Olgular Eşliğinde Genvoya Kullanımı Etkililik ve Güvenlik

Dr Atahan Çağatay

2019

Olgu-I

- 28 yaşında erkek hasta,
- Şikayeti: Halsizlik, ara ara diş eti kanaması,
- Dört yıldır idyopatik trombositopenik purpura tanısıyla Hematoloji uzmanı tarafından yakından takip edilmekteymiş. Yaklaşık bir yıl önce bir anal fissür nedeniyle bir hastanede (Eğitim ve Araştırma Hastanesi) opere edilmiş. 8 ay önce ise almakta olduğu ilaçların etkisiz kaldığı düşüncesiyle (İTP) aynı hastanede splenektomi yapılmış.

Olgu-I

Hasta, kanama diyatezinin gelişmesi üzerine takip eden hematoloji uzmanının (Yurt dışında kongrede olması nedeniyle) önerisiyle bir başka hastanede çalışan hematolog arkadaşına ilgilenmesi için yönlendirilmiş. Hızlı bir değerlendirme sonucunda, ilk değerlendirmede serolojik bazı testlerin bakılmasını da istemiş ve istenen testlerin sonuçları değerlendirildiğinde: anti-HIV testi pozitif gelmiş.

Olgu-I

Doğrulama testi de pozitif olduğunu saptadığımız hasta takibimize alındı (Hematologu tarafından bize yönlendirilmişti).

Fizik muayenede:

Hasta Cushingoid görünümde idi, yüz pleotorik, ensede dolgunlaşma fark edildi. Splenektomi insizyonu gözlendi.

Diğer sistem muayenelerinde özellik yoktu.

Olgu-I

İlaç ve Alışkanlıklar:

Prednizolon 20 mg/gün

Eltrombopag: 50 mg/gün

Laboratuvar

Hastanın laboratuvar bulguları:

Tam idrar analizi: pH:7
Sedim: Normal
Sedimantasyon 8 mm/saat
CD4: **68/mikrolitre**
HIV RNA **296 000** kopya/mikrolitre
Lökosit 17 500/mikrolitre
Nötrofil: 14 650 (%83.7)
Lenfosit: 1500 (%8.5)
Hemoglobin: 11.6 gr/dl
Trombosit: **98 000/mikrolitre**
Antitoxoplasma IgG:pozitif
AntiCMV IgG: pozitif
VDRL: Negatif
TPHA: Negatif

Olgu-I

- Hastaya Elvitagravir/C/TAF/Emtrisitabin
  - Günde 1 adet
  - Kotrimoksazol 1X1

başlandı.

Altı ay sonra….

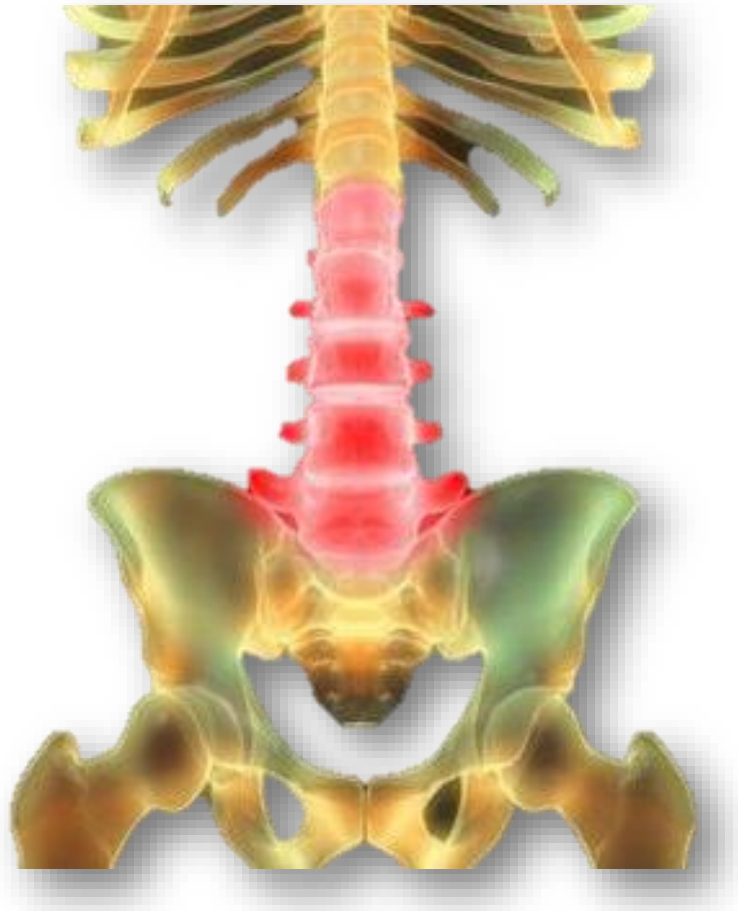
- Hastanın prednizolon ve eltrombopag tedavisi kesildi (kademeli kesildi ve yaklaşık 2 aydır iki ilacı da kullanmamaktaydı)

- Son Değerleri:
  - HIV RNA: SAPTANAMAZ düzeyde
  - CD4+T lenfosit: 290 /mikrolitre
  - **Trombosit: 379 000/mikrolitre**
  - Lökosit: 14 100/mikrolitre
  - Hb: 11.4 gr/dl

Antiretroviral Tedavide Hangi Parametrelere Dikkat Edilmeli?

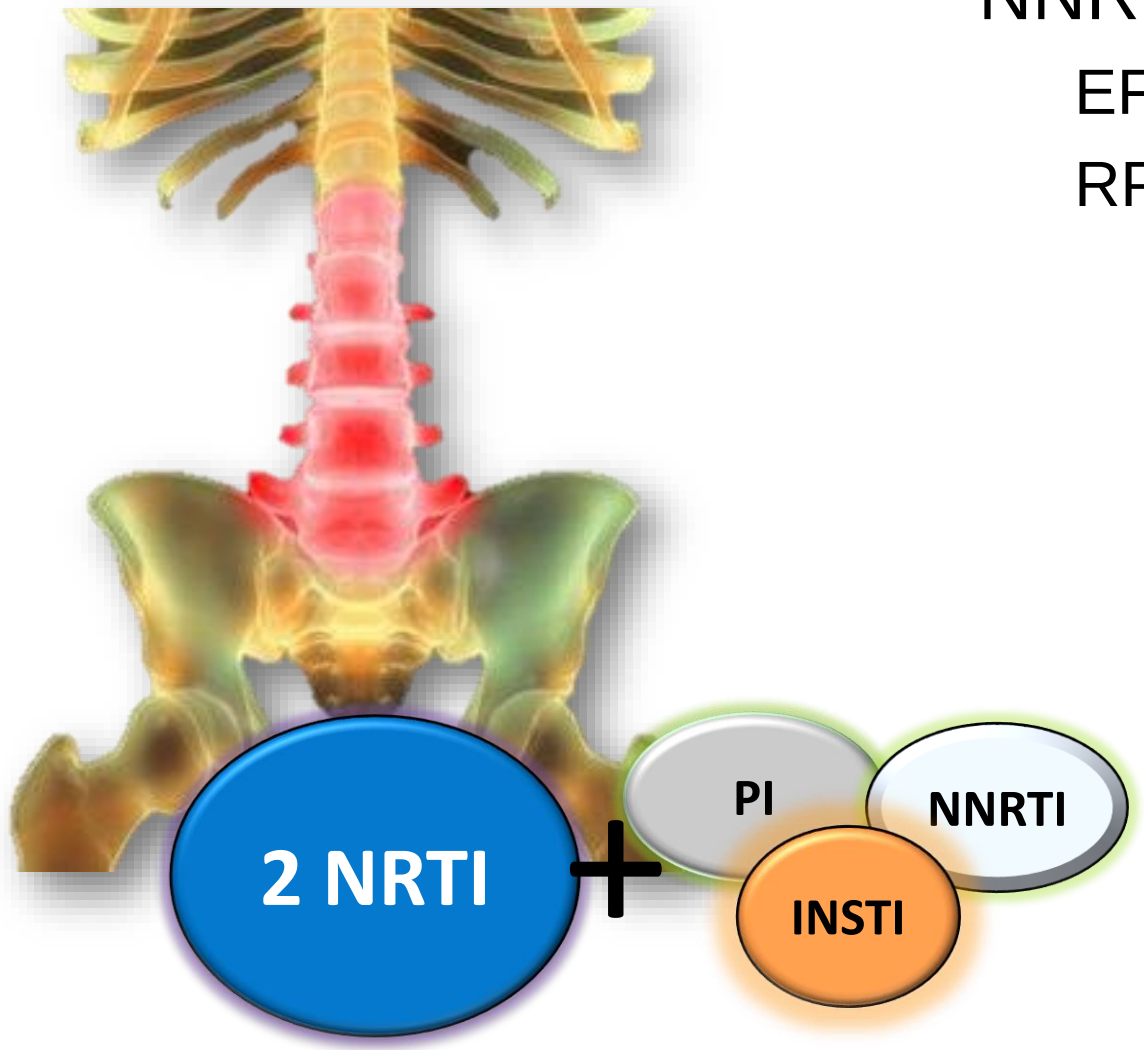
- Etkinlik
- HLA-B 5701
- Kronik HBV koinfeksiyonu
- İlaç direnç anamnezi
- Hali hazırda kullanılan NRTI ilaç hangisi?
  - Emtrisitabin/TDF
  - Abakavir/lamivudin
  - Diğer NRTI
  - NNRTI (efavirenz, rilpivirin)
- Hali hazırda kullanılan 3. ART ilacı hangisi?
  - Dolutegravir
  - Ritonavir destekli PI
  - Elvitegravir/cobicistat
  - Efavirenz veya nevirapin
  - Raltegravir
  - Rilpivirin
- ART'nin hangi komponentinin değiştirilmesi gerekir?

Omurga için seçeneklerimiz neler?



- ABC/3TC
  - HIV RNA < 100.000, güç?
  - HLA-B*5701
  - Kardiyovasküler risk?
- TDF/FTC
  - Kemik ve Böbrek ?
- TAF/FTC
  - Tenofovir'in etkinliği
  - Kemik ve böbrek üzerine nötr

Üçüncü ajanda seçeneklerimiz?



NNRTI
- EFV
- RPV

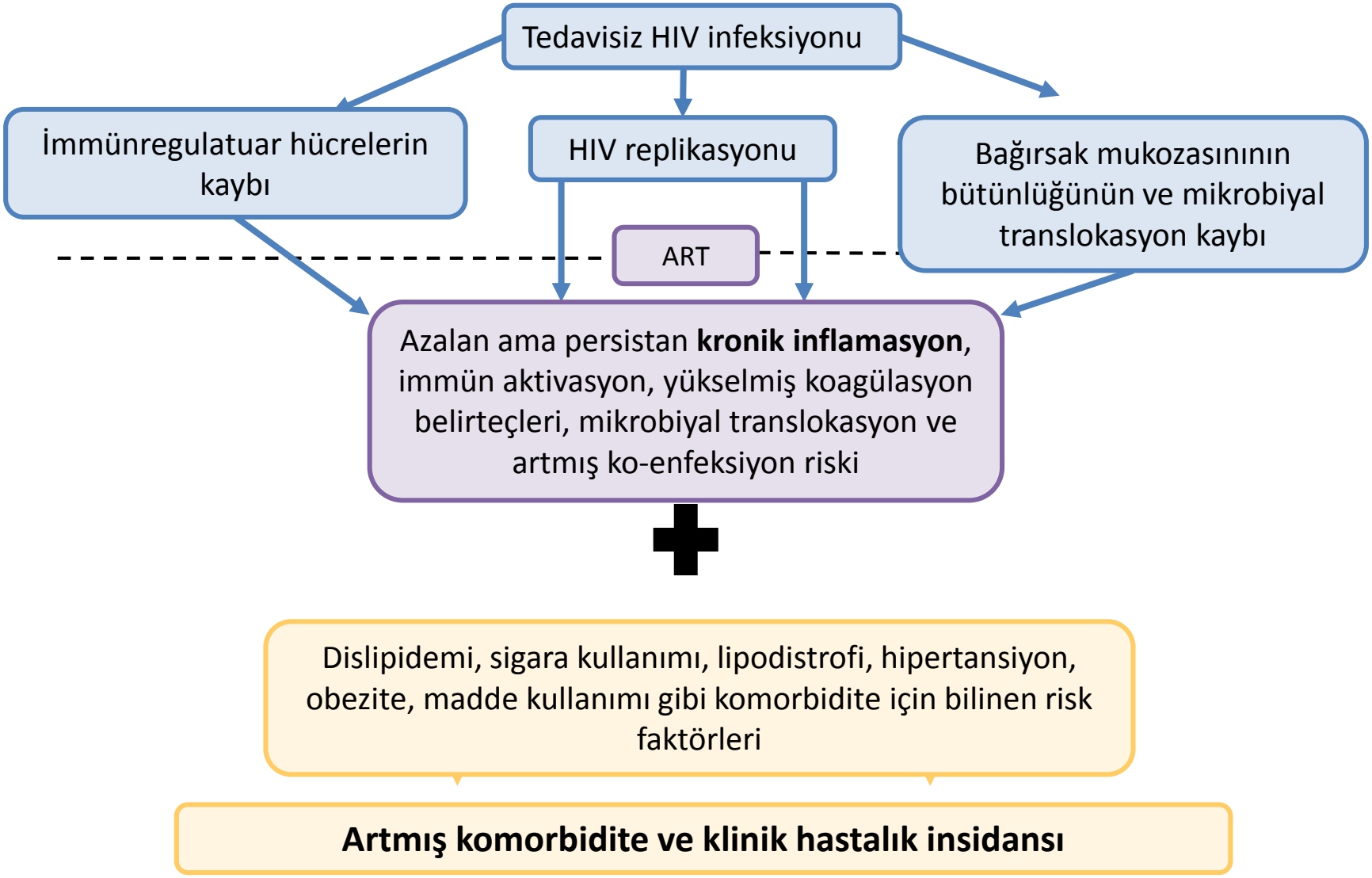
PI/r
- LPV/r
- ATV/r
- DRV/r

INSTI
- EVG/c
- DTG
- RAL

INSTI

- Kılavuzlarda integraz çağı
- Tolerabilite
  - DTG&CNS etkisi?
- Direnç
  - Toplumda integraz direnci?
- İlaç ilaç etkileşimi
  - Cobicistat < Ritonavir (CYP 3A inhib.)

Kronik inflamasyon, HIV pozitif hastalarda artmış komorbidite riskiyle ilişkilidir



Deeks SG. Annu Rev Med 2011;62:141–155

İnflamatuvar Belirteçler Açısından Eşdeğer Azalma !!

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Research Paper

Equivalent Decline in Inflammation Markers with Tenofovir Disoproxil Fumarate vs. Tenofovir Alafenamide

Nicholas T. Funderburg [a,*], Grace A. McComsey [b,c], Manjusha Kulkarni [a], Tammy Bannerman [a], Jessica Mantini [a], Bernadette Thornton [a], Hui C. Liu [d], Yafeng Zhang [d], Qinghua Song [d], Liang Fang [d], Jason Dinoso [d], Andrew Cheng [d], Scott McCallister [d], Marshall W. Fordyce [d], Moupali Das [d]

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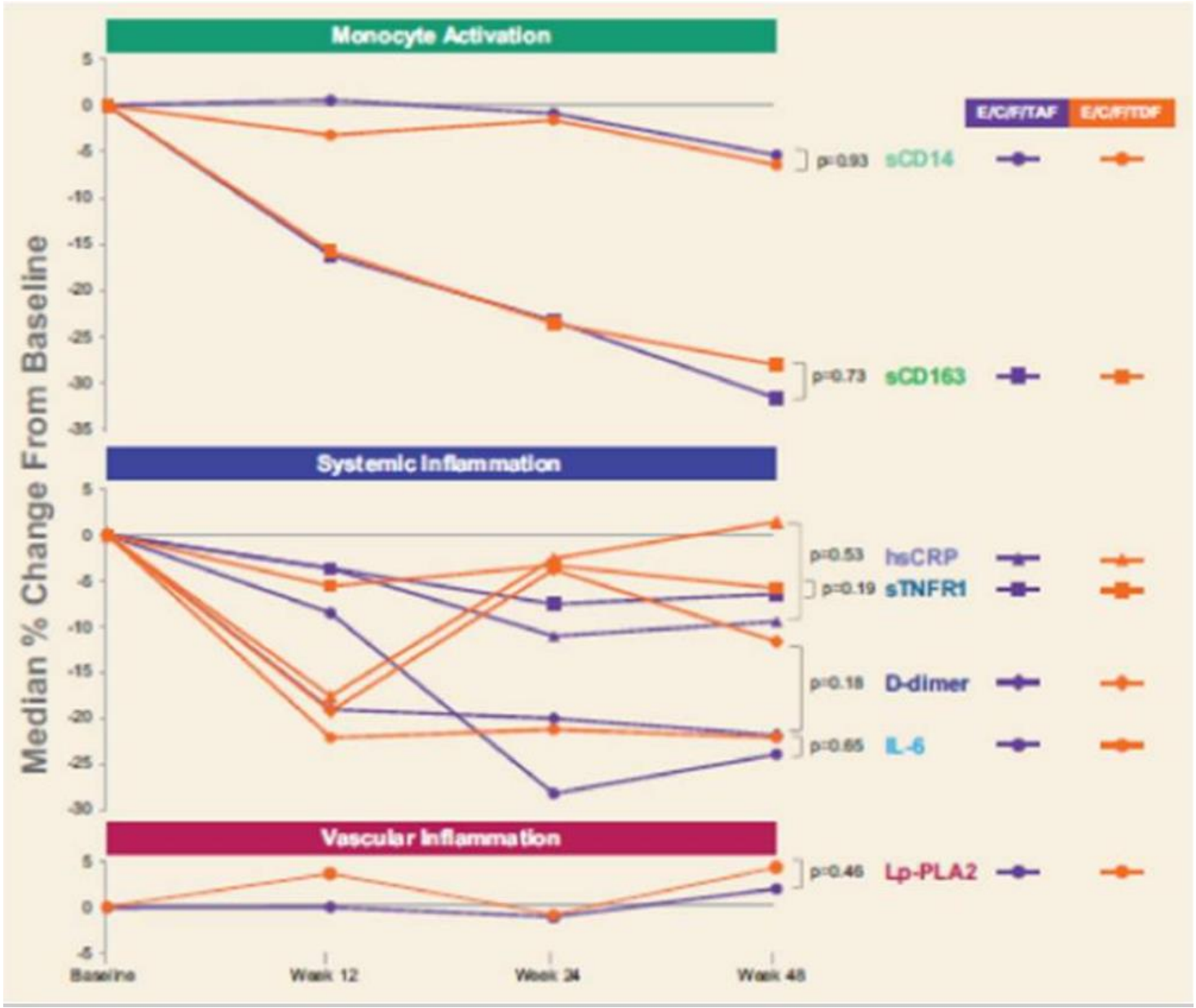

Fig. 2. Percent changes in markers of inflammation and immune activation. Plasma samples were thawed and levels of A) soluble CD14 (sCD14), soluble CD163 (sCD163), B) C reactive protein (hsCRP), tumor necrosis factor receptor type 1 (TNFr-I), D-dimer, interleukin-6 (IL-6) and C) lipoprotein-associated phospholipase A2 (Lp-PLA2) were measured by ELISA. Differences in percent changes were assessed by Wilcoxon rank-sum test.

İnflamatuvar Belirteçler

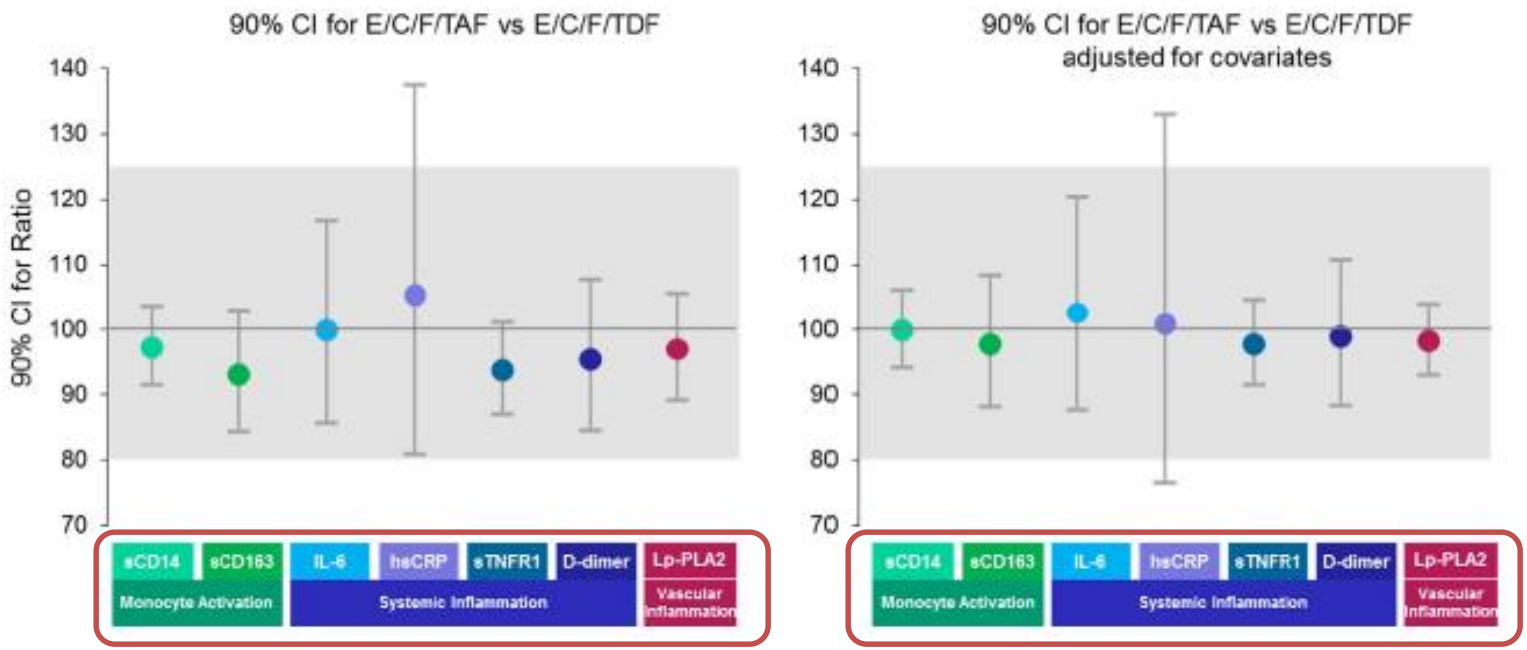

Fig. 3. Changes in levels of biomarkers: equivalence by two one-sided test. Using TOST, equivalence is established at α significance level if a $(1-2\alpha) * 100\%$ confidence interval (CI) for the ratio of treatment 1/treatment 2 is contained within a range around 100%, such as (80%–125%).

TAF'lı ART Rejiminin Etkililik ve Güvenlik Değerlendirmesi

Review

Journal of Pharmacy Practice
1-6

DOI: 10.1177/0897190017710519
journals.sagepub.com/home/jpp
SAGE

A Review of the Efficacy and Safety of Genvoya® (Elvitegravir, Cobicistat, Emtricitabine, and Tenofovir Alafenamide) in the Management of HIV-1 Infection

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Etkililik!
(Naif Hastada)

Efficacy

Use of Genvoya in Treatment-Naive HIV-1-Infected Adults

Sax et al combined 2 phase III trials for a prespecified pooled efficacy and safety analysis.[7] These 2 randomized, double-blinded, phase III noninferiority trials evaluated the efficacy and safety of EVG/c/TAF/FTC and compared TAF to TDF in similar treatment regimens. This trial randomized patients to receive EVG/c/TAF/FTC or EVG/c/TDF/FTC once a day. Baseline characteristics of the study population included primarily young white males with estimated glomerular filtration rate (eGFR) greater than 110 mL/min and CD4 cell counts greater than 200 cells per µL. Over 90% of patients included in the study had symptomatic HIV-1 status and less than 5% of the patients had AIDS. The primary efficacy end point was the proportion of patients with HIV-1 RNA less than 50 copies/mL at week 48. A high success rate was evident in both the EVG/c/TAF/FTC and EVG/c/TDF/FTC groups (800 patients [92%] and 784 patients [90%], adjusted difference: 2%, 95% confidence interval: [CI] −0.7% to 4.7%).

The results of the trial demonstrated significant differences in efficacy in the EVG/c/TAF/FTC group compared to the EVG/c/TDF/FTC group for women (95% vs 87%) and individuals who had a viral load less than 100 000 copies/mL (94% vs 91%); percentage differences were 3.1% (95% CI 0.2-6.0) and 7.9% (95% CI 0.2-15.6), respectively ($P = .024$). At week 48, CD4 cell counts were significantly higher in the EVG/c/TAF/

Sax ve ark: TAF –TDF kıyaslaması: İki Faz III çalışma derlenmiş; virolojik süpresyon (92 ve %90), kadınlar arasında (%95'e %87), virolojik yükleri 100 000 kopya/ml'nin altında olanlarda (%94'e %91) (p: 0.024)

CD4 açısından; 48. hafta verilerinde TAF'lı grup TDF'li gruba kıyasla daha yüksek bulunmuş: 234'e 211 (p: 0.24)

Etkililik!
(Virolojik Baskılı Hasta)

Use of Genvoya in Virologically Suppressed Adults

In this randomized, multicenter, active-controlled, open-label, phase III, noninferiority trial, patients were randomized to receive EVG/c/TAF/FTC or remain on a previous TDF-containing regimen.[10] Similar to the study by Sax et al, baseline characteristics of the study population included primarily young white males with eGFR greater than 100 mL/min. Most patients also had CD4 cell counts >350 cells per μL and were virologically suppressed, defined as HIV-1 RNA <50 copies/mL. All patients were on a TDF-containing regimen for 98 weeks prior to enrollment. These 4 baseline regimens were EVG/c/TDF/FTC, efavirenz/TDF/FTC, atazanavir (ATV)/c/TDF/FTC, or ATV/ritonavir (r)/TDF/FTC. Patients were assigned (2:1) to continue 1 of the 4 TDF-containing regimens or switch to EVG/c/TAF/FTC. This study evaluated whether the efficacy, safety, and tolerability in patients switching to the EVG/c/TAF/FTC regimen were noninferior to patients who remained on a regimen containing TDF. The primary end point was undetectable viral load (HIV-1 RNA <50 copies/mL) at week 48 in patients who received at least 1 dose of the study drug.

Virologic suppression at week 48 occurred in 97% of patients assigned to the EVG/c/TAF/FTC group and 93% of patients in the TDF-containing regimen group (adjusted difference: 4.1%, 95% CI: 1.6-6.7, $P = .0002$). Virologic failure was similar between the EVG/c/TAF/FTC and TDF-containing arms, 10 patients (1%) and 6 patients (1%), respectively. In the EVG/c/TAF/FTC arm, 1 patient (<1%) had virologic failure at

Randomize, çok merkezli, aktif kontrollü, açık etiketli, faz III, noninferiyorite çalışması
Hastaların bir kısmı TAF'a geçilmiş, diğer kısmı TDF'li rejim ile devam etmiş, hastalar bu şekilde randomize edilmiş.

48. Haftada **virolojik süpresyon** TAF'lı rejimde %97, TDF'li diğer rejimlerde %93 (p: 0.0002)
Virolojik başarısızlık %1 ile benzer oranda

3 Çalışma;

Table 1. Adverse Event Profile of EVG/c/TAF/FTC Versus EVG/c/TDF/FTC.

	Sax et al[7]		Mills et al[10]		Pozniak et al[11]	
	TAF, n = 866 (%)	TDF, n = 867 (%)	TAF, n = 959 (%)	TDF, n = 477 (%)	TAF < 50 mL/min, n = 80 (%)	TAF ≥ 50 mL/min, n = 162(%)
Patients with any AE(s)						
Death	5 (<1)	3 (<1)	4 (<1)	0	0	0
Serious AE	N/A	N/A	65 (7)	35 (7)	9 (11)	20 (12)
Study discontinuations due to AE	7 (<1)	11 (<2)	9 (1)	12 (3)	6 (8)	2 (1)
Most common AE(s)						
Diarrhea	147 (17)	164 (19)	96 (10)	42 (9)	10.4 (13)	17.8 (11)
Nausea	132 (15)	151 (17)	50 (5)	16 (3)	4.8 (6)	14.6 (9)
Headache	124 (14)	108 (13)	69 (7)	20 (4)	2.4 (3)	14.6 (9)
Upper respiratory tract infection	99 (11)	109 (13)	151 (16)	54 (11)	2.4 (3)	19.4 (12)
Nasopharyngitis	78 (9)	80 (9)	88 (9)	39 (8)		
Cough	67 (8)	60 (7)	64 (7)	25 (5)	4 (5)	9.7 (6)
Vomiting	62 (7)	54 (6)				
Arthralgia	61 (7)	39 (5)	59 (6)	24 (5)	6.4 (8)	16.2 (10)
Back pain	60 (7)	57 (7)	52 (5)	25 (5)	3.2 (4)	13 (8)
Insomnia	57 (7)	48 (6)	50 (5)	30 (6)		
Rash	55 (6)	46 (5)				
Pyrexia	45 (5)	41 (5)				
Dizziness	44 (5)	37 (4)			8 (10)	6.5 (4)
Syphilis			46 (5)	30 (6)		
Bronchitis			58 (6)	26 (5)	7.2 (9)	13 (8)
Depression			42 (4)	30 (6)		
Osteopenia			56 (6)	22 (5)	8.8 (11)	11.3 (7)
Sinusitis			48 (5)	25 (5)		
Fatigue					4 (5)	9.7 (6)
Pain in extremity					4 (5)	13 (8)
Renal cyst					4.8 (6)	9.7 (6)

Olgu-II

- 62 yaşında erkek hasta
- Katarakt ameliyatı öncesinde yapılan serolojik tarama testinde HIV pozitif olduğu saptanmış
- Takip için tarafımıza yönlendirilmiş
- Hasta değerlendirildikten sonra doğrulama testi yapıldı, tedavi için ek tetkikler istendi.

Laboratuvar

Hastanın laboratuvar bulguları:

Tam idrar analizi: pH:6

Sedim: 1 eritrosit 1 lökosit

Sedimantasyon 15 mm/saat

CD4: **165/mikrolitre**

HIV RNA **108 000** kopya/mikrolitre

Lökosit 9 200/mikrolitre

- Nötrofil: 7 200 (%78)
- Lenfosit: 1 000 (%10.8)
- Hemoglobin: 13 gr/dl
- Trombosit: **180 000/mikrolitre**

Kreatinin: 1.3 mg/dl

Antitoxoplasma IgG:pozitif

AntiCMV IgG: pozitif

VDRL: Negatif

TPHA: Negatif

TÜRK NEFROLOJİ DERNEĞİ

Turkish Society of Nephrology

GLOMERÜL FİLTRASYON HIZI (KISA MDRD FORMÜLÜ İLE HESAPLANMIŞ)

FORMÜL : Glomerüler Filtrasyon Hızı = $186 * SerumKreat^{-1.154} * Yaş^{-0.203} * Cinsiyet * Irk$

SONUÇ: Glomerüler Filtrasyon Hızı = 59.45 mL/min/1.73 m^2

* Kreatinin mg/dl :	1.3
* Yaş Yıl :	62
* Cinsiyet :	Erkek (1)
* Irk :	Siyah olmayan (1)

Vazgeç Hesapla

DOI: 10.1111/hiv.12643
HIV Medicine (2018)

ORIGINAL RESEARCH

Comparison of 48-week efficacies of elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide and nucleoside/nucleotide reverse transcriptase inhibitor-sparing regimens: a systematic review and network meta-analysis

S Gallien,[1,2] M Massetti,[3] P Flandre,[4] H Leleu,[3] D Descamps[5,6] and E Lazaro[7,8]

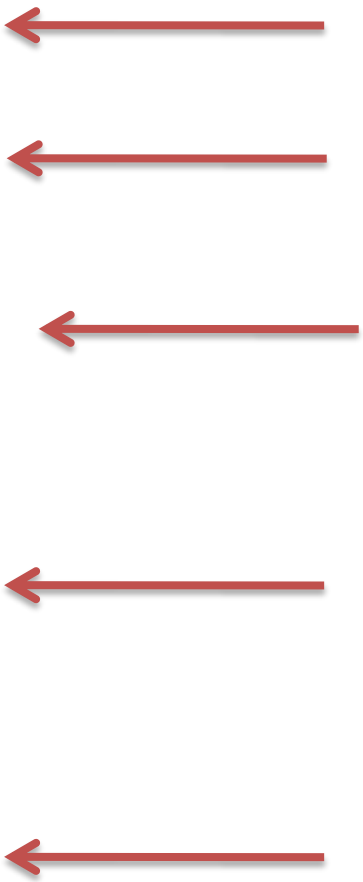
[1]*Henri Mondor University Hospital, Créteil, France,* [2]*University of Paris-Est Créteil Val de Marne Medical School, Créteil, France,* [3]*Public Health Expertise, Paris, France,* [4]*INSERM Sorbonne University, UPMC University Paris 06, UMR-S 1136, Pierre Louis Institute of Epidemiology and Public Health, Paris, France,* [5]*Bichat Claude Bernard University Hospital, Paris, France,* [6]*University Paris Diderot Medical School, Paris, France,* [7]*Bordeaux University Hospital, Bordeaux, France and* [8]*University of Bordeaux, Bordeaux, France*

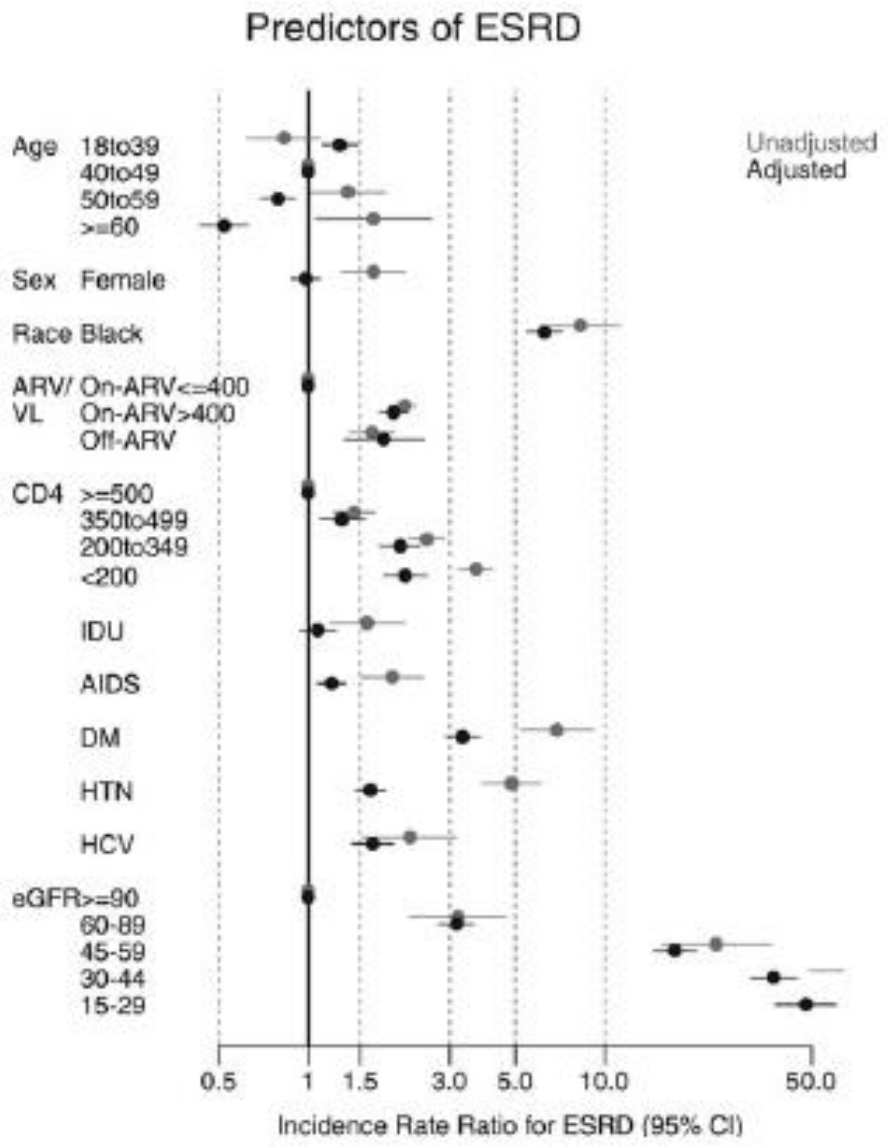
Conclusions

The NMA results suggest that E/C/F/TAF represents a more effective option than NRTI-sparing regimens in terms of 48-week efficacy in treatment-naïve patients. Furthermore, TAF pharmacological properties, as well as tolerability results in clinical studies, suggest a safety profile similar to that of NRTI-sparing regimens. Thus, the E/C/F/TAF combination might represent a more appropriate option than NRTI-sparing regimens for initiation of antiretroviral therapy in treatment-naïve HIV-infected patients.

Table 3. Unadjusted Incidence Rates of End-Stage Renal Disease Among HIV-Infected Patients in Care

Characteristic	Incidence Rate per 100 000 PY (95% CI)	
	Overall (N = 286)	Well-Suppressed[a] (n = 22)
Overall	179 (160–201)	68 (45–104)
Sex		
Male	157 (136–180)	56 (34–93)
Female	259 (211–320)	127 (61–269)
Race		
White	45 (32–64)	13 (3–51)
Black	437 (384–498)	204 (121–345)
Ethnicity		
Hispanic	80 (49–130)	65 (21–202)
Risk behavior		
IDU	263 (202–343)	161 (60–428)
Non-IDU	166 (146–189)	61 (38–96)
Age, y		
18–39	142 (114–177)	45 (17–120)
40–49	172 (143–206)	52 (25–109)
50–59	234 (185–295)	83 (37–184)
≥60	285 (190–429)	195 (81–469)
eGFR category, mL/min		
≥90	73 (57–93)	11 (3–42)
60–89	233 (176–308)	51 (17–159)
45–59	1875 (1340–2625)	772 (290–2056)
30–44	4778 (3396–6720)	2008 (647–6225)
15–29	14 674 (10 197–21 117)	3193 (449–22 668)





Genel popülasyonda risk faktörleri: Diabetes mellitus, hipertansiyon, HCV infeksiyonu

104/111 Tedavi deneyimsiz hastalarda ECFTAF çalışması
TDF kolunda renal nedenlerle tedaviyi bırakan hastaların oranları

Subject	Gender	$eGFR_{CG}$, mL/min	Age, years	Race	Renal adverse event on TDF
1*	Male	116	45	White	Renal tubular disorder
2*	Male	104	51	White	Fanconi syndrome, glycosuria
3	Male	98	27	American Indian/Alaska Native	Proteinuria
4	Male	94	50	White	Blood creatinine increased, BMD decreased
5	Male	92	50	White	GFR decreased
6*	Male	88	33	White	Renal tubular disorder
7	Male	83	36	White	Blood creatinine increased, GFR decreased
8	Male	83	41	Black	Renal failure
9*	Male	82	53	White	Renal tubular disorder
10	Female	73	53	Other	Renal failure
11	Male	66	37	Black	Nephropathy
12	Male	63	59	White	Bladder spasm

1. Arribas J et al. J Acquir Immune Defic Syndr 2017;75(2):211–8; yayınından uyarlanmıştır.
2. Gilead Sciences, data on file.

Contributions of traditional and HIV-related risk factors on non-AIDS-defining cancer, myocardial infarction, and end-stage liver and renal diseases in adults with HIV in the USA and Canada: a collaboration of cohort studies

Keri N Althoff, Kelly A Gebo, Richard D Moore, Cynthia M Boyd, Amy C Justice, Cherise Wong, Gregory M Lucas, Marina B Klein, Mari M Kitahata, Heidi Crane, Michael J Silverberg, M John Gill, William Christopher Mathews, Robert Dubrow, Michael A Horberg, Charles S Rabkin, Daniel B Klein, Vincent Lo Re, Timothy R Sterling, Fidel A Desir, Kenneth Lichtenstein, James Willig, Anita R Rachlis, Gregory D Kirk, Kathryn Anastos, Frank J Palella Jr, Jennifer E Thorne, Joseph Eron, Lisa P Jacobson, Sonia Napravnik, Chad Achenbach, Angel M Mayor, Pragna Patel, Kate Buchacz, Yuezhou Jing, Stephen J Gange for the North American AIDS Cohort Collaboration on Research and Design

Summary

Background Adults with HIV have an increased burden of non-AIDS-defining cancers, myocardial infarction, end-stage liver disease, and end-stage renal disease. The objective of this study was to estimate the population attributable fractions (PAFs) of preventable or modifiable HIV-related and traditional risk factors for non-AIDS-defining cancers, myocardial infarction, end-stage liver disease, and end-stage renal disease outcomes.

Lancet HIV 2019; 6: e93–104

Published Online
January 22, 2019
http://dx.doi.org/10.1016/S2352-3018(18)30295-9

Lancet HIV 2019;6:e93-104

	NADC		MI		ESLD		ESRD	
	No diagnosis (n=60 095)	Diagnosis (n=1405)	No diagnosis (n=29 168)	Diagnosis (n=347)	No diagnosis (n=34 657)	Diagnosis (n=387)	No diagnosis (n=35 365)	Diagnosis (n=255)
Demographics								
Age								
<40 years	29 429 (49%)	317 (23%)	13 749 (47%)	63 (18%)	16 641 (48%)	124 (32%)	16 344 (46%)	94 (37%)
40–49 years	20 584 (34%)	550 (39%)	10 217 (35%)	144 (41%)	12 474 (36%)	160 (41%)	13 042 (37%)	101 (40%)
50–59 years	8239 (14%)	390 (28%)	4220 (14%)	106 (31%)	4528 (13%)	80 (21%)	4835 (14%)	41 (16%)
≥60	1843 (3%)	148 (11%)	982 (3%)	34 (10%)	1014 (3%)	23 (6%)	1144 (3%)	19 (7%)
Male	46 330 (77%)	1093 (78%)	23 475 (80%)	298 (86%)	27 354 (79%)	334 (86%)	27 974 (79%)	178 (70%)
Race and ethnicity								
White	25 075 (42%)	692 (49%)	13 429 (46%)	193 (56%)	14 560 (42%)	207 (53%)	15 022 (42%)	30 (12%)
Black	21 658 (36%)	534 (38%)	10 831 (37%)	123 (35%)	11 693 (34%)	108 (28%)	11 452 (32%)	205 (80%)
Hispanic	7683 (13%)	111 (8%)	3106 (11%)	20 (6%)	4379 (13%)	43 (11%)	4756 (13%)	12 (5%)
Other	3033 (5%)	44 (3%)	1308 (4%)	10 (3%)	1269 (4%)	7 (2%)	1333 (4%)	1 (0%)
Unknown or missing	2646 (4%)	24 (2%)	494 (2%)	1 (0%)	2756 (8%)	22 (6%)	2802 (8%)	7 (3%)
HIV transmission risk								
MSM	31 370 (52%)	742 (53%)	16 103 (55%)	193 (56%)	17 514 (51%)	180 (47%)	17 114 (48%)	67 (26%)
IDU	6885 (11%)	204 (15%)	2971 (10%)	44 (13%)	4231 (12%)	97 (25%)	3912 (11%)	52 (20%)
Heterosexual contact	15 397 (26%)	343 (24%)	7559 (26%)	84 (24%)	9224 (27%)	73 (19%)	9065 (26%)	108 (42%)
Other, unknown, or missing	6443 (11%)	116 (8%)	2535 (9%)	26 (7%)	3688 (11%)	37 (10%)	5274 (15%)	28 (11%)

Lancet HIV 2019;6:e93-104

Traditional Risk Factors								
Smoking								
Never	13 604 (23%)	236 (17%)	6891 (24%)	55 (16%)	6916 (20%)	57 (15%)	7645 (22%)	41 (16%)
Ever	37 013 (62%)	1106 (79%)	21 884 (75%)	292 (84%)	20 588 (59%)	289 (75%)	20711 (59%)	182 (71%)
Missing	9478 (16%)	63 (4%)	393 (1%)	0 (0%)	7153 (21%)	41 (11%)	7009 (20%)	32 (13%)
Elevated TC	10 037 (17%)	325 (23%)	7287 (25%)	211 (61%)	7032 (20%)	66 (17%)	6779 (19%)	108 (42%)
Hypertension	5230 (9%)	237 (17%)	2809 (10%)	89 (26%)	2234 (6%)	53 (14%)	2365 (7%)	68 (27%)
Diabetes	1660 (3%)	68 (5%)	766 (3%)	27 (8%)	855 (2%)	20 (5%)	928 (3%)	29 (11%)
Stage 4 CKD	889 (1%)	35 (2%)	610 (2%)	20 (6%)	634 (2%)	26 (7%)	479 (1%)	83 (33%)
Statin Prescription	2260 (4%)	95 (7%)	1449 (5%)	50 (14%)	812 (2%)	11 (3%)	1090 (3%)	16 (6%)
HCV infection	10379 (17%)	356 (25%)	5392 (18%)	92 (27%)	6700 (19%)	197 (51%)	6189 (18%)	88 (35%)
HBV infection	4814 (8%)	156 (11%)	1766 (6%)	30 (9%)	3535 (10%)	108 (28%)	2225 (6%)	31 (12%)
HIV-related risk factors								
Low CD4 count	13 337 (22%)	396 (28%)	7034 (24%)	112 (32%)	8875 (26%)	139 (36%)	8805 (25%)	93 (36%)
Detectable HIV RNA	34 408 (57%)	809 (58%)	16 523 (57%)	184 (53%)	19 862 (57%)	217 (56%)	19 422 (55%)	176 (69%)
Clinical AIDS diagnosis	10158 (17%)	353 (25%)	6284 (22%)	109 (31%)	7392 (21%)	102 (26%)	7695 (22%)	94 (37%)
ART regimen								
Treatment naive	25 216 (42%)	452 (32%)	11 478 (39%)	90 (26%)	14 170 (41%)	96 (25%)	13 065 (37%)	75 (29%)
PI-based ART	12 394 (21%)	406 (29%)	5842 (20%)	114 (33%)	7707 (22%)	117 (30%)	7606 (22%)	51 (20%)
NNRTI-based ART	10 289 (17%)	217 (15%)	5121 (18%)	44 (13%)	5465 (16%)	50 (13%)	6756 (19%)	35 (14%)
Other ART	5591 (9%)	155 (11%)	2402 (8%)	43 (12%)	2858 (8%)	56 (14%)	3278 (9%)	35 (14%)
Treatment experienced but not prescribed ART	6558 (11%)	174 (12%)	4325 (15%)	56 (16%)	4457 (13%)	68 (18%)	4660 (13%)	59 (23%)

Lancet HIV 2019;6:e93-104

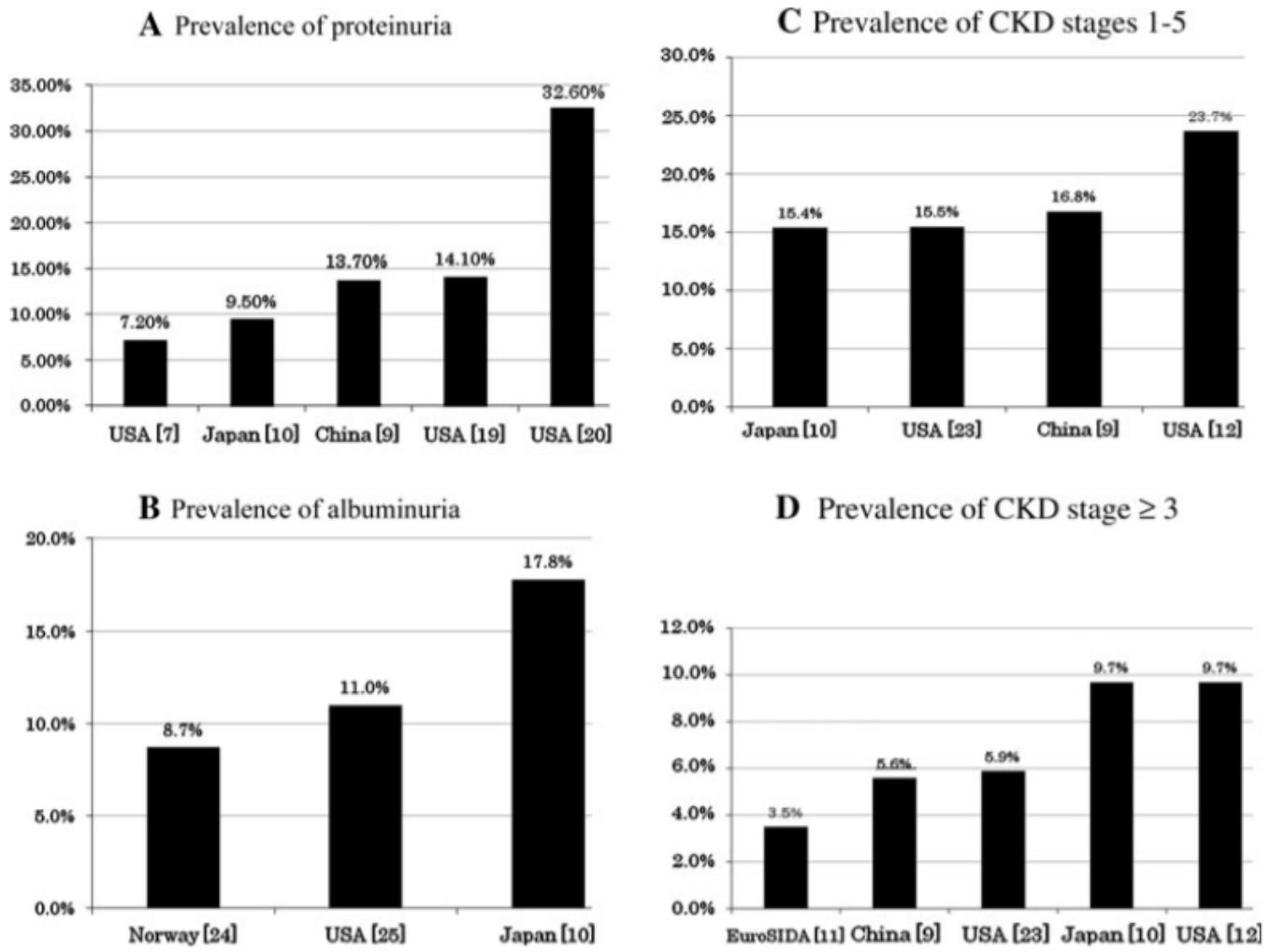


Fig. 1 Comparisons of prevalence of proteinuria (**a**), albuminuria (**b**), CKD stages 1–5 (**c**), and CKD stages ≥3 (**d**) across previous studies. The *number in brackets* indicates the reference number

HIV-Pozitif Hastada KBY İle İlişkili Faktörler

Table 2 Factors associated with CKD in HIV-infected patients

Variable	References
Black race	[4–6, 12, 25, 28, 30]
Older age	[9–11, 26–28, 55, 64, 65]
Low CD4 cell count	[9–11, 25, 27, 73]
High HIV-RNA viral load	[12, 25, 27]
Diabetes mellitus (+)	[10–12, 27, 55, 64, 65]
Hypertension (+)	[11, 12, 25, 27, 29, 30]
Hepatitis C virus co-infection (+)	[25, 55, 73]
Proteinuria	[9–12, 26, 64, 65]
Albuminuria	[10, 29, 30, 55]
eGFR <90 ml/min/1.73 m^2	[29, 55, 64]
Elevation of urinary tubular markers	[57–64]
Use of TDF	[3, 11, 48, 51, 52, 55]

Clin Exp Nephrol (2012) 16:363–372

HIV VE NEFROPATİ

HIV'e Özgü Glomerular Hastalıklar

- HIVAN
- HIVIC
- TMA

HIV'e Özgü Olmayan Glomerular Hastalıklar

- HCV'yla İlişkili MPGN/Kriyoglobulinemia
- Diyabetik nefropati
- Glomerular skleroz
- Membranöz glomerulopati
- Minimal Change Hastalıklar
- IgA nefropatisi
- Postinfeksiyöz glomerulopati

Clin Exp Nephrol (2012) 16:363–372

HIV İnfeksiyonu Sırasında Böbrek Hastalıkları

Table 1. Spectrum of renal lesions in HIV infection.

Kidney disorder	Associations/subtypes
Tubulo-interstitial disease	
Acute kidney injury	Sepsis, toxins, drugs
Proximal tubular injury	Tenofovir, adefovir, codofovir, didanosine
Chronic tubular injury	Amphotericin, tenofovir, adefovir, cidofovir
Crystal nephropathy	Indinavir, atazanavir, sulphadiazine, ciprofloxacin, acyclovir (IV)
Interstitial nephritis	Infections (including HIV, BK virus), following ART, drugs
Glomerular lesion	
HIV-FSGS (focal segmental glomerulosclerosis) or "classic" HIVAN (HIV-associated nephropathy: FSGS with collapsing glomerulopathy, microcystic tubular dilatation, interstitial inflammation)	APOL1 risk variants
HIV-ICD (HIV-immune complex disease) (this group may have co-infection with Hepatitis B or C)	Mesangial proliferative Membranoproliferative (types I and III) Lupus-like Exudative-proliferative Crescentic IgA Membranous
Various glomerulonephropathies (this is a heterogeneous group with different etiologies)	Minimal change disease Membranous nephropathy Immunotactoid nephropathy Amyloidosis
HIV-TTP/HUS	TTP: Thrombotic thrombocytopenic purpura HUS: Hemolytic uremic syndrome

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Diagnosis of HIV infection

↓

Screen for risk factors for kidney disease

- Age ≥50 years
- CD4 count <200 cells/μL
- Comorbidities: diabetes mellitus, hypertension, and HCV co-infection
- eGFR <90 mL/min/1.73 m^2
- Proteinuria or albuminuria (dipstick test, protein to creatinine ratio, albumin to creatinine ratio in spot urine)
- Elevation of urinary tubular markers (NAG, β_2M, α_1M)
- Use of TDF with or without protease inhibitors

↓

Early identification of CKD

Determine CKD stage

Referral to a nephrologist if any doubt concerning diagnosis and treatment

↓

Count the number of risk factors

- No risk factors → Screen risk factors annually
- Single or multiple risk factors → Periodic monitoring using urinalysis and eGFR

↓

- Treat in collaboration with experts of nephrology, cardiology or diabetology
- Treat/prevent comorbidities: strict control of blood pressure and blood sugar level
- Avoid use of nephrotoxic drugs
- Adjust medication regimens/doses according to eGFR

HIV'le İlişkili BB Hastalığının Erken Tanımlama Algoritması

Clin Exp Nephrol (2012) 16:363–372

HIV İnfeksiyonu Sırasında Böbrek Hastalıkları

- Kronik böbrek hastalıkları, HIV infeksiyonu seyrinde önemli bir komplikasyon olarak karşımıza çıkmaktadır; %3.5-%48.5 (HIV'in komplikasyonu olarak, diğer komorbid hastalıklar olarak, HIV infeksiyonunun bir sonucu olarak)

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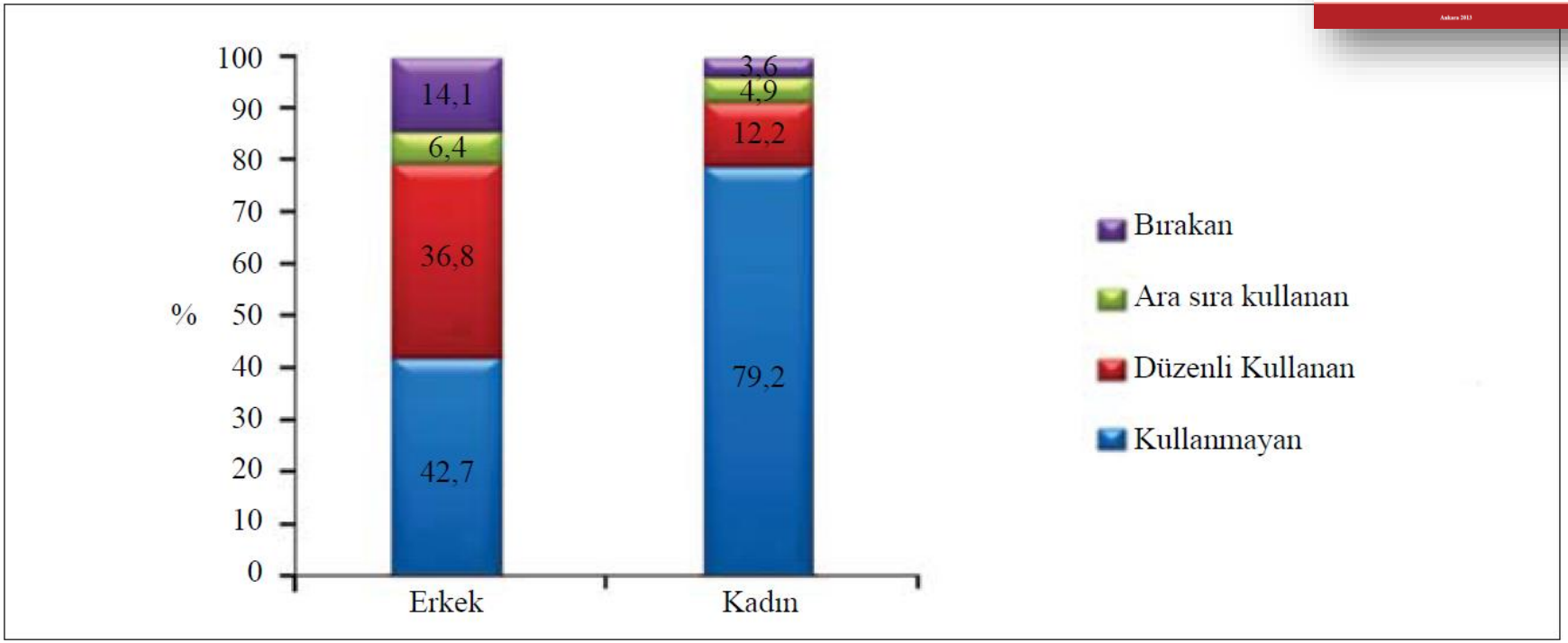
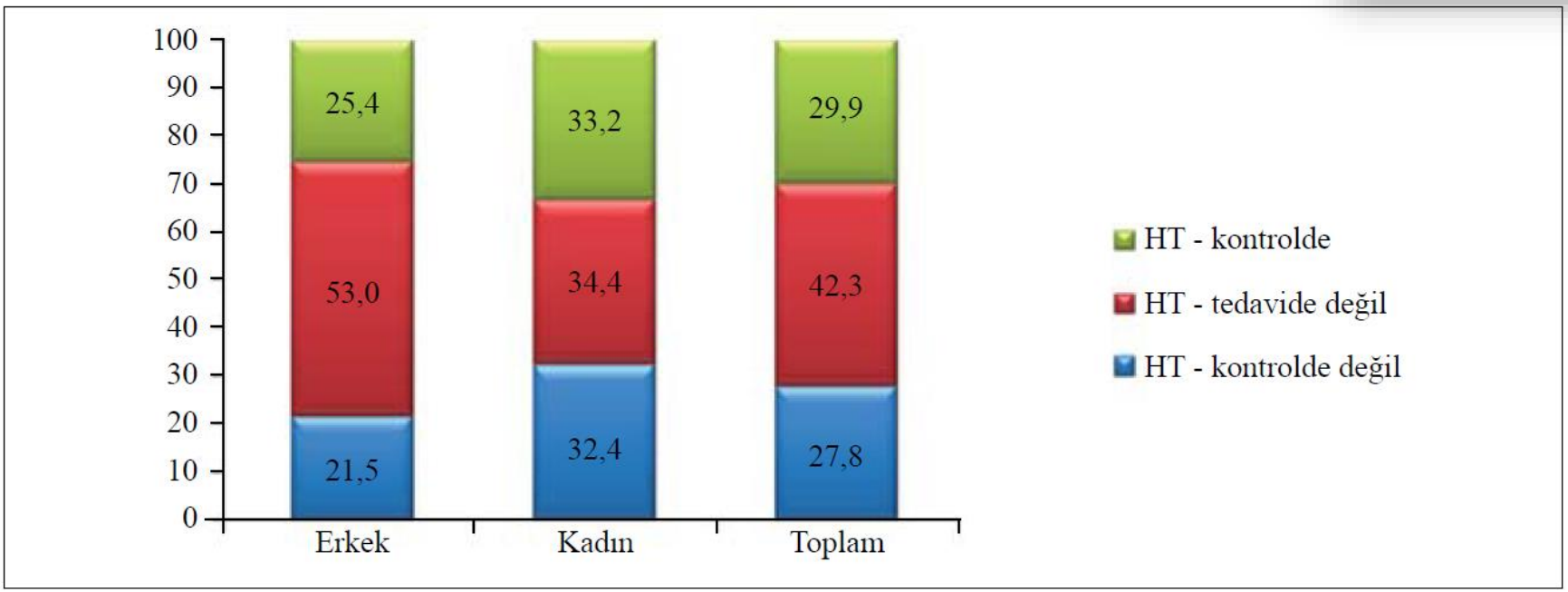
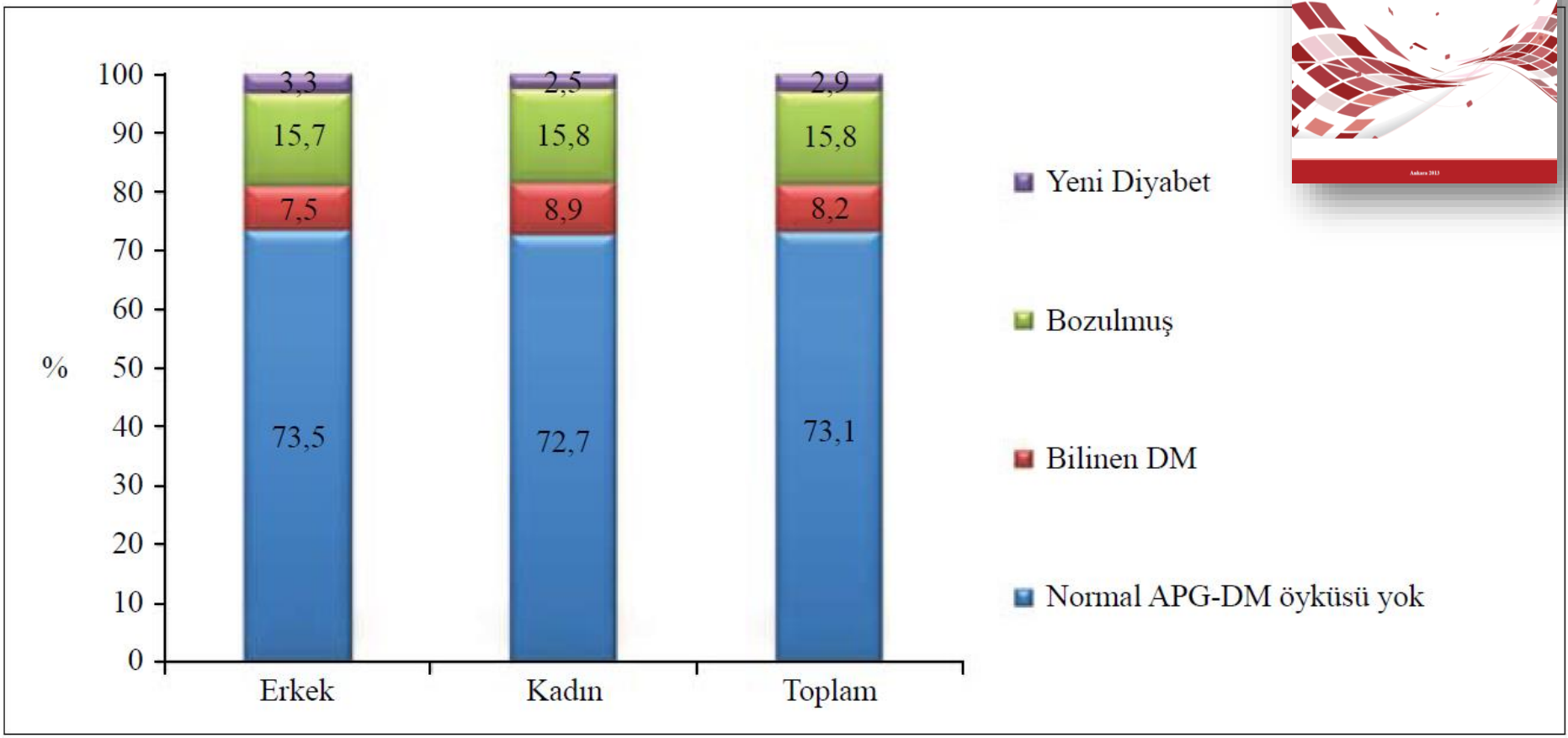


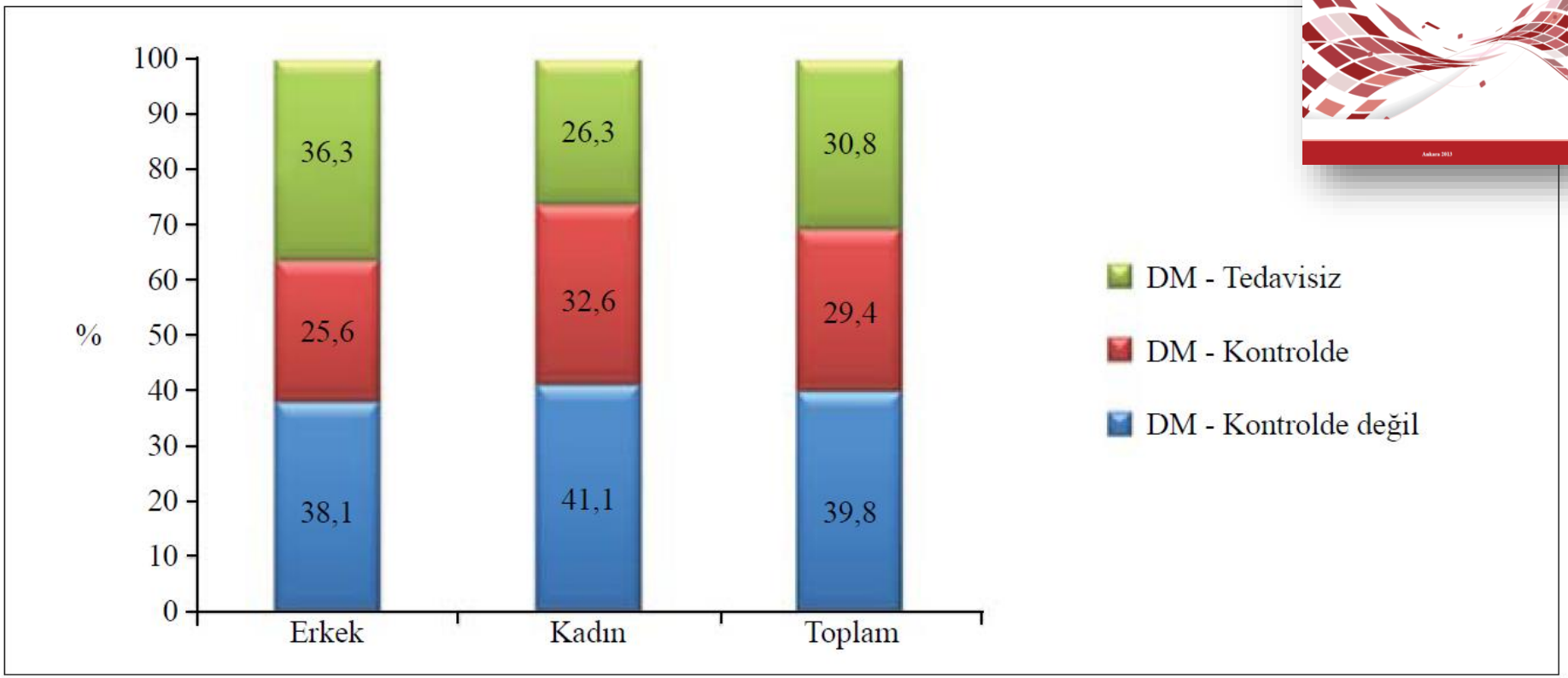
Şekil 4.1 Kadın ve erkeklerin sigara kullanma durumu, Türkiye 2011.



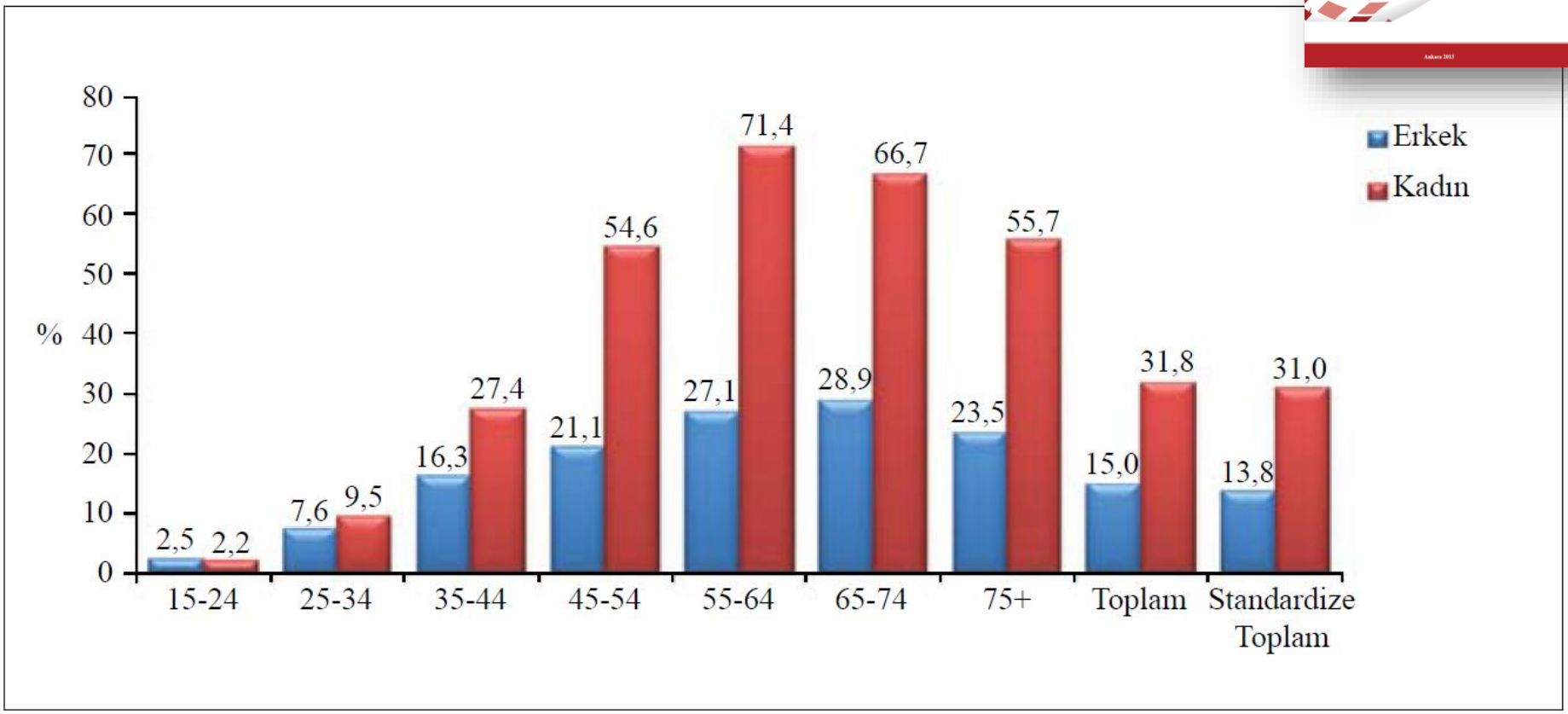
Şekil 6.6 Hipertansiyonu olan kişilerde cinsiyete göre kontrolde ve tedavide olma oranları, Türkiye 2011.



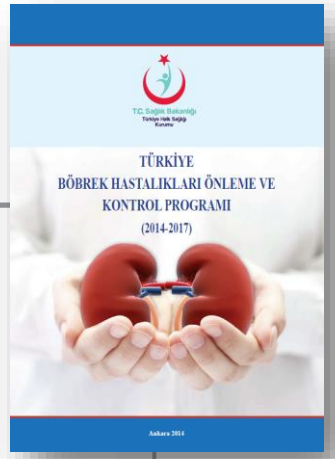
Şekil 7.1 Araştırma grubunda cinsiyete göre, öykü ve APG sonuçları, Türkiye 2011.

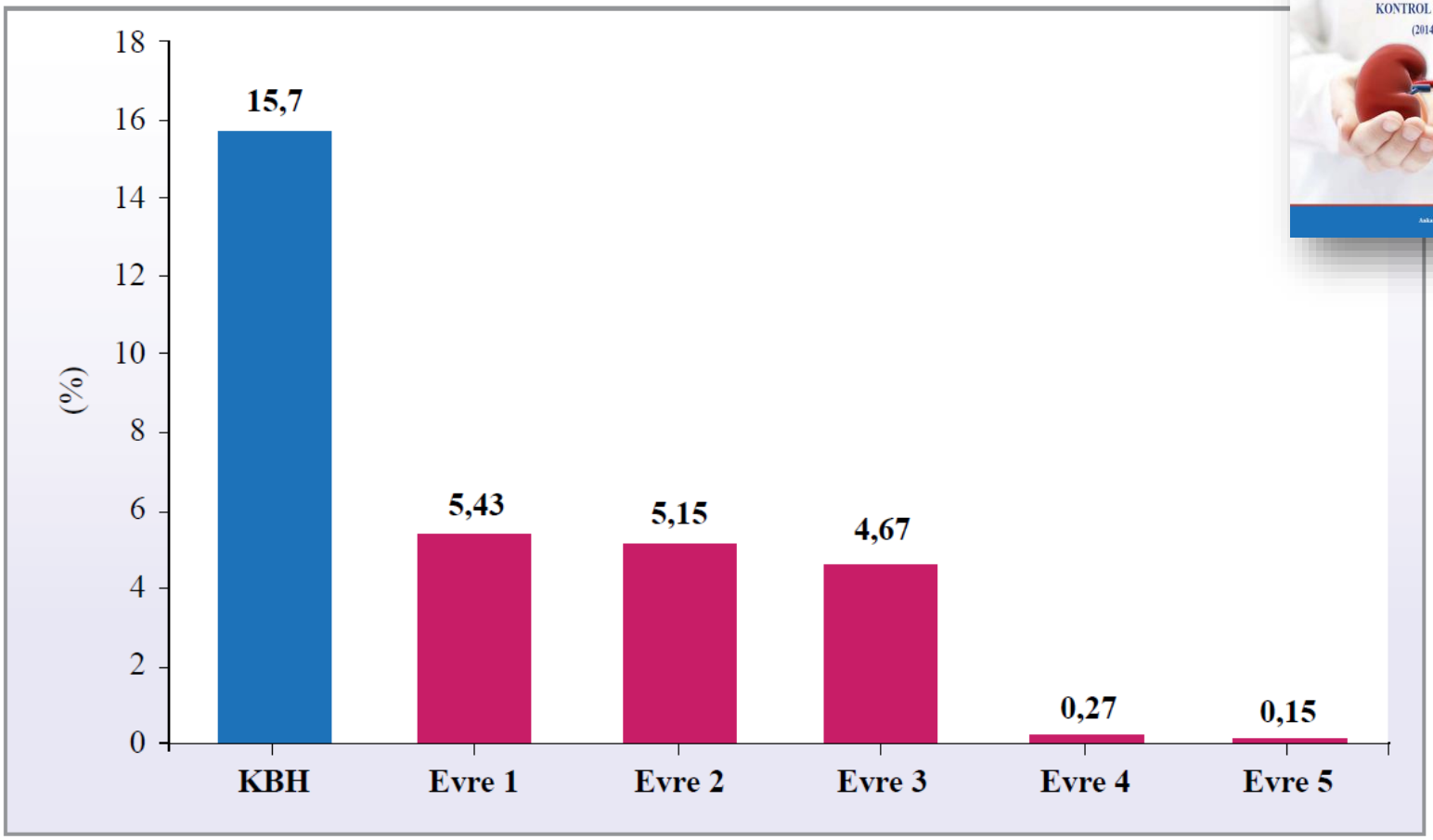


Şekil 7.6 Diyabetli kişilerde cinsiyete göre kontrolde ve tedavide olma, Türkiye 2011.



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





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

Olgu-II

- Hastaya Elvitagravir/C/TAF/Emtrisitabin
  - Günde 1 adet
  - Kotrimoksazol 1X1

başlandı.

Bir yıl sonra….

Laboratuvar

Hastanın laboratuvar bulguları:

Tam idrar analizi: pH:6

Sedim: normal

CD4: **620/mikrolitre**

HIV RNA : **SAPTANAMAZ**

Lökosit 8 000/mikrolitre

Nötrofil: 5 000 (%62,5)

Lenfosit: 2 100 (%26)

Hemoglobin: 13 gr/dl

Trombosit: 240 000/mikrolitre

TÜRK NEFROLOJİ DERNEĞİ

Turkish Society of Nephrology

GLOMERÜL FİLTRASYON HIZI (KISA MDRD FORMÜLÜ İLE HESAPLANMIŞ)

FORMÜL : **Glomerüler Filtrasyon Hızı = 186 * SerumKreat$^{-1.154}$ * Yaş$^{-0.203}$ * Cinsiyet * Irk**

SONUÇ: Glomerüler Filtrasyon Hızı = 80.21 mL/min/1.73 m^2

* Kreatinin mg/dl :	1
* Yaş Yıl :	63
* Cinsiyet :	Erkek (1)
* Irk :	Siyah olmayan (1)

Vazgeç Hesapla

Siz olsaydınız ne yapardınız?

Beni dinlediğiniz teşekkür ederim