İntegraz İnhİbİtörlerİ: Gerçek yaşam Verİlerİ

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DHHS 2016

İlk Seçenek

İntegraz inhibitör temelli

- DTG + ABC/3TC (AI)

(sadece HLA-B*5701 negatif olan hastalar)

- DTG + TDF/FTC (AI) veya **TAF/FTC (AII)**
- EVG/cobi/TDF/FTC (AI)

(sadece KrKl ≥70 mL/dak ise)

- EVG/cobi/**TAF/FTC**

(sadece KrKl ≥30 mL/dak ise)

- RAL + TDF/FTC (AI) veya **TAF/FTC (AII)**

Proteaz inhibitör temelli

- DRV/r + TDF/FTC (AI) veya **TAF/FTC (AII)**

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İlk seçenekler	**İntegraz inhibitör temelli** • DTG/ABC/3TC • DTG+(TDF/FTC veya TAF/FTC) • EVG/cobi/TDF/FTC veya EVG/cobi/TAF/FTC • RAL+(TDF/FTC veya TAF/FTC) • RPV/TDF/FTC veya RPV/TAF/FTC (viral yük<100.000 kopya/ml ve CD4 hücre sayısı >200/mm^3) **Proteaz inhibitör temelli** DRV/r veya DRVc + TDF/FTC veya TAF/FTC

Raltegravir
Dolutegravir
Elvitegravir

Pubmed; retrospektif, gözlemsel çalışmalar

RALTEGRAVİR

Jpn. J. Infect. Dis., 69, 33–38, 2016

Original Article

Raltegravir and Abacavir/Lamivudine in Japanese Treatment-Naïve and Treatment-Experienced Patients with HIV Infection: a 48-Week Retrospective Pilot Analysis

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[2]*Department of Infection Control Science, Juntendo University Faculty of Medicine, Tokyo, Japan*

SUMMARY: Abacavir/lamivudine (ABC/3TC) is a nucleoside reverse transcriptase inhibitor used for treating human immunodeficiency viral (HIV) infections. Hypersensitivity reactions such as skin eruptions caused by ABC are well-known, but rarely occur in Asians. Raltegravir (RAL) is an integrase strand transfer inhibitor, that is now increasingly, used for treating HIV infections because it has few adverse effects. This retrospective analysis assessed the efficacy and safety of combined ABC/3TC and RAL in both treatment-naïve and -experienced Japanese patients with HIV infections. In all 11 treatment-naïve patients (100%), virological suppression to undetectable level was achieved. Liver transaminases, renal function, and serum lipid profiles showed no exacerbations up to 48 weeks of treatment. In 12 patients who were switched from previous regimens to ABC/3TC and RAL, HIV viral load was undetectable in 11 patients (91.6%), but remained detectable in 1 patient with poor adherence. Major reasons for switching regimens to ABC/3TC and RAL were hyperlipidemia and nausea. After switching, these adverse effects improved, and no new adverse effects were observed. Despite the small number of participants in this study, the results support the combination of ABC/3TC and RAL as a possible treatment choice in Japanese individuals with HIV-infection.

- Retrospektif, **tek merkez**
- Nisan 2009- Haziran 2012
- ABC/3TC+RAL başlanan **23 hasta**
  - **11** naif
  - **12** ART deneyimli
    (1 hastada viral yük saptanabilir düzeyde)

Naif hasta (n=11)

Table 2. Antiviral and immunological effects of ABC/3TC and RAL in the Naïve Group[1)]

Case No.	Age	Sex[2)]	HIV viral load (copies/mL)		CD4 T-cell count (cells/mm³)	
			0 week	48 weeks	0 week	48 weeks
1	46	W	630,000	UD[3)]	46	141
2	60	M	430,000	UD	395	629
3	39	M	370,000	UD	274	748
4	28	M	150,000	UD	319	584
5	39	M	120,000	UD	294	785
6	55	M	36,000	UD	27	252
7	63	M	17,000	UD	12	216
8	23	M	15,000	UD	337	433
9	35	M	14,000	UD	98	269
10	30	M	11,000	UD	160	376
11	39	M	6,900	UD	330	439

1): ABC, abacavir; 3TC, lamivudine; RAL, raltegravir.
2): M, man; W, woman.
3): Undetectable (<20 copies/mL).

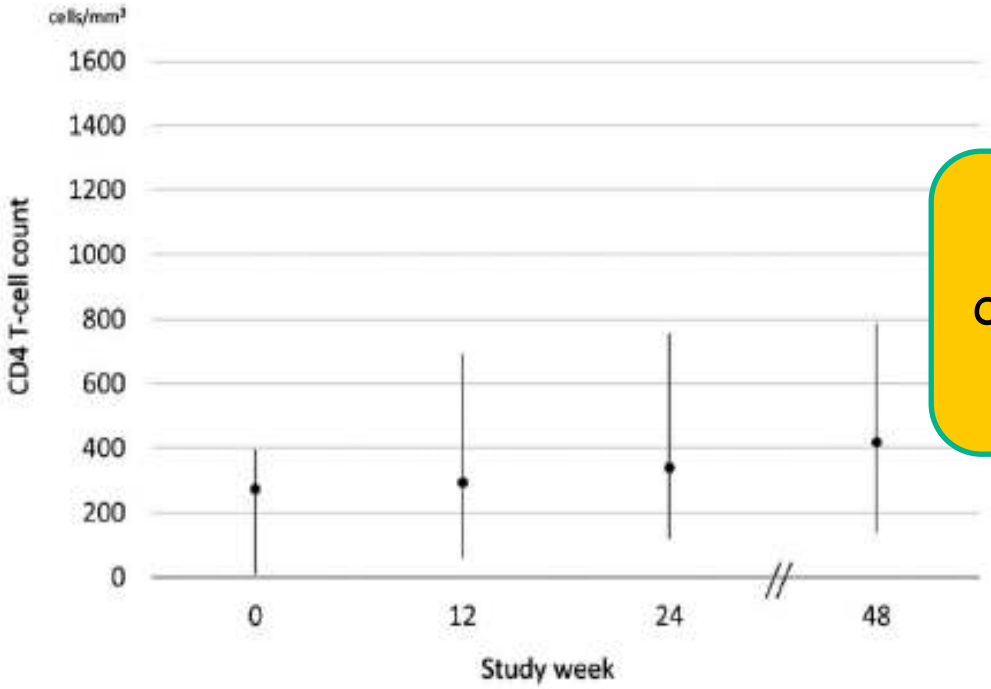

Fig. 2. Median and range of CD4-lymphocyte counts of the Naïve Group. The median CD4-lymphocyte count increased after starting treatment with abacavir/lamivudine (ABC/3TC) and raltegravir (RAL).

Karaciğer enzim yüksekliği, dislipidemi, renal fonksiyonda azalma gözlenmedi

Tedavi deneyimli hasta (n=12)

Table 4. Previous regimen, antiviral effect, and immunological effect of ABC/3TC and RAL in the Switched Group

Case No.	Age	Sex[1)]	Previous regimen[2)]	Reason for switching regimen	HIV viral load (copies/mL)		CD4 T-cell count (cells/mm^3)	
					0 week	48 weeks	0 week	48 weeks
1	44	W	ABC/3TC + FPV/r	Dizziness	130,000	250	147	422
2	31	M	ABC/3TC + FPV/r	Diarrhea	UD[3)]	UD	532	445
3	39	M	ABC/3TC + EFV	Hyperlipidemia	UD	UD	671	798
4	59	M	ABC/3TC + EFV	Hyperlipidemia	UD	UD	547	714
5	45	M	TDF/FTC + LPV/r	Hyperlipidemia	UD	UD	601	423
6	68	M	TDF/FTC + LPV/r	Hyperlipidemia	UD	UD	377	561
7	33	W	ZDV/3TC + LPV/r	Nausea	UD	UD	1,441	1,224
8	52	M	ZDV/3TC + LPV/r	Nausea	UD	UD	586	448
9	40	W	ZDV/3TC + LPV/r	Renal dysfunction	UD	UD	1,218	1,400
10	44	M	ZDV/3TC + EFV	Nightmare	UD	UD	508	593
11	47	W	ZDV/3TC + NVP	Hyperlipidemia	UD	UD	994	534
12	40	M	d4T + 3TC + EFV	Insomnia	UD	UD	414	472

1): M, man; W, woman.
2): ABC, abacavir; 3TC, lamivudine; FPV/r, fosamprenavir + ritonavir; EFV, efavirenz; TDF, tenofovir; FTC, emtricitabine; LPV/r, lopinavir + ritonavir; NVP, nevirapine; ZDV, zidovudine; d4T, stavudine.
3): Undetectable (<20 copies/mL).

ABC/3TC+RAL viral yükü yüksek hastalar dahil etkin

RAL'in lipid profili üzerinde olumsuz etkileri düşük

Fig. 4. Median CD4 lymphocyte counts of the Switched Group. All patients maintained high CD4 T-cell count after switching regimen to abacavir/lamivudine (ABC/3TC) and raltegravir (RAL).

Original research article

INTERNATIONAL JOURNAL OF STD & AIDS

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Five years' real-life experience with raltegravir in a large HIV centre

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Abstract

Raltegravir was the first licensed integrase inhibitor. Real-life experience is informative and complements trial data. We therefore evaluated raltegravir use in adults in a large HIV treatment centre. From pharmacy and departmental HIV database records, we identified all adults taking ≥1 dose of raltegravir from first availability to the end of November 2012. Data were collected using a standardised case report form. Two hundred and fifteen individuals provided 502 patient-years (median 2.6 years/person) of raltegravir use. Of 215 individuals, 166 (77%) were male, median age 43 years; 189 (88%) were antiretroviral therapy (ART)-experienced and 26 (12%) ART-naive, with median baseline CD4 counts of 324 and 54 cells/μL, respectively. Of ten individuals using once-daily raltegravir, four, with good adherence remained virologically suppressed after a median 28 months, four stopped against medical advice, one stopped to simplify and one failed virologically. In hepatitis co-infection, 35 individuals (92 patient-years) took raltegravir without evidence of hepatotoxicity. Six women started raltegravir during pregnancy for intensification (5/6) or switch for tolerability without complications. Of ten individuals stopping raltegravir after virological failure, 2/4 with successful sequencing showed resistance. Raltegravir appears safe and effective, without evidence of toxicity above that in published trials, including in pregnancy and co-infections. Once-daily dosing seems effective where adherence is good.

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- Retrospektif, gözlemsel çalışma
- 2009-2012
- **215 hasta**, %77 erkek
  - ≈ %12 ART naif; ortanca CD4: 54/mm^3 (23-258)
  - ≈ **%88 ART deneyimli**; ortanca CD4: 323/mm^3 (132-569)
  - 6 gebe
  - 10 hasta günde tek doz RAL
- Ortanca takip süresi: **2,6 yıl** (0,8-3,5 yıl)

Table 1. Accompanying regimens in antiretroviral therapy (ART)-naive and ART-experienced individuals starting raltegravir.

Regimen type	Detail	Number of individuals
ART-naive ($N = 26$)		
NRTI backbone only	Total	20
	TDF + FTC	17
	ABC + 3TC	3
PI-based	Total	6
	DRV/R 800/100 mg once daily	6/6
	(DRV/R plus NRTIs	4/6)
ART experienced ($N = 189$)		
NRTI backbone only	Total	53
	TDF + FTC	31
	ABC + 3TC	9
	Other	13
PI-based	Total	116 (%61)
	DRV/R 800/100 mg once daily	20/116
	DRV/R 600/100 mg twice daily	37/116
	DRV/R other dose or unknown	1/116
	ATZ/R 300/100 mg once daily	38/116
	Other PI[a]	20/116
Among PI-based regimens, other accompanying drugs		
	EFV (with ATZ/R + TDF)[b]	1/116
	NVP[c]	2/116
	ETV	31/116
	MRV[d]	6/116
	ENF[e]	4/116
Other regimens[f]	Total	20

1 akut hepatit
3 baş ağrısı
1 döküntü (?)
1 karaciğer enzim yüksekliği (EBV?)

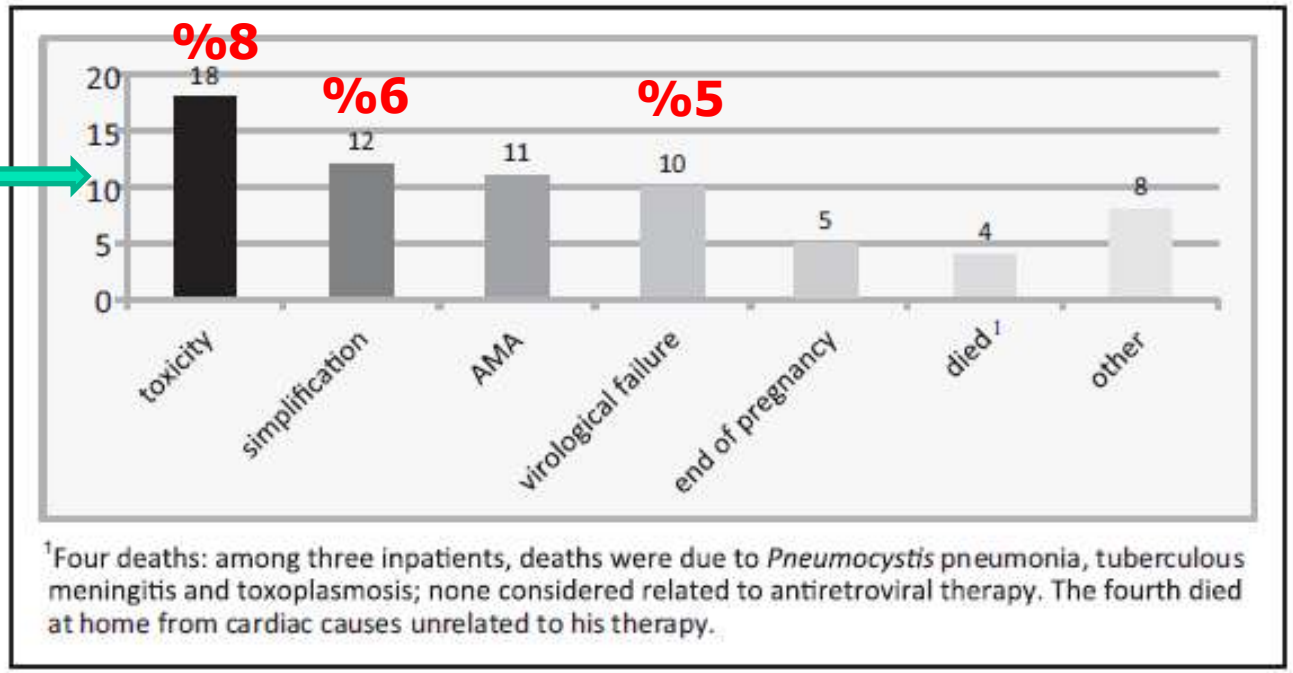

Figure 2. Reasons for stopping raltegravir in 68 individuals who stopped during the period reviewed. AMA = against medical advice.

RAL başlanan hastaların %32'si tedaviyi bıraktı.

İleri evre hastalıkta güvenilir

Gebelerde etkin

Uyum sağlanırsa tek doz etkin (?)

Direnç gelişen hastaların öyküsünde diğer ART sınıf ilaçlarına direnç mevcut

Original research article

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Efficacy of raltegravir-containing regimens in antiretroviral-naïve and -experienced individuals in routine clinical practice

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Abstract

Raltegravir is one of the standard antiretroviral therapy (ART) options in treatment-experienced and -naïve patients. However, efficacy data from clinical practice are scarce. Therefore, the efficacy of raltegravir-containing ART in clinical practice was investigated retrospectively. In all, 295 treatment-naïve and -experienced patients were analysed using two different cut-offs for virological failure (200 or 50 copies/ml). The response at week 24 and onwards was evaluated as a 'time to loss of virological response' analysis and estimated as a survival function. Additionally, dual therapy regimens (raltegravir plus boosted protease inhibitor) were compared to standard combinations in experienced patients performing a snapshot analysis at weeks 24 and 48, as well as a time to loss of virological response analysis. A total of 86.2% of the 64 treatment-naïve patients maintained virological suppression using a cut-off of 200 copies/ml (c/ml), while 67.7% maintained virological suppression with a 50 copies/ml cut-off from week 24 until the end of observation. Among the 231 treatment-experienced patients, 84.8% maintained virological suppression from week 24 onwards using a cut-off of 200 copies/ml; and 71.0% using 50 copies/ml, respectively. In the subgroup snapshot analysis at week 24, 98.3% (86.7% using a cut-off of 50 copies/ml) and at week 48, 93.3% (80.0%) of patients responded to dual therapy. Patients who were receiving a standard background therapy responded in 88.3% (81.3%) at week 24 and in 86.0% (80.7%) at week 48. Differences were not significant. This study shows again the overall long-term efficacy of raltegravir-based ART and furthermore gives reference for a comparable efficacy of dual and standard nucleos(t)ide reverse transcriptase inhibitor–backbone regimens in experienced patients on raltegravir over a period of 48 weeks in a real-life cohort where patients with severe comorbidities were included.

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- Retrospektif, tek merkez
- Ekim 2007-Ekim 2012
- **295 hasta;** %73 erkek

  64 ART naif

  231 ART deneyimli (%78)

  (% 55 virolojik olarak baskılanmış)
- Ortanca yaş: 45 yıl (38-52)

Characteristic	Total	Naïve	Experienced
Hepatitis B and C	1 (0.3)	0 (0.0)	1 (0.4)
Last ART – no. (%)			
(Double-) NRTI + PI		–	81 (35.1)
(Double-) NRTI + NNRTI		–	36 (15.6)
Double PI		–	29 (12.6)
Triple/quadruple NRTI		–	59 (25.5)
Double-NRTI + 3rd agent		–	5 (2.2)
Structured treatment interruption		–	17 (7.4)
Double NRTI		–	2 (0.9)
Single PI		–	2 (0.9)
Background therapy – no. (%)			
Dual therapy (PI/r)	66 (22.4)	6 (9.4)	60 (26.0)
NRTI-backbone	197 (66.8)	58 (90.6)	139 (60.2)
DRV/r + NNRTI	14 (4.7)	0 (0.0)	14 (6.1)
NRTI + PI (or + MVC or + T20)	15 (5.1)	0 (0.0)	15 (6.5)
PI + T20	3 (1.0)	0 (0.0)	3 (1.3)

ART, antiretroviral therapy; CDC, Centres of Disease Control and Prevention; DRV/r, darunavir/raltegravir; MVC, maraviroc; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

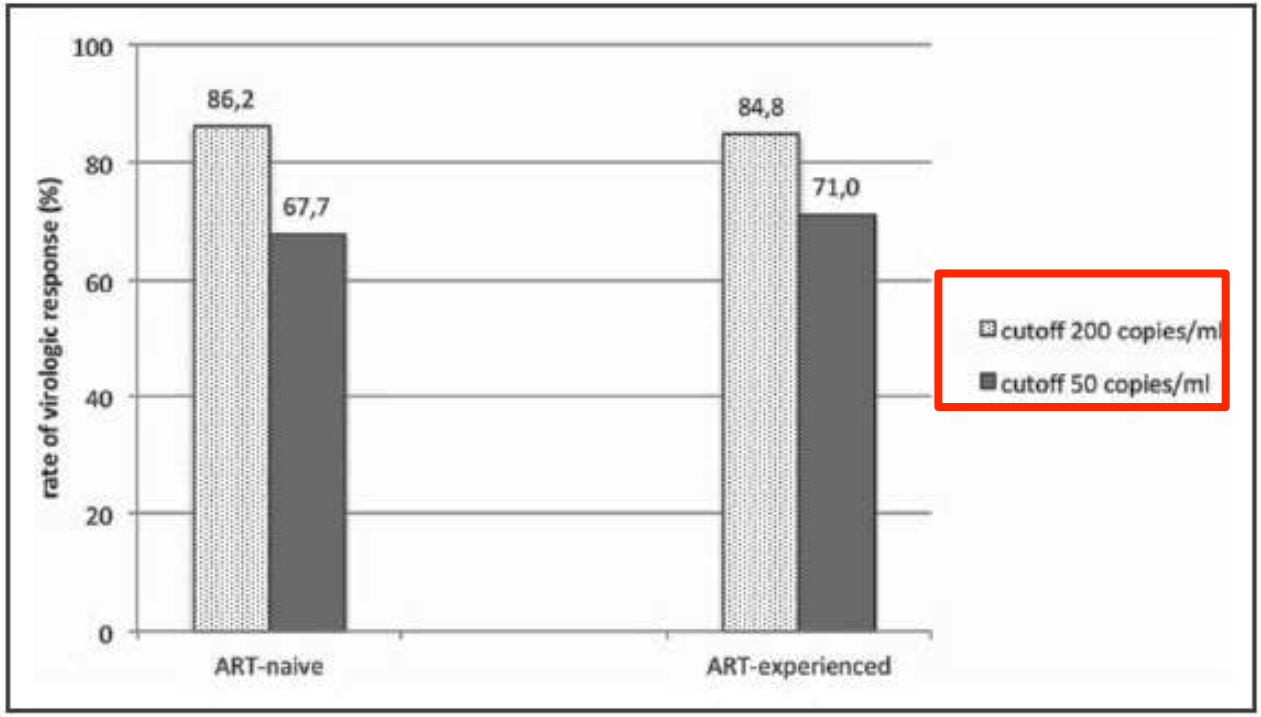

Figure 1. Response to RAL-therapy from week 24 on: 'Time to loss of virologic response' (TLOVR) analysis from week 24 on until the end of the observation period. Percentage of patients showing virologic response to RAL therapy for the whole time of observation.

		Background therapy					
		Dual therapy		Standard background therapy		Total	
Virologic response at week 48		60		171		231	
Cut-off 200 copies/ml	Virologic response	56	93.3%	147	86.0%	203	87.9%

Heterojen hasta grubu gerçek yaşam verileri:

ART naif hastalar başta olmak üzere deneyimli hastalarda da 48. hafta verilerine göre etkin

RAL+PI etkin bir seçenek

(24. hafta ve sonrasında >200 kopya/ml) saptanan toplam 44 hastanın 23'ünde yapılan direnç testi sonuçları:

12 hastada RAL direnci (3 naif)

Raltegravir central nervous system tolerability in clinical practice: results from a multicenter observational study

Giordano Madeddu[a], Barbara Menzaghi[b], Elena Ricci[c], Laura Carenzi[c], Canio Martinelli[d], Antonio di Biagio[e], Giustino Parruti[f], Giancarlo Orofino[g], Maria S. Mura[a], Paolo Bonfanti[h], for the C.I.S.A.I Group

Central nervous system (CNS) symptoms have been reported in clinical trials and case reports in patients receiving raltegravir. We investigated CNS symptoms in 453 HIV-infected patients. Of these 47 (10.4%) developed at least one drug-related CNS symptom. Predictors of CNS symptoms were concomitant therapy with tenofovir or with proton pump inhibitors that can increase raltegravir concentration. Thus, our data suggest a possible correlation between high raltegravir plasma concentrations and CNS symptoms, and therefore their monitoring in clinical practice.

- 18 Enfeksiyon Hastalıkları Bölümü, İtalya
- Surveillance Cohort Long-Term Toxicity of Antiretrovirals (SCOLTA): **online farmakovijilans program**
- **453 hasta**,%67 erkek
- Ortalama yaş: 48,2 yıl
- Ortanca izleme süresi: 23 ay

MSS yan etkileri

Toplam 47 (%10,4)

- **%3,8 baş ağrısı**
- **%3,3 depresyon**
- %1,8 anksiyete
- %1,5 baş dönmesi
- %1,3 uykusuzluk
- %0,2 uyku bozuklukları

Tedaviyi bırakma nedenleri

Toplam oran: %14

- **%3,3 yan etki**
  4 MSS yan etkisi: 2 baş ağrısı, 1 ajitasyon, 1 intihar girişimi
- **%3,3 hasta seçimi/düşük uyum**
- **%2,9 virolojik başarısızlık**
- %0,9 tedavi basitleştirme
- %2 ölüm
- %2 diğer

RAL alan hastalarda MSS yan etkileri açısından yakın takip

Eş zamanlı ilaç kullanımı risk faktörü olabilir (tenofovir?, PPI?)

anlamlı faktörler

DOLUTEGRAVİR

Original research article

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SAGE

Early clinical experience of dolutegravir in an HIV cohort in a larger teaching hospital

SEJ Todd, P Rafferty, E Walker, M Hunter, WW Dinsmore, CM Donnelly, EJ McCarty, SP Quah and CR Emerson

Abstract

Dolutegravir (DTG) is the third HIV integrase inhibitor (INI) available for prescription in Belfast since July 2014. It has shown high virological efficacy in both treatment-naïve and -experienced patients. We carried out a retrospective case chart analysis of HIV-1-positive adults commenced on DTG between July 2014 and September 2015. Patients were identified from records as either treatment-naïve or antiretroviral therapy (ART) experienced. Outcomes included: (1) virological response (HIV-1 RNA viral load at 0, 4, 8 and 12 weeks), (2) immunological response (CD4+ cell count at 0, 4, 8 and 12 weeks) and (3) tolerability (side effects and discontinuation). The main exclusion criteria were patients transferring care already established on DTG from other treatment centres or inadequate follow-up information (defined as attendance at <50% of clinical and serological follow-up visits). One hundred and fifty-seven commenced DTG out of 823 patients on ART; 106 (68%) were switched to DTG from another regimen, and 51 (32%) were ART-naïve. One naïve and 14 treatment-experienced patients were excluded from the analysis due to failure to attend clinical follow-up. Analysis of HIV-1 RNA viral load (HIV-1 VL) was divided into three groups: 50 new starters, 68 suppressed at switch and 24 not suppressed at switch. *New starters:* Baseline median HIV-1 RNA VL 71,259 copies/mL ($19{,}536_{Q25}$–$196{,}413_{Q75}$); 73% were virally undetectable (HIV-1 RNA VL <70 copies/mL) by week 4. *Switching patients:* Of those with an HIV-1 RNA undetectable viral load prior to switching, two were detectable with a mean viral load of 443,730 copies/mL after four weeks. Of the 24 patients detectable at switch (median HIV-1 VL 2212 [311_{Q25}–$43{,}467_{Q75}$]), 10 were detectable after four weeks. For those with a recordable viraemia, the median HIV-1 VL reduced to 376 (220_{Q25}–1181_{Q75}). At week 12, four patients were detectable with a median VL of 12,390 (567_{Q25}–$52{,}285_{Q75}$). Overall, 56 (35%) reported side effects; 40 (25%) reported either difficulty with low mood, anxiety or sleep disturbance. Sixteen (10%) discontinued DTG, with 13 (8%) due to intolerable side effects. DTG is a useful drug in naïve or switch patients. It has the potential to effectively suppress the viral load within the first four weeks of treatment and thus reduces infectiousness. Within the cohort, DTG was generally well tolerated but side effects such as low mood, anxiety and sleep disturbance were high, with 8% of patients discontinuing treatment.

- Retrospektif
- Temmuz 2014- Eylül 2015
- **157 DTG başlanan hasta**
- Ortanca yaş: 40 yıl, % 78 erkek
- **51(%32) ART naif**
  - %61 ABC/3TC, %37 TDF/FTC
- **106 (%68) ART deneyimli**
  - %65 ABC/3TC, %35 TDF/FTC

Table 2. Median CD4 cell count (cells/μl), HIV-1 RNA viral load (copies/mL) and serum creatinine (μmol/L), in naïve and treatment-experienced (switch) patients at baseline and week 12.

	Baseline		Week 12	
	Naïve (n = 50)	Switch (n = 92)	Naïve (n = 50)	Switch (n = 92)
Median CD4 cell count (cells/μl)	435	490	590	490
Median HIV viral load (copies/mL)	71,259	<70	<70	<70
Median serum creatinine (μmol/L)				
TDF/FTC backbone	77	81	79	87
ABC/3TC backbone	81	82	89	91

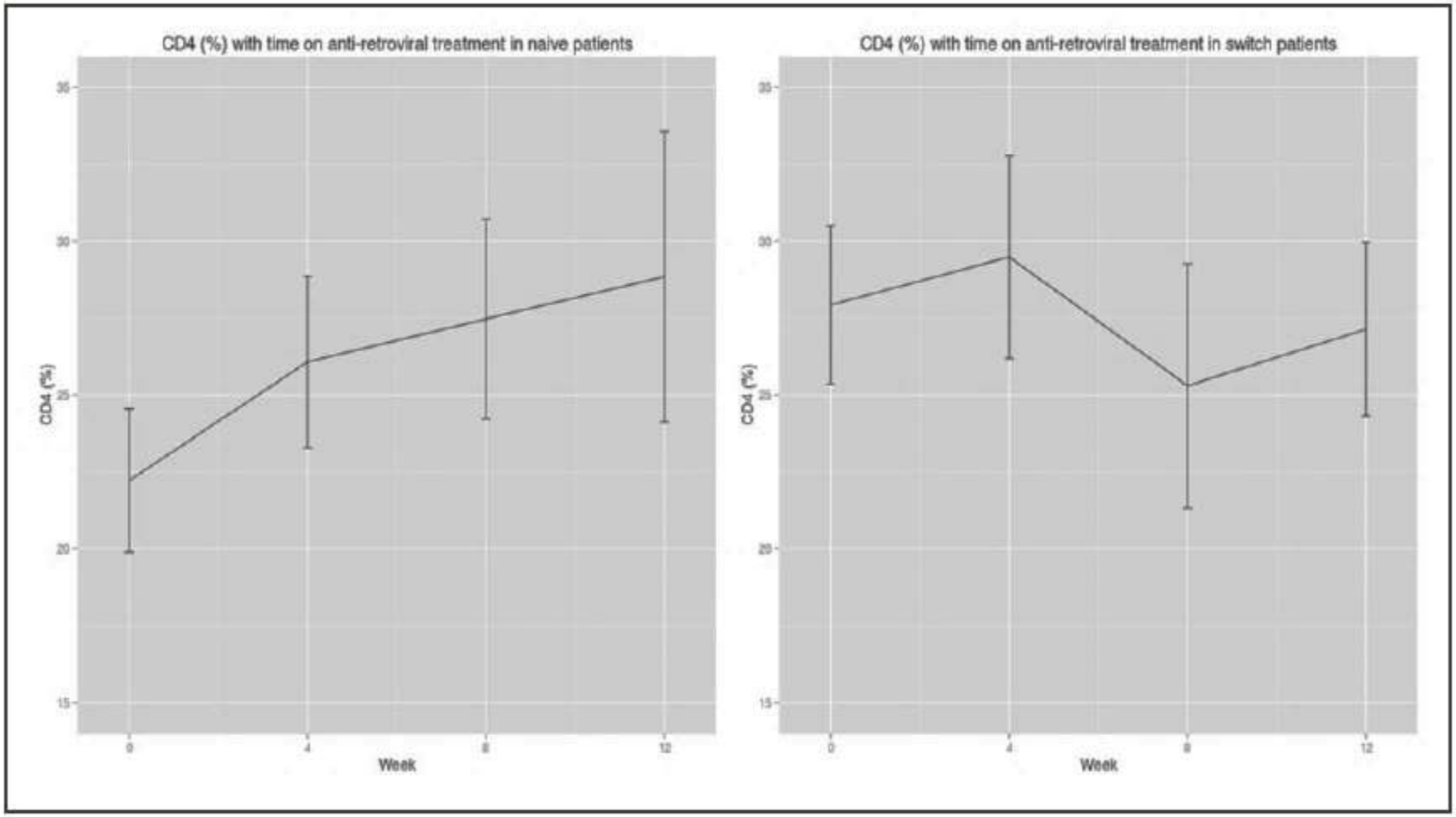

Figure 1. Mean CD4 cell count (%) in naïve and treatment-experienced patients at weeks 0, 4, 8 and 12. Bars represent confidence intervals (95% CI).

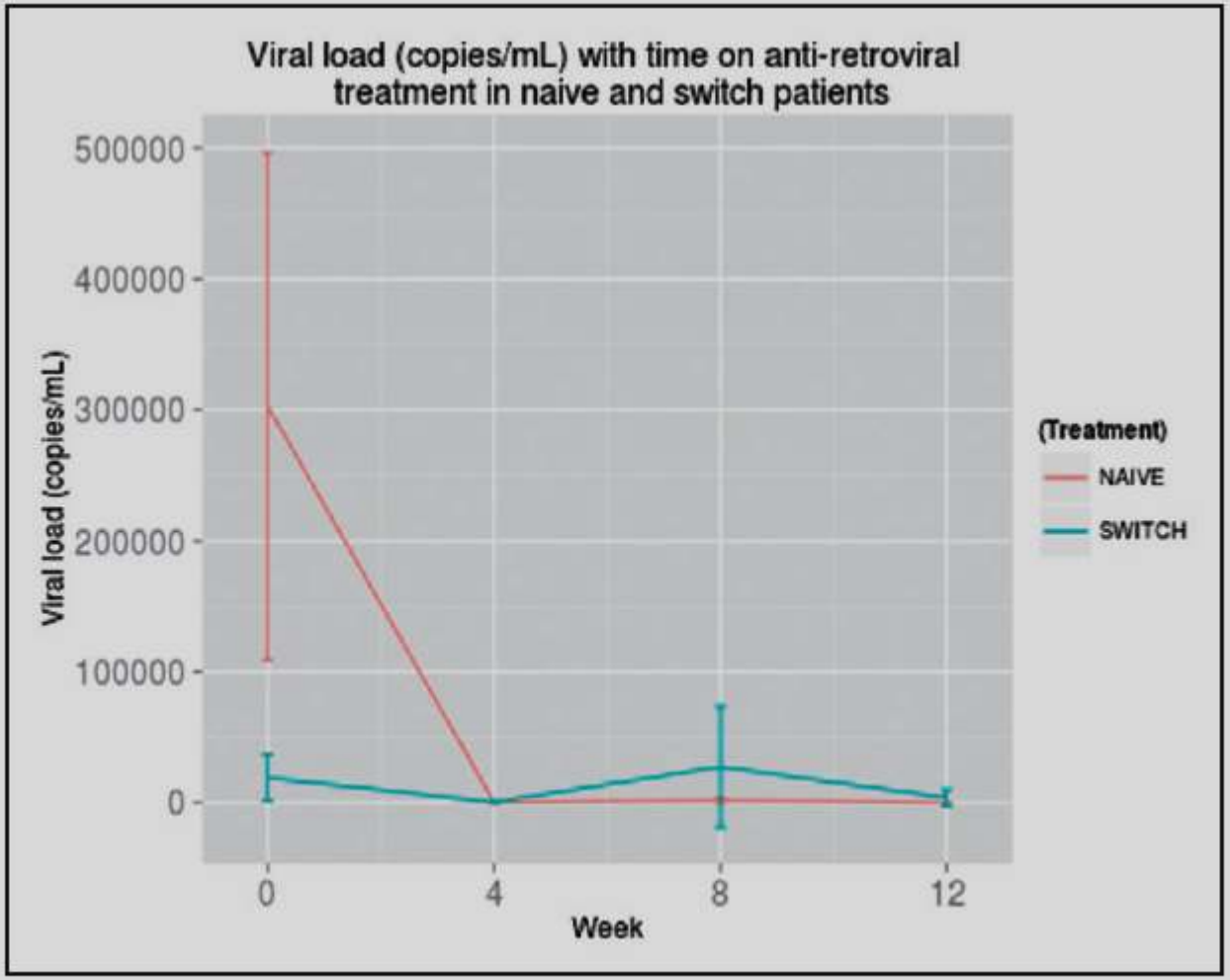

Figure 2. Mean HIV-1 RNA viral load (copies/mL) per week on antiretroviral treatment in naïve and switch patients. Bars represent 95% confidence intervals.

ART naif (n=50)

- Bazal ortanca HIV RNA: **71.259 kopya/ml**
- 4. hafta: ortanca HIV RNA: **<70 kopya/ml**

- HIV RNA **4. haftada %73**
  12. haftada %94
  oranında hastada saptanamaz düzeyde

- **12. hafta**:

1 hastada HIV RNA: 512 kopya/ml

bazal HIV RNA 4.084.746 kopya/ml, 7 ay sonra HIV RNA (-)

ART deneyimli (n=92)

- Hastaların %74'ünde switch sırasında viral yük saptanamaz düzeylerde
- 12. hafta:

  4 hastada ortanca HIV RNA:12.390 kopya/ml
(tüm hastalarda direnç ve uyumsuzluk (+))

Yan etkiler

Yan etki oranı: %35

- **%25 MSS**

  duygu durumunda bozulma, anksiyete, uyku bozuklukları
- %20 gastrointestinal
- % 3 döküntü
- % 2 terleme

Yan etki nedeniyle tedaviyi bırakma

Klinik çalışmalarla uyumlu etkinlik, viral yükte hızlı düşme

Yan etkiye bağlı tedaviyi bırakma oranları klinik çalışmalara kıyasla daha yüksek (%2-3---%8)

Original Article

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Experience of dolutegravir in HIV-infected treatment-naive patients from a tertiary care University Hospital in Ireland

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Abstract

Objective: Dolutegravir, an HIV integrase inhibitor, is a relatively new treatment option. To assess the tolerability, side effects, and time to viral decline to non-detectable in patients newly started on dolutegravir.

Methods: Retrospective health care record of 61 consecutive HIV treatment-naive patients started on dolutegravir was reviewed and analysed on SPSS.

Results: The mean initial viral load was 160826.05 copies/mL (range, 79–1,126,617 copies/mL). HIV viral load became non-detectable in 63.9% of patients on dolutegravir within 3 months. In all, 60.7% of patients reported no side effects on dolutegravir; 98.4% of the patients claimed full compliance to their antiretrovirals.

Conclusion: Dolutegravir was found to be efficacious and well tolerated in HIV-infected treatment-naive patients.

Keywords

Pharmacoepidemiology/drug safety, dolutegravir, HIV, viral load, naive, integrase inhibitor, tolerability

Date received: 6 September 2016; accepted: 28 September 2016

- Retrospektif
- Mayıs 2014- Mayıs 2015
- **61 ART naif hasta**
  Ortanca yaş: 37,8 yıl
  Erkek: %72
- **%90 TDF/FTC** %8 ABC/3TC
- **Hastalarda ART'ye uyum oranı: %98,4**

- Ortalama HIV RNA: **160.826.05** kopya /ml (79- 1,126,617)

- Hastaların **% 41'inde HIV RNA> 100.000** kopya/ml

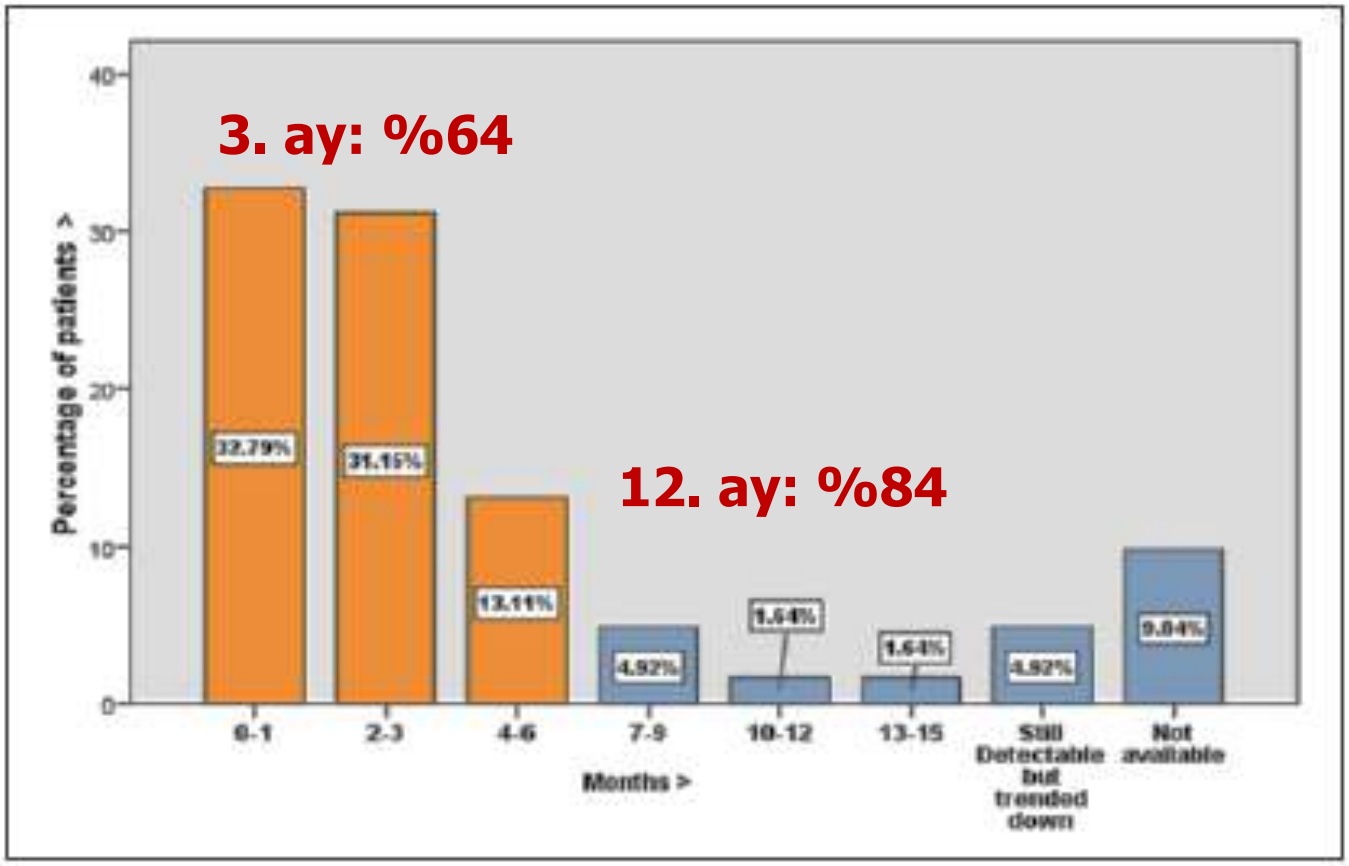

Figure 1. Number of months to viral load becoming non-detectable on DTG.

Table 1. Side effects reported by patients.

Side effects reported	Frequency	Percent
[illegible]	[illegible]	[illegible]

Klinik çalışmalarla uyumlu etkinlik

48. haftada viral yükün negatifleşme oranları klinik çalışmalarla kıyaslandığında daha düşük (%84---%88-90)

GI: gastrointestinal.

Yan etki oranı: %39,3
Tedaviyi sadece 1 hasta bıraktı
(döküntü, baş ağrısı, yaygın ağrı)

Intolerance of dolutegravir-containing combination antiretroviral therapy regimens in real-life clinical practice

Mark G.J. de Boer[a], Guido E.L. van den Berk[b], Natasja van Holten[a], Josephine E. Oryszcyn[b], Willemien Dorama[a], Daoud ait Moha[b] and Kees Brinkman[b]

Objective: Dolutegravir (DGV) is one of the preferred antiretroviral agents in first-line combination antiretroviral therapy (cART). Though considered to be a well tolerated drug, we aimed to determine the actual rate, timing and detailed motivation of stopping DGV in a real-life clinical setting.

Design: A cohort study including all patients who started DGV in two HIV treatment centers in The Netherlands.

Methods: All cART-naïve and cART-experienced patients who had started DGV were identified from the institutional HIV databases. Clinical data, including motivation and timing of discontinuation of DGV, were extracted from the patient files. Factors that potentially influenced discontinuation of DGV were compared between patients who stopped or continued DGV by multivariate and Kaplan–Meier analyses.

Results: In total, 556 patients were included, of whom 102 (18.4%) were cART-naïve at initiation of DGV. Median follow-up time was 225 days. Overall, in 85 patients (15.3%), DGV was stopped. In 76 patients (13.7%), this was due to intolerability. Insomnia and sleep disturbance (5.6%), gastrointestinal complaints (4.3%) and neuropsychiatric symptoms such as anxiety, psychosis and depression (4.3%) were the predominant reasons for switching DGV. In regimens that included abacavir, DGV was switched more frequently (adjusted relative risk 1.92, 95% confidence interval 1.09–3.38, *P* log-rank 0.01). No virologic failures were observed.

Conclusion: A relatively high rate of preliminary discontinuation of DGV due to intolerability was detected in our patient population. In particular, DGV was stopped more frequently if the regimen included abacavir. Multiple factors may explain these unexpected postmarketing observations, which warrant further investigation.

AIDS 2016, **30**:2831–2834

Keywords: dolutegravir, integrase inhibitor, side effects, toxicity

- Hollanda, 2 merkez
- Ağustos 2014- Mart 2016
- **556 hasta**
  - 102 (%18,4) ART naif
  - **%82 tedavi deneyimli**
- Ortanca yaş: 48 yıl; K/E: 7
- **%64 ABC** %29,4 TDF %10,6 PI/r

- Hasta izlem süresi: **ortanca 225 gün** (133-296)
- DTG kesilme zamanı: **ortanca 73 gün** (5-327)

Hastaların %15,3'ü ilacı bıraktı (% 95'i ilacı 48. hafta içinde)

Table 1. Reported adverse reactions leading to discontinuation of dolutegravir[a].

Adverse drug reaction	*n* (%)
Sleep disturbance, insomnia	31 (5.6)
Gastrointestinal complaints	21 (3.8)
Joint, tendon and/or muscle pain	11 (2.0)
Psychological/psychiatric symptoms[b]	14 (2.5)
Neurologic symptoms	10 (1.8)
General malaise (headache and severe fatigue)	24 (4.3)
Respiratory tract complaints	5 (0.9)
Other	9 (1.6)

Table 2. Risk factors for discontinuation of dolutegravir since start or switch to a dolutegravir-containing regimen.

Klinik çalışmalara kıyasla yan etkilere bağlı DTG'i kesme oranı göreceli olarak daha yüksek

ABC içeren rejimlerde DTG'i bırakma oranı daha yüksek

OLVG (vs. LUMC)	55 (14.2)	332	1.14 (0.72–1.83)	0.57

95% CI, 95% confidence interval; cART, combination antiretroviral therapy; DGV, dolutegravir; LUMC, Leiden University Medical Center; OLVG, OLVG Medical Center RR, relative risk; ABC, abacavir; TDF, tenofovir disoproxil; PI, protease inhibitor. Manufacturers of Atripula: Bristol-Myers Squibb and Gilead Sciences Ltd.
[a]Adjusted RR for sex, age and naïve for cART, yes or no.

ELVİTEGRAVİR

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Safety and Tolerability of Stribild in the Southeast United States

Caroline Boyd Derrick, PharmD, BCPS[1], Zhiqiang Kevin Lu, PhD[2], Celeste Rudisill Caulder, PharmD[2], Elizabeth Kelly Hester, PharmD, FCCP, BCPS[3], Tyler David Wagner[4], and Paul Brandon Bookstaver, PharmD, FCCP, BCPS[2]

Abstract

Purpose: The purpose of this study is to assess postmarketing safety and tolerability of Stribild (elvitegravir [EVG]/cobicistat [COBI]/tenofovir disoproxil fumarate [TDF]/emtricitabine [FTC]). **Methods:** A retrospective, pharmacoepidemiologic study in 2 outpatient HIV clinics in the Southeast United States was conducted among adults receiving EVG/COBI/TDF/FTC. We evaluated incidence and treatment-related adverse events, including change in serum creatinine (SCr). **Results:** Patients were primarily treatment experienced (n = 173, 60%), African American (n = 210, 73%), and males (n = 187, 65%). One hundred ninety-five (68%) patients had any increase in SCr, and 65 (23%) had an increase of ≥0.3 mg/dL. Mean SCr change from baseline to peak was 0.2 mg/dL. Being treatment experienced (odds ratio [OR] = 2.21, 95% confidence interval [CI]: 1.12-4.38) was associated with SCr ≥0.3 mg/dL, while body mass index ≥30 kg/m^2 (OR = 0.41, 95% CI: 0.18-0.93) was protective. Twenty (7%) patients discontinued therapy, 3 due to acute kidney injury. **Conclusion:** Our results demonstrate limited adverse events and low discontinuation rates associated with EVG/COBI/TDF/FTC.

- **Çok merkezli, retrospektif, gözlemsel farmakoepidemiyolojik kohort**
- Eylül 2012-Ağustos 2013
- >18 yaş, **286 hasta**

  %65 erkek

  %41 ART naif

  % 50'si TDF kullanıyor, 1/3'ünde viral yük: (-)
- Ortalama yaş: 39 yıl (18-75)
- Ortalama izlem süresi: **226 gün**

Table 1. Baseline Characteristics.[a]

Baseline Characteristics	All (n = 286)	Increase in SCr ≥0.3 (n = 65)	Increase in SCr ≥0.5 (n = 13)
Mean age (SD), years	38.6 (12.4)	38.0 (12.0)	42.8 (12.0)
Gender, n (%)			
Male	187 (65.4%)	42 (64.6%)	10 (76.9%)
Female	99 (34.6%)	23 (35.4%)	3 (23.1%)
Race, n (%)			
White	63 (22.0%)	18 (27.7%)	5 (38.5%)
Black	210 (73.4%)	43 (66.2%)	8 (61.5%)
Hispanic	8 (2.8%)	3 (4.6%)	0
Others	5 (1.8%)	1 (1.5%)	0
Mean weight (SD), kg	84.6 (25.7)	78.5 (20.4)	81.3 (23.8)
Mean height (SD), cm	173.2 (8.9)	172.0 (9.3)	176.0 (7.8)
Mean BMI (SD), kg/m^2	28.2 (8.2)	26.6 (6.8)	26.0 (6.9)
BMI, kg/m^2			
≤25.0	129 (45.1%)	30 (46.2%)	7 (53.9%)
25.1-29.9	60 (21.0%)	22 (33.9%)	2 (15.3%)
≥30.0	97 (33.9%)	13 (20.0%)	4 (30.8%)
Mean AST (SD), IU/L	28.4 (24.7)	29.4 (15.1)	32.7 (13.4)
Mean ALT (SD), IU/L	31.9 (30.1)	32.1 (23.9)	47.2 (37.6)
Renal function values			
Mean SCr (SD), mg/dL	0.9 (0.2)	0.8 (0.2)	1.0 (0.3)
Mean BUN (SD), mg/dL	12.5 (3.7)	12.1 (3.3)	14.3 (3.1)
Median CrCl (range), mL/min	106.6 (43-221)	118.0 (55-212)	110.8 (55-145)
CrCl <70 mL/min, n (%)	24 (8.4%)	4 (6.2%)	3 (23.1%)

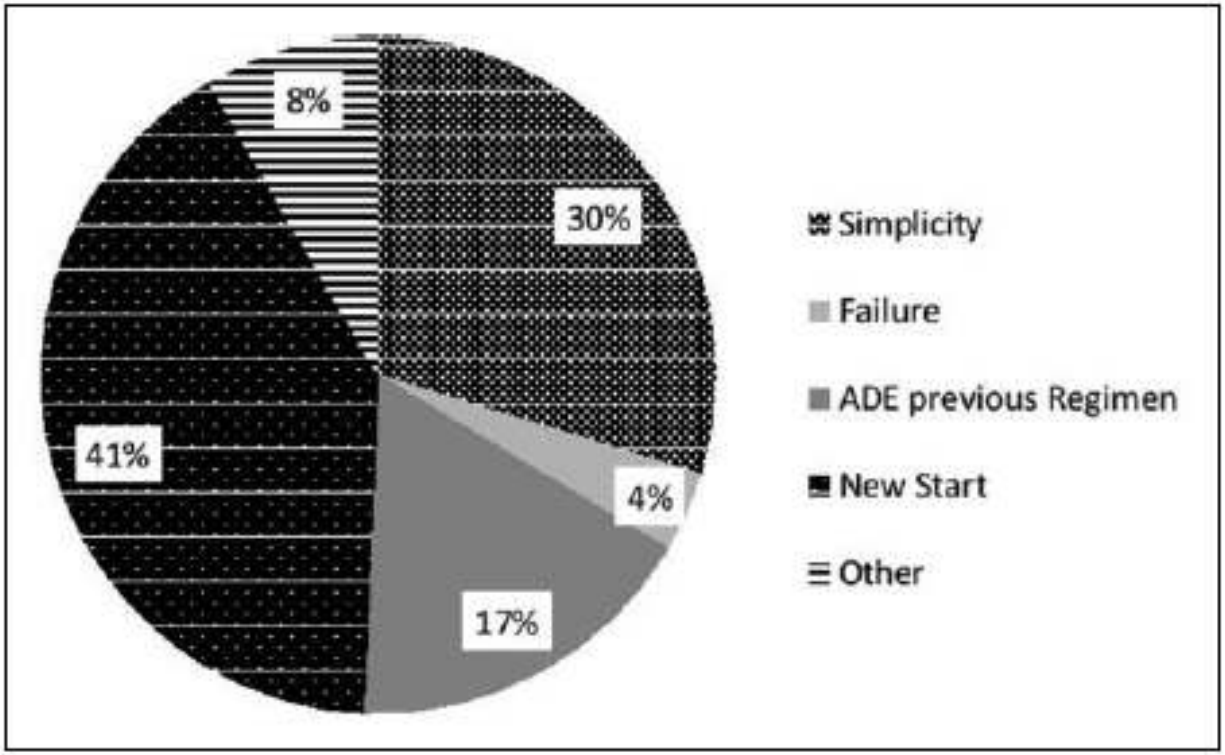


Figure 1. Reasons for starting EVG/COBI/TDF/FTC. Reinitiation of therapy occurred in 3% of patients (included in the new start patients). Other includes less strict meal requirements, pregnancy, prior noncompliance, work-related changes, and not documented.
ADE, adverse drug event; COBI, cobicistat; EVG, elvitegravir; FTC, emtricitabine; TDF, tenofovir disoproxil fumarate.

Baseline Characteristics	All (n = 286)	Increase in SCr ≥0.3 (n = 65)	Increase in SCr ≥0.5 (n = 13)
Concomitant nephrotoxins			
SMX/TMP	51 (17.8%)	15 (23.1%)	3 (23.1%)
NSAIDS	32 (11.2%)	6 (9.2%)	0
ACE-I	49 (17.1%)	14 (21.5%)	4 (30.8%)
Acyclovir/valacyclovir	7 (2.5%)	0	0
Diuretics	19 (6.6%)	4 (6.2%)	2 (15.4%)
Initiated SMX/TMP with Stribild	21 (7.3%)	7 (10.8%)	2 (15.4%)
Comorbidities, n (%)			
Cardiovascular disease	113 (39.5%)	27 (41.5%)	7 (53.9%)
Hepatic insufficiency	20 (7.0%)	2 (3.1%)	0
Cerebrovascular disease	10 (3.5%)	3 (4.6%)	1 (7.7%)
Psychiatric disorders	117 (40.9%)	19 (29.2%)	1 (7.7%)
HIV-related data			
Treatment naive, n (%)	113 (39.5%)	33 (50.8%)	7 (53.9%)
Mean CD4 count (SD), cells/μL	440 (323)	373 (312)	347 (355)
CD4 count <200 cells/μL	82 (28.7%)	25 (38.5%)	7 (53.9%)
Median viral load (range), copies/mL	5154 (10-3 395 350)	34 795 (10-896 000)	111 238 (10-821 508)
Viral load ≤20 copies/mL, n (%)	89 (31.1%)	21 (32.3%)	4 (30.8%)

Abbreviations: ACE-I, angiotensin-converting enzymes inhibitors; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BUN, blood urea nitrogen; CrCl, creatinine clearance; HIV, human immunodeficiency virus; NSAIDs, nonsteroidal anti-inflammatory drugs; SCr, serum creatinine; SMX/TMP, sulfamethoxazole-trimethoprim.

[a]Creatinine clearance calculated using Cockcroft-Gault formula.[14]

Table 2. Renal Outcomes on EVG/COBI/TDF/FTC Therapy.[a,b,c]

	All Patients
Mean SCr change ± SD (baseline to first follow-up), mg/dL	0.1 ± 0.2280
Mean SCr change ± SD (baseline to peak SCr), mg/dL	0.2 ± 0.6286
Mean CrCl decrease ± SD (baseline to first follow-up), mg/dL	5.1 ± 52.7280
Mean CrCl decrease ± SD (baseline to peak SCr), mg/dL	16.1 ± 19.2280
Increase in SCr ≥ 0.3 mg/dL, n (%)	65 (22.7%)
Increase in SCr ≥ 0.5 mg/dL, n (%)	13 (4.5%)

Abbreviations: COBI; cobicistat; CrCL, creatinine clearance; EVG, elvitegravir; FTC, emtricitabine; SCr, serum creatinine; SD, standard deviation; TDF, tenofovir disoproxil fumarate.

[a]Average time to the first follow-up was 65 days.

[b]Average number of days between baseline and peak was 111.

[c]Average number of days between EVG/COBI/TDF/FTC start and last follow-up was 226.

KrKl'de ortalama azalma: 16,1 ml/dak

KrKl'de ortalama azalma: 45 ml/dak

KrKl'de ortalama azalma: 48 ml/dak

Table 3. Associated Factors in Patients with a SCr Increase of ≥0.3 mg/dL

Characteristics	OR	95% CI	*P* Value
Age, years			
18-40	1.00	-	-
≥40	1.05	0.55-2.02	.88
Race			
White	1.00	-	-
Blacks	0.70	0.35-1.42	.45
Hispanic	1.76	0.32-9.76	.36
Others	0.63	0.06-7.09	.67
Gender			
Male	1.00	-	-
Female	1.56	0.81-3.02	.18
BMI, kg/m^2			
≤25.0	1.00	-	-
25.1-29.9	1.87	0.92-3.81	.17
≥30.0	0.41	0.18-0.93	.002
CD4 count/μL			
<200	1.00	-	-
≥200	0.51	0.24-1.07	.07
Viral load, copies/mL			
<20	1.00	-	-
≥20	0.57	0.27-1.21	.15
CrCl at baseline, mL/min			
<70	1.00	-	-
≥70	1.45	0.43-4.89	.55
ARV exposure history			
Treatment naive	1.00	-	-
Treatment experienced	2.21	1.12-4.38	.02
SMX/TMP			
No	1.00	-	-
Yes	0.97	0.40-2.33	.95
ACE-I			
No	1.00	-	-
Yes	1.94	0.85-4.43	.12

Abbreviations: ACE-I, angiotensin-converting enzymes inhibitors; ARV, antiretroviral; BMI, Body Mass Index; CI, confidence interval; CrCl, creatinine clearance; OR, odds ratio; SMX/TMP, sulfamethoxazole-trimethoprim.

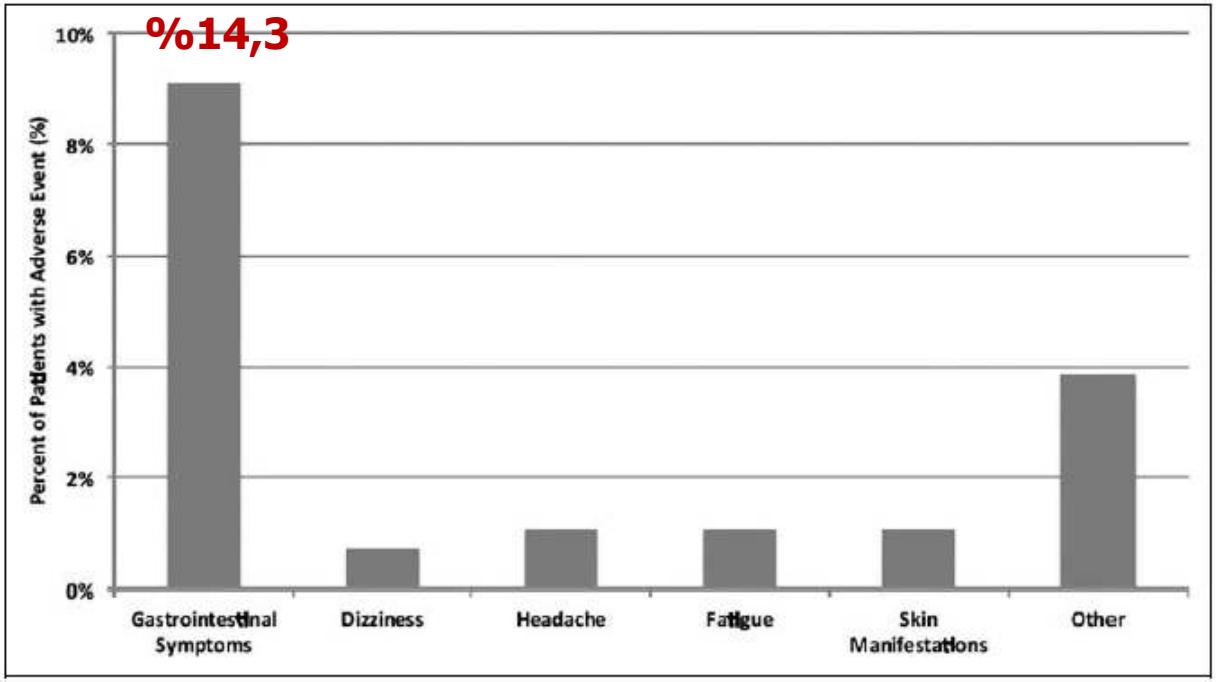
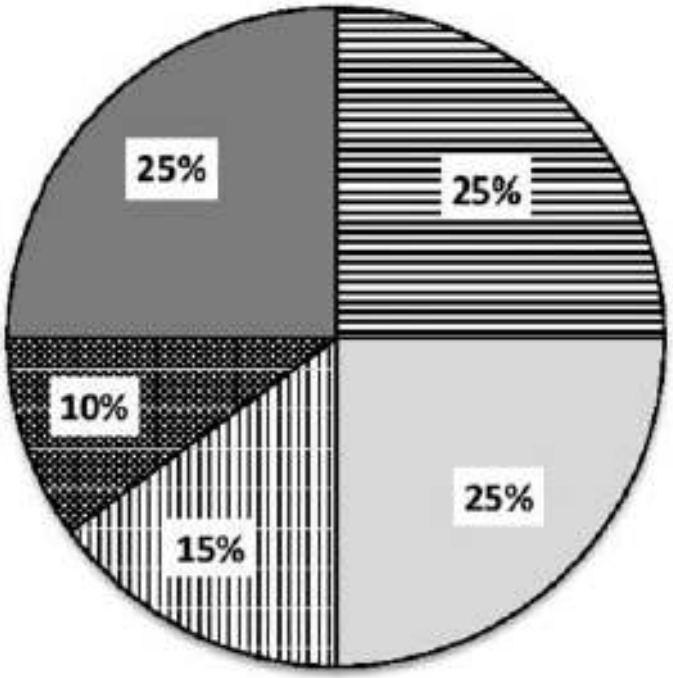


Figure 2. Nonrenal adverse events on EVG/COBI/TDF/FTC therapy. Other reasons include gallbladder pain, weight gain, body aches, altered mental status, edema, and hot flashes. COBI, cobicistat; EVG, elvitegravir; FTC, emtricitabine; TDF, tenofovir disoproxil fumarate.

Tedaviyi bırakma nedenleri

20 patients (7%)



- Non-Renal Adverse Events — fatigue, gastrointestinal , dizziness
- Virologic Failure — with documented integrase resistance
- AKI — 3 naive pts: 1TMP-SXT, 2 ACE inh
- Monetary Issues
- Undefined

Figure 3. Reasons for EVG/COBI/TDF/FTC discontinuation. AKI, acute kidney injury; COBI, cobicistat; EVG, elvitegravir; FTC, emtricitabine; TDF, tenofovir disoproxil fumarate.

Table 4. EVG/COBI/TDF/FTC Clinical and Laboratory Outcomes.[a,b]

	All Patients

Serum kreatinin düzeylerinde artış ve renal yan etkiler klinik çalışmalardakine benzer

İleri evre hastalıkta serum kreatinin düzeylerinde artış ihtimali daha yüksek

İlacı bırakma oranları benzer, daha düşük

Yan etkiler hafif düzeyde

Abbreviation: COBI; cobicistat; EVG, elvitegravir; FTC, emtricitabine; SD, standard deviation; TDF, tenofovir disoproxil fumarate.
[a]Average time to first follow-up = 65 days or 2.1 months.
[b]Average time to last follow-up = 223 days or 7.3 months.

İNSTİ

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HIV Medicine (2017), 18, 56–63

ORIGINAL RESEARCH

Higher rates of neuropsychiatric adverse events leading to dolutegravir discontinuation in women and older patients

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Objectives

Dolutegravir (DTG), a second-generation integrase strand transfer inhibitor (INSTI), is now among the most frequently used antiretroviral agents. However, recent reports have raised concerns about potential neurotoxicity.

Methods

We performed a retrospective analysis of a cohort of HIV-infected patients who had initiated an INSTI in two large German out-patient clinics between 2007 and 2016. We compared discontinuation rates because of adverse events (AEs) within 2 years of starting treatment with dolutegravir, raltegravir or elvitegravir/cobicistat. We also evaluated factors associated with dolutegravir discontinuation.

Results

A total of 1950 INSTI-based therapies were initiated in 1704 patients eligible for analysis within the observation period. The estimated rates of any AE and of neuropsychiatric AEs leading to discontinuation within 12 months were 7.6% and 5.6%, respectively, for dolutegravir (n = 985), 7.6% and 0.7%, respectively, for elvitegravir (n = 287), and 3.3% and 1.9%, respectively, for raltegravir (n = 678). Neuropsychiatric AEs leading to dolutegravir discontinuation were observed more frequently in women [hazard ratio (HR) 2.64; 95% confidence interval (CI) 1.23–5.65; P = 0.012], in patients older than 60 years (HR: 2.86; 95% CI: 1.42–5.77; P = 0.003) and in human leucocyte antigen (HLA)-B*5701-negative patients who initiated abacavir at the same time (HR: 2.42; 95% CI: 1.38–4.24; P = 0.002).

- Retrospektif, 2 merkez
- Ocak 2007-Nisan 2016
- 1704 hasta
- **1950 İNSTİ temelli tedavi**
- 228 hasta 2, 9 hasta 3 INSTI temelli ART
- INSTI başlanan naif hastalar:
  EVG (%23)
  DTG (%21)
  RAL (%13)

Table 1 Outcome and adverse events (AEs) for individuals who received prescriptions of integrase strand transfer inhibitors (INSTIs) between January 2007 and April 2016 in both centres

	Dolutegravir	Elvitegravir	Raltegravir
Total INSTI therapies (*n*)	1073	342	776
INSTI started within RCT (*n*)	13	14	17
INSTI started elsewhere (*n*)	48	21	66
Insufficient data, lack of follow-up (*n*)	27	20	15
Follow-up per exposure (months) [median (range)]	11.5 (0–25.4)	16.0 (0.4–33.4)	36.3 (0.2–107.3)
Exposures on INSTI analysed (*n*)	985	287	678
Alive and on INSTI at time of data cut [% (*n*)]	91.0 (896)	83.3 (239)	54.0 (366)
Death while on INSTI [% (*n*)]	0.9 (9)	0.3 (1)	4.7 (32)

Tedavi bıraktırmayı gerektiren yan etki oranı: toplam %6,3

	Dolutegravir	Elvitegravir	Raltegravir
Reasons for discontinuation of INSTI (per exposure) over entire follow-up period			
Other reasons [% (*n*)]	0.2 (2)	2.4 (7)	1.5 (8)
Discontinuation because of AEs (any) [% (*n*)]	6.8 (67)	9.4 (27)	4.1 (28)
All AEs leading to discontinuation over entire follow-up period			
Renal [% (*n*)]	0.2 (2)	3.5 (10)	0.0 (0)
Gastrointestinal [% (*n*)]	0.7 (7)	2.8 (8)	0.9 (6)
Hepatic [% (*n*)]	0.1 (1)	0.0 (0)	0.1 (1)
Skin [% (*n*)]	0.3 (3)	0.7 (2)	0.1 (1)
Other [% (*n*)]	0.5 (5)	1.4 (4)	0.9 (6)
Neuropsychiatric [% (*n*)]	5.0 (49)	1.0 (3)	2.1 (14)
Neuropsychiatric adverse events*			
Insomnia, sleep disturbances	36	2	4
Poor concentration, slow thinking	8	0	0
Dizzyness	13	1	3
Headache, paraesthesia	16	1	6
Depression	7	0	1

Hayatı tehdit eden semptom yok
DTG kesildikten sonra semptomlar hızla geriledi

Table 3 Relative hazards (RHs) of variables significantly associated with dolutegravir (DTG) discontinuation [because of any adverse event (AE) or neuropsychiatric AEs] and remaining in the final Cox model

	RH	95% CI	*P*
Any AE			
Female, vs. male gender	2.81	1.46–5.41	0.002
Older age (> 60 years), vs. younger age	2.88	1.56–5.34	< 0.001
ABC with DTG initiated, vs. no ABC	2.63	1.61–4.29	0.0001
DTG start in 2016, vs. in 2014/2015	8.93	3.76–21.28	< 0.0001
Neuropsychiatric AEs			
Female, vs. male gender	2.64	1.23–5.65	0.01
Older age (> 60 years), vs. younger age	2.86	1.42–5.77	0.003
ABC with DTG initiated, vs. no ABC	2.42	1.38–4.24	0.002
DTG start in 2016, vs. in 2014/2015	11.36	4.31–29.41	< 0.0001

ABC, abacavir; CI, confidence interval.

İlk 1 yılda DTG'yi yan etkiler (özellikle nöropsikiyatrik) nedeniyle bırakma oranı klinik çalışmalara oranla daha yüksek (%1,2-2,5---%6)

DTG'yi bırakma oranı kadın veya >60 yaş hastalarda 3 kat daha fazla

Sınıflar arası çapraz reaksiyon yok

STRIBILD GERÇEK YAŞAM VERİLERİ: ACTHIV-IST VERİ TABANI

- **ACTHIV-IST (ACTion against HIV in ISTanbul) İstanbul; 5 merkez:**
  - Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi
  - Bezm-i Alem Üniversitesi Vakıf Gureba Hastanesi
  - İstanbul Üniversitesi Cerrahpaşa Tıp Fakültesi
  - Göztepe Medeniyet Üniversitesi Tıp Fakültesi
  - Şişli Hamidiye Etfal Eğitim ve Araştırma Hastanesi

- Mayıs 2015-Aralık 2016
- Stribild başlanan 6. ve/veya 12. aylık izlem verileri bulunan hastalar

Merkezler	n	%
Şişli Hamidiye Etfal Eğitim ve Araştırma Hastanesi	172	**44.4**
İstanbul Üniversitesi Cerrahpaşa Tıp Fakültesi	64	16.5
Göztepe Medeniyet Üniversitesi Üniversitesi Tıp Fakültesi	63	16.3
Bezm-i Alem Üniversitesi Vakıf Gureba Hastanesi	45	11.6
Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi	43	11.1
Total	**387**	**100.0**

- **387 hasta**; %91 erkek, %48,6 MSM
- Ortanca yaş: 32 yıl (18-77)
- **Stribild kullanım süresi:2736 hasta-ay**
- **Ortanca izlem süresi: 12 ay (2-40)**

Değerlendirmeye alınan toplam:210 hasta

- %91,5 erkek, %49 MSM
- Ortanca yaş: 33 yıl (18-77)

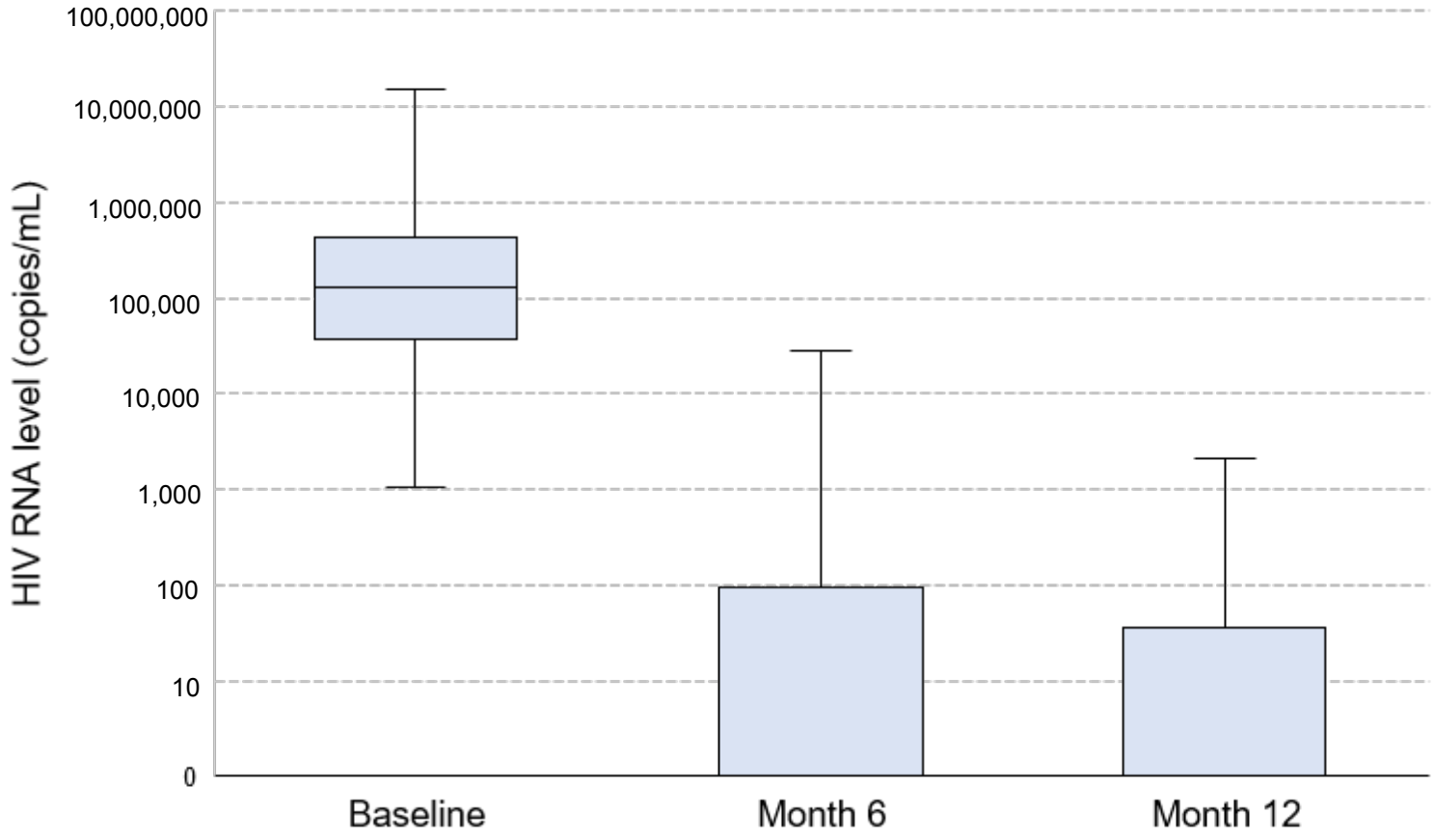
- **Naif:133 (%63)**
- **Tedavi deneyimli:77 (%37)**

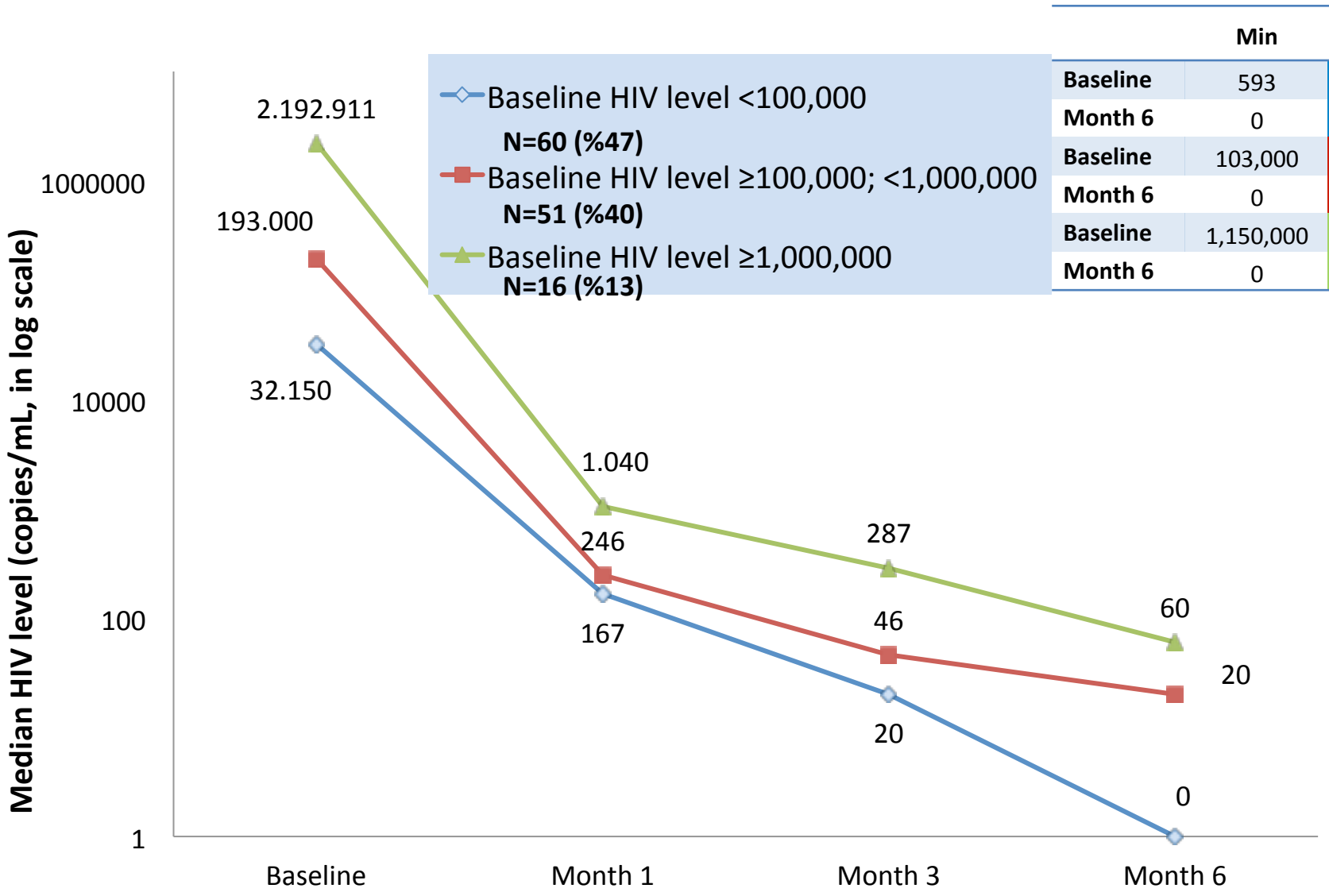
Naif hastalar

- **N=133**, % 95,5 erkek
- Ortanca yaş: 32 yıl (18-77)
- % 54 MSM

HIV RNA level (copies/mL) in treatment status subgroups

	Median	Minimum	Maximum
Naive			
Baseline	129,000	310	15,236,051
Month 6	0	0	492,225
Month 12	0	0	2,138





	Min	Max
Baseline	593	92,889
Month 6	0	28,713
Baseline	103,000	952,000
Month 6	0	492,225
Baseline	1,150,000	8,688,605
Month 6	0	3,524

Figure HIV RNA level (copies/mL) of patients with 6th month measurements regarding baseline HIV RNA level subgroups in treatment naïve patients

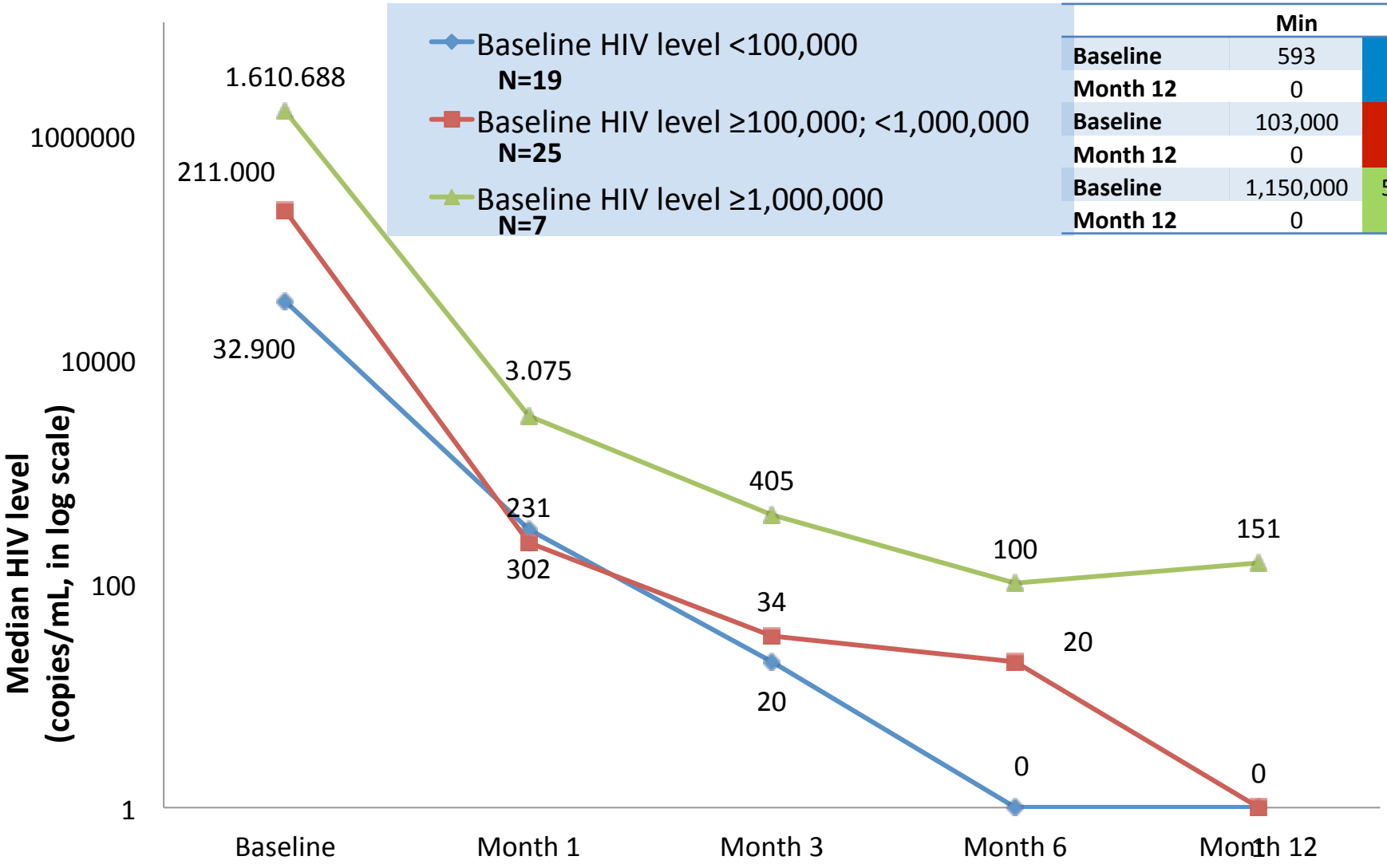


Figure HIV RNA level (copies/mL) of patients with 12th month measurements regarding baseline HIV RNA level subgroups in treatment naïve patients

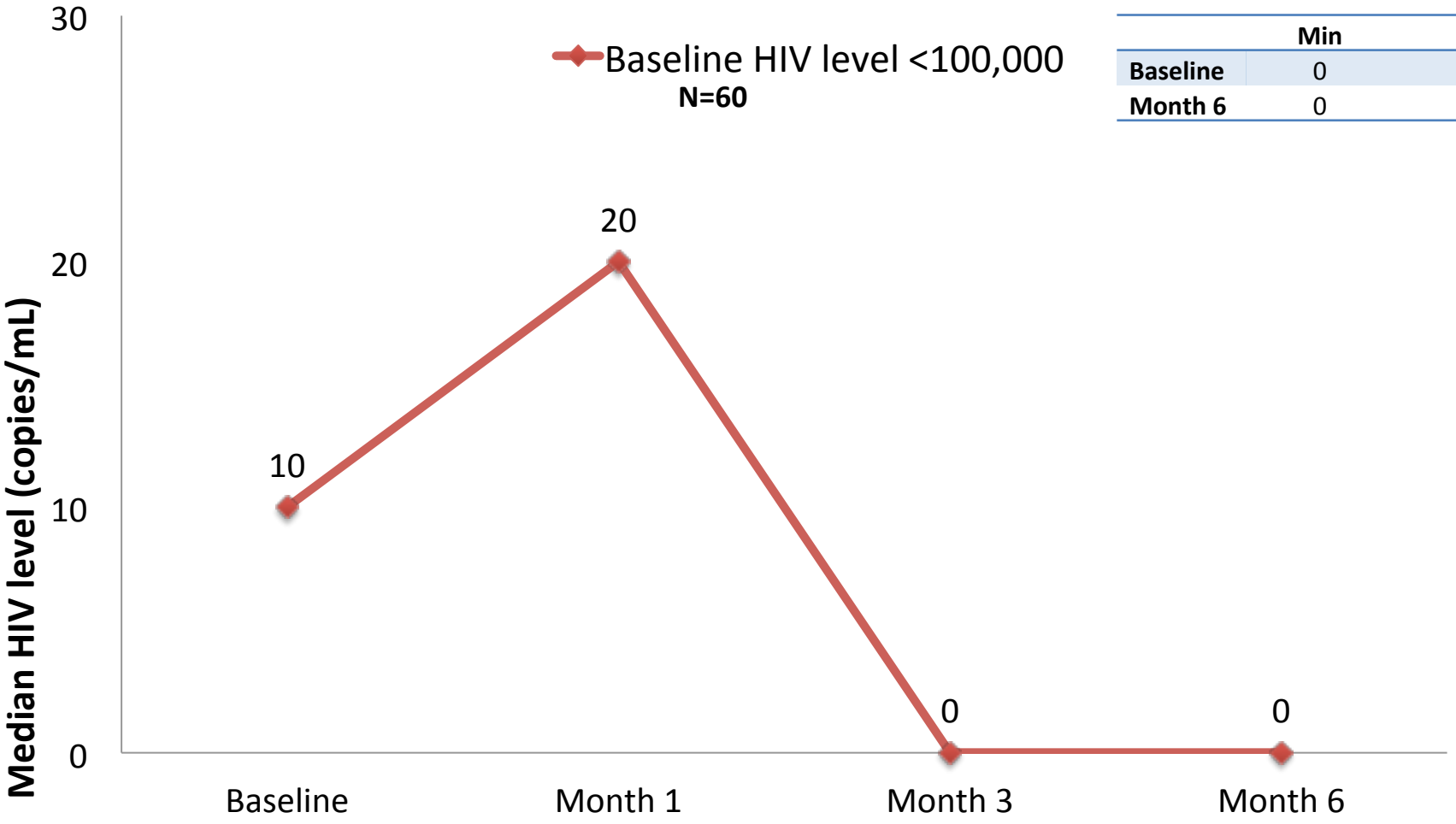
Tedavi deneyimli hastalar

- **N=77**

  60 tedaviyi basitleştirme

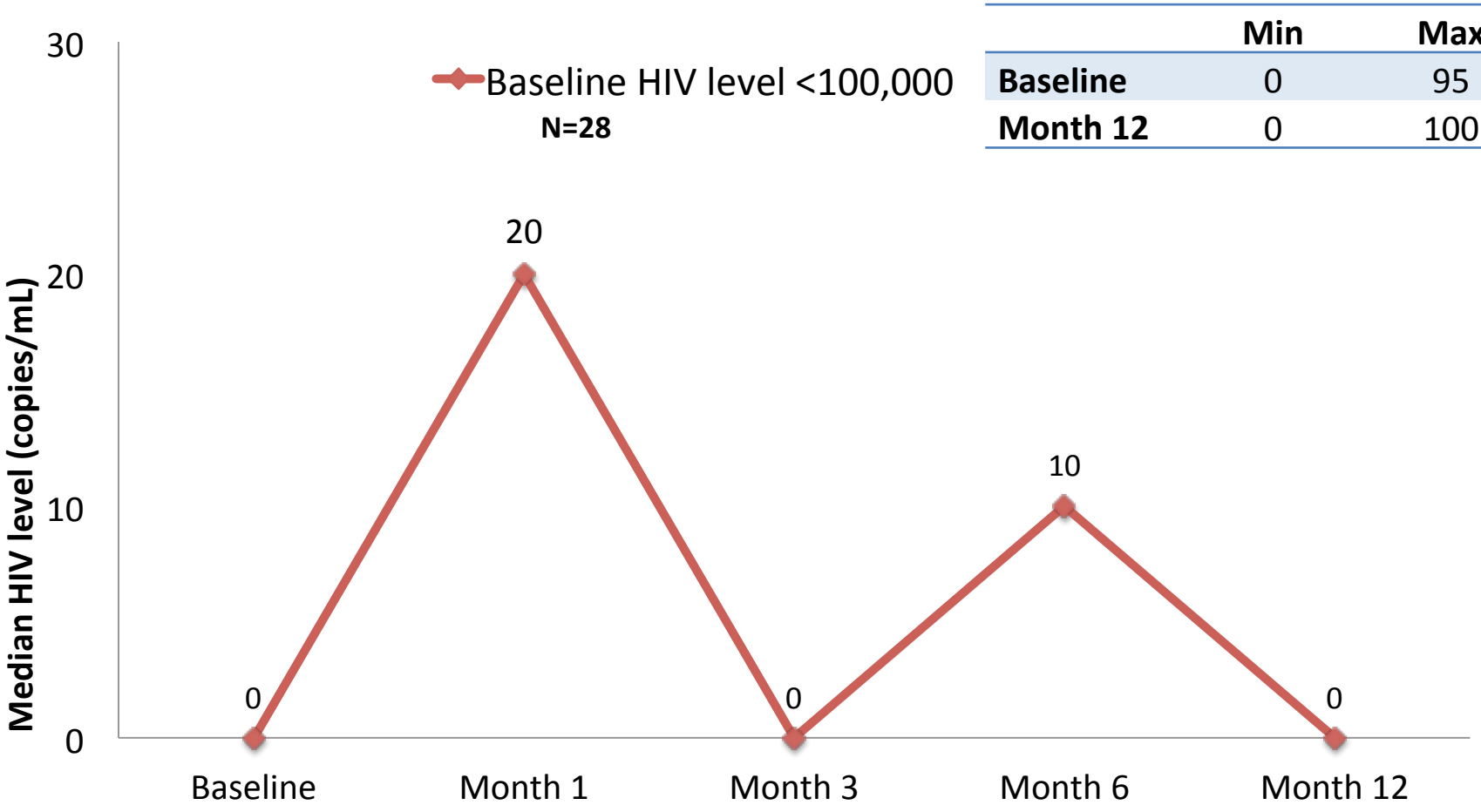
  17 tedaviye yanıtsız
- % 86,4 erkek, % 45,4 MSM
- Ortanca yaş: 35 yıl (20-76)
- %97 TDF/FTC %48 LPV/r %47 EFV

Tedaviyi basitleştirme (n=60)



	Min	Max
Baseline	0	95
Month 6	0	777

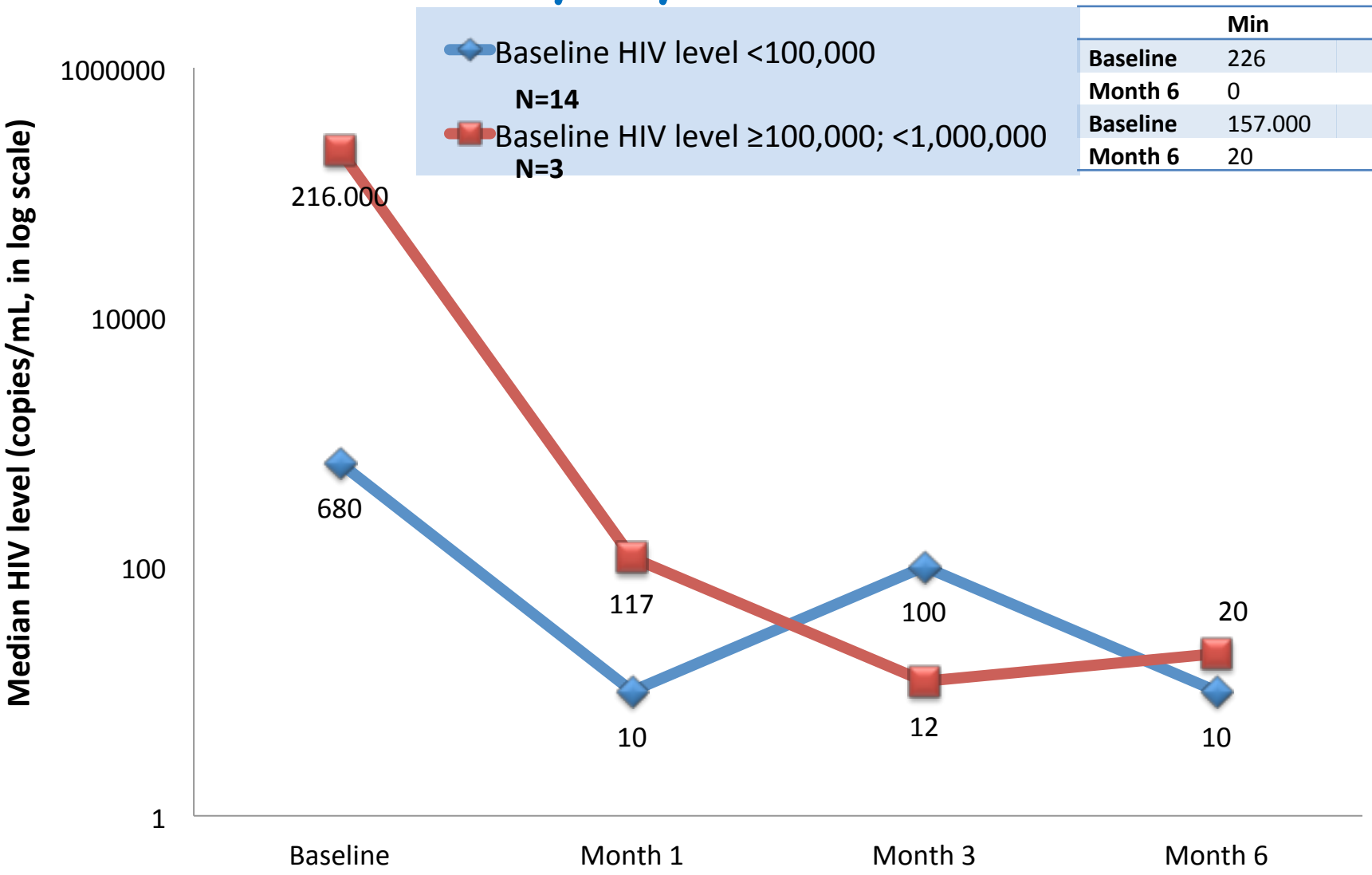
Figure HIV RNA level (copies/mL) of patients with 6th month measurements regarding baseline HIV RNA level subgroups in treatment experienced (switch) patients



	Min	Max
Baseline	0	95
Month 12	0	100

Figure HIV RNA level (copies/mL) of patients with 12th month measurements regarding baseline HIV RNA level subgroups in treatment experienced (switch) patients

Tedaviye yanıtsız (n=17)



	Min	Max
Baseline	226	74,600
Month 6	0	759
Baseline	157.000	224,000
Month 6	20	58

Figure HIV RNA level (copies/mL) of patients with 6th month measurements regarding baseline HIV RNA level subgroups in treatment experienced (treatment failure) patients

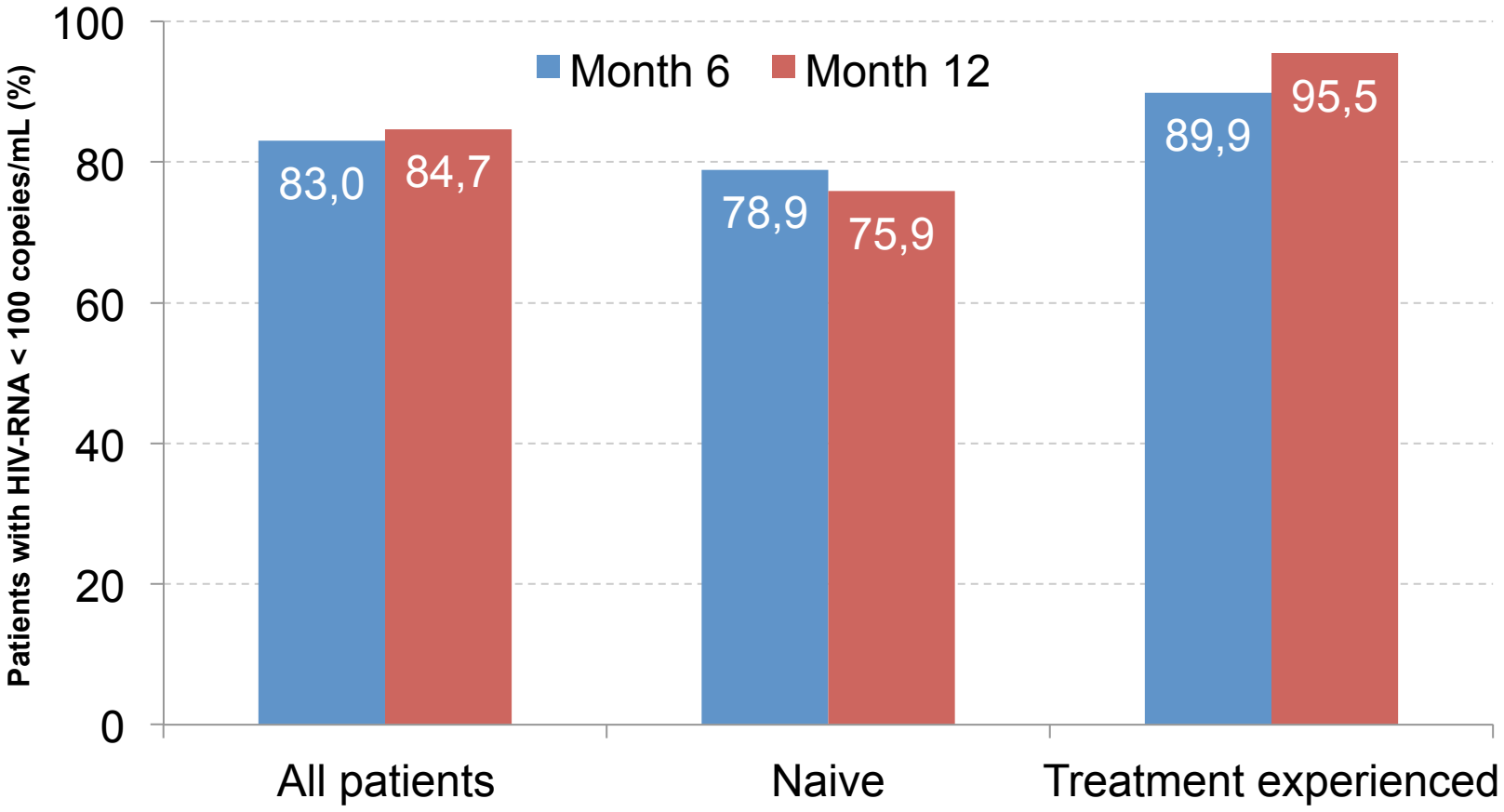
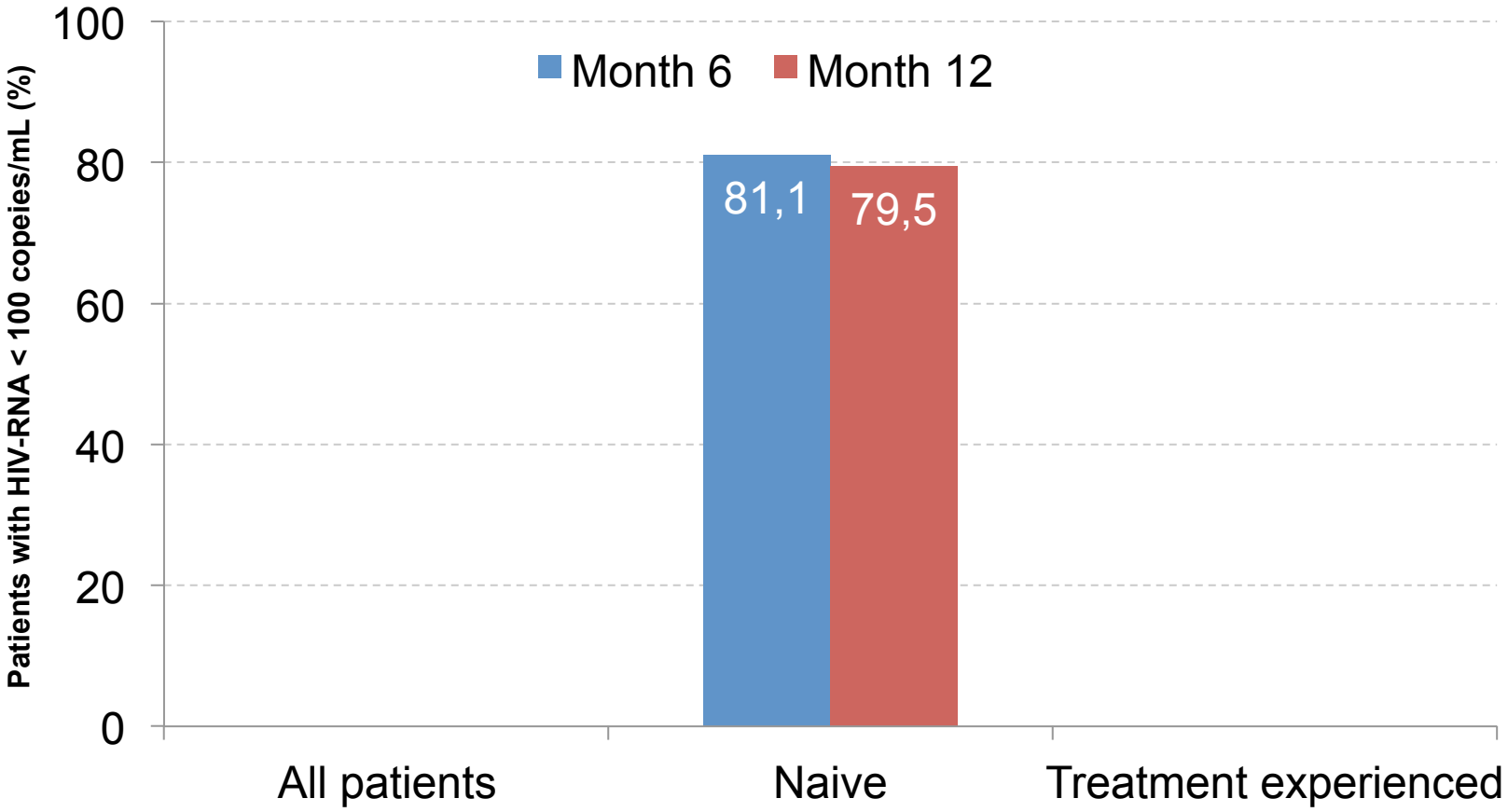


Figure. Percentage of patients with HIV RNA < 100 copies/ml



HIV RNA < 1.000.000 kopya/ml olan hastalar

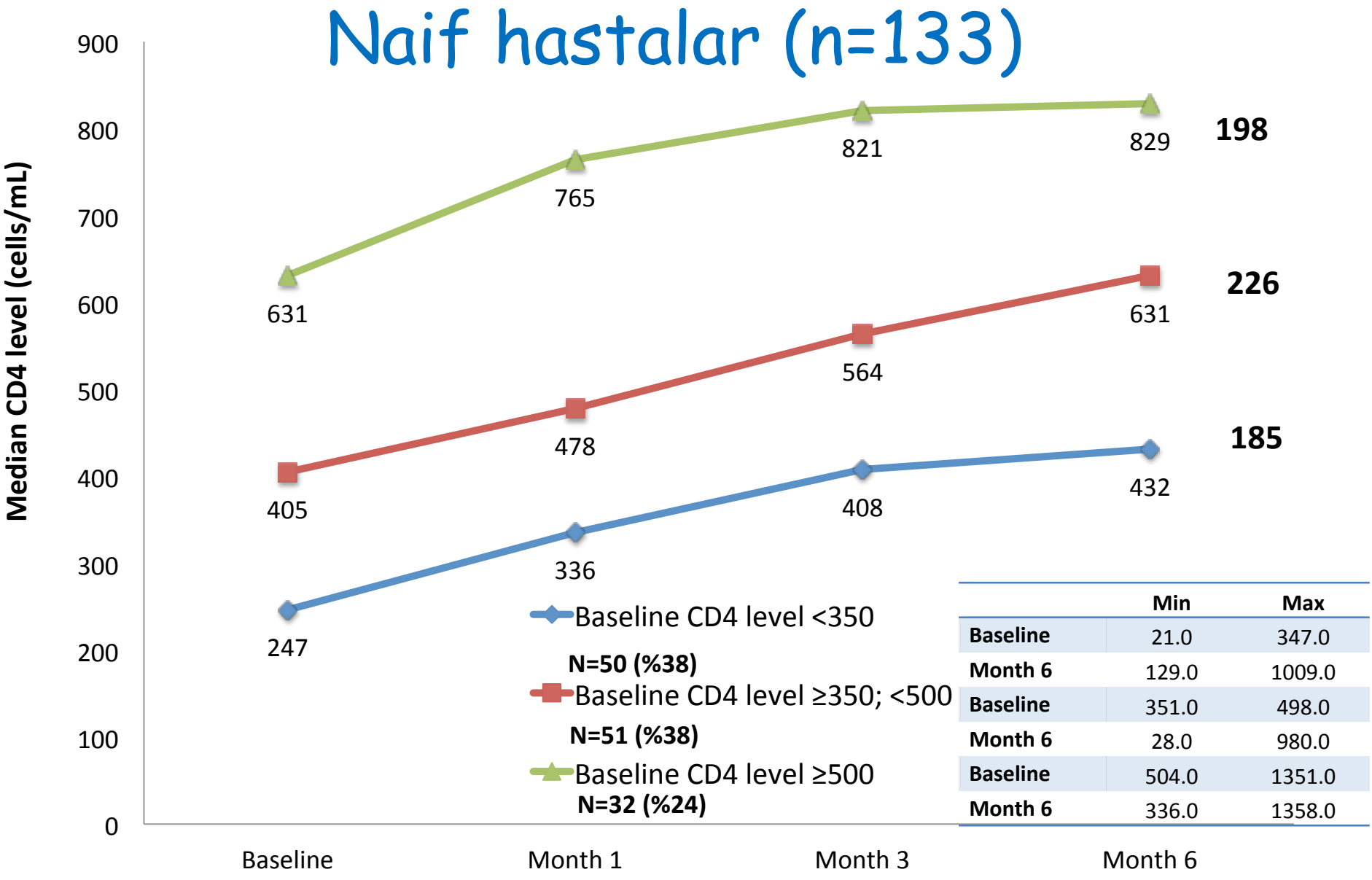


Figure CD4+ T lymphocyte level (cells/mL) of patients with 6th month measurements regarding baseline CD4+ T lymphocyte level subgroups in treatment naïve patients

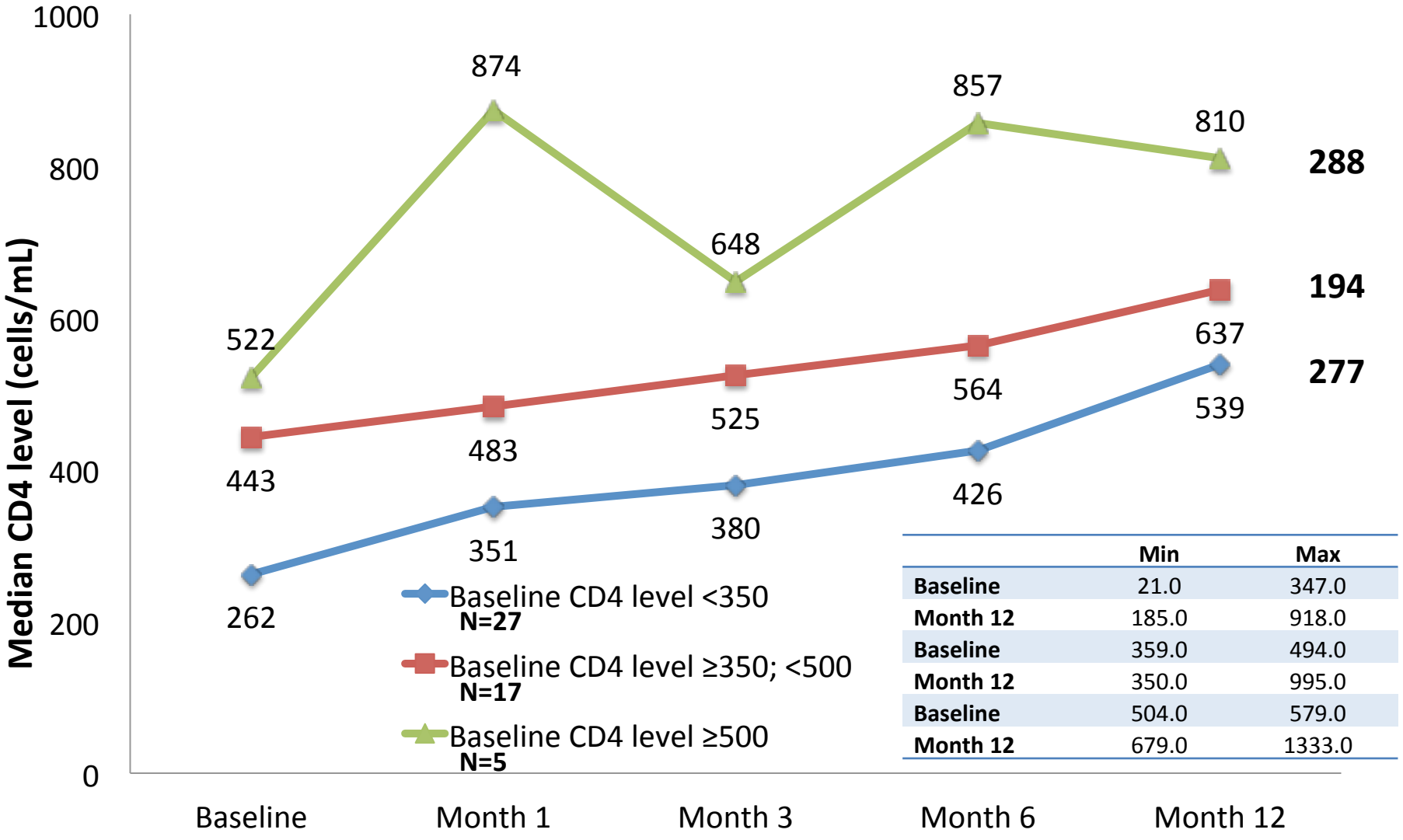
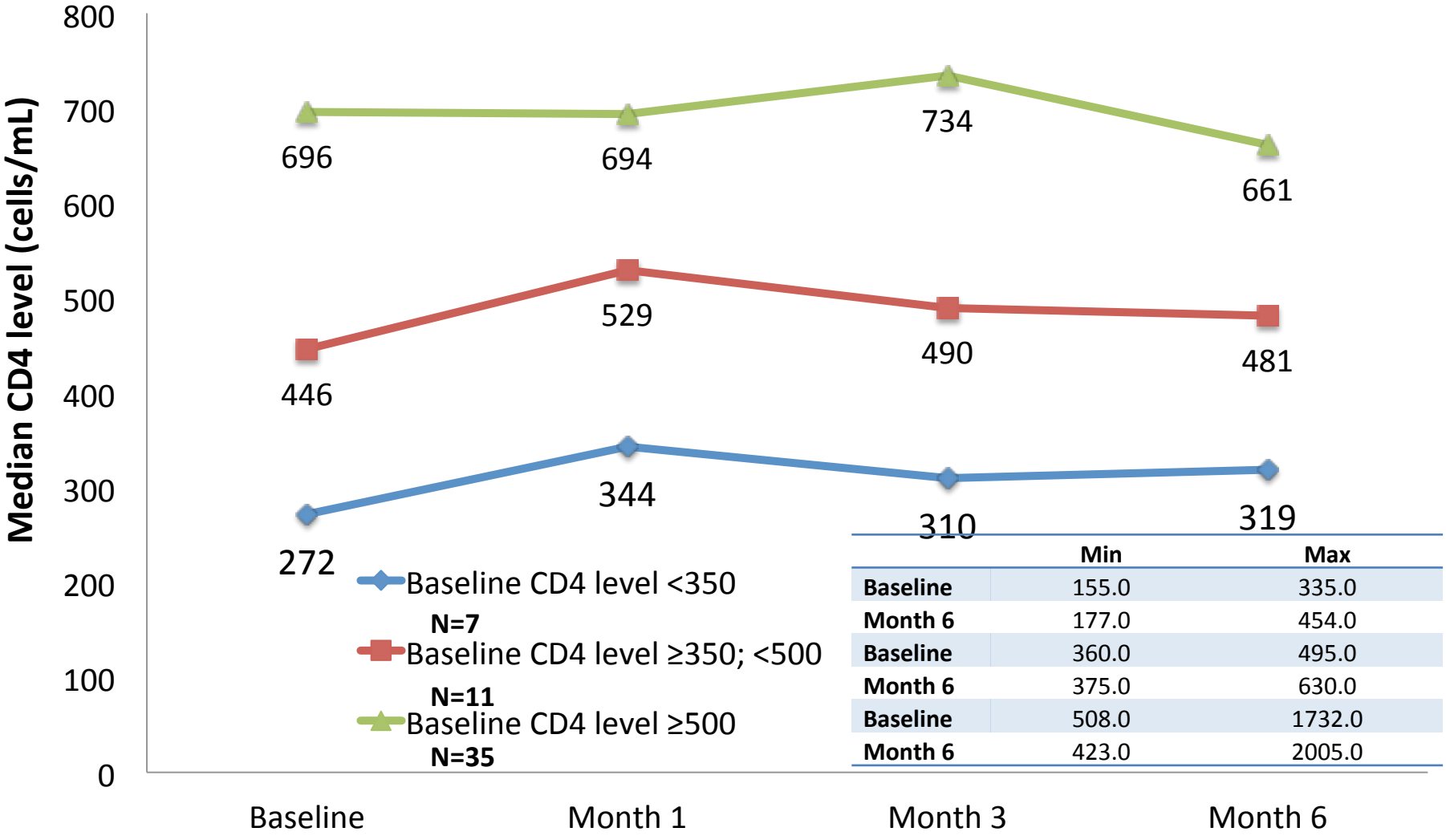


Figure CD4+ T lymphocyte level (cells/mL) of patients with 12th month measurements regarding baseline CD4+ T lymphocyte level subgroups in treatment naïve patients

Switch (n= 53)



	Min	Max
Baseline	155.0	335.0
Month 6	177.0	454.0
Baseline	360.0	495.0
Month 6	375.0	630.0
Baseline	508.0	1732.0
Month 6	423.0	2005.0

Figure CD4+ T lymphocyte level (cells/mL) of patients with 6th month measurements regarding baseline CD4+ T lymphocyte level subgroups in treatment experienced (switch) patients

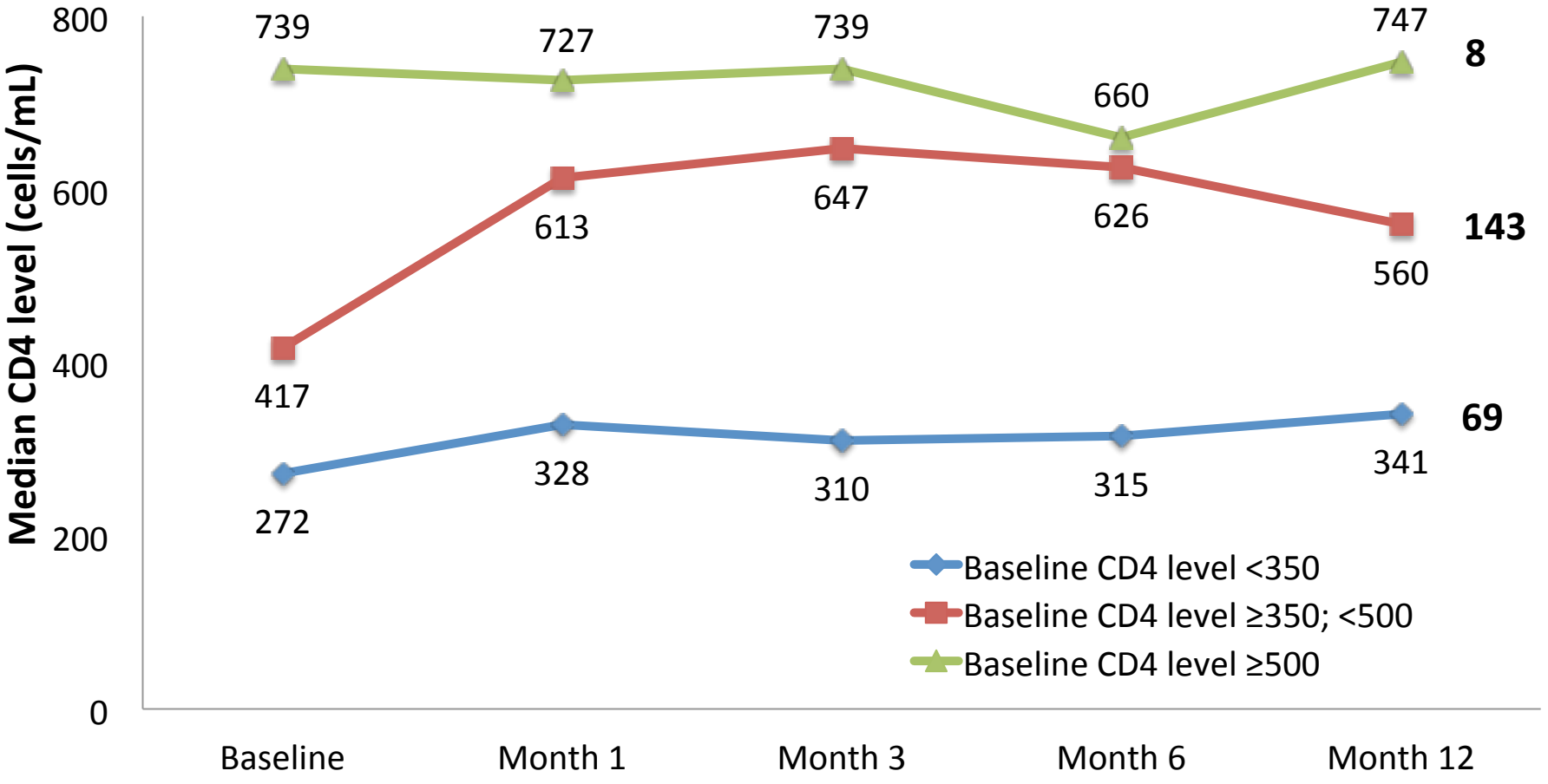


Figure CD4+ T lymphocyte level (cells/mL) of patients with 12th month measurements regarding baseline CD4+ T lymphocyte level subgroups in treatment experienced (switch) patients (N=29)

Baseline	Month 1	Month 3	Month 6	Month 9	Month 12
30,300	20	0	218		
24,290		0	358		
83,000	677	20	378		
73,700	276	111	456	20	
14,911	14,911		904	177	
8,700	14,400	20	14,400	0	
33,200	451		16,800	20	20
18,424	18,424	13,124	28,713		
345,832	366	100	117		
110,000	253	157	128		
171,000			220		
409,131	0	0	224	176	
794,654		107	250		
386,781	0	146	295	100	
182,000	228	20	356	20	
137,000	157	279	438		0
311,580	510	217	451		
424,000	648	110	751	206	20

List of patients with HIV RNA at month 6 > 100 copies/mL (18 naive)

Yan etkiler (n=387)

System Organ Class Preferred term	n	% in 387
Any adverse event	**61**	**15.8**
Gastrointestinal disorders	**22**	**5.7**
Nausea	8	2.1
Diarrhoea	7	1.8
Dyspepsia	4	1.0
Flatulence	3	0.8
Abdominal pain	2	0.5
Abdominal discomfort	1	0.3
Nervous system disorders	**11**	**2.8**
Headache	5	1.3
Dizziness	4	1.0
Abnormal Dreams	1	0.3
Paraesthesia	1	0.3
Amnesia	1	0.3
General disorders and administration site conditions	**10**	**2.6**
Asthenia	5	1.3
Hyperthidrosis	3	0.8
Death	2	0.5
Treatment failure	1	0.3
Pyrexia	1	0.3
Skin and subcutaneous tissue disorders	**9**	**2.3**
Pruritus	6	1.6
Rash	2	0.5
Alopecia	2	0.5
Pain of skin	1	0.5
Psychiatric disorders	**7**	**1.8**
Somnolence	3	0.8
Insomnia	1	0.3
Middle insomnia	1	0.3
Anxiety	1	0.3
Anger	1	0.3
Hypersomnia	1	0.3

System Organ Class Preferred term	n	% in 387
Investigations	**7**	**1.8**
Weight increased	2	0.5
Red blood cell count increased	1	0.3
Blood cholesterol increased	1	0.3
Weight decreased	1	0.3
Hepatic enzyme increased	1	0.3
Mean cell volume abnormal	1	0.3
Musculoskeletal and connective tissue disorders	**5**	**1.3**
Osteoporosis	1	0.3
Arthralgia	1	0.3
Pain in extremity	1	0.3
Back pain	1	0.3
Neck pain	1	0.3
Renal and urinary disorders	**2**	**0.5**
Nephropathy toxic	1	0.3
Dysuria	1	0.3
Metabolism and nutrition disorders	**2**	**0.5**
Thirst	1	0.3
Decreased appetite	1	0.3
Reproductive system and breast disorders	**1**	**0.3**
Ejaculation failure	1	0.3
Vascular disorders	**1**	**0.3**
Syncope	1	0.3
Infections and infestations	**1**	**0.3**
Lower respiratory tract infection	1	**0.3**
Eye disorders	**1**	**0.3**
Eye swelling	1	0.3
Injury, poisoning and procedural complications	**1**	**0.3**
Dermatitis contact	1	0.3
Cardiac disorders	**1**	**0.3**
Palpitations	1	0.3

Yan etkiler (n=387)

Yan etki oranı: %15,8

- **Gastrointestinal**: %5,7
- **MSS**: %4,6

  anksiyete, uyku bozuklukları, baş ağrısı, baş dönmesi
- **Döküntü, alopesi**: %2,3
- **Diğer**: %3,2

İlacı bırakma oranları

Toplam: %1,6 (n=6)

- **2 hasta**: eksitus
- **1 hasta**: ilaç etkileşimi
- **1 hasta**: kreatinin yüksekliği
- **1 hasta**: karaciğer enzim yüksekliği
- **1 hasta**: hekim önerisi

TEŞEKKÜR EDERİM

SONUÇLAR

- Tek tabletli rejimlere uyum oranı daha yüksek
- Tüm İNSTİ'li rejimlerde etkinlik oranları klinik çalışmalar ile benzer

Raltegravir

- RAL alan hastalarda MSS yan etkileri açısından yakın takip ?

- Eş zamanlı ilaç kullanımı risk faktörü olabilir

  (tenofovir?, PPI?)

Dolutegravir

- Klinik çalışmalara kıyasla özellikle nöropsikiyatrik yan etkilere bağlı DTG'i kesme oranı göreceli olarak daha yüksek

- ABC içeren rejimlerde veya kadın veya >60 yaş hastalarda DTG'i bırakma oranı daha yüksek

Elvitegravir

- Renal yan etkiler klinik çalışmalardakine benzer
- İleri evre hastalıkta serum kreatinin düzeylerinde artış ihtimali daha yüksek

Elvitegravir

- Klinik çalışmalarda etkililik %84-89
- Gerçek yaşam verilerinde etkililik ≈ %80

  Hasta profili, uyumu?

  Viral yük > 100.000->1.000.000
- Yan etki oranı ve tedaviyi bırakma oranı daha düşük