
Genvoya®
elvitegravir 150mg/kobisistat 150mg/emtrisitabin 200mg/tenofovir alafenamid 10mg tablet
ETKİLİLİK
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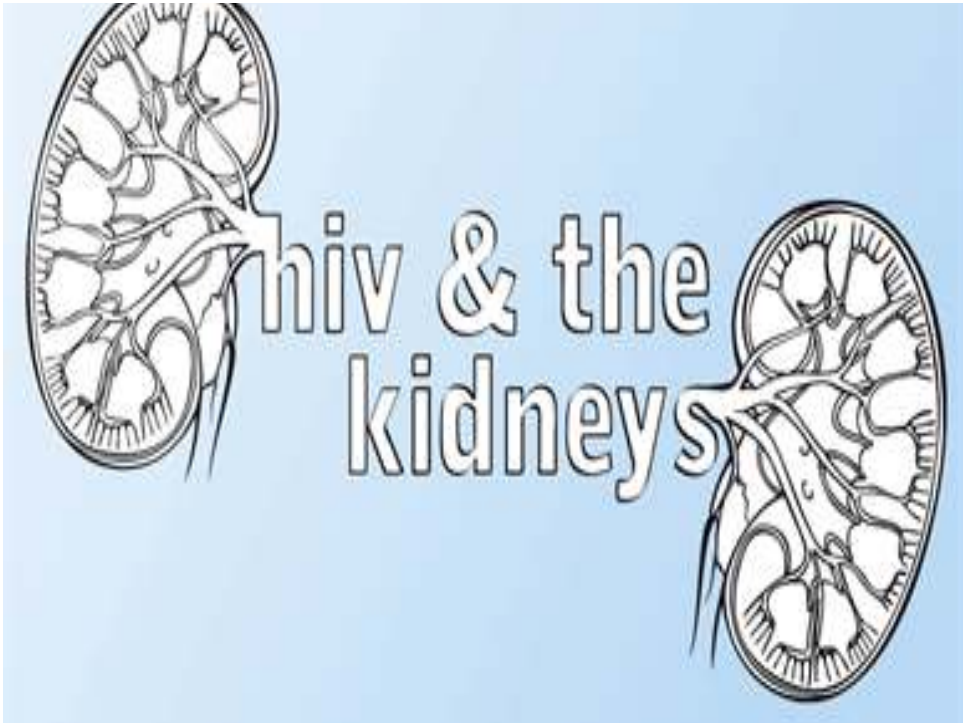
KOLAYLIK
GELECEĞE TAŞIYAN GÜÇ

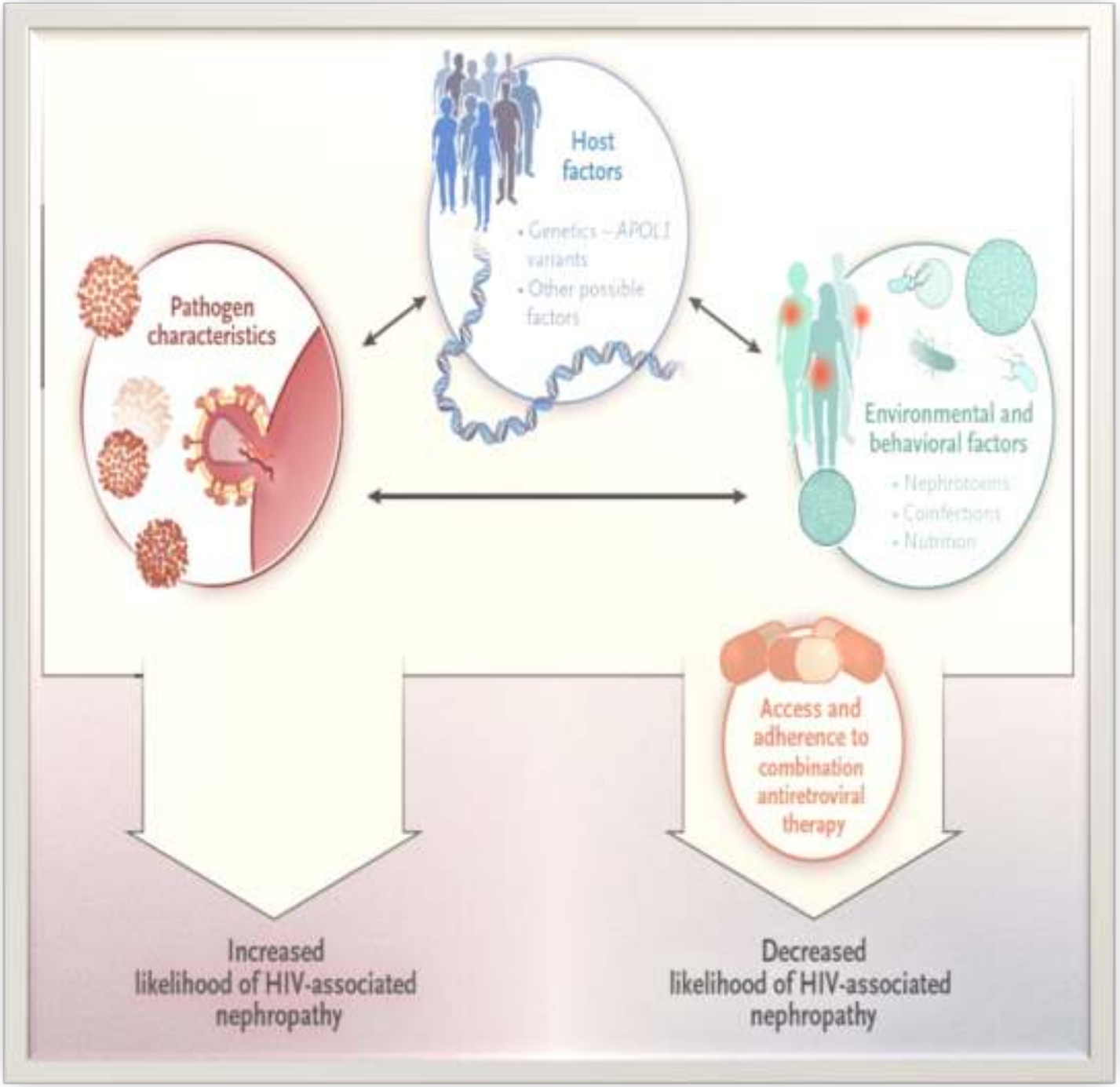
HIV ve Böbrek

Dr. İzzet Hakkı Arıkan

Marmara Üniversitesi Tıp Fakültesi

Nefroloji Bilim Dalı




Host factors
• Genetics – APOL1 variants
• Other possible factors
Pathogen characteristics
Environmental and behavioral factors
• Nephrotoxins
• Coinfections
• Nutrition
Access and adherence to combination antiretroviral therapy
Increased likelihood of HIV-associated nephropathy
Decreased likelihood of HIV-associated nephropathy

Kidney disease in the setting of HIV infection: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference

OPEN

Charles R. Swanepoel[1], Mohamed G. Atta[2], Vivette D. D'Agati[3], Michelle M. Estrella[4], Agnes B. Fogo[5], Saraladevi Naicker[6], Frank A. Post[7], Nicola Wearne[1], Cheryl A. Winkler[8], Michael Cheung[9], David C. Wheeler[10], Wolfgang C. Winkelmayer[11] and Christina M. Wyatt[12]; for Conference Participants[13]

Kidney International (2018) **93,** 545–559;

HIV pozitif kişilerde akut ve kronik böbrek hastalığı riski artmıştır

Antiretroviral group	Kidney damage mechanism	Kidney manifestations
NRTI		
Abacavir	Inhibition of mitochondrial DNA polymerase; oxidative phosphorylation and endogenous nucleotide kinases	AKI, AIN (case report)
Didanosine		Fanconi or Fanconi-like syndrome
Lamivudine		Type B lactic acidosis
Stavudine		Nephrogenic diabetes insipidus (case reports)
Zidovudine		
NtRTI		
Tenofovir	Direct proximal tubular epithelial cells toxicity Intracellular accumulation Mitochondrial depletion	Fanconi syndrome Nephrogenic diabetes insipidus AKI Osteomalacia
NNRTI		
Efavirenz	Unknown	Minimal change disease (case report)
Nevirapine	Hypersensitivity	Urolithiasis (case report) AKI (case reports)
Protease inhibitors		
Indinavir	Intratubular drug precipitation due to poor solubility (mainly for indinavir, atazanavir)	AKI and CKD Acute and chronic interstitial nephritis Nephrolithiasis, asymptomatic crystalluria, crystal nephropathy Papillary necrosis
Atazanavir		
Nelfinavir		
Amprenavir		
Saquinavir		
Lopinavir		
Ritonavir		
Integrase inhibitors		
Raltegravir	Skeletal muscle toxicity	Rhabdomyolysis and AKI (case reports)

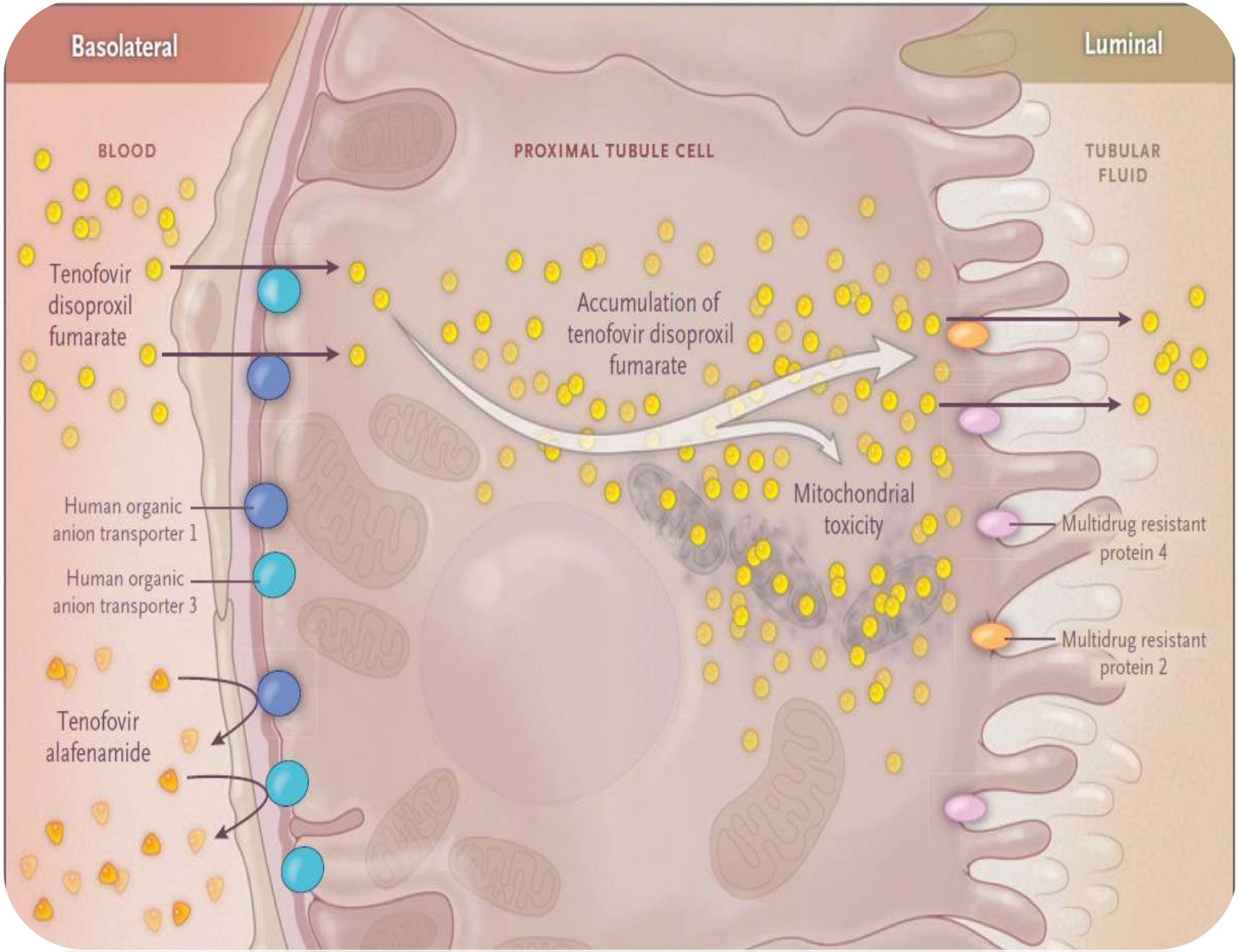
Campos P, et al. Clin J Kidney 2016;9:7772-781

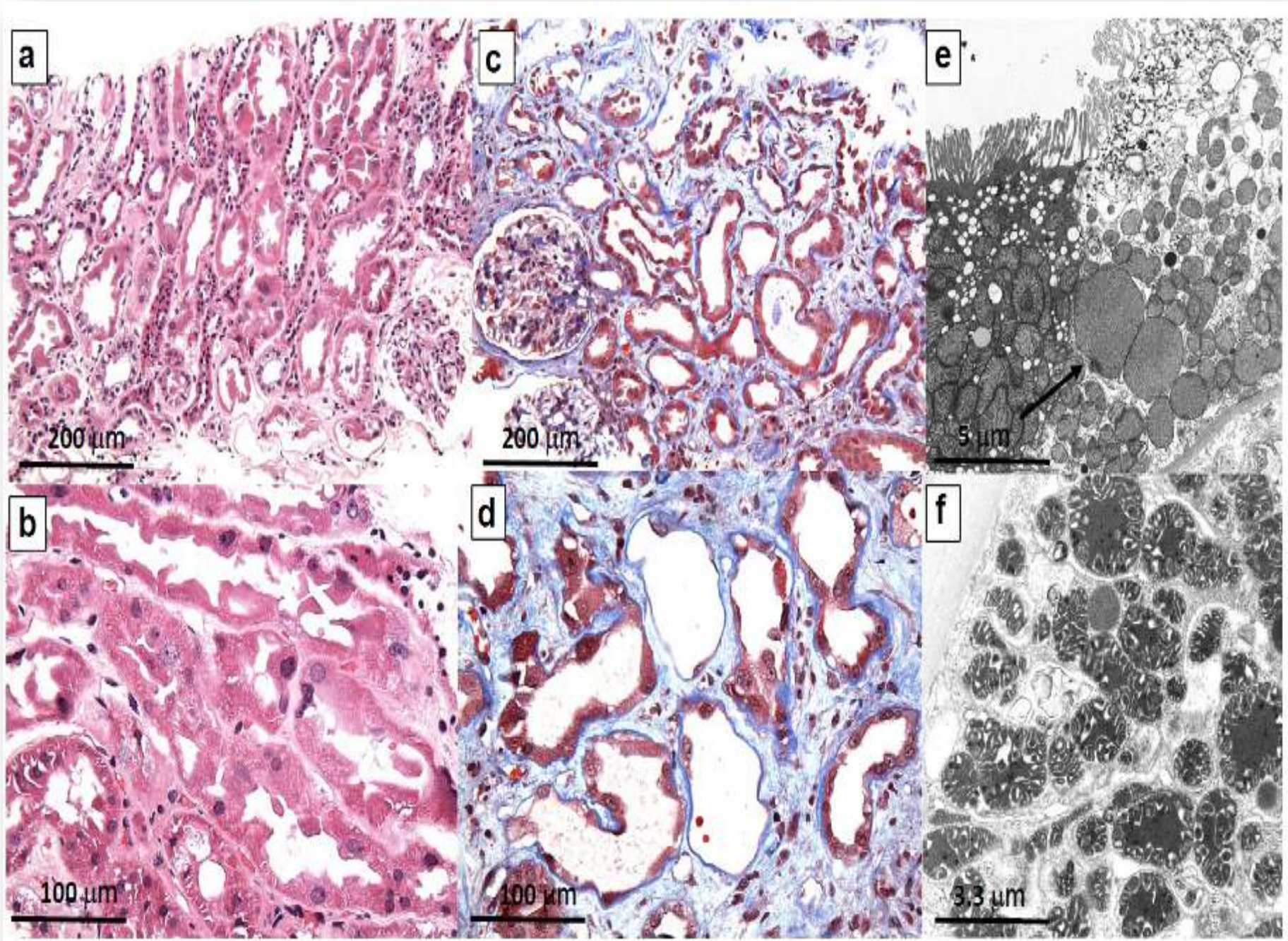
Tenovofir Disoproxil Fumarata (TDF) Nefrotoksisitesi

- Önemli kümülatif nefrotoksisite potansiyeli
- Subklinik proksimal tübüler fonksiyon bozukluğu

  Düşük derecede proteinüri ve ciddi fosfatüri sık
- Tübülopati için risk faktörleri

  Yaş, immün yetersizlik, diyabet, uzun süreli kullanım, didanosine veya ritonovir boosted protease inhibitörleri ile beraber kullanımı
- Ciddi tübülopati eGFR'de azalma, osteomalazi ve kemik kırıklarına yol açabilir
- eGFR'de azalma ve proteinüri (hızlı da olabilir)


Basolateral
Luminal
BLOOD
PROXIMAL TUBULE CELL
TUBULAR FLUID
Tenofovir disoproxil fumarate
Accumulation of tenofovir disoproxil fumarate
Mitochondrial toxicity
Human organic anion transporter 1
Human organic anion transporter 3
Multidrug resistant protein 4
Multidrug resistant protein 2
Tenofovir alafenamide


a
200 µm
c
200 µm
e
5 µm
b
100 µm
d
100 µm
f
3.3 µm

ART ve Nefrotoksisite

- TAF, abacavir ve darunavir varlığında

  - KBH (eGFR < 60 ml/dk) veya hızlı eGFR azalmasında (>3-5 ml/dk/1.73 m2 her yıl) veya KBH için yüksek riskli olanlarda TDF, atazanavir ve lopinavir/ritonavir kullanılmaması

Tenovofir Disoproxil Fumarata (TDF) Nefrotoksisitesi

Renal fonksiyonlarda iyileşme

- TDF kesilmesi veya
- TDF'nin tenofovir alafenamide (TAF)'e değiştirilmesi

HIV + KBH

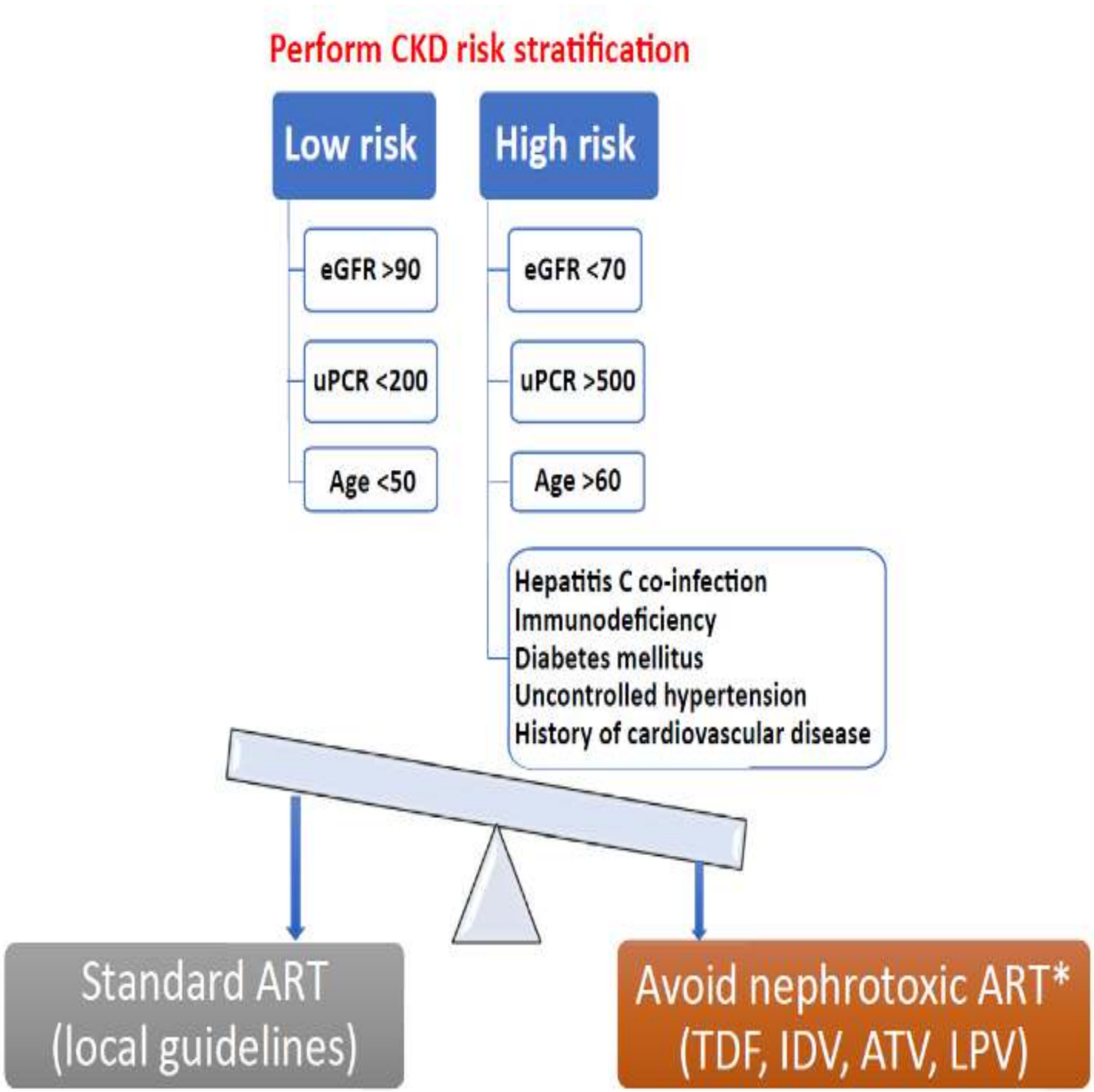
Geleneksel Risk Faktörleri

- Yaş
- Diyabet
- Hipertansiyon
- KV hastalık
- Geçirilmiş ABH

HIV ile ilişkili Risk Faktörleri

- Düşük CD4 sayısı
- Yüksek viral yük
- IV ilaç kullanımı
- HCV ko-infeksiyonu
- cART
  - Tenofovir
  - İndanavir
  - Lopinavir/ritonavir
  - Atanazavir/ritonavir
  - Abacavir

Sıklığı %4.7- 7.9 (eGFR < 60 ml/dk)- Kuzey Amerika ve Avrupa
-Düşük GFR veya proteinüri (%33)


Perform CKD risk stratification
Low risk
High risk
eGFR >90
uPCR <200
Age <50
eGFR <70
uPCR >500
Age >60
Hepatitis C co-infection
Immunodeficiency
Diabetes mellitus
Uncontrolled hypertension
History of cardiovascular disease
Standard ART
(local guidelines)
Avoid nephrotoxic ART*
(TDF, IDV, ATV, LPV)

Kronik Böbrek Hastalığı Taraması

- HIV tanısı anında
- ART başlangıcında ve modifikasyonunda

HIV Hastalarında Renal Değerlendirme

- **Serum kreatinin temelli ölçümler ve hesaplamalar**

  - 24 saatlik idrarda kreatinin klirensi (ölçüm)

  - eGFR (yaş, cinsiyet, ırk, serum kreatinin)

  MDRD

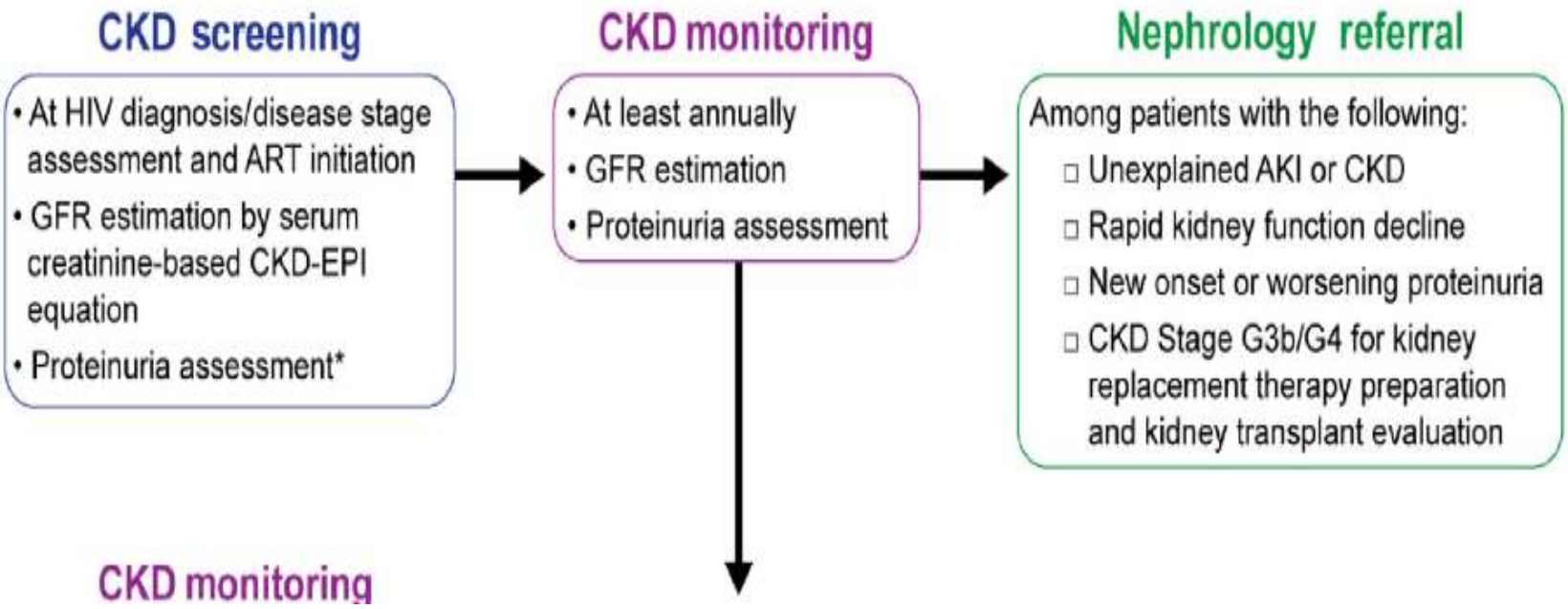
  CKD-EPI (önerilen)

  Cockcroft and Gault formula (+ağırlık; - ırk) (malnutrisyonda)

HIV Hastalarında İdrar Analizi

- Tüm hastalara
- Proteinüri ve/veya hematüri
- Kantitatif proteinüri (idrar albümin/kreatinin veya protein/kreatinin oranı)
- TDF alanlarda idrar glukoz ve serum fosfor

Kidney International (2018) **93,** 545–559;



CKD monitoring

Low CKD risk	• Yearly during follow-up (if clinically stable and virologically suppressed)** • Before and 1 month after ART modification • GFR estimation • Proteinuria assessment
High CKD risk	• Twice yearly during follow-up (if clinically stable and virologically suppressed)** • Before and 1 month after ART modification • GFR estimation • Proteinuria assessment
On TDF plus ritonavir or cobicistat	• Twice yearly during follow-up (if clinically stable; more frequently if eGFR decline or marked hypophosphatemia is present) • GFR estimation • Proteinuria assessment • Serum phosphorus • Urinalysis • Fractional excretion of phosphate and urinary low-molecular weight protein in those suspected to have developed proximal tubulopathy
Established CKD	• Follow KDIGO guidelines for monitoring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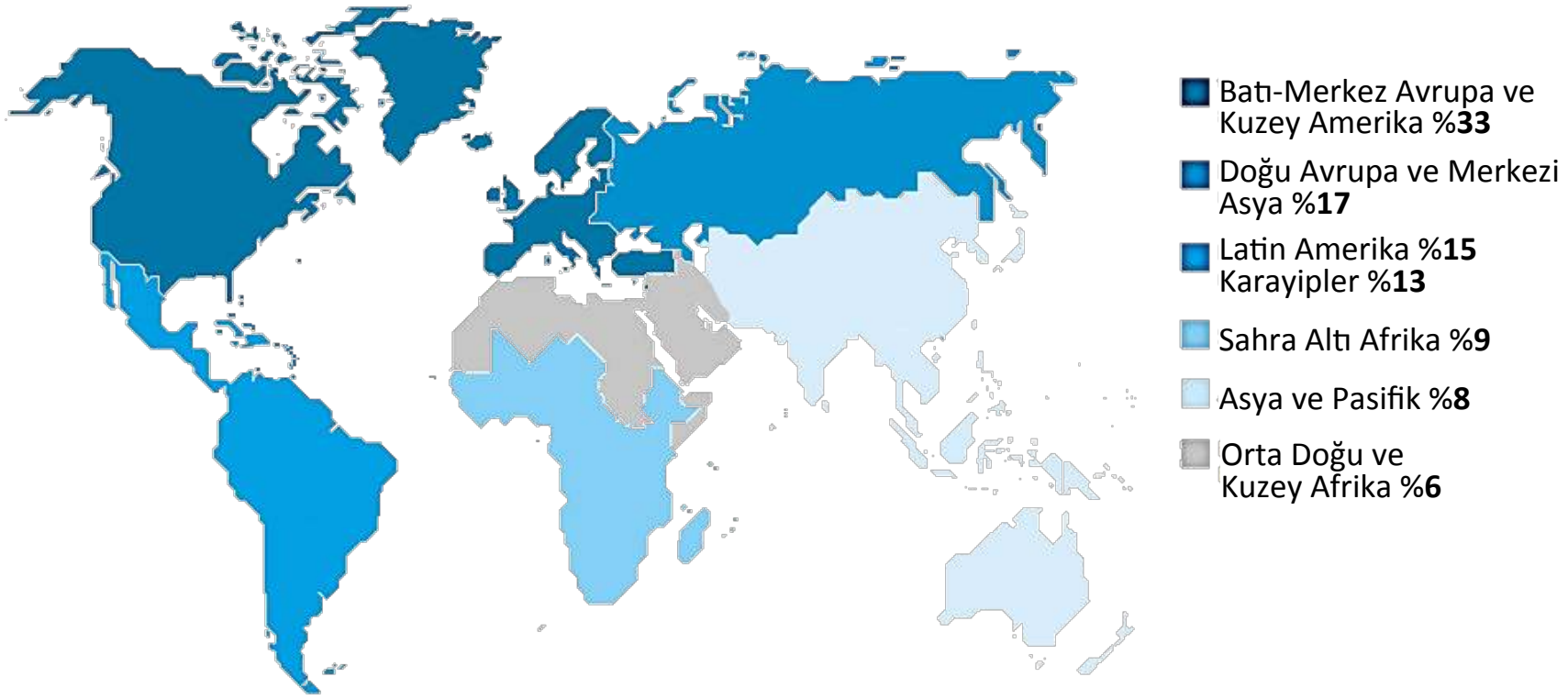
HIV Tedavisinde Karşılanmamış İhtiyaçlar ve HIV Tedavisi

Dr Özlem Altuntaş Aydın
SBÜ Bakırköy Dr Sadi Konuk EAH

Yaşlı HIV pozitif hastaların oranı artmaktadır

Bölgelere göre tahmini 50 yaş üstü HIV pozitif hasta yüzdeleri, 2012



HIV and Aging. A special supplement to the UNAIDS report on global AIDS epidemic 2013

HIV enfeksiyonu ve ART uzun dönemde çok sayıda farklı sağlık alanını etkiler

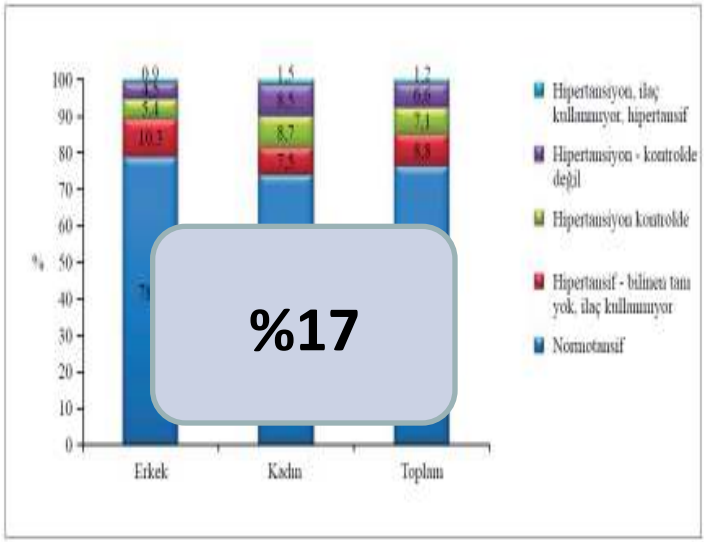
ART kullanan ve 3 veya daha fazla komorbiditesi olan hastalar[1]

Komorbiditedeki artışın en önde gelen nedenleri kardiyovasküler hastalık ve kronik böbrek hastalığıdır[1]

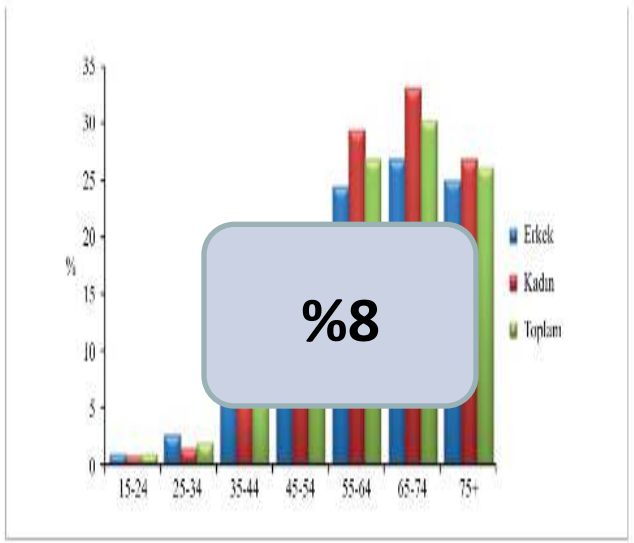
HIV+ kişilerde bugün ve gelecekte komorbiditeyi azaltmak için şimdi ne yapabilirsiniz?

1. Smit M, Cassidy R, Cozzi-Lepri A, et al. Quantifying the future clinical burden of an ageing HIV-positive population in Italy: a mathematical modelling study. HIV Drug Therapy, Glasgow 2016, October 23-26, 2016. Abstract PT68.

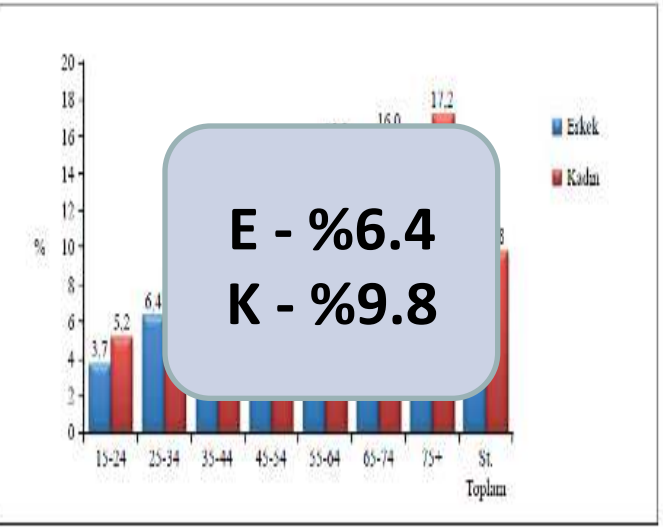
HIV ile ilişkili olmayan komorbiditeler



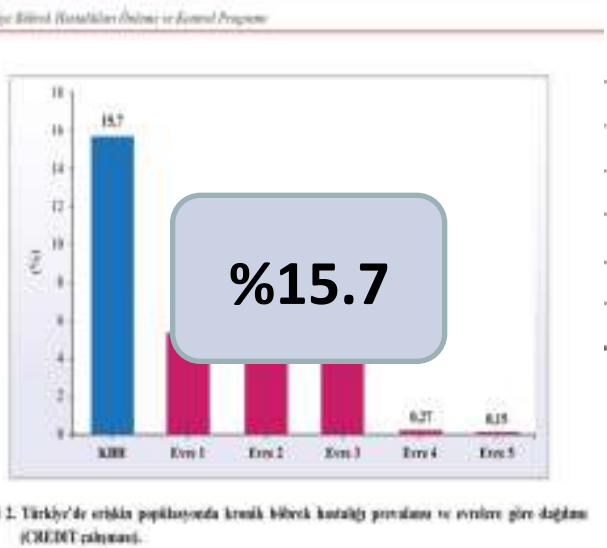
Şekil 6.1 Ölçümle elde edilen sonuçlar ve öyküye göre toplumda kan basıncının dağılımı, Türkiye 2011.



Şekil 7.4 Cinsiyete ve yaş gruplarına göre diyabet prevalansı, Türkiye 2011.



Şekil 13.1 Erkek ve kadınlarda yaşa göre anjina pektoris sıklığı, Türkiye 2011.



Şekil 2. Türkiye'de erişkin popülasyonda kronik böbrek hastalığı prevalansı ve evrelere göre dağılımı (CREDIT çalışması).

es Res 2013;5:481-488;

Osteoporos Int. 2012 Mar;23(3):949-55. doi: 10.1007/s00198-011-1655-5. Epub 2011 May 19.

Incidence of hip fracture and … the FRACTURK study.

Tuzun S[1], Eskiyurt N, Akarirmak U, Saridogan … iety.

Author information

Abstract

The incidence of hip fractures in Turkey in … FRAX® models for Turkey should be revised.

INTRODUCTION: The MEDOS study in 19… xceptionally low rates of hip fracture. The aim of the FRACTURK study was to estim… e of osteoporosis in Turkey.

METHODS: Hip fracture cases in 2009 we… of 26,424 residents aged 50 years or more in 12 different regions of Turkey and… ed by DXA in an age-stratified sample of 1,965 men and women.

RESULTS: Hip fracture incidence in the co… urvey. The age-specific incidence in men and women was substantially higher than … maining lifetime probability of a hip fracture was 3.5% in men and 14.6% in w… res estimated in Turkey, 73% of which were found in women. Assuming no chang… p fractures was expected to increase to nearly 64,000 in 2035. The prevalence of … nen and women, respectively, aged 50 years or more.

CONCLUSION: Although Turkey is still among the countries with low hip fracture rates in Europe, the incidence has increased markedly in the last 20 years. This finding can be used to recalibrate fracture risk assessment models for Turkey.

BRAZ J INFECT DIS. 2013;17(6):707–711

The Brazilian Journal of INFECTIOUS DISEASES

www.elsevier.com/locate/bjid

ELSEVIER

Brief communication

Prevalence and risk factors of osteopenia/osteoporosis in Turkish HIV/AIDS patients

Ozlem … lu[b], Mery…

[a] Hasek…
[b] Hasek…
[c] Hasek…

126 HIV-enfekte olguda DXA
Ort yaş 40.1, %85 erkek, %35.7 AIDS, %63.5 ART kullanıyor
Ort CD4:313/mm3, HIVRNA: 5.2 log10 kp/ml
%53.9 osteopeni, %23.8 osteoporoz
Erkeklerde (öz genç ve MSM) osteoporoz daha sık
Yüksek viral yük, ART kullanımı ve süresi osteoporoz ile ilişkili

Which HIV patients should be screened for osteoporosis: an international perspective

Elena Alvarez[a], Waldo H. Belloso[b], Mark A. Boyd[c], Ahmet Ç. Inkaya[d], Evelyn Hsieh[e], Andrew Kambugu[f], Greg Kaminski[g], Esteban Martinez[h], Hans-Jürgen Stellbrink[i], Sharon Walmsley[j], Todd T. Brown[k], and Patrick W.G. Mallon[a,l]

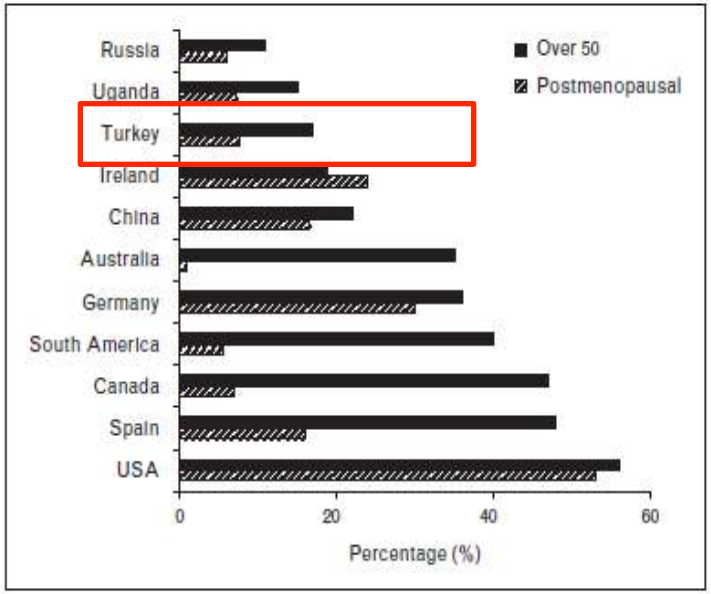


FIGURE 1. Geographical distribution of HIV patients over the age of 50 and postmenopausal women based on HIV cohort data provided by HIV and bone expert clinicians from 11 countries.

Eurasia

Turkey

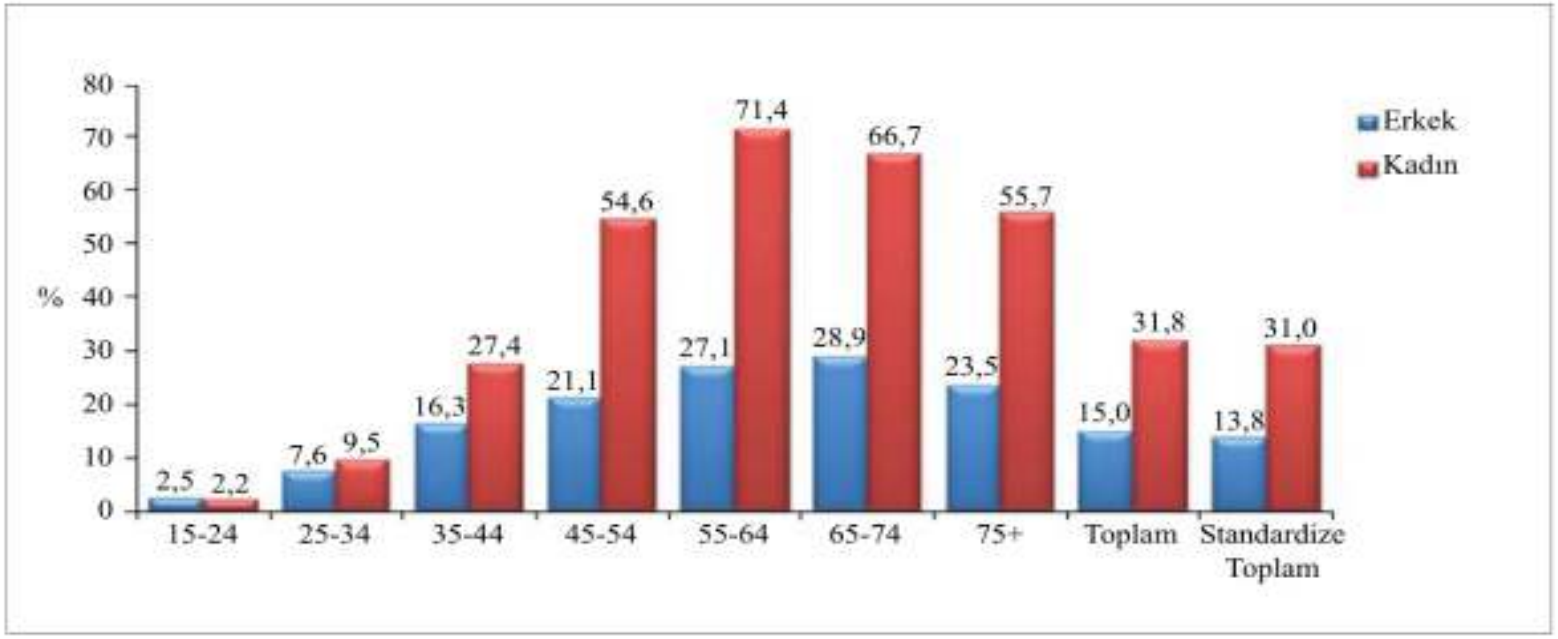
Source: HIV cohort of study participants from the Hacettepe University in Ankara.

The HIV cohort of the Hacettepe University attends 440 PLWH of whom approximately 17% are aged over 50 and 1.7% are postmenopausal women. Nearly 15% of the overall treatment cohort are women, with approximately half adhering to faith-led clothing practices that involve covering almost the entire body, greatly reducing overall sun exposure. Although almost half of those newly diagnosed with HIV have low BMD, only a handful of fractures have been observed, most in those with advanced HIV or older age. Although there are no

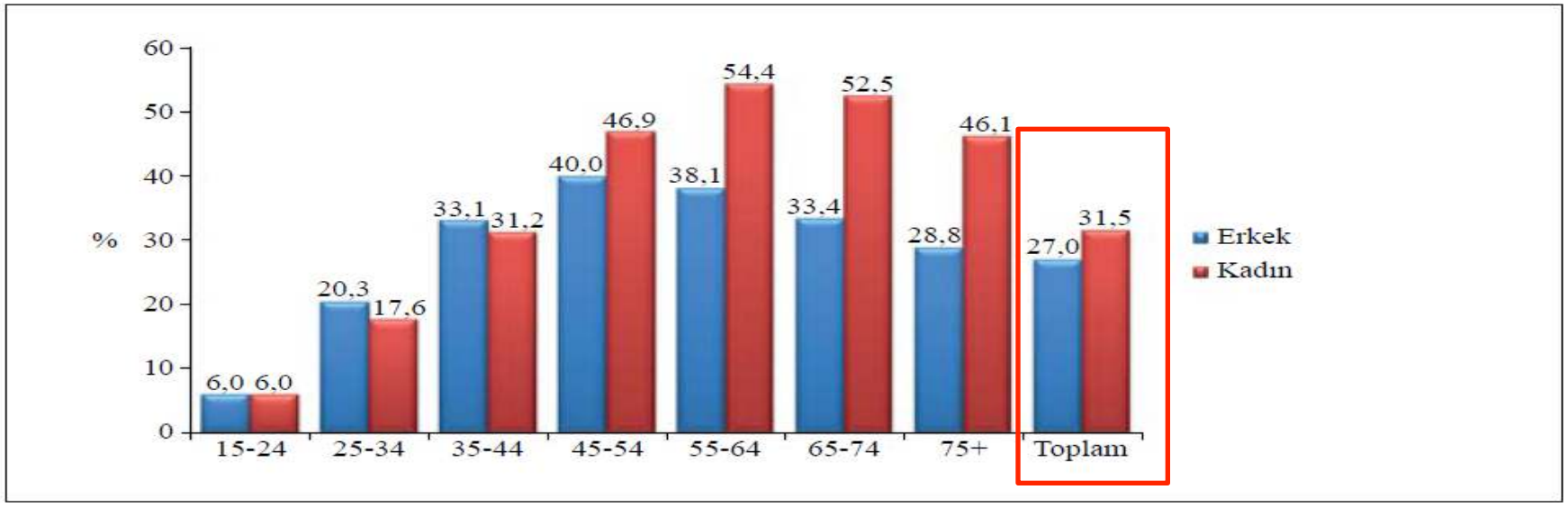
Although centres reported significant numbers of PLWH aged over 50 (Table 1), overall most centres report only a limited experience of fractures, with only one centre (USA) reporting significant fragility fractures. It is notable, however, that this clinic population also has one of the highest proportions of both older patients (56% over 50 years old) and postmenopausal women (53%) of any of the centres contributing perspectives.

10.1 Giriş

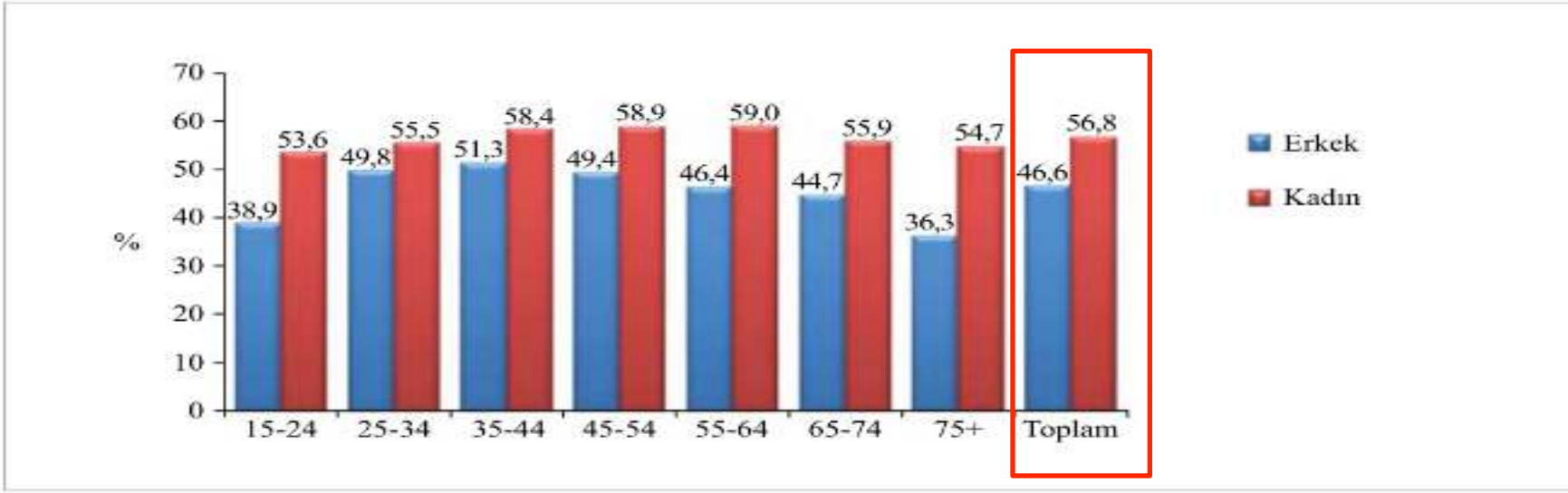
Metabolik Sendrom (MS) kardiyovasküler hastalıkların önemli risk etmenlerinden biridir (1). MS varlığı KKH gelişme riskini 2 kat artırmaktadır. Metabolik sendromu; abdominal obezite, hiperglisemi ya da insülin direnci ya da tip 2 diyabet varlığı, yüksek kan basıncı ve dislipidemi gibi metabolik risk etmenleri oluşturmaktadır (2). Gelişmekte olan ülkelerde modern yaşam biçim değişikliklerine bağlı olarak yüksek kalorili ve yağdan zengin besin alımı ve düşük düzeyde fiziksel aktivite MS görülme sıklığında artışa yol



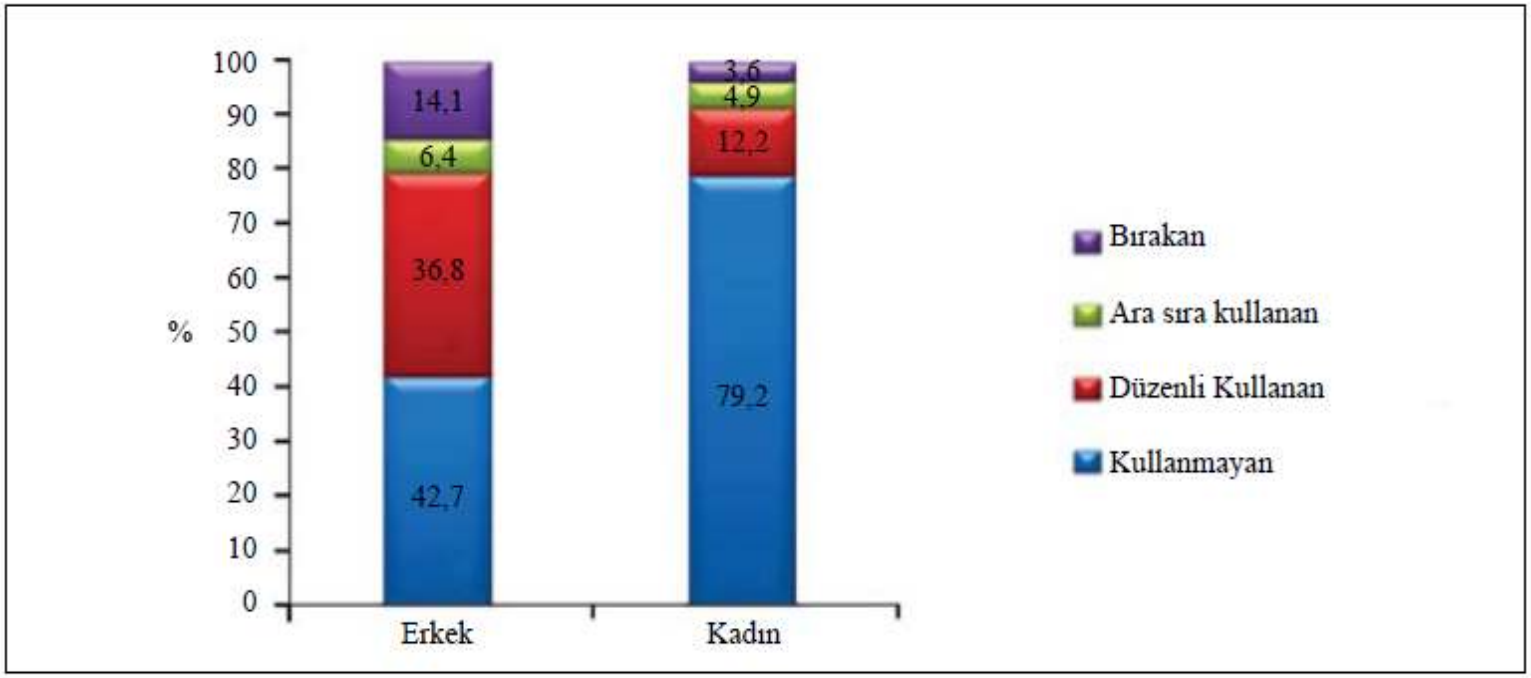
Şekil 10.1 Yaşa ve cinsiyete göre metabolik sendrom sıklığı, Türkiye 2011.



Şekil 8.1 Yaşa ve cinsiyete göre yüksek total kolesterol görülme sıklığı, Türkiye 2011.



Şekil 8.5 Yaşa ve cinsiyete göre düşük HDL kolesterol görülme sıklığı, Türkiye 2011.



Şekil 4.1 Kadın ve erkeklerin sigara kullanma durumu, Türkiye 2011.

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60 *Current HIV Research*, 2014, *12*, 60-64

Epidemiological Profile of Naïve HIV-1/AIDS Patients in Istanbul: The Largest Case Series from Turkey[§]

Mucahit Yemisen[1], Özlem Altuntaş Aydın[2], Alper Gündüz[3], Nail Özgüneş[4], Bilgul Mete[*,1], Bahadir Ceylan[5], Hayat Kumbasar Karaosmanoğlu[2], Dilek Yıldız[3], Fatma Sargın[4], Resat Özaras[1] and Fehmi Tabak[1]

reported by the female patients was heterosexual intercourse, and almost all of them acquired the disease from their husbands.

active smoker … nd 291 (35.1%), respe… findings that brought the patient to the hospital were fever, weight

%62.7

Olgu 1

- 26 Y, erkek
- Bekar, Yönetici, sık seyahat
- Bulaş yolu homoseksüel temas

Boğaz ağrısı, kilo kaybı (10 günde 5 kg) nedeniyle tetkik sırasında tanı

Bir ay önce babası MI nedeniyle ex (51 y)
Amcası ve dedesi de 50 yaş civarında MI nedeniyle ex
Annesi tip II DM, HT

- Sigara 12 paket/yıl, alkol – sosyal içici

- Fizik muayene:

  A: 36.6 C T.A: 120/80 mmHg

  Servikal bilateral, 1cm’den küçük, multipl, mobil, ağrısız LAP

  Diğer bulgular doğal

Hb: 13.1 g/dL
Hct: %37
WBC: 5600/mm^3
(%61 PNL, %34 Lenfosit)
Plt: 177 000/mm^3

Sedimentasyon: 10 mm/h
VDRL: negatif
TPHA: negatif

HBsAg: negatif
AntiHBctotal: pozitif
AntiBs: pozitif

AntiHCV: negatif
AntiHAV total: pozitif
Toksoplasma IgG: pozitif
Rubella IgG: pozitif
CMV IgG: pozitif

AKŞ: 82 mg/dL
Üre: 32 mg/dL
Krea: 0.8 mg/dL
ALT: 11 U/L
AST: 19 U/L
T. protein: 8.1 g/dl
Albumin: 4.6 g/dl

T. Kolesterol: 155 mg/dL
LDL: 103 mg/dL
HDL: 28 mg/dL
TG: 118 mg/dL
Ca: 9.2 mg/dL
P: 4 mg/dL
PTH: 56 pg/mL

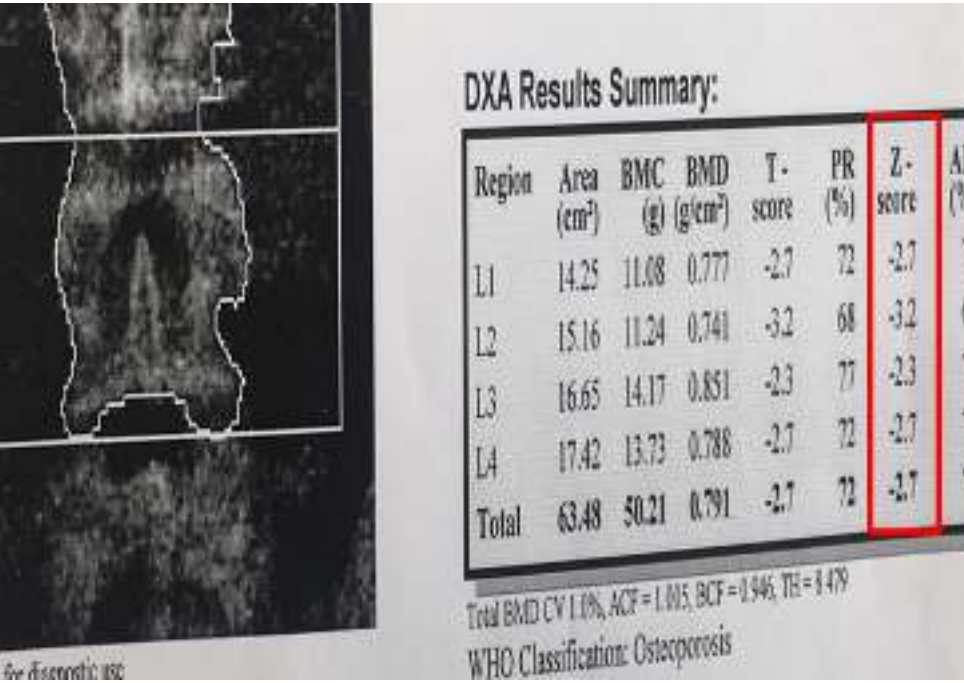
TİT: N bulgular

CD4: 453/mm^3

HIVRNA: HIVRNA: 80712 kp/ml

Akc grf: Doğal

HLAB5701: negatif



DXA Results Summary:

Region	Area (cm^2)	BMC (g)	BMD (g/cm^2)	T-score	PR (%)	Z-score	AM (%)
L1	14.25	11.08	0.777	-2.7	72	-2.7	72
L2	15.16	11.24	0.741	-3.2	68	-3.2	68
L3	16.65	14.17	0.851	-2.3	77	-2.3	77
L4	17.42	13.73	0.788	-2.7	72	-2.7	72
Total	63.48	50.21	0.791	-2.7	72	-2.7	72

Total BMD CV 1.0%, ACF = 1.005, BCF = 0.946, TH = 8.479

WHO Classification: Osteoporosis

DXA Results Summary:

Region	Area (cm^2)	BMC (g)	BMD (g/cm^2)	T-score	PR (%)	Z-score	AM (%)
Neck	5.34	3.94	0.738	-1.4	79	-1.3	81
Troch	11.74	6.78	0.577	-1.6	74	-1.5	75
Inter	20.28	22.45	1.107	-0.5	93	-0.5	93
Total	37.36	33.16	0.888	-1.0	86	-0.9	87
Ward's	1.00	0.74	0.740	-0.3	94	-0.1	99

Total BMD CV 1.0%, ACF = 1.005, BCF = 0.946, TH = 6.483

Hangi ART ?

EACS European AIDS Clinical Society

Initial Combination Regimen for ART-naïve

A) Recommended regimens (one of the following to be selected)

Regimen	Dosing
2 NRTIs + INSTI	
ABC/3TC/DTG	ABC/3TC/DTG 600/300/50 mg, 1 tablet qd
TAF/FTC or TDF/FTC	TAF/FTC 25/200 mg, 1 tablet qd or TDF/FTC 300/200 mg, 1 tablet qd
+ DTG	+ DTG 50 mg, 1 tablet qd
TAF/FTC/EVG/c or TDF/FTC/EVG/c	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
TAF/FTC or TDF/FTC	TAF/FTC 25/200 mg, 1 tablet qd or TDF/FTC 300/200 mg, 1 tablet qd
+ RAL	+ RAL 400 mg, 1 tablet bid
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
2 NRTIs + PI/r or PI/c	
TAF/FTC or TDF/FTC	TAF/FTC 10/200 mg, 1 tablet qd or TDF/FTC 300/200 mg, 1 tablet qd
+ DRV/c or + DRV/r	DRV/c 800/150 mg, 1 tablet qd or + DRV 800 mg, 1 tablet qd + RTV 100 mg, 1 tablet qd

What to Start: Initial Combination Regimens for the Antiretroviral-Naive Patient (Last updated March 27, 2018; last reviewed March 27, 2018)

The panel has issued the following statement on bictegravir: https://aidsinfo.nih.gov/news/2044/adult-arv-panel-classifies-bic-taf-ftc-as-recommended-initial-regimen-for-hiv.

Panel's Recommendations

- An antiretroviral (ARV) regimen for a treatment-naive patient generally consists of two nucleoside reverse transcriptase inhibitors (NRTIs) in combination with a third active ARV drug from one of three drug classes: an integrase strand transfer inhibitor (INSTI), 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 and Adolescents (the Panel) classifies the following regimens as Recommended Initial Regimens for Most People with HIV (in alphabetical order):
  - Dolutegravir/abacavir/lamivudine[a]—only for patients who are HLA-B*5701-negative (AI)
  - Dolutegravir plus tenofovir/emtricitabine[a,b] (AI)
  - Elvitegravir/cobicistat/tenofovir/emtricitabine[b] (AI)
  - Raltegravir plus tenofovir/emtricitabine[a,b] (AI for tenofovir disoproxil fumarate, AII for tenofovir alafenamide)[a,b]
- To address individual patient characteristics and needs, the Panel also provides a list of Recommended Initial Regimens in Certain Clinical Situations (Table 6).
- Given the many excellent options for initial therapy, selection of a regimen for a particular patient should be guided by factors such as virologic efficacy, toxicity, pill burden, dosing frequency, drug-drug interaction potential, resistance testing results, comorbid conditions, access, and cost. Table 7 provides guidance on choosing an ARV regimen based on selected clinical case scenarios. Table 8 highlights the advantages and disadvantages of different components in a regimen.

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

[a] Lamivudine may substitute for emtricitabine or vice versa.

[b] Tenofovir alafenamide (TAF) and tenofovir disoproxil fumarate (TDF) are two forms of tenofovir approved by the Food and Drug Administration. TAF has fewer bone and kidney toxicities than TDF, while TDF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.

HIV Tedavisi
HAART = 2 NRTI + PI/NNRTI/INSTI

Omurga için nelere dikkat edelim?

Table 8. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (page 1 of 4)

Note: All drugs within an ARV class are listed in alphabetical order.

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
Dual-NRTI	ABC/3TC	• Coformulated with DTG	• May cause life-threatening HSRs in patients positive for the HLA-B*5701 allele. As a result, HLA-B*5701 testing is required before use. • In the ACTG 5202 study, patients with baseline HIV RNA ≥100,000 copies/mL showed inferior virologic responses when ABC/3TC was given with EFV or ATV/r as opposed to TDF/FTC. This difference was not seen when ABC/3TC was used in combination with DTG. • ABC use has been associated with CV disease and cardiac events in some, but not all, observational studies.
	TAF/FTC	• Coformulated with EVG/c or RPV • Active against HBV; a recommended dual-NRTI option for patients with HIV/HBV coinfection • Smaller decline in renal function, less proteinuria, and smaller reductions in BMD than after initiation of TDF/FTC • Approved for patients with eGFR ≥30 mL/min	• TDF is associated with lower lipid levels than TAF, perhaps because TDF results in higher plasma levels of tenofovir, which lowers lipids.
	TDF/FTC	• Coformulated with EFV, EVG/c, and RPV as STRs • Active against HBV; a recommended dual-NRTI option for patients with HIV/HBV coinfection • Better virologic responses than with ABC/3TC in patients with baseline viral load ≥100,000 copies/mL when combined with ATV/r or EFV • Associated with lower lipid levels than ABC or TAF	• Renal toxicity, including proximal tubulopathy and acute or chronic renal insufficiency • Osteomalacia has been reported as a consequence of proximal tubulopathy. • Decreases BMD more than other NRTI combinations

i ABC contraindicated if HLA-B*5701 positive. Even if HLA-B*5701 negative, counselling on HSR risk still mandatory. ABC should be used with caution in persons with a high CVD risk (> 20%).

ii Use this combination only if HBsAg-negative.

iii In certain countries TDF is labelled as 245 mg rather than 300 mg to reflect the concentration of the active metabolite (tenofovir disoproxil). When available, combinations containing TDF can be replaced by the same combinations containing TAF. TAF is used at 10 mg when co-administered with drugs that inhibit P-gp, and at 25 mg when co-administered with drugs that do not inhibit P-gp. The decision whether to use TDF or TAF depends on individual characteristics as well as availability. So far, there are only limited long-term data on TAF.

TAF*** should be considered as a first choice**** over TDF in individuals with:

- established or high risk of CKD, see page 50;
- co-medication with nephrotoxic drugs or prior TDF toxicity, see page 51;

Modern ART

Tek Tablet, Güçlü, Güvenli olmalı

TDF/FTC/EVG/cob

2015

DTG/ABC/3TC

2016

EVG/cob/FTC/TAF

2017

Modern ART

Tek Tablet, Güçlü, Güvenli

GENVOYA

EVG/cob/FTC/TAF

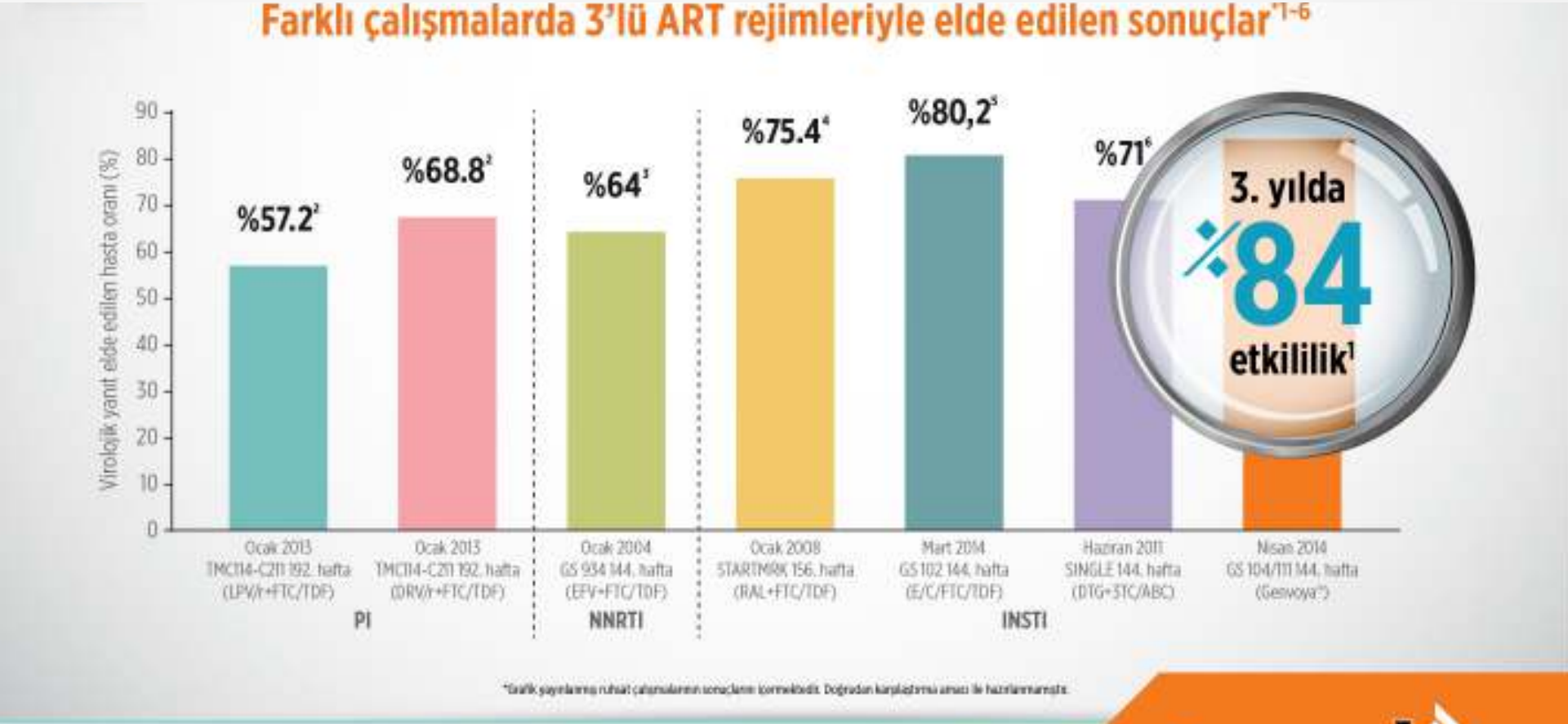
2017

TAF/emtrisitabin/kobisistat/elvitegravir

Alendronat 70 mg/hafta + Kalsiyum + D vitamini

	1. Ay	**3.ay**	**6.ay**
CD4(mm3)		543	586
HIVRNA(kp/ml)	116	-	-

Genvoya tedavi deneyimsiz hastalarda 3. yılın sonunda korunan kalıcı ve güçlü etkililik sağlar



*Grafik yayınlanmış ruhsat çalışmalarının sonuçlarını içermektedir. Doğrudan karşılaştırma amacı ile hazırlanmamıştır.

1. Arribas J, et al. J Acquir Immune Defic Syndr 2017; 75(2): 211–218.
2. Orkin C et al. HIV Med. 2013 Jun;14(7):449-58.
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4. Rockstroh JK, et al. Clin Infect Dis 2011; 53(8): 807–816.
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6. Walmsley SE, et al. J Acquir Immune Defic Syndr 2015; 70(5): 515–519.

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Olgu 2

2009 yılı

42 Y, erkek
Gıda mühendisi, evli
HIV enfeksiyonu ve HBV enf tanısı (evlilik öncesi test)
Olası bulaş yolu – heteroseksüel temas

Özgeçmişinde özellik yok
Annesi HCC ex, babası HT

Sigara 20 paket/yıl, alkol, ilaç, madde kullanımı yok

Fizik muayene doğal

Hb:13.2
Hct: %39
WBC. 4700/mm3
(% 44 PNL,%52 L)

Plt: 182 000

HBsAg: pozitif
HBeAg:negatif
AntiHBctotal: pozitif
AntiBs: negatif
HBVDNA: 6785 kp
AntiHCV: negatif
AntiHAV total: pozitif
Delta Ab: negatif

Sedimentasyon: 17 mm/h
VDRL: negatif
TPHA: negatif

Toksoplasma IgG: pozitif
Rubella IgG: pozitif
CMV IgG: pozitif

AKŞ: 93 mg/dL
Üre: 49 mg/dL
Krea: 0.9 mg/dL
ALT:29 U/L
AST: 28 U/L
T. protein:8.2 g/dl
Albumin: 4.6 g/dl
AFP: 2.3

T. kolesterol: 168 mg/dL
LDL: 109 mg/dL
HDL: 31 mg/dL
TG: 139 mg/dL
Ca: 9.2 mg/dL
P: 4 mg/dL

TİT: normal

Akc grf: doğal
Batın USG: doğal

Fizik muayene doğal

CD4: 477/mm3

HIVRNA: 250807 kp/ml

Recommendations for Initiation of Therapy in Naive HIV-Infected Patients

SYMPTOMATIC	• CDC stage B and C: treatment recommended • If OI, initiate as soon as possible*
ASYMPTOMATIC	• CD4 < 200: Treatment recommended, without delay. • CD4 201-350: treatment recommended. • CD4 350-500: - Treatment recommended if hepatitis C co-infection, hepatitis B co-infection requiring therapy, HIV-associated nephropathy or other specific organ deficiency; - Treatment should be considered if VL>105 c/ml and/or CD4 decline >50-100/mm3/year or age >50 or, pregnancy, high cardiovascular risk, malignancy. • CD4 > 500: - Treatment should generally be deferred, independently of plasma HIV RNA; closer follow-up of CD4 if VL > 105 c/ml. - Treatment can be offered if presence of ≥ 1 of the above co-morbid conditions (CD4 350-500). • Whatever CD4 and Plasma HIV RNA, treatment can be offered on an individual basis, especially if patient is seeking and ready for ARV therapy

HIV/HBV

HIVRNA yüksek

Eşi HIV (-)

2010

TDF/FTC+ EFV
(Sarhoşluk hissi)

	1. ay	3. ay	6.ay	1.yıl	3.yıl	5.yıl
CD4		529	612	686	649	711
HIVRNA	14672	445	-	-	-	-
HBVDNA		-	-	-	-	-

Kan biyokimyasal değerler – Normal TİT: Normal
DXA: Normal

2016 Temmuz

Tek tablet isteği

Sarhoşluk hissinin devam etmesi

Switch Strategies for Virologically Suppressed Persons

Definition of virologically suppressed

Clinical trials exploring switching strategies have defined suppression as a HIV-VL < 50 copies/mL for at least 6 months.

Indications

1. **Documented toxicity** caused by one or more of the antiretrovirals included in the regimen. Examples of these reactive switches: lipoatrophy (d4T, AZT), central nervous system adverse events (EFV), diarrhoea (PI/r) and jaundice (ATV).
2. **Prevention of long-term toxicity.** Example of this proactive switch: prevention of lipoatrophy in patients receiving d4T or AZT.
3. **Avoid serious drug-drug interactions**
4. **Planned pregnancy**
5. **Ageing and/or co-morbidity** with a possible negative impact of drug(s) in current regimen, e.g. on CVD risk, metabolic parameters
6. **Simplification:** to reduce pill burden, adjust food restrictions and improve adherence.

5. Switches of single drugs with the same genetic barrier (for example T-20 for RAL) is usually virologically safe in the absence of resistance to the new compound.
6. Clinicians should carefully review the possibility of drug-drug interactions with the new regimen.
7. If the switch implies discontinuing TDF, clinicians should check the HBV status (avoid discontinuation of TDF in persons with chronic HBV and assess HBV vaccination status).
8. HIV-positive persons should be seen soon (e.g. 4 weeks) after treatment switches to check for maintenance of suppression and possible toxicity of the new regimen.
9. If a HIV-positive person receives and tolerates a regimen that is no longer a preferred option, there is no need to change. Example: persons tolerating EFV-containing regimens.

Strategies not recommended

a. Intermittent therapy, sequential or prolonged treatment interruptions
b. Two-drug combination, i.e. 1 NRTI + 1 NNRTI or 1 NRTI + 1 PI without RTV or 1 NRTI + RAL, or 2 NRTIs or MVC + RAL
c. Triple NRTIs combinations

TDF/FTC/EVG/c

	1. ay	3. ay	6.ay
CD4		702	729
HIVRNA	-	-	-
HBVDNA	-	-	-

2017 Ocak

Krea:1.1 mg/dl

GFR: 75 mL/dk

UP/C: 45

	2017 Nisan	Temmuz	Eylül	Ekim
CD4	727	762		719
HIVRNA	-	-		-
HBVDNA	-	-		-
Kreatinin	1.2	1.2	1.3	1.34
GFR	67.8	68	61.9	59.7
UP/C	48	45	50	53

Table 15. Antiretroviral Therapy-Associated Adverse Events That Can Be Managed with Substitution of Alternative Antiretroviral Agent (page 3 of 3)

Adverse Event	ARV Agent(s) or Drug Class		Comments
	Switch from	Switch to	
Renal Effects Including proximal renal tubulopathy and elevated creatinine	TDF[a]	ABC,[h] or TAF (for patients with CrCl >30 mL/min), NRTI-sparing regimens, or regimens using only 3TC or FTC as the NRTI may be considered if appropriate.	TDF may cause tubulopathy. Switching from TDF to TAF is associated with improvement in proteinuria and renal biomarkers. The long-term impact of TAF on patients with pre-existing renal disease,

HLA B5701: negatif

ABC/3TC/DTG + Entekavir ???
RAL+LPV/r+Entekavir ????

EACS European AIDS Clinical Society

Treatment of HBV/HIV Co-infection

1. All persons with HBV/HIV co-infection should receive ART that includes TDF or TAF unless history of tenofovir intolerance.

10. In case of non-response to HBV vaccinations, ART should contain TDF or TAF.

Modern ART

Tek Tablet, Güçlü, Güvenli

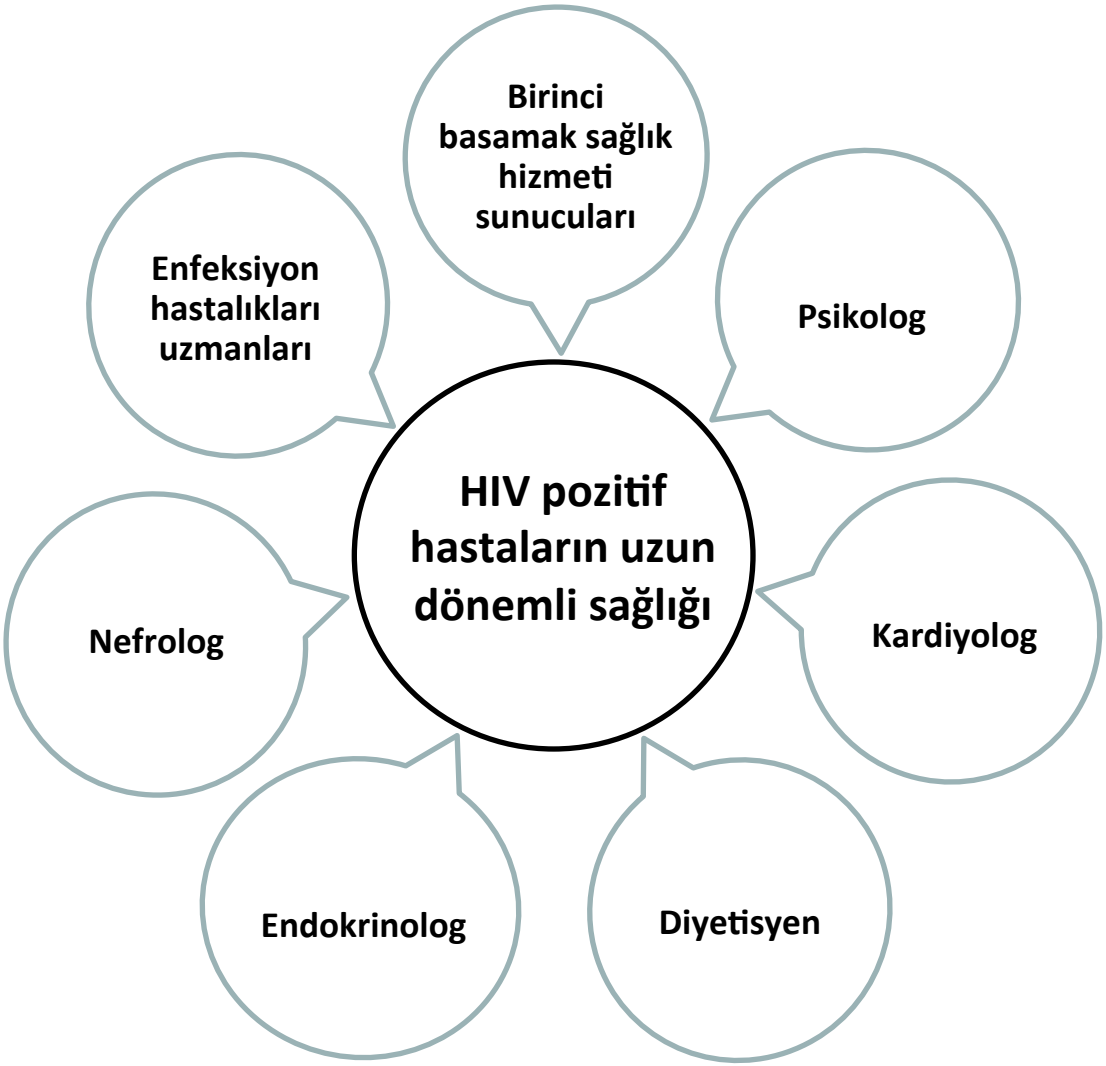
GENVOYA

EVG/cob/FTC/TAF

2017

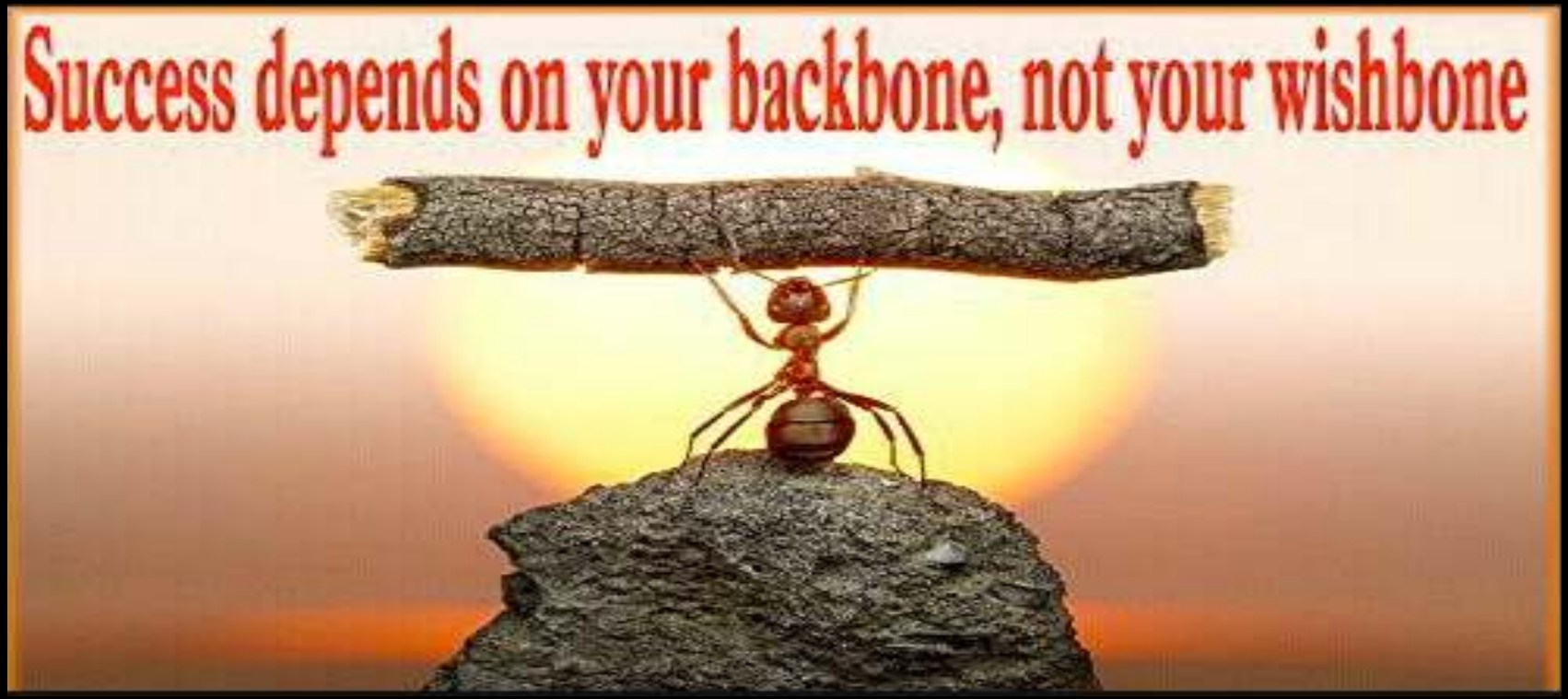
	Kasım	Aralık	Ocak 2018	Nisan
CD4			702	
HIVRNA			-	-
HBVDNA	-		-	-
Kreatinin	1.25	1.19	1.1	1.06
GFR	64.7	68.5	75	78
UP/Krea	42	33	28	15

HIV pozitif hastaların bakımında disiplinlerarası yaklaşım



- Tüm alanlardaki riskin azaltılması ve genel sağlığın iyileştirilmesi amacıyla çalışan **multidisipliner** bir ekibin dahil olduğu standart bakım, yaşlanan HIV pozitif hasta popülasyonuna uzun dönemde fayda sağlayacaktır

Guaraldi G. Germs 2011;1:6–8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- Hastalıkların taranmasını,
- Teşhis edilmesini ve/veya
- Uygun tedavilere ulaşılmasını

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%84

144. haftada virolojik yanıt[1]

Tedavi deneyimli hastalarda

%93

96. haftada virolojik yanıt[2]

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İVCr **30** ml/dk

olan hastalarda onaylı tek tablet rejimi[3]

0

Renal Tübülopati vakası[1,2]

KOLAY KULLANIM

TEDAVİ ÖNCESİ TEST GEREKTİRMEYEN TEK TABLET REJİMİ[3]

YAŞAM KALİTESİNDE ARTIŞ[4]

GÜVENLİLİK

DAHA İYİ KEMİK MİNERAL YOĞUNLUĞU[1]

DAHA İYİ RENAL GÜVENLİLİK[1]

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