarda güvenlilik ve etkinlik belirlenmemiştir
Renal fonksiyonlar	TAF/FTC +EVG © CrCL > 30 ml/dk TDF/FTC+EVG © CrCL > 50 ml/dk	CrCl > 50 ml/dk	TAF/FTC+RAL CrCL > 50 ml/dk TDF/FTC+RAL CrCL > 30 ml/dk
HLA gen tipi	Önemi yok	Tedaviyi başlamadan önce her hastaya HLA-B*5701 genini taşıyıp taşımadığı açısından test yapılmalıdır. HLA-B*5701 genini taşıyan hastalara kesinlikle başlanmamalıdır.	Önemi yok

Rehberlerde ilk seçenek tedaviler 2NRTI + İntegraz İnhibitörü

	TAF/FTC TDF/FTC EVG ©	ABC/3TC/DTG	TAF/FTC TDF/FTC+RAL
Miyokart Enfarktüsü (MI)	Bir bağlantı bulunmamaktadır.	Gözlemsel çalışmalar ABC ile MI riskinde artış arasında bağlantı olduğunu düşündürmektedir. Bu çalışmalar daha çok tedavi deneyimli hastalarda yapılmış çalışmalardır. **ABC/3TC/DTG** başlayacağınız hastada MI ile ilişkili diğer risk faktörlerini azaltmaya çalışın. • sigaranın bırakılması, • hipertansiyonun kontrol altına alınması, • hiperlipidemi	Bir bağlantı bulunmamaktadır.

Rehberlerde ilk seçenek tedaviler 2NRTI + İntegraz İnhibitörü

	TAF/FTC TDF/FTC EVG ©	ABC/3TC/DTG	TAF/FTC TDF/FTC+RAL
Hipersensitivite	Özel bir uyarı bulunmamaktadır	Tedavi öncesi HLA-B*5701 testi mutlaka yapılmalıdır. Pozitif olanlara kesinlikle başlanmamalıdır. Negatif olan kişilerde de halen hipersensitivite gelişme riski vardır. Hipersensitivite reaksiyonundan şüphe edildiğinde (bronşit, faranjit, gastrointestinal problemler, influenza benzeri semptomlar dahil) HLA B5701 geni negatif olsa bile tedavi kesilmelidir.	Raltegravir ilişkili hipersensitivite olabilir

Rehberlerde ilk seçenek tedaviler
2NRTI + İntegraz İnhibitörü

	TAF/FTC TDF/FTC EVG ©	ABC/3TC/DTG	TAF/FTC TDF/FTC+RAL
HBV Koenfeksiyonu	Ko enfekte hastalarda tedavisinin kesilmesi Hep B alevlenmesine sebep olabilir.	Ko enfekte hastada Lamivudin tek başına yeterli olmaz. Hep B için ayrıca ilaç eklenmesi önerilir.	Ko enfekte hastalarda tedavisinin kesilmesi Hep B alevlenmesine sebep olabilir.
Hepatik yetmezlik	Hafif ve orta hepatik yetmezlikte doz ayarlaması gerekmez. (Child A ve B) Ciddi hepatik yetmezlikli hastalarda önerilmez (Child C)	Hafif hepatik yetmezlikli hastalarda ABC doz azaltılması gerekebilir (Child A) Orta ve ağır hepatik yetmezlikli hastalarda önerilmez. (Child B ve C)	Hafif ve orta hepatik yetmezlikte doz ayarlaması gerekmez. (Child A ve B) Ağır karaciğer yetmezliğine farmakokinetiği çalışılmamıştır
Güçlendirici Booster © ®	© Cobicistat içerir. Bu nedenle eklenen her tedavi ilaç etkileşimi açısından değerlendirilmelidir. Özellikle tüberküloz tedavisi alan hastalarda kullanımı önerilmez.	**Güçlendirici Booster © ® içermez.**	**Güçlendirici Booster © ® içermez**
Lipid profiline etkisi	Lipid ler üzerine olumsuz etkileri var		
Kemik mineral yoğunluğu	**TDF/FTC sıkıntılı** **TAF/FTC sorunsuz**		**TDF/FTC sıkıntılı** **TAF/FTC sorunsuz** **RAL miyopati rabdomiyoliz**

Hastaya Göre Tedavi

- Direnç testi
- Viral yük + CD4
- HLA-B*5701
- Böbrek fonksiyonlarını değerlendir
- Kemik mineral danstometri
- Fırsatçı enfeksiyonlar
- Kardiak risk faktörleri
- Hiperlipidemi
- Psikiyatrik sorunu var mı?
  - Nöbet geçirme öyküsü
  - HIV demans
- Gebelik?

Hastaya Göre Tedavi

Direnç testi çıkmadan acilen tedavi başlayacaksanız

Direnç riski yüksek olan NNRTI bazlı tedavileri tercih etmeyiniz

HLA-B*5701 + ise

Abacavir içeren rejimleri kullanmayınız

Hastaya Göre Tedavi

Böbrek fonksiyonlarını değerlendirilmeli
Bozukluk varsa

TDF'den

KAÇINILMALI

HLA-B*5701 negatif ise ABC
GFR>30 ml/dak ise TAF

Hastaya Göre Tedavi

Kemik mineral Danstometrisini değerlendir
Osteoporoz varsa

TDF'den KAÇINILMALI

HLA-B*5701 negatif ise ABC
GFR>30 ml/dak ise TAF

Hastaya Göre Tedavi

CD4<200 hücre/mm^3

RPV bazlı tedavi

DRV/r+RAL

ÖNERİLMEZ

HIV RNA>100 000 kopya/ml

RPV bazlı tedavi

ABC/3TC + EFV veya ATV/r

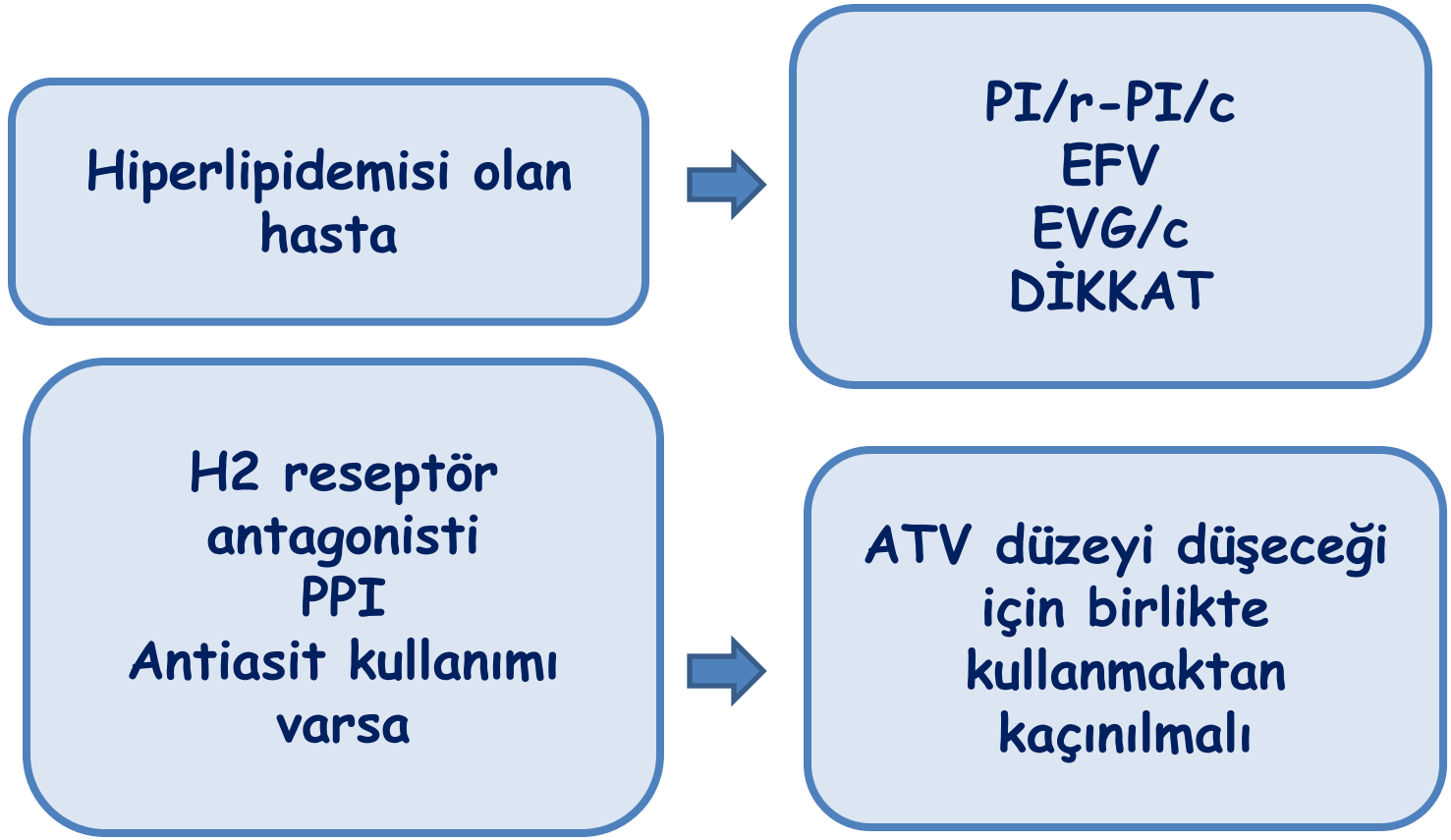
DRV/r + RAL

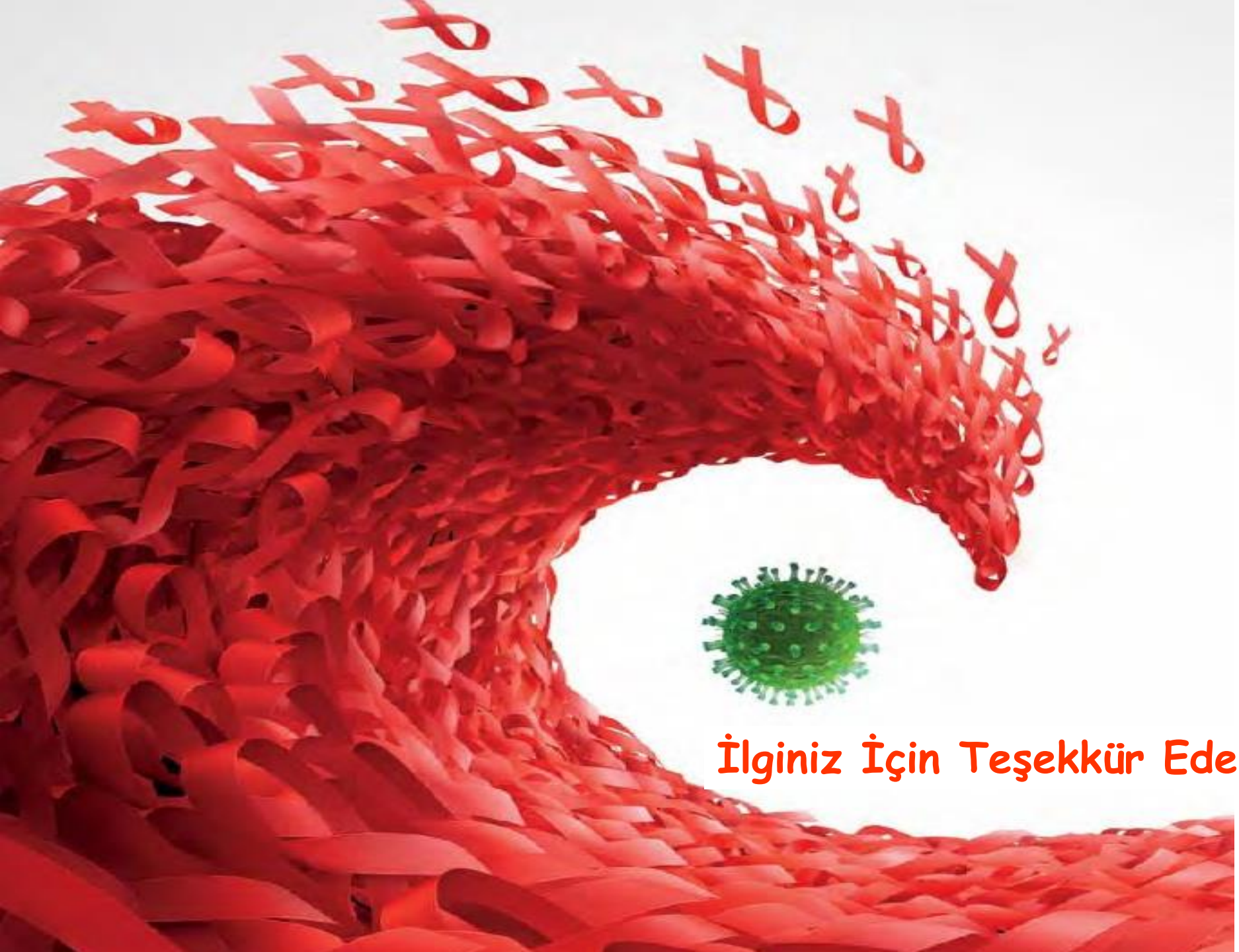
ÖNERİLMEZ

Hastaya Göre Tedavi

Psikiyatrik sorunları veya HIV demansı olan hasta	→	EFV ve RPV bazlı ilaçlar KAÇINILMALI
Yüksek kardiyak riski olan hasta	→	ABC ve proteaz inhibitörlü tedavilerden KAÇINILMALI
QT uzanası varsa	→	EFV ve RPV bazlı ilaçlar KAÇINILMALI

Hastaya Göre Tedavi





İlginiz İçin Teşekkür Ederim

Tüberküloz

- Sadece İNAH proflaksisi alıyorsa tüm rejimler başlanabilir
- RİF ile TAF birlikte kullanımı önerilmiyor
- EFV kullanılıyorsa doz arttırmak gerekmiyor
- RAL kullanıyorsa 2x800mg
- DTG kullanıyorsa 2x50mg
- CD4<50 ART hemen TB başlandıktan sonraki 2 hafta içinde
- CD4>50 TB tedavisinin 8. haftası içinde
- Gebe hastada hemen ART