TEDAVİ

REHBERLER NE DER ?

HEKİM NE İSTER ?

HASTA NE İSTER ?

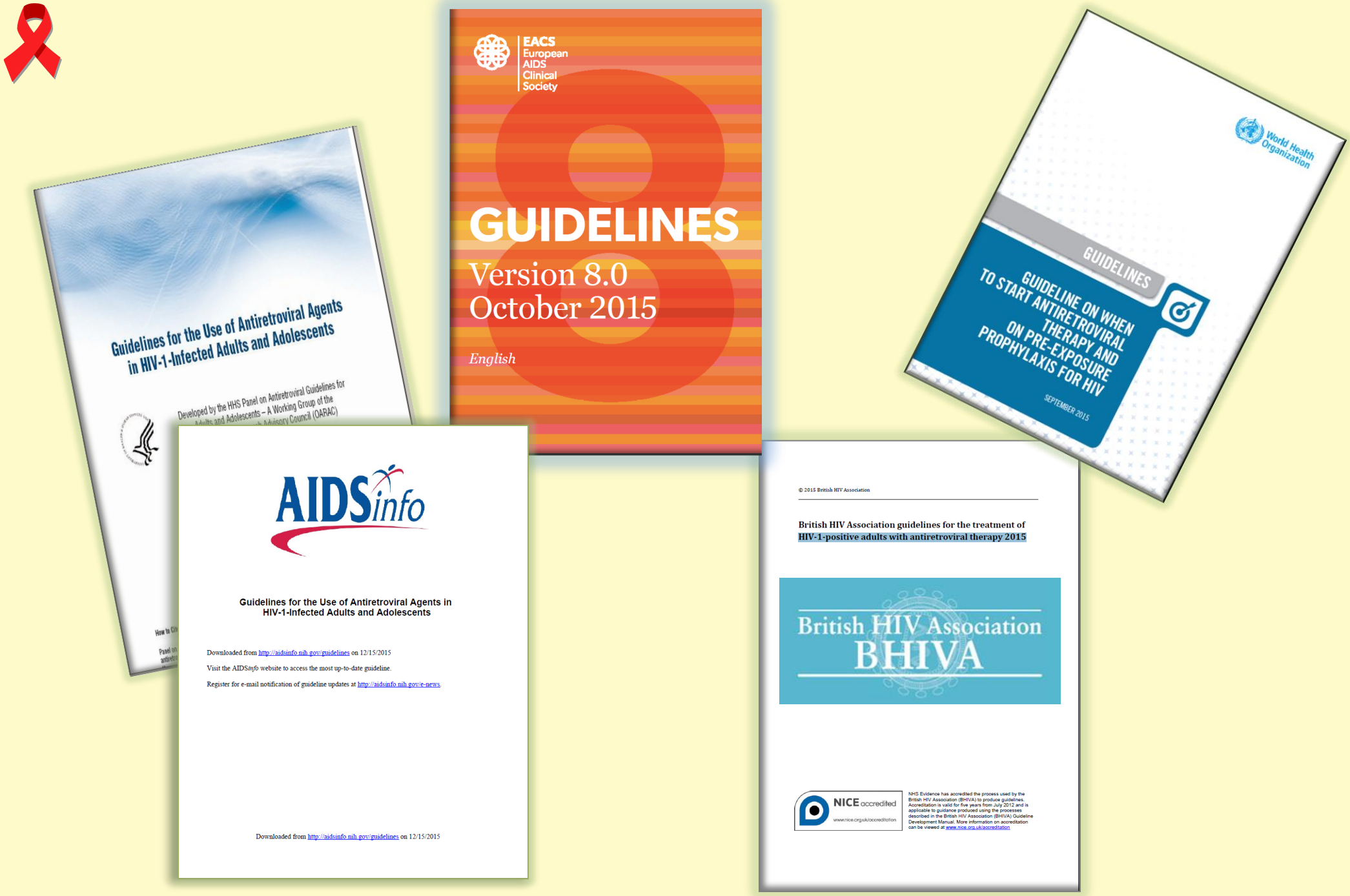
BAŞAK DOKUZOĞUZ

ANKARA NUMUNE EĞİTİM ARAŞTIRMA HASTANESİ

ANTİRETROVİRAL TEDAVİ

NE ZAMAN BAŞLAYALIM ?

NE BAŞLAYALIM ?


Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents
Developed by the HHS Panel on Antiretroviral Guidelines for
EACS
European
AIDS
Clinical
Society
GUIDELINES
Version 8.0
October 2015
English
World Health Organization
GUIDELINES
GUIDELINE ON WHEN TO START ANTIRETROVIRAL THERAPY AND ON PRE-EXPOSURE PROPHYLAXIS FOR HIV
SEPTEMBER 2015
AIDSinfo
Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents
Downloaded from http://aidsinfo.nih.gov/guidelines on 12/15/2015
Visit the AIDSinfo website to access the most up-to-date guideline.
Register for e-mail notification of guideline updates at http://aidsinfo.nih.gov/e-news.
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© 2015 British HIV Association
British HIV Association guidelines for the treatment of HIV-1-positive adults with antiretroviral therapy 2015
British HIV Association
BHIVA
NICE accredited
www.nice.org.uk/accreditation
NHS Evidence has accredited the process used by the British HIV Association (BHIVA) to produce guidelines. Accreditation is valid for five years from July 2012 and is applicable to guidance produced using the processes described in the British HIV Association (BHIVA) Guideline Development Manual. More information on accreditation can be viewed at www.nice.org.uk/accreditation

T.C. Sağlık Bakanlığı
Türkiye Halk Sağlığı Kurumu

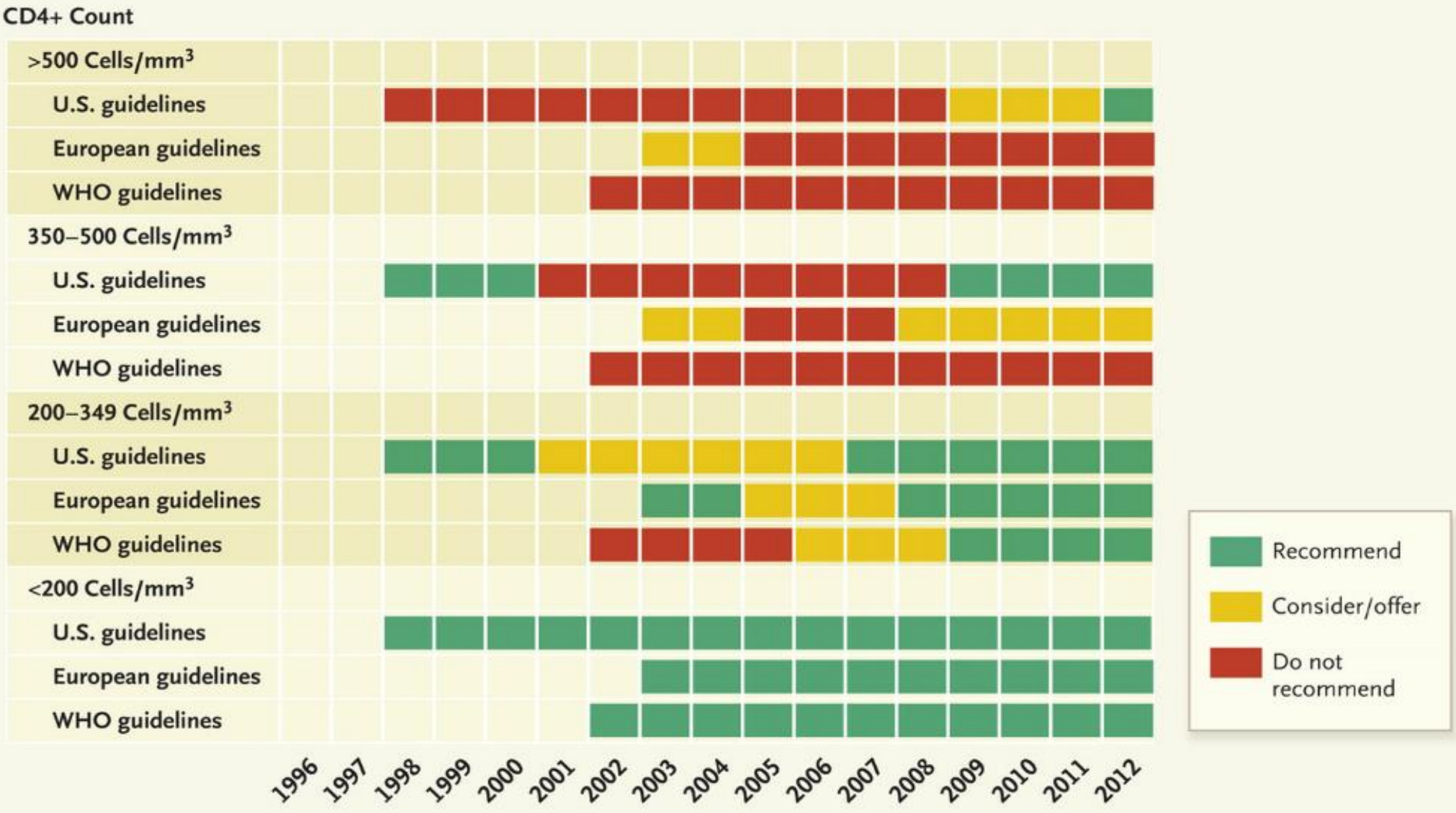
HIV / AIDS TANI TEDAVİ REHBERİ

Ankara 2013

Tedavinin Hedefleri

- Viral yük etkin ve sürekli olarak baskılamak
- İmmünolojik fonksiyonu düzeltmek ve korumak
- HIV ilişkili morbidite ve mortaliteyi azaltmak
- Hayat kalitesini arttırmak
- Yaşam süresini uzatmak
- Vertikal HIV bulaşını engellemek
- HIV bulaşını önlemek

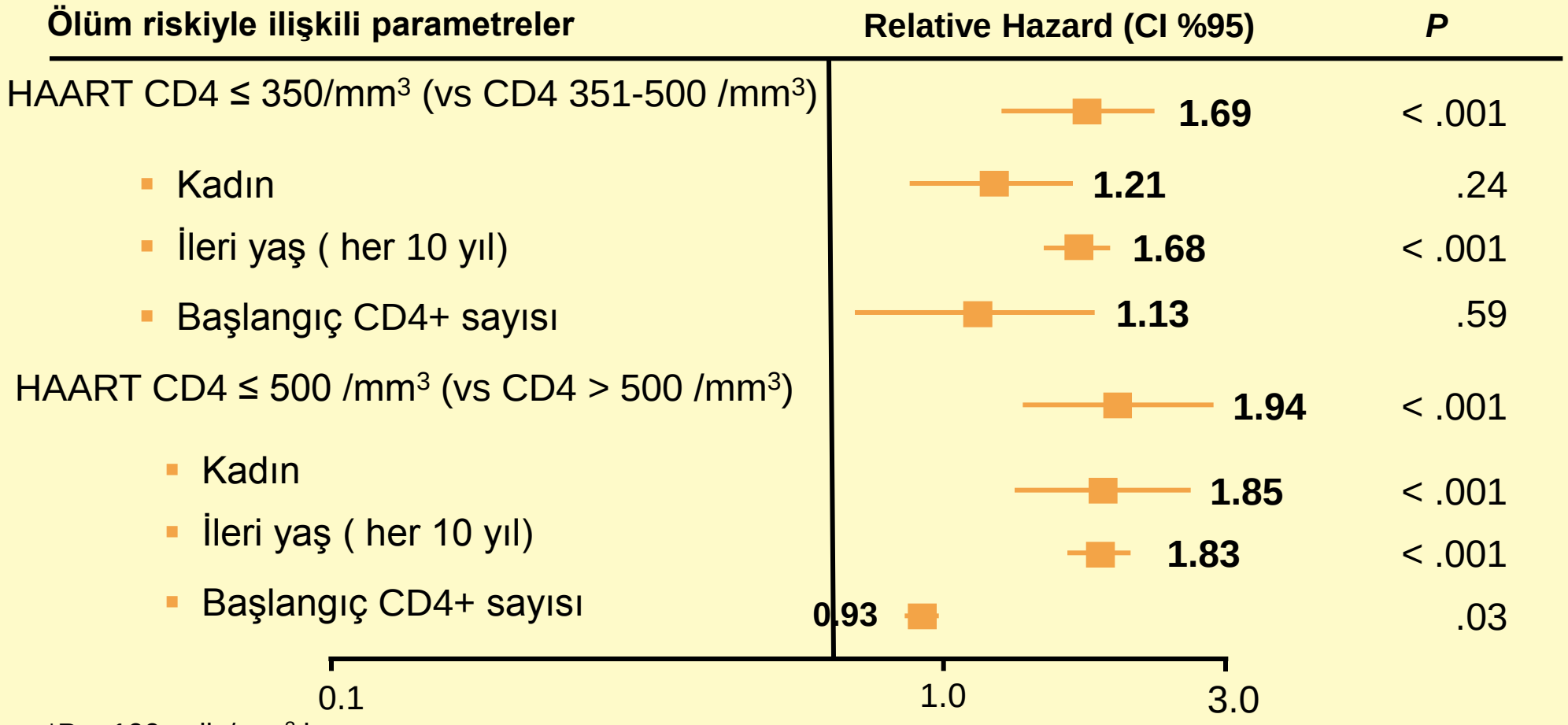
REHBERLERİN ASEMPTOMATİK HIV+ OLGULARDA CD4+SAYISINA GÖRE ART BAŞLAMA ÖNERİLERİ



. De Cock KM, El-Sadr WM. , When to Start ART in Africa — An Urgent Research Priority N Engl J Med 2013

NA- ACCORD

North America AIDS Cohort Collaboration on Research and Design

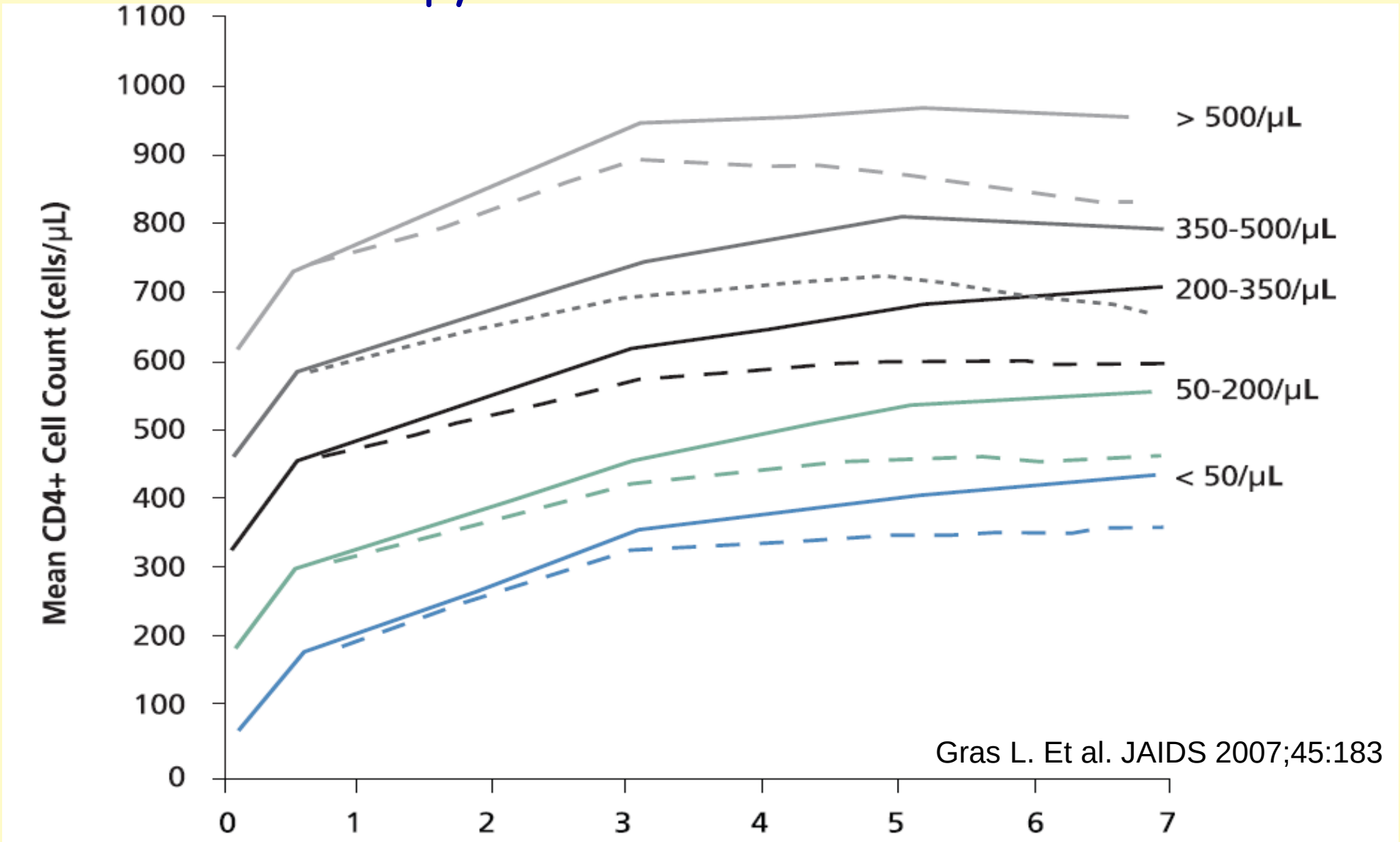


*Per 100 cells/mm3 increase.

Kitahata MM, et al. N Engl J Med. 2009;360:1815-1826.

ATHENA

AIDS Therapy Evaluation in the Netherlands



Gras L. Et al. JAIDS 2007;45:183

ART Ne Zaman Başlayalım?

	DHHS 2014	EACS 2013	BHIVA 2014	DSÖ 2013-14
Semptomatik	+	+	+	+
Asemptomatik				
CD4 < 350/mm³	+ AI	+	+	+
CD4 350–500 /mm³	+ AII	+/- Hasta ile görüşerek değerlendirilir	+/- Eşlik eden durumlara göre	+
CD4 > 500 /mm³	+ BIII	+/- Hasta ile görüşerek değerlendirilir	+/- Tbc İzlem kısıtlılığı	

N Engl J Med. 2015 Aug 27;373(9):808-22. doi: 10.1056/NEJMoa1507198. Epub 2015 Jul 20.

A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa.

TEMPRANO ANRS 12136 Study Group, Danel C, Moh R, Gabillard D, Badje A, Le Carrou J, Ouassa T, Ouattara E, Anzian A, Ntakpé JB, Minga A, Kouame GM, Bouhoussou F, Em
Dohoun L, Kamaga
Koné F, Guéhi C, K
Yededji SY, Assi R
S, Aka K, Aoussi E
V, Moh-Semdé C,
Collaborator

Abstract

BACKGROUND: I
with a 2-by-2 fact
HIV-infected adul

METHODS: We i
criteria for startin
groups: deferred A
The primary end p
defining cancer, n
outcomes betwee

RESULTS: A tota
of 204 primary en
with a baseline CI
invasive bacterial
was lower with ea
baseline CD4+ co
95% CI, 0.48 to 0
1.01). The 30-mo

CONCLUSIONS:
ART and no IPT,
Agency for Resea

Strategic Timing of Antiretroviral Treatment (START)

This study is ongoing, but not recruiting participants.

Sponsor:

University of Minnesota - Clinical and Translational Science Institute

Collaborators:

National Institute of Allergy and Infectious Diseases (NIAID)
Copenhagen HIV Programme (CHIP) -- Copenhagen, Denmark
Medical Research Council
The Kirby Institute for Infection and Immunity in Society
The Institute for Clinical Research at the Veterans Affairs Medical Center -- Washington, D.C., USA
French National Institute for Health and Medical Research-French National Agency for Research on AIDS and Viral Hepatitis (Inserm-ANRS)
German Federal Ministry of Education and Research
NEAT - European AIDS Treatment Network
National Health and Medical Research Council, Australia
National Institutes of Health Clinical Center (CC)
National Cancer Institute (NCI)
National Heart, Lung, and Blood Institute (NHLBI)
National Institute of Mental Health (NIMH)
National Institute of Neurological Disorders and Stroke (NINDS)
National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
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Gilead Sciences
GlaxoSmithKline
Merck Sharp & Dohme Corp.
Tibotec Pharmaceutical Limited

CD4 Sayısına Bakılmaksızın Tüm Hastalara ART Başlayın

- **HIV ilişkili morbidite ve mortaliteyi azaltmak**
- **HIV infekte kişilerden bulaşın önlenmesi**

4.0 When to start

British HIV Associ

What's New in the Guidelines? (Last updated January 28, 2016; last reviewed

4.1

4.1.1

4.1.2

ART
y a
hted
ing

ART to [illegible] or all HIV-infected patients, regardless of CD4 count. Revisions to this section focus on the data support[illegible]RT for all patients.

Follow[illegible] the updated recommenda

Recommenc
Infection wit

Recommendations are
dence, the degree of p
high risk for, developing

Symptomatic HIV dis conditions, incl. tuberculosis)		
Any CD4 count	Current CD4 count	
	< 350	≥ 350
SR	SR	R

SR = Strongly Recommended
R = Recommended

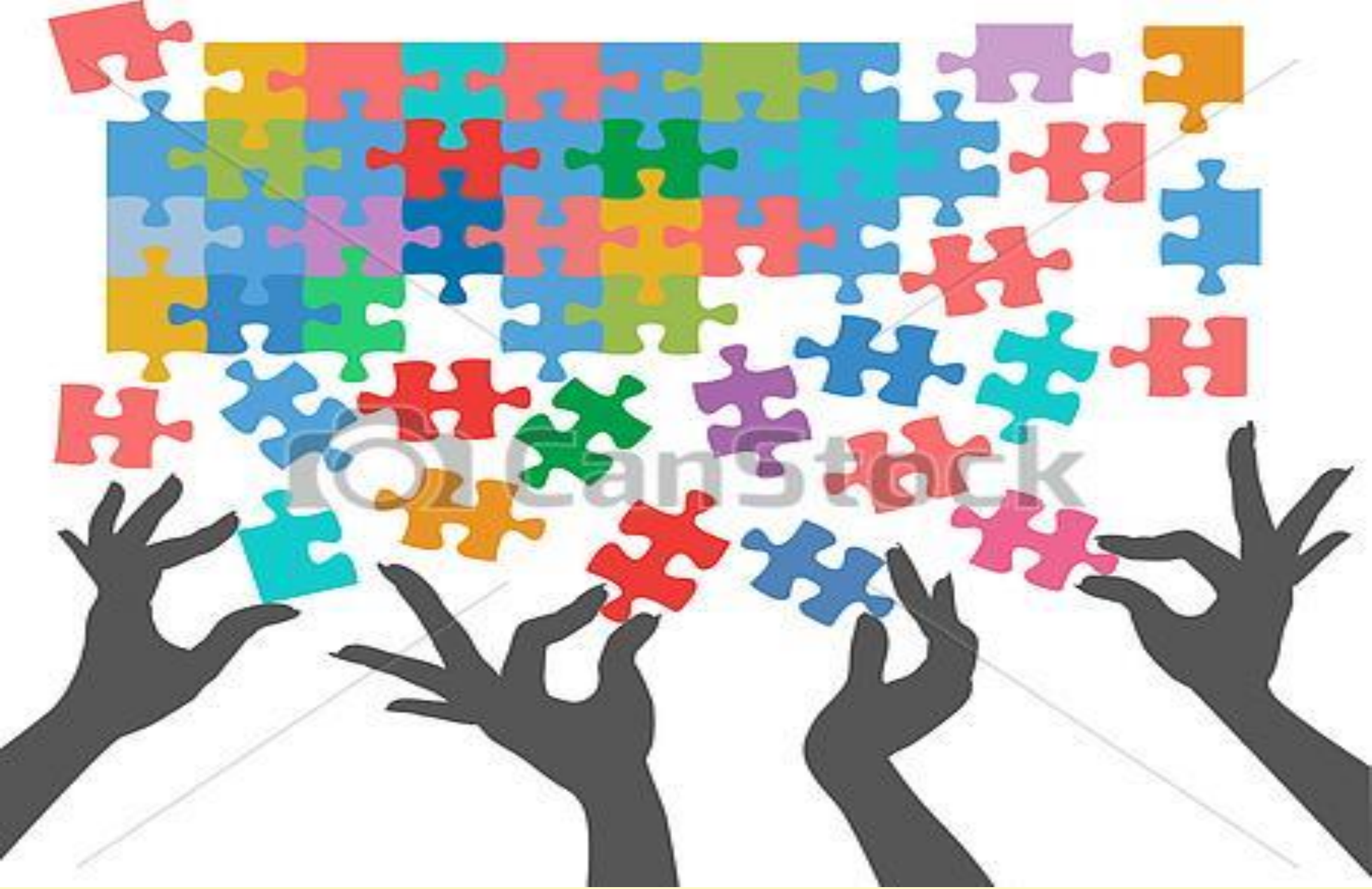
Recommendation 1: When to start ART among people living with HIV

Target population	Specific recommendation	Strength of the recommendation	Quality of the evidence
			Moderate NEW
			Moderate
			Moderate
			UPDATED
			Low
	cell count		NEW
	As a priority, ART should be initiated in all adolescents with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and individuals with CD4 count ≤350 cells/mm³	*Strong*	*Moderate*
Children (1 to <10 years old)	ART should be initiated in all children 1 to <10 years old living with HIV at any CD4 cell count	*Conditional*	*Low* NEW
	As a priority, ART should be initiated	*Strong*	*Moderate*

- Tedavi hasta bazında değerlendirilir
- Klinik ve/veya psikososyal durumuna göre ertelenebilir
- Ancak mümkün olduğunca erken başlanmalıdır

Hemen Tedavi Başlanması Gerekir !

- **Gebelik**
- **AIDS tanımlayıcı durumlar**
  - HIV ilişkili demans, malignite
- **HIV nefropatisi (HIVAN)**
- **Akut / erken infeksiyon**
- **HIV/ HBV koinfeksiyonu**
- **HIV/HCV koinfeksiyonu**



- **GÜUÇME82**

- 2004 CD4: 475 /mm³
  688 /mm³
  555 /mm³
  422 /mm³
- → 2009 CD4: 250 /mm³
- 2015 CD4: 741 /mm³

- **ADELAR73**

- 2011 CD4: 612 /mm³
  508 /mm³
- → 2013 CD4: 482 /mm³
- 2015 CD4: 948/mm³

NRTI

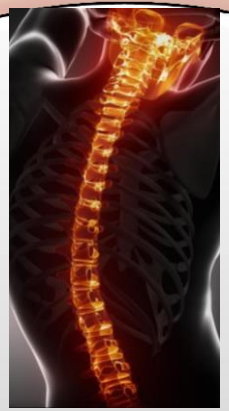
NNRTI

PI

INI

FI

CCR5
antagonisti



2 NRTI

+

veya

NNRTI

veya

PI

INI

ART - İlk Seçenek

	NRTI	INSTI	PI	NNRTI
DHHS	TDF/FTC ABC/3TC**	DTG** EVG/c EVG/c/TAF/FTC RAL	DRV/r	
EACS	TDF/FTC ABC/3TC**	DTG** EVG/c RAL	DRV/r	RPV
BHIVA	TDF/FTC	DTG EVG/c RAL	ATZ/r DRV/r	RPV
WHO	TDF/3TC (FTC)	DTG		EFV

ART - Alternatif

	NRTI	INSTI	PI	NNRTI
DHHS	ABC/3TC* TDF/FTC&		DRV/c* ATV/r& ATV/c&	EFV RPV
EACS	ABC/3TC" TDF/FTC#	RAL"	DRV/c ATV/r ATV/c LPV/r#	EFV
BHIVA	ABC/3TC			EFV
WHO	2NRTI	RAL	ATV/r LPV/r DRV/r	

OLGU

- **MİDOBA65**
- **Asemptomatik**
- **CD_4 : 375/mm^3**
- **VY : 5.9x 10^6**

a) TDF/FTC + DRV/r

b) TDF/FTC + LPV/r

c) TDF/FTC + EFV

d) TDF/FTC + DTG

e) TDF/FTC + EVG/c

f) TDF/FTC

g) ABC+ 3T

h) ZDV/3TC

Tedavi Başlarken DİKKAT !

- **CD4<200/mm³**
  - **RPV ∅**
  - **DRV/r+RAL ∅**

  } Virolojik başarısızlık

- **VY> 100 000 kopya/ml**
  - **RPV ∅**
  - **ABC/EFV ∅**
  - **ATV/r ve DRV/r+ RAL ∅**

  } Virolojik başarısızlık

Tedavi Başlarken DİKKAT !

- **HLA-B 5701 pozitif**
  - **ABC** ∅ ⟶ Fatal olabilen allerjik reaksiyon

- **Direnç testi sonucu beklenemeyen hasta**
  - **NNRTI** ∅ ⟶ Aktarılan direnç mutasyonları
  - INSTI ???

Eşlik Eden Durumlar

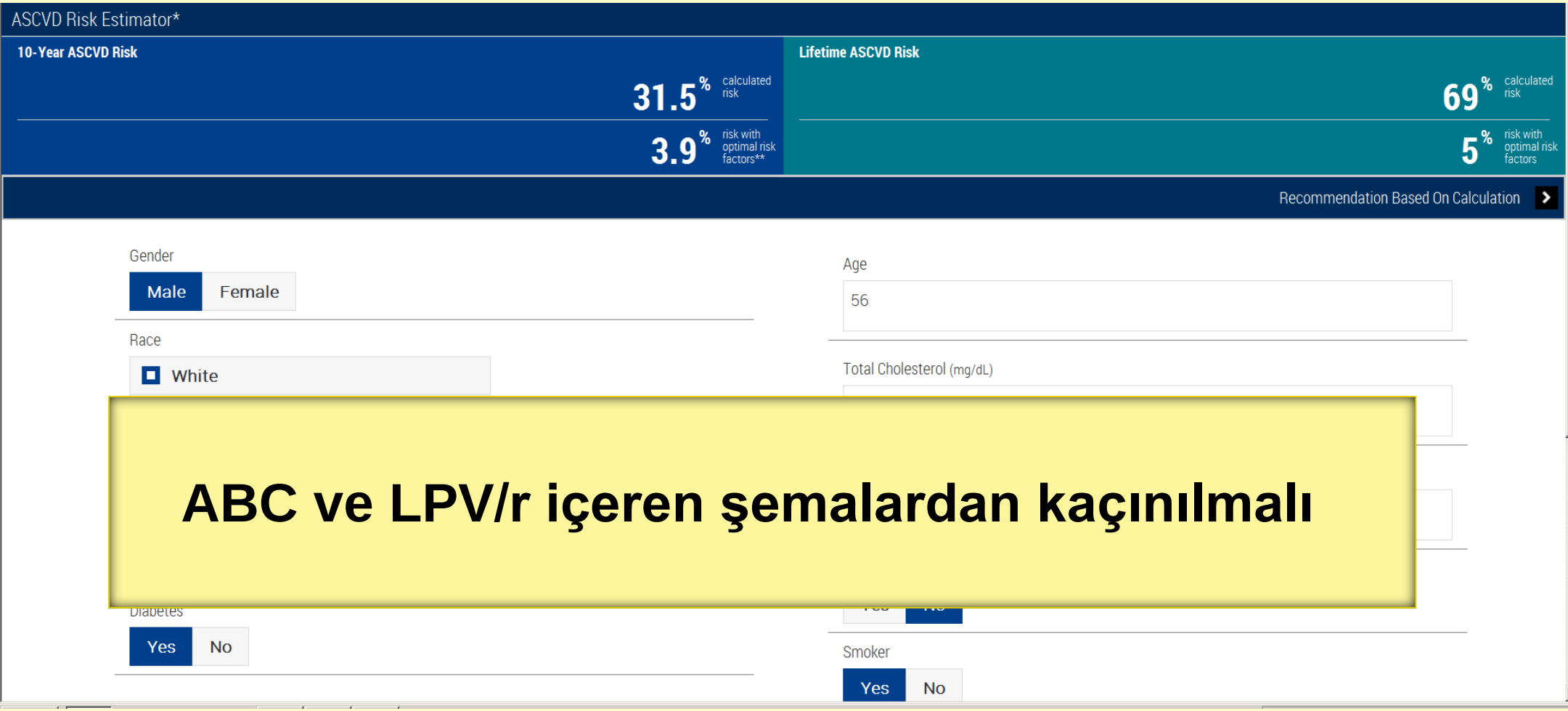
- **Fırsatçı hastalık**
  - **Tbc**
- **Eşlik eden infeksiyonlar**
  - **HBV, HCV**
- **Malignite varlığı**
  - meme, hepatobiliyer, kolorektal, prostat, servical, anal
- **Kardiyovasküler durumu**
- **Böbrek**
- **Karaciğer**
- **Diabet**
- **Dislipdemi**
- **Kemik metabolizması**
- **Depresyon**
- **Madde kullanımı**

Tedavi Yan Etki/ Komplikasyon

- Kardiyovasküler
- Diabet
- Dislipdemi
- Lipodistrofi
- Kemik metabolizması
- Laktik asidoz

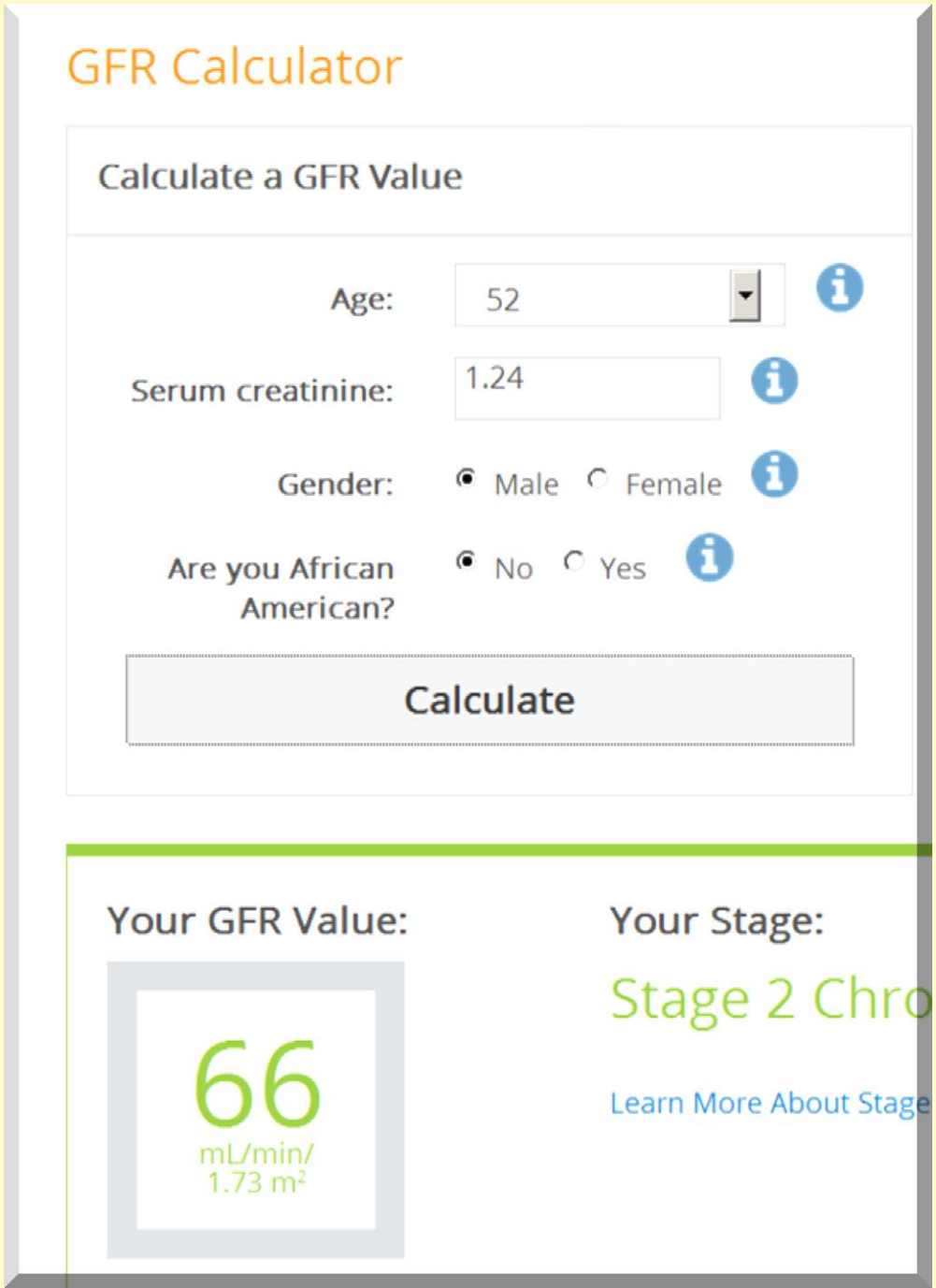
risk önlenmesi

Kardiyak Risk Değerlendirmesi



ABC ve LPV/r içeren şemalardan kaçınılmalı

http://tools.acc.org/ASCVD-Risk-Estimator/



GFR <70 mL/dk

- **EVG/c/TDF/FTC**
- **ATV/c ve TDF**
- **DRV/c ve TDF**

kaçınılmalıdır

www.davita.com/gfr-calculator/

Kronik Böbrek Hastaları İçin Seçenekler

- **ABC/3TC**
  - **HLB*5701 negatifse**
  - **HIV RNA> 100 000 k/mL ise EFV veya ATV/r birlikte kullanma**
  - **CrCl < 50 mL/dk ise ABC+ 3TC kullan** (3TC doz ayarlaması için)
- **Diğer seçenekler**
  - **DRV/r + RAL** (HIV RNA <100,000 /mL ve CD4 >200/mm^3)
  - **LPV/r + 3TC**

Böbrek Yetmezliğinde Doz Ayarlaması

		eGFR[i] (mL/min)				Haemodialysis
		≥ 50	30-49	10-29	< 10	
NRTIs						
ABC		300 mg q12h	No dose adjustment required			
ddI[ii]	≥ 60 kg	400 mg q24h	200 mg q24h	150 mg q24h	100 mg q24h	100 mg q24h[iv]
	< 60 kg	250 mg q24h	125 mg q24h	100 mg q24h	75 mg q24h	75 mg q24h[iv]
d4T	≥ 60 kg	30 mg q12h	15 mg q12h	15 mg q24h	15 mg q24h	15 mg q24h[iv]
	< 60 kg	40 mg q12h	20 mg q12h	20 mg q24h	20 mg q24h	20 mg q24h[iv]
FTC		200 mg q24h	200 mg q48h	200 mg q72h	200 mg q96h	200 mg q96h[iv]
3TC		300 mg q24h	150 mg q24h	100 mg q24h[iii]	50-25 mg q24h[iii]	50-25 mg q24h[iii], [iv]
TDF[v]		300[viii] mg q24h	300[viii] mg q48h	Not recommended (300[viii] mg q72-96h, if no alternative)	Not recommended (300[viii] mg q7d, if no alternative)	300[viii] mg q7d[iv]
ZDV		300 mg q12h	No dose adjustment required		100 mg q8h	100 mg q8h[iv]
ABC/3TC		600/300 mg q24h	Use individual drugs			
ZDV/3TC		300/150 mg q12h				
ABC/3TC/ZDV		300/150/300 mg q12h				
TDF/FTC		300[viii]/200 mg q24h	300[viii]/200 mg q48h	Use individual drugs		
NNRTIs						
EFV		600 mg q24h	No dose adjustment required			
ETV		200 mg q12h	No dose adjustment required			
NVP		200 mg q12h	No dose adjustment required			
TDF/FTC/RPV		300[viii]/200/25 mg q24h	Do not use			

	eGFR[i] (mL/min)				Haemodialysis
	≥ 50	30-49	10-29	< 10	
PIs[v]					
ATV/r	300/100 mg q24h	No dose adjustment required[vi]			
DRV/r	800/100 mg q24h	No dose adjustment required[vi]			

Karaciğer Yetmezliğinde Doz Ayarlaması

NRTIs	
ABC	Child-Pugh Class A: 200 mg bid (use oral solution)
	Child-Pugh Class B or C: Contraindicated
ddI	Contraindicated If used no dosage adjustment
d4T	Contraindicated If used no dosage adjustment
FTC	No dosage adjustment
3TC	No dosage adjustment
TDF	No dosage adjustment
TDF/FTC	No dosage adjustment
ZDV	Reduce dose by 50% or double the interval between doses if Child-Pugh Class C
NNRTIs	
EFV	No dosage adjustment; use with caution in persons with hepatic impairment
TDF/FTC/EFV	
ETV	Child-Pugh Class A or B: no dosage adjustment Child-Pugh Class C: no data
NVP	Child-Pugh Class B or C: contraindicated
RPV	Child-Pugh Class A or B: no dosage adjustment Child Pugh Class C: no data

PIs	
ATV	Child-Pugh Class B: 300 mg qd
	Child-Pugh Class C: not recommended
	RTV boosting is not recommended in persons with hepatic impairment (Child-Pugh Class B or C)
DRV	Child-Pugh Class A or B: no dosage adjustment
	Child-Pugh Class C: not recommended
DRV/c	Child-Pugh Class A or B: no dosage adjustment
	Child-Pugh Class C: not recommended
FPV	**PI-naïve persons:**
	Child-Pugh Class A or B: 700 mg bid
	Child-Pugh Class C: 350 mg bid
	PI-experienced persons:
	Child-Pugh Class A: 700 mg bid + RTV 100 mg qd
	Child-Pugh Class B: 450 mg bid + RTV 100 mg qd
	Child-Pugh Class C: 300 mg bid + RTV 100 mg qd
IDV	Child-Pugh Class A or B: 600 mg q8h
	Child-Pugh Class C: no data
LPV/r	No dosage recommendation; use with caution in persons with hepatic impairment
RTV	Refer to recommendations for the primary PI
SQV	Child-Pugh Class A or B: use with caution
	Child-Pugh Class C: contraindicated

- **Hiperlipidemi**
  - **PI/r - ABC - EFV - EVG/c ……***olumsuz etkisi olduğu göz önüne alınmalı*
- **Osteoporoz**
  - **TDF……** *uzak durmayı düşün*
- **Psikiyatrik hastalık**
  - **EFV……** *kaçınılmalı*
- **HIV ilişkili demans**
  - **EFV ……..** *kaçınılmalı DRV/r ve DTG içeren şemalar tercih edilebilir*

Madde Bağımlılığı Tedavisinde Doz Ayarlama

Characteristics of drugs used as opioid substitution therapy (OST)[i]

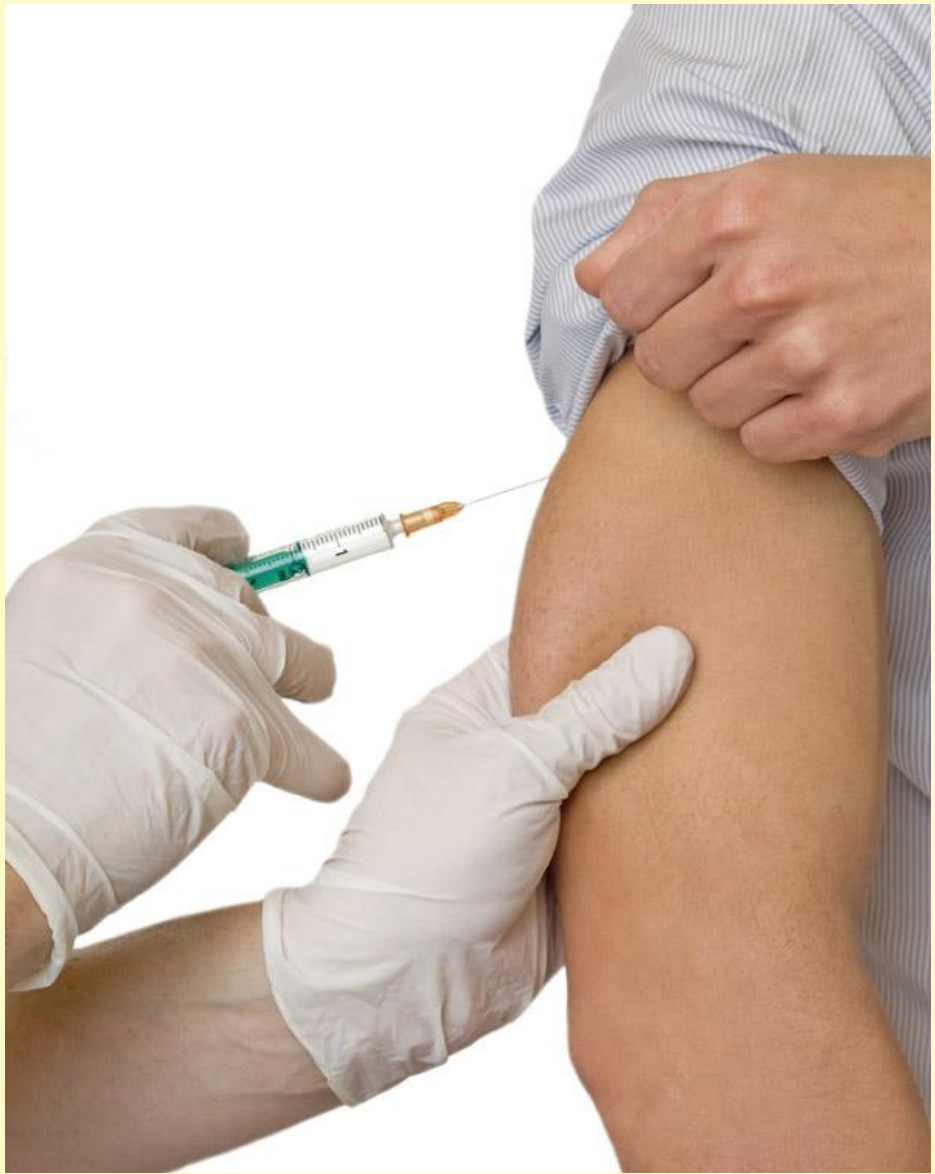
Feature	Methadone	Buprenorphine
Dose required to prevent withdrawal symptoms according to degree of opioid dependency	Linear relationship (from 10-300 mg per day)	Linear relationship for persons with less opioid dependency only – ceiling effect (max daily dose 24 mg)
Interaction with ARVs	Methadone plasma concentrations are reduced if used together with NNRTIs or PIs: • NVP & EFV: ↓ 50% • ETV: ↓ < 10%[ii] • LPV/r: ↓ 50% • SQV/r, DRV/r, FPV/r: ↓ 15-25% • ATV, IDV: ↓ < 10%	Buprenorphine (B) and active metabolite norbuprenorphine (N) plasma concentrations are reduced if combined with NNRTIs and increased if combined with some PIs • EFV: ↓ up to 50% (B) and 70% (N) • ATV/r, IDV, SQV/r: ↑ 50-100% (B&N) • DRV/r: ↑ 50% (N) • **CAVE:** B reduces ATV; do not use without RTV or COBI boosting
	CAVE: withdrawal symptoms if combined with ARV that decreases plasma concentration and risk of drug toxicity if such ARVs are interrupted – reverse if ARVs increase plasma concentration	
Risk of overdose	Yes	No if used as a co-formulation with naloxone
Causing QT prolongation on ECG	Yes (dose-response relationship)[iii]	No
Risk of obstipation	High	High
Type of administration	Tablet or liquid	Tablet applied sublingual
Risk of further impairment in persons with existing liver impairment	Yes	Yes

i See Drug-drug Interactions between Analgesics and ARVs

İlaç Etkileşimleri

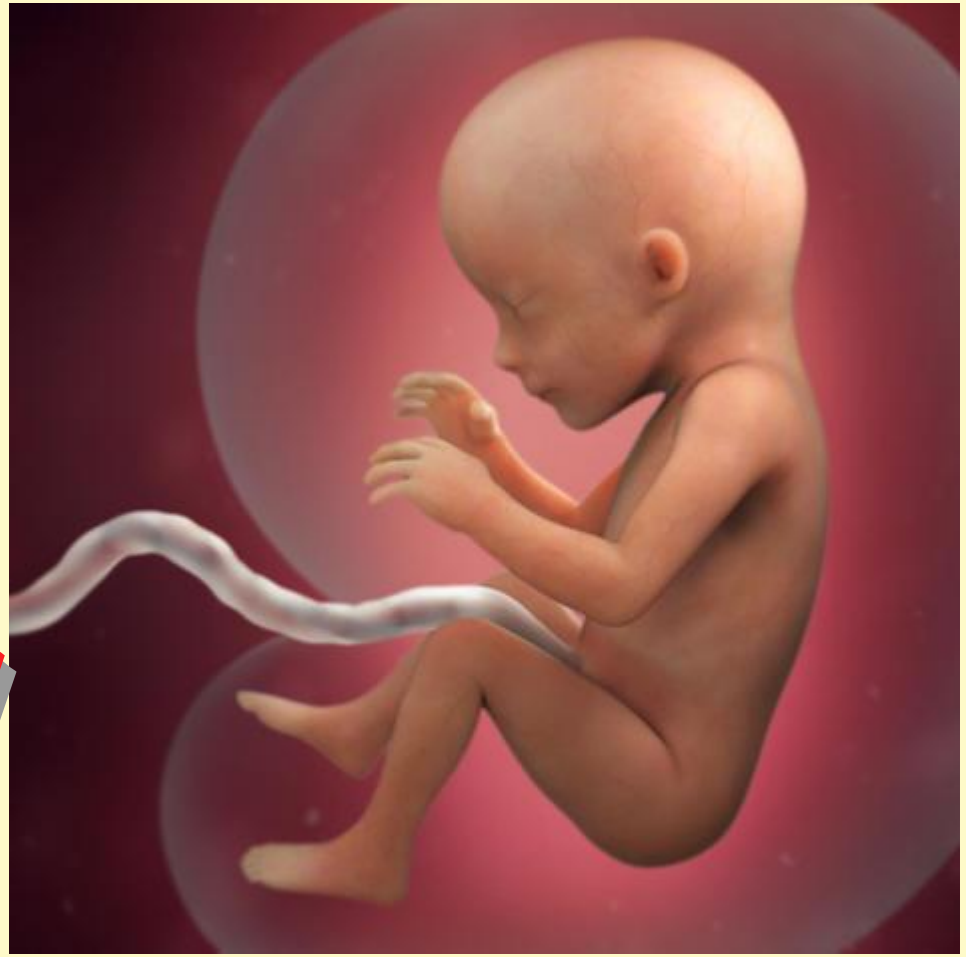
Antidepressants	Darunavir	Ritonavir	Efavirenz	Emtricitabine (FTC)	Tenofovir	Raltegravir
Escitalopram	▢	▢	▢	◇	◇	◇
Mirtazapine	▢	▢	▢	◇	◇	◇
Antipsychotics/Neuroleptics	**Darunavir**	**Ritonavir**	**Efavirenz**	**Emtricitabine (FTC)**	**Tenofovir**	**Raltegravir**
Quetiapine	●	●	▢	◇	◇	◇
Antiretrovirals (Integrase Inhibitors)	**Darunavir**	**Ritonavir**	**Efavirenz**	**Emtricitabine (FTC)**	**Tenofovir**	**Raltegravir**
Raltegravir	◇	◇	▢	◇	◇	n/a
Antiretrovirals (NNRTIs)	**Darunavir**	**Ritonavir**	**Efavirenz**	**Emtricitabine (FTC)**	**Tenofovir**	**Raltegravir**
Efavirenz	▢	▢	n/a	◇	◇	▢
Antiretrovirals (Nucleoside/tide Analogues)	**Darunavir**	**Ritonavir**	**Efavirenz**	**Emtricitabine (FTC)**	**Tenofovir**	**Raltegravir**
Emtricitabine (FTC)	◇	◇	◇	n/a	◇	◇
Tenofovir	▢	▢	◇	◇	n/a	◇
Antiretrovirals (Protease Inhibitors)	**Darunavir**	**Ritonavir**	**Efavirenz**	**Emtricitabine (FTC)**	**Tenofovir**	**Raltegravir**
Darunavir	n/a	▢	▢	◇	▢	◇
Lopinavir	●	▢	▢	◇	▢	◇
Ritonavir	▢	n/a	▢	◇	▢	◇

Bağışıklama



- İnfluenza
- Pnömokok
- Meningokok
- HPV
- HBV
- HAV
- VZV

Gebelik



OLGU

- **MİDOBA65**
- **Asemptomatik**
- **CD_4 : 375/mm^3**
- **VY : 5.9x 10^6**
- **Antidepresan**
- **LAD %30 daralık**
- **Osteopeni ....Femur, lomber**

Hekim Ne İster

- Açık davranmasını
- Kontrole düzeli gelmesini
- Tedavi uyumunu

Ayrımcılık

- Toplumda
- Sağlık kuruluşlarında

Hasta Ne İster

- **GİZLİLİK**
  - **Hastanede**
  - **Aile- sosyal çevrede**
  - **Kayıtlarda**
  - **İş yerinde**
- **Moral destek**
- **İŞ ?????**
- **Tedavi süresi ????**

ART Başlarken

BİLGİLENDİRME

- ART'nin yararı
- Uyumun önemi
- Uyumu bozan faktörler

Uyumu sağlayacak stratejiler önerilebilir

- Tedavi süresiz devam etmeli
  - Bağışıklık sisteminin korunması
  - Virüsün baskılanması

ART Başlarken

BİLGİLENDİRME

- **Hasta bu tedavi ile**
  - **tam şifa bulmayacağını**
  - **virüsün yok edilemediğini anlamalıdır**

- **Bulaştırmamak için önlem almalı**

Hasta Ne İster

- Tanıdığı hekimi görmek
  - Tüm sıkıntılarını anlatmak
- Cinsel yaşamda değişiklik olmasın
- Evlenmek ….. Çocuk
- Kontrole gelmek ?????
- Seyahat
- Tek doz tedavi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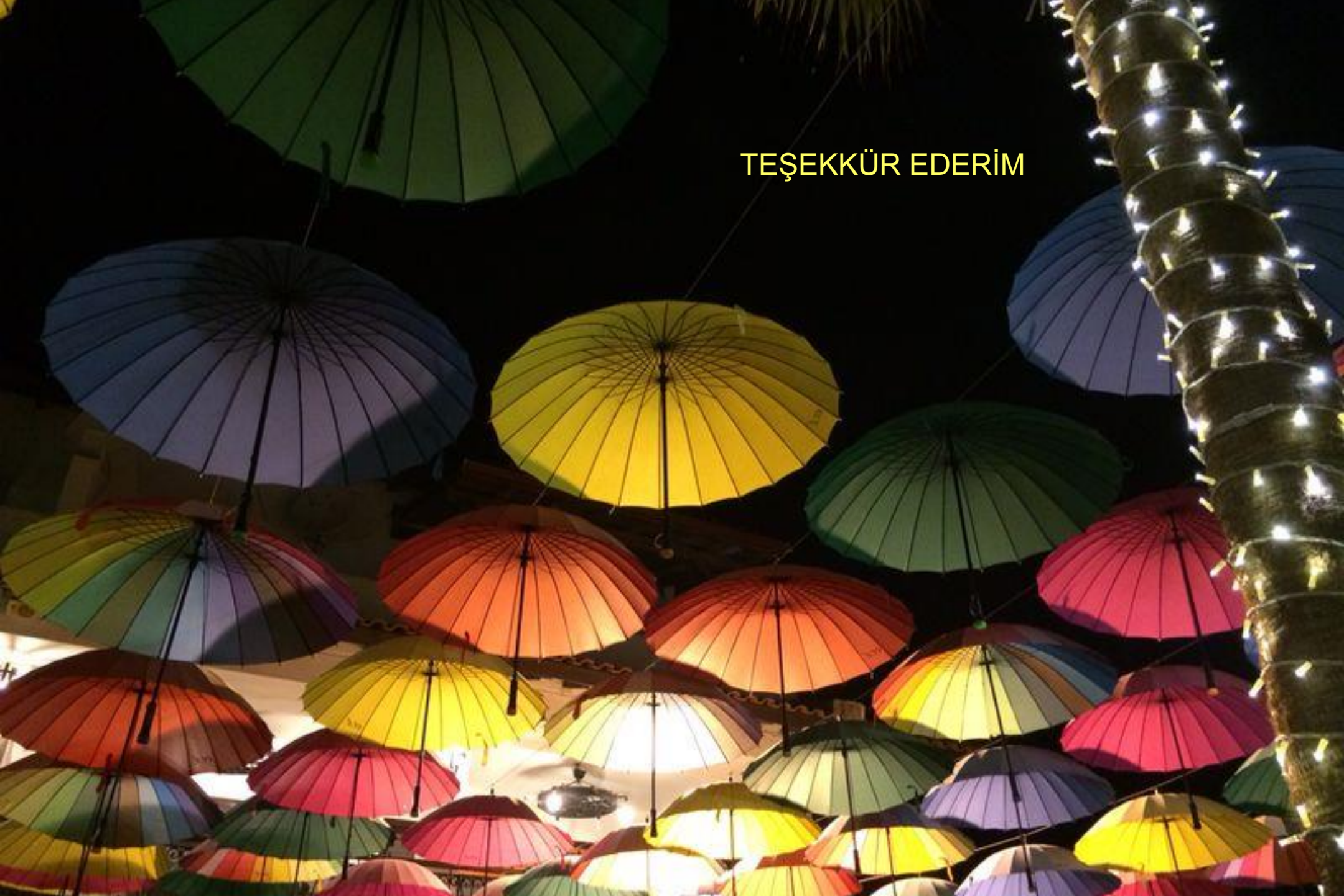
€ 39,95


TEŞEKKÜR EDERİM