Fırsatçı Enfeksiyonların Primer Proflaksisinde Değişiklikler

Dr. Özlem Altuntaş Aydın

Bakırköy Dr Sadi Konuk Eğitim ve Araştırma Hastanesi

HIV-Associated Opportunistic Infections—Going, Going, But Not Gone: The Continued Need for Prevention and Treatment Guidelines

John T. Brooks,[1] Jonathan E. Kaplan,[1] King K. Holmes,[2] Constance Benson,[3] Alice Pau,[4] and Henry Masur[4]

[1]Centers for Disease Control and Prevention, Atlanta, Georgia; [2]University of Washington, Seattle; [3]University of California–San Diego; and [4]National Institutes of Health, Bethesda, Maryland

ART öncesi döneme göre fırsatçı enfeksiyonlarda 10 kat azalma

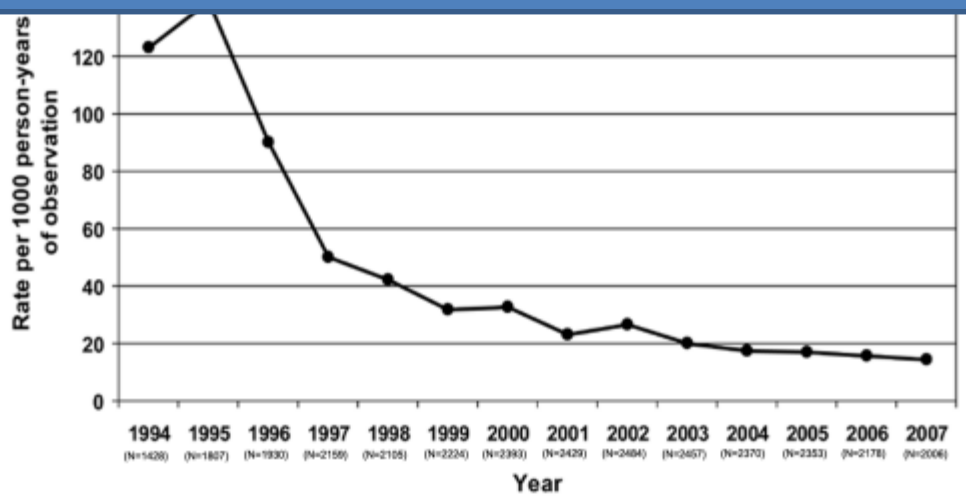

Figure 1. Incidences of first AIDS-defining opportunistic infection, according to year, among all patients in care, HIV Outpatient Study, 1994–2007

ART fırsatçı enfeksiyonların sadece sıklığını değil, seyrini de değiştirmektedir

Clin Microbiol Infect. 2007 May;13(5):510-5. Epub 2007 Feb 12.

Evolving characteristics of toxoplasmosis in patients infected with human immunodeficiency virus-1: clinical course and Toxoplasma gondii-specific immune responses.

Hoffmann C[1], Ernst M, Meyer P, Wolf E, Rosenkranz T, Plettenberg A, Stoehr A, Horst HA, Marienfeld K, Lange C.

⊕ Author information

Abstract

Toxoplasmic encephalitis (TE) is the most important opportunistic infection of the central nervous system in patients infected with human immunodeficiency virus (HIV)-1. This study evaluated the effect of highly active anti-retroviral therapy (HAART) and Toxoplasma gondii-specific immune responses on the occurrence of TE. The clinical characteristics of all patients diagnosed with TE in two centres since 1990 (n = 140) were analysed. Patients were grouped according to the date of diagnosis (period 1, 1990-1993; period 2, 1994-1996; period 3, 1997 onwards). Immune responses to T. gondii were evaluated in a subgroup (n = 12) by interferon (IFN)-gamma-specific ELISPOT tests. There were marked differences in the estimated Kaplan-Meier overall survival (OS), with a 1-year OS (5-year OS) of 41% (7%) in period 1, 56% (29%) in period 2, and 90% (78%) in period 3 (p <0.0001). In period 3, TE was found to be the first AIDS-defining illness more frequently than in earlier periods (74% vs. 38%, p 0.0002). Persistent neurological deficits caused by TE were present in 37% of the patients. Patients with an acute episode of TE or a TE relapse had significantly lower responses in the T. gondii-specific ELISPOT than patients who discontinued maintenance therapy and were relapse-free (p 0.0044). Survival of HIV patients with TE has improved markedly since the introduction of HAART, but persistent neurological deficits are often present in surviving patients. While preventive therapy remains essential, evaluation of T. gondii-specific immune responses may be an important step in improving estimates of the individual risk of TE and TE relapses.

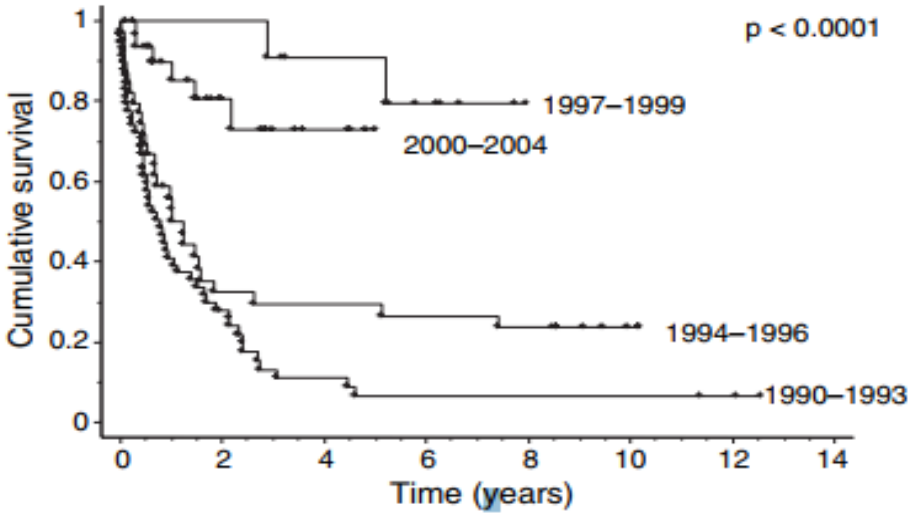

Fig. 1. Cumulative overall survival of patients diagnosed with toxoplasmic encephalitis at different time periods.

%80

%30

%8

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Poster Exhibition Presentation

PE14/16 - Opportunistic Infections and Malignancies Associated with HIV Infection in Istanbul, Turkey: Data Collected from ACTHIV-IST Study Group

O. Altuntas Aydin[1], B. Mete[2], A. Gunduz[3], F. Sargın[4], B. Ceylan[5], H. Kumbasar Karaosmanoglu[1], M. Yemisen[2], D. Yıldız[3], N. Ozgunes[4], R. Ozaras[2], F. Tabak[2]

[1]Haseki Education and Research Hospital, Istanbul, Turkey, [2]IU, Cerrahpasa Medical School, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey, [3]Sisli Etfal Education and Research Hospital, Istanbul, Turkey, [4]Medeniyet University, Goztepe Education and Research Hospital, Istanbul, Turkey, [5]Bezmialem Vakif University, Faculty of Medicine, Istanbul, Turkey

Objectives: The clinical course of HIV/AIDS and patterns of opportunistic infections (OIs) and cancers vary from patient to patient and from country to country. Hence, we aimed to study the profile of OIs and malignancies of HIV/AIDS patients according to their first admission to 5 centers following-up HIV infected patients in Istanbul, Turkey.
Methods: Between the term of January 2000-June 2013, 829 HIV infected patients who were followed-up by ACTHIV-IST (ACTion against HIV in Istanbul) study group were included in this study. Clinical and laboratory data of patients were collected retrospectively from the patients' files and were transferred to a HIV data base system.
Results: Less than one fourth of the patients were female (15.6%), mean age at the diagnosis was 38.1±11.1 years (range:17-79). Out of 829 patients, 171 (20.6%) were admitted with OIs or malignancies. The mean CD4 T-cell count and mean HIV RNA level of patients admitted with OIs or malignancies were 248.22±255.16/mm^3 and 8.34x10^5±1.4x10^6 copies/ml, respectively. On the other hand, other patients' mean CD4 T-cell count was 405.73±258.96/mm^3 (p< 0.05) and their mean HIVRNA level was 3,78x10^5±0.92x10^6 copies/ml (p< 0.05). The most frequent OIs or cancers observed at first admission were candida infections (6.7%), tuberculosis (4.4%), zona zoster (2.9%), *Pneumocystis jiroveci* pneumoniae (2%) and kaposi's sarcoma (1.3%). All opportunistic infections and malignancies of the patients at their first admission are demonstrated in table 1, 2 and 3.

Opportunistic infections	N	%
Candidiasis	56	6.7
Oral candidiasis	47	
Esophagial candidiasis	6	
Vaginal candidiasis	3	
Tuberculosis	32	3.9
Pulmonary tuberculosis	27	
Extrapulmonary tuberculosis	5	
Zona zoster	24	2.9
Pneumocystis jiroveci pneumoniae	17	2

Opportunistic infections	N	%
Cytomegalovirus infections	6	0.7
Cerebral toxoplasmosis	5	0.6
Genital herpes	3	0.4
Condyloma accuminata	2	0.2
Salmonella septicemia	2	0.2
Scabies	2	0.2
Neurosyphilis	1	0.1

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Poster Exhibition Presentation

PE14/9 - Spectrum of Opportunistic Diseases in Newly Diagnosed Patients in a Multicenter Cohort of HIV-infected Patients from Turkey

M. Fincancı[1], V. Korten[2], N. Uzun Kes[3], T. Yıldırmak[4], D. Gökengin[5], N. Taşdelen Fışgın[6], B. Dokuzoğuz[7], F. Kaptan[8], HIV-TR Cohort Study Group

[1]Istanbul Education and Research Hospital, Istanbul, Turkey, [2]Marmara University Hospital, Istanbul, Turkey, [3]Şişli Education and Research Hospital, Istanbul, Turkey, [4]Okmeydanı Education and Research Hospital, Istanbul, Turkey, [5]Ege University Hospital, Izmir, Turkey, [6]19 Mayıs University Hospital, Samsun, Turkey, [7]Ankara Numune Education Training and Research Hospital, Ankara, Turkey, [8]Izmir Education Training and Research Hospital, Izmir, Turkey

Objectives: A recently established (2012) multicenter cohort of HIV-infected patients living in Turkey (HIV-TR) provided an opportunity to collect more information on opportunistic diseases (ODs) and comorbidities. The aim of this study is to document the clinical spectrum and frequency of HIV-related diseases in HIV infected patients who are newly diagnosed and treatment naive.

Methods: HIV-infected patients presented in 2011 were included retrospectively. Data from 21 hospitals throughout the country were gathered in a central, web-based database. Conditions in the categories A, B and C defined in the Centers for Disease Control (CDC) classification system and comorbidities were diagnosed by physicians working in the hospitals involved in the cohort.

Results: HIV-TR Cohort enrolled 273 patients who were diagnosed in 2011 and their median CD4+ T cell count was 353 cell/mm³. Of them, 237 (87%) were asymptomatic at presentation. Nineteen (7 %) of asymptomatic patients had a history of primary HIV infection. One patient presented with acute primary HIV infection. Eight patients presented with a CDC category B condition. There were 43 AIDS defining ODs in 27 patients (9.9%): (recurrent pneumonia:7, tuberculosis:6, *Pneumocystis jiroveci* pneumonia:6, wasting syndrome:6, cerebral toxoplasmosis:5, candida esophagitis:4, lymphoma:3, *Cytomegalovirus* infection:3, HIV encephalopathy:2, candida pneumonia:1). Mean CD4 counts of the patients with ODs were significantly lower (91 vs 431 cell/mm³) ($p < 0.05$) and their median age was higher (44 y vs 38 y, $p < 0.05$) than the asymptomatic group. HBsAg was positive in 5.3%, anti-HCV was positive in 2.7% and syphilis serology was positive in 8% of the patients.

Conclusion: Although the spectrum of ODs in Turkey is wide, their frequencies are lower than they are in many countries. This may be due to relatively early presentation of our patients. Low CD4 cell counts that indicate late presentation clearly increase the risk for ODs.

Ciddi fırsatçı enfeksiyonlarla veya AIDS ile başvuran olguların %90'ı HIV-enfekte olduğunu bilmeyen hastalar

Halen HIV-enfekte olduğunu bilmeyen olgular var

*Ülkemizde yapılan modelleme çalışmaları ile gerçek HIV-enfekte olgusu sayısı yaklaşık **X2***

Bazı fırsatçı enfeksiyonlar için indikatör CD4 sayısı cut-off değeri	
<250 /mm^3	PCP, özefagial kandidiyaz, PML, HSV
<100/mm^3	Serebral toksoplazmoz, kriptokokoz, milier TB, HAND
<50/mm^3	CMV retinit, atipik TB
CD4 sayısından bağımsız	Kaposi sarkomu, akc TB, HZV, bakteriyel pnömoni

Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents

Recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America

How to Cite the Adult and Adolescent Opportunistic Infection Guidelines:

Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf. Accessed (insert date) [include page numbers, table number, etc. if applicable]

It is emphasized that concepts relevant to HIV management evolve rapidly. The Panel has a mechanism to update recommendations on a regular basis, and the most recent information is available on the AIDS*info* website (http://aidsinfo.nih.gov).

Access AIDS*info* mobile site

HIV MEDICINE

Volume 12, Supplement 2, September 2011

British HIV Association and British Infection Association Guidelines for the Treatment of Opportunistic Infection in HIV-seropositive Individuals 2011

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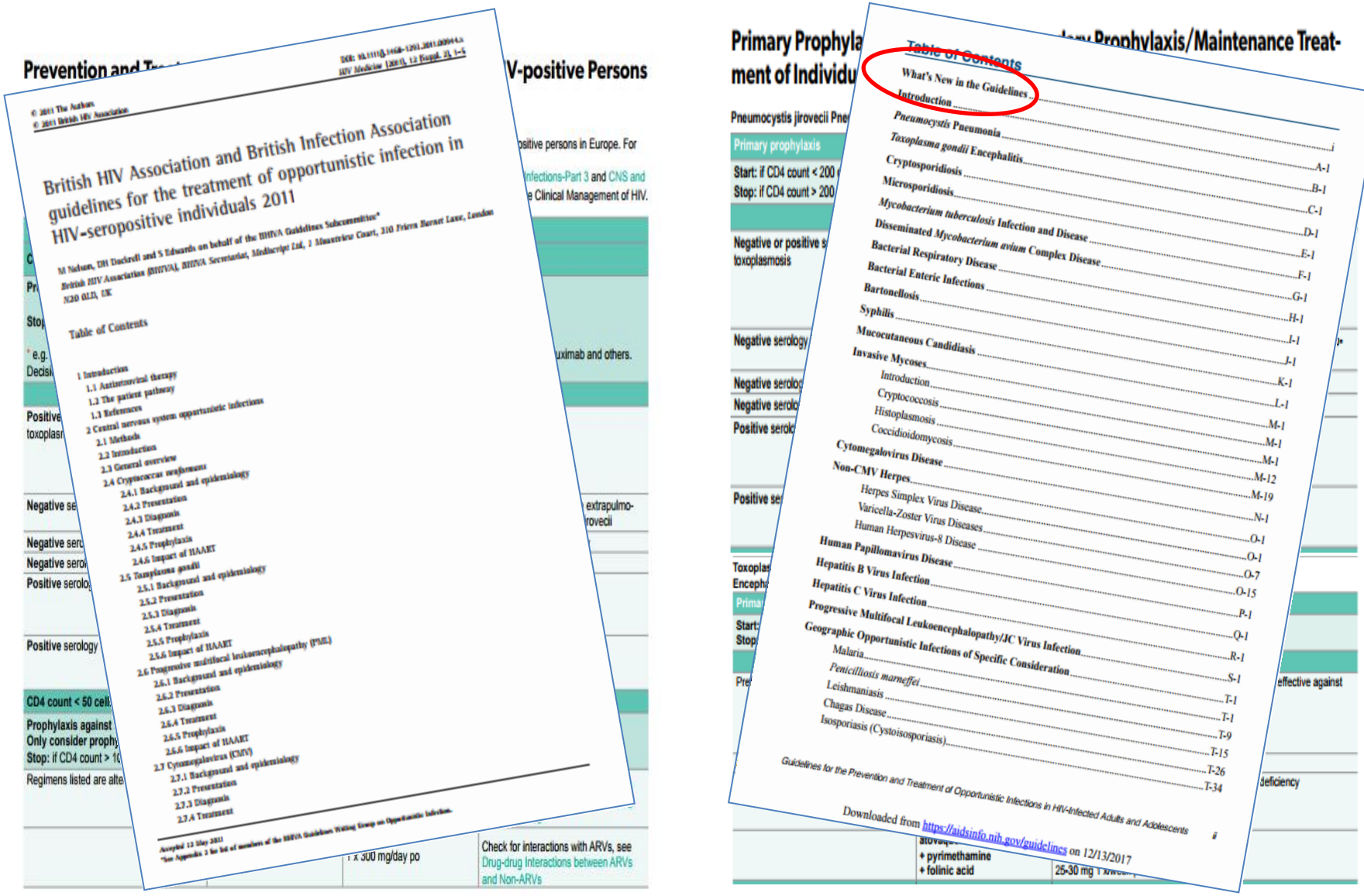
GUIDELINES

Version 9.0
October 2017

English



Prevention and Tr... ...V-positive Persons

...positive persons in Europe. For

...Infections-Part 3 and CNS and ...e Clinical Management of HIV.

...ximab and others.

...extrapulmo- ...rovecii

...effective against

...deficiency

Check for interactions with ARVs, see Drug-drug Interactions between ARVs and Non-ARVs

1 x 300 mg/day po

+ pyrimethamine
+ folinic acid

25-30 mg 1 x...

British HIV Association and British Infection Association guidelines for the treatment of opportunistic infection in HIV-seropositive individuals 2011

DOI: 10.1111/j.1468-1293.2011.00944.x
HIV Medicine 12(Suppl. 2), 1–5

M Nelson, DH Dockrell and S Edwards on behalf of the BHIVA Guidelines Subcommittee*
British HIV Association (BHIVA), BHIVA Secretariat, Mediscript Ltd, 2 Mountview Court, 310 Friern Barnet Lane, London N20 0LD, UK

Table of Contents

Accepted 12 May 2011

*See Appendix 2 for list of members of the BHIVA Guidelines Writing Group on Opportunistic Infection.

Primary Prophyla... ...Prophylaxis/Maintenance Treat- ment of Individu...

Pneumocystis jirovecii Pne...

Primary prophylaxis

Start: if CD4 count < 200 ...
Stop: if CD4 count > 200 ...

Negative or positive s... toxoplasmosis

Negative serology ...

Negative serolo...

Negative serolo...

Positive serolo...

Positive se...

Toxoplas...
Encephe...

Primar...

Start:
Stop:

Pre...

Table of Contents

Pneumocystis pneumonia (PCP)

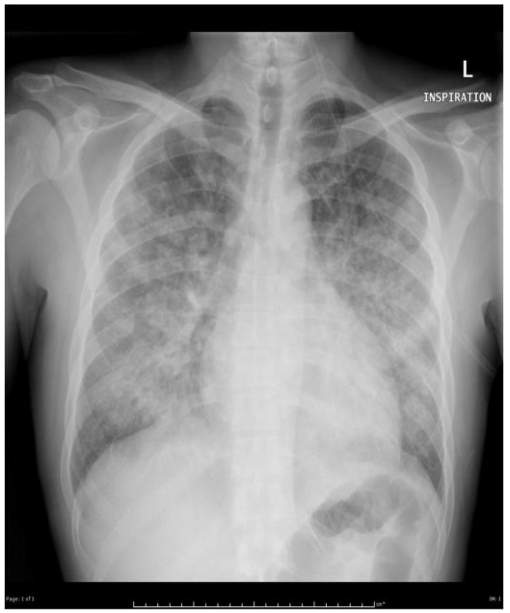
P. carinii fare

P. jirovecii insan

Sağlıklı çocukların 2-4 yaş arasında 2/3'ünde *P. jirovecii* Ab mevcut

<u>PCP risk faktörleri:</u>

- CD4<200/mm^3, CD4 < %14
- Geçirilmiş PCP
- Rekürren bakteriyel pnömoni
- Kilo kaybı
- Oral kandida enf
- Yüksek HIVRNA



Preventing Disease

Indication for Primary Prophylaxis

HIV-infected adults and adolescents, including pregnant women and those on ART, should receive chemoprophylaxis against PCP if they have CD4 counts <200 cells/mm³ **(AI)**.[12,13,41] Persons who have a CD4 cell percentage of <14% should also be considered for prophylaxis **(BII)**.[12,13,41] Initiation of chemoprophylaxis at CD4 counts between 200 and 250 cells/mm³ also should be considered when starting ART must be delayed and frequent monitoring of CD4 counts, such as every 3 months, is impossible **(BII)**.[13] Patients receiving pyrimethamine-sulfadiazine for treatment or suppression of toxoplasmosis do not require additional prophylaxis for PCP **(AII)**.[42]

Recommendations for Prevention and Treatment of *Pneumocystis* Pneumonia (PCP)

Preventing 1st Episode of PCP (Primary Prophylaxis)

Indications for Initiating Primary Prophylaxis:

- CD4 count <200 cells/mm³ **(AI)** *or*
- CD4% <14% of total lymphocyte count **(BII)** *or*
- CD4 count >200 but <250 cells/mm³, if ART cannot be initiated, and if CD4 cell count monitoring (e.g., every 3 months) is not possible **(BII)**.

Note—Patients who are receiving pyrimethamine/sulfadiazine for treatment or suppression of toxoplasmosis do not require additional prophylaxis for PCP **(AII)**.

Preferred Therapy:

- TMP-SMX, 1 DS PO daily[a] **(AI)** *or*
- TMP-SMX, 1 SS PO daily[a] **(AI)**.

Alternative Therapy:

- TMP-SMX 1 DS PO three times weekly **(BI)** *or*
- Dapsone[b,c] 100 mg PO daily or 50 mg PO BID (BI) *or*
- Dapsone[b] 50 mg PO daily + (pyrimethamine 50 mg + leucovorin 25 mg) PO weekly **(BI)** *or*
- (Dapsone[b] 200 mg + pyrimethamine 75 mg + leucovorin 25 mg) PO weekly **(BI)** *or*
- Aerosolized pentamidine[c] 300 mg via Respigard II™ nebulizer every month **(BI)** *or*
- Atovaquone 1500 mg PO daily with food **(BI)** *or*
- (Atovaquone 1500 mg + pyrimethamine 25 mg + leucovorin 10 mg) PO daily with food **(CIII)**.

Indication for Discontinuing Primary Prophylaxis:

- CD4 count increased from <200 cells/mm³ to ≥200 cells/mm³ for at least 3 months in response to ART **(AI)**
- Can consider if CD4 count 100-200 cells/mm³ and HIV RNA remain below limit of detection for at least 3-6 months **(BII)**

Indication for Restarting Primary Prophylaxis:

- CD4 count <100 cells/mm³ regardless of HIV RNA **(AIII)**
- CD4 count 100-200 cells/mm³ and with HIV RNA above detection limit of the assay **(AIII)**.

Discontinuing Primary Prophylaxis

Primary *Pneumocystis* prophylaxis should be discontinued for adult and adolescent patients who have responded to ART with an increase in CD4 counts from <200 cells/mm³ to >200 cells/mm³ for >3 months **(AI)**. In observational and randomized studies supporting this recommendation, most patients had CD4 counts >200 cells/mm³ for more than 3 months before discontinuing PCP prophylaxis.[56-65] The median CD4 count at the time prophylaxis was discontinued was >300 cells/mm³, most patients had a CD4 cell percentage

PCP, toksoplazmoz ve bakteriyel enf korumadaki yararı sınırlı
Proflaksi bırakıldığında:

- Tablet sayısı
- Maliyet
- İlaç toksisitesi
- İlaç etkileşimleri
- Dirençli patojenlerin seleksiyonu azalıyor

Clin Infect Dis. 2010 Sep 1;51(5):611-9. doi: 10.1086/655761.

Is it safe to discontinue primary Pneumocystis jiroveci pneumonia prophylaxis in patients with virologically suppressed HIV infection and a CD4 cell count <200 cells/microL?

Opportunistic Infections Project Team of the Collaboration of Observational HIV Epidemiological Research in Europe (COHERE), Mocroft A, Reiss P, Kirk O, Mussini C, Girardi E, Morlat P, Stephan C, De Wit S, Doerholt K, Ghosn J, Bucher HC, Lundgren JD, Chene G, Miro JM, Furrer H.

⊕ Collaborators (64)

Erratum in
Clin Infect Dis. 2010 Nov 1;51(9):1114.

12 Avrupa ülkesinin kohortu,
1997'den sonra ART başlanmış **23 412 hasta**
107 016 takip-yıl, 253 PCP gelişmiş
Primer proflaksi CD4 ≤100/mm³ olanlarda PCP insidansını azaltıyor
ART kullanan, virolojik supresyon sağlanmış, CD4 101-200/mm³ olan olgularda
Primer PCP insidansı çok düşük

ART ile VL supresyon sağlanmış
CD4<200/mm^3 primer PCP proflaksisi bırakılmış 4 çalışma

discontinuation, but suppression of plasma viremia with antiretroviral therapy may allow for discontinuation of PCP prophylaxis even with CD4 count <200 cells/μL.

Methods: A systematic review was performed to determine the incidence of PCP in HIV-infected individuals with CD4 count <200 cells/μL and fully suppressed VL on antiretroviral therapy but not receiving PCP prophylaxis.

Results: Four articles examined individuals who discontinued PCP prophylaxis with CD4 count <200 cells/μL in the context of fully suppressed VL on antiretroviral therapy. The overall incidence of PCP was 0.48 cases per 100 person-years (PY) (95% confidence interval (CI) (0.06–0.89). This was lower than the incidence of PCP in untreated HIV infection (5.30 cases/100 PY, 95% CI 4.1–6.8) and lower than the incidence in persons with CD4 count <200 cells/μL, before the availability of highly active antiretroviral therapy (HAART), who continued prophylaxis (4.85/100 PY, 95% CI 0.92–8.78). In one study in which individuals were stratified according to CD4 count <200 cells/μL, there was a greater risk of PCP with CD4 count ≤100 cells/μL compared to 101–200 cells/μL.

Conclusion: Primary PCP prophylaxis may be safely discontinued in HIV-infected individuals with CD4 count between 101–200 cells/μL provided the VL is fully suppressed on antiretroviral therapy. However, there are inadequate data available to make this recommendation when the CD4 count is ≤100 cells/μL. A revision of guidelines on primary PCP prophylaxis to include consideration of the VL is merited.

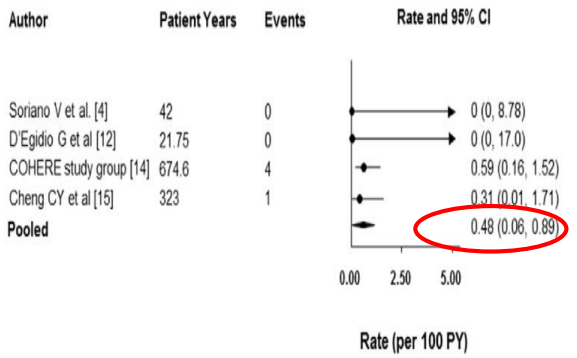


Figure 2. Incidence of PCP in HIV-infected Individuals on Antiretroviral Therapy who Discontinue Prophylaxis with CD4+ Count <200 cells/μL with Suppressed Viral Load.
doi:10.1371/journal.pone.0028570.g002

PCP insidansı
- ART kullanmayan - **5.3** /100 hasta yılı
- ART öncesi dönemde CD4<200/mm3, Proflaksi kullananlarda - **4.85** /100 hasta yılı

Opportunistic Infection	Indication for Discontinuing Primary Prophylaxis	Indication for Restarting Primary Prophylaxis	Indication for Discontinuing Secondary Prophylaxis/Chronic Maintenance Therapy	Indicatio Restart Second Prophylaxis/ Maintena
Pneumocystis Pneumonia	CD4 count increased from <200 to >200 cells/µL for >3 months in response to ART **(AI)** Can consider when CD4 count 100-200 cells/µL if HIV RNA remain below limits of detection for at least 3-6 months **(BII)**	CD4 count <100 cells/mm^3 **(AIII)** CD4 count 100-200 cells/ µL and with HIV RNA above detection limit of the assay **(AIII)**.	CD4 count increased from <200 cells/µL to >200 cells/µL for >3 months in response to ART **(BII)** Can consider when CD4 count 100-200 cells/µL if HIV RNA remain below limits of detection for at least 3-6 months **(BII)** **If PCP occurs** at a CD4 count >200 cells/ µL while not on ART, discontinuation of prophylaxis can be	CD4 count <10 **(AIII)** CD4 count 100 µL and with HI above detectio the assay **(AII**

Primary Prophylaxis, Treatment and Secondary Prophylaxis/Maintenance Treatment of Individual OIs

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Pneumocystis jirovecii Pneumonia (PcP)

Primary prophylaxis
Start: if CD4 count < 200 cells/µL, CD4 percentage < 14%, oral thrush or relevant concomitant immunosuppression (see above) **Stop:** if CD4 count > 200 cells/µL over 3 months or CD4 count 100-200 cells/µL and HIV-VL undetectable over 3 months

Toxoplasma gondii ensefaliti

Sıklıkla latent doku kistlerinin reaktivasyonu ile ortaya çıkar
Primer enfeksiyon akut serebral veya dissemine hastalık

Toxoplasma Ab seroprevalansı
ABD %11
Avrupa, Latin Amerika, Afrika %50-80

Turkiye Parazitol Derg. 2011;35(2):65-7. doi: 10.5152/tpd.2011.17.

[Toxoplasma gondii IgG seroprevalence in HIV/AIDS patients].

[Article in Turkish]
Aydın OA[1], Karaosmanoğlu HK

⊕ **Author information**

164 hastada - **%52**
CD4<100/mm^3 olanlarda - **%64**

Abstract

OBJECTIVE: Our aim was t who applied to our outpatient clinic.

METHODS: Between Janua gondii IgG antibodies by using the ELISA method.

RESULTS: Of the total of 164 HIV/AIDS patients, 135 were male, 29 were female with a mean age of 36 years (range: 20-72 years). 85 (52%) of cases, T. gondii IgG was evaluated positive. In addition, positive T. gondii IgG was seen in 23 of 36 patients (64%) whose count of CD4+T cell was below 100.

CONCLUSION: Life threatening clinical conditions, mostly toxoplasma encephalitis, develop in cases who are T. gondii IgG seropositive with a count of CD4+ T cell lower than 100. The presence of T. gondii IgG should be investigated in all HIV infected patients due to the high risk of reactivation.

PMID: 21776588 DOI: 10.5152/tpd.2011.17

HAART öncesinde

- İleri evre HIV enfekte
- Toxo-IgG (+)
- Proflaksi almayanlarda TE **%33**

Seronegatif olanlarda toksoplazmoz insidansı düşükdür
Ortaya çıkarsa;

- Primer enf
- Ab oluşturulamamış, latent enfeksiyonun reaktivasyonu
- Test hatası?

Discontinuing Primary Prophylaxis

Prophylaxis against TE should be discontinued in adult and adolescent patients receiving ART whose CD4 counts increase to >200 cells/μL for more than 3 months **(AI)**. Multiple observational studies[31-33] and two randomized trials[34,35] have reported that primary prophylaxis can be discontinued, with minimal risk for development of TE, in patients receiving ART whose CD4 counts increase from <200 cells/μL to >200 cells/μL for more than 3 months. In these studies, most patients were taking HIV protease inhibitor-containing regimens and the median CD4 count at the time prophylaxis was discontinued was >300 cells/μL. At the time prophylaxis was discontinued, most patients had sustained suppression of plasma HIV RNA levels below the detection limits of available assays; the median follow-up was 7 to 22 months. CD4 count increases to >200 cells/μL were studied because regimens used for prophylaxis of TE also provide PCP prophylaxis, and the risk of PCP in untreated patients increases once the CD4 count is <200 cells/μL. Thus, the recommendation specifies discontinuing prophylaxis after an increase to >200 cells/μL. When CD4 counts are >200 cells/μL for at least 3 months, primary TE prophylaxis should be discontinued because it adds little value in preventing toxoplasmosis and increases pill burden, potential for drug toxicity and interaction, likelihood of development of drug-resistant pathogens, and cost.

A combined analysis of 10 European cohorts found a low incidence of TE in patients with CD4 counts between 100 and 200 cells/mm^3, who were receiving ART and had HIV RNA plasma viral loads <400 copies/mL, and who had stopped or never received TE prophylaxis, suggesting that primary TE prophylaxis can be safely discontinued in patients with CD4 counts 100 to 200 cells/mm^3 and HIV plasma RNA levels below limits of detection with commercial assays.[36] Similar observations have been made with regard to stopping primary or secondary prophylaxis for PCP.[36-38] Data on which to base specific recommendations are inadequate, but one approach would be to stop primary prophylaxis in patients with CD4 counts of 100 to 200 cells/mm^3 if HIV plasma RNA levels remain below limits of detection for at least 3 to 6 months **(BII)**.[36]

Toxoplasma gondii
Encephalitis

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Primary prophylaxis			
Start: if CD4 count < 200 cells/μL, or CD4 percentage < 14%, oral thrush, or relevant concomitant immunosuppression (see above) **Stop:** if CD4 count > 200 cells/μL over 3 months or CD4 count 100-200 cells/μL and HIV-VL undetectable over 3 months			
	Drug	**Dose**	**Comments**
Preferred prophylaxis	**TMP-SMX**	1 double-strength tablet (ds) (800/160 mg) 3 x/week po or 1 single-strength tablet (ss)	All regimens are also effective against PcP

Sonuç olarak

July 25, 2017

1. ***Pneumocystis* Pneumonia:** Sections of the *Pneumocystis* guidelines have been updated to modernize some of the language and to more closely reflect the standard of care in 2017, which includes early cART initiation for all patients. In addition, suggested criteria for stopping both primary and secondary prophylaxis in patients with HIV viral loads below detection limits and CD4 counts between 100 and 200 cells/mm^3 are provided.
2. ***Toxoplasma gondii* Encephalitis:** Sections of the toxoplasmosis guidelines have been updated to modernize some of the language and to more closely reflect the standard of care in 2017, which includes early cART initiation for all patients. Greater detail is provided on management of toxoplasmosis during pregnancy. In addition, suggested criteria for stopping primary prophylaxis in patients with HIV viral loads below detection limits and CD4 counts between 100 and 200 cells/mm^3 are provided.
3. **Table 1, Table 2 and Table 4:** Updated to reflect the changes in the sections.

Yeni Yılda ...

... Diliyorum


prophylaxis


Opportunistic Infections
candidiasis
coccidioidomycosis
TB
cryptosporidiosis
tuberculosis
histoplasmosis
pneumonia

Opportunistic Infection	Indication for Discontinuing Primary Prophylaxis	Indication for Restarting Primary Prophylaxis	Indication for Discontinuing Secondary Prophylaxis/Chronic Maintenance Therapy	Indication for Restarting Secondary Prophylaxis/Chronic Maintenance
Toxoplasma gondii **Encephalitis**	CD4 count increased to >200 cells/μL for >3 months in response to ART **(AI)** Can consider when CD4 count 100-200 cells/μL if HIV RNA remain below limits of detection for at least 3-6 months **(BII)**	CD4 count <100 cells/ μL **(AIII)**. CD4 count 100-200 cells/ μL and with HIV RNA above detection limit of the assay **(AIII)**.	Successfully completed initial therapy, receiving maintenance therapy and remain free of signs and symptoms of TE, and CD4 count >200 cells/μL for >6 months in response to ART **(BI)**.	CD4 count <200 cells/ **(AIII)**


Sevgi
Mutluluk
Dostluk
Sabır
İyi niyet
Hoşgörü
Yardımlaşma
Başarı

TE

- Toxoplasmic encephalitis (TE) is caused by the protozoan Toxoplasma gondii. Disease appears to occur almost exclusively because of reactivation of latent tissue cysts.1-4 Primary infection occasionally is associated with acute cerebral or disseminated disease.
- In the era before antiretroviral therapy (ART), the 12-month incidence of TE was approximately 33% in patients with advanced immunosuppression who were seropositive for T. gondii and not receiving prophylaxis with drugs against the disease. A low incidence of toxoplasmosis is seen in patients who are seronegative for T. gondii. If patients are truly seronegative, their toxoplasmosis presumably represents one of three possible scenarios:
- 1) Primary infection, 2) Re-activation of latent disease in individuals who cannot produce detectable antibodies, or 3) Testing with insensitive assays.7

- Clinical disease is rare among patients with CD4 T lymphocyte (CD4) cell counts >200 cells/µL. Patients with CD4 counts< 50 cells/µL are at greatest risk.

Recommendations for Preventing and Treating *Toxoplasma gondii* Encephalitis (page 1 of 2)

Preventing 1st Episode of *Toxoplasma gondii* Encephalitis (Primary Prophylaxis)

Indications for Initiating Primary Prophylaxis:

- *Toxoplasma* IgG positive patients with CD4 count <100 cells/mm^3 **(AII)**

Note: All the recommended regimens for preventing 1st episode of toxoplasmosis are also effective in preventing PCP.

Preferred Regimen:

- TMP-SMX 1 DS PO daily **(AII)**

Alternative Regimens:

- TMP-SMX 1 DS PO three times weekly **(BIII)**, *or*
- TMP-SMX SS PO daily **(BIII)**, *or*
- Dapsone[a] 50 mg PO daily + (pyrimethamine 50 mg + leucovorin 25 mg) PO weekly **(BI)**, *or*
- (Dapsone[a] 200 mg + pyrimethamine 75 mg + leucovorin 25 mg) PO weekly **(BI)**, *or*
- Atovaquone[b] 1500 mg PO daily **(CIII)**, *or*
- (Atovaquone[b] 1500 mg + pyrimethamine 25 mg + leucovorin 10 mg) PO daily **(CIII)**

Indication for Discontinuing Primary Prophylaxis:

- CD4 count >200 cells/mm^3 for >3 months in response to ART **(AI)**; *or*
- Can consider if CD4 count is 100-200 cells/mm^3 and HIV RNA levels remain below limits of detection for at least 3-6 months **(BII)**.

Indication for Restarting Primary Prophylaxis:

- CD4 count <100 to 200 cells/mm^3 **(AIII)**

- A combined analysis of 10 European cohorts found a low incidence of TE in patients with CD4 counts between 100 and 200 cells/mm3 , who were receiving ART and had HIV RNA plasma viral loads< 400 copies/mL, and who had stopped or never received TE prophylaxis, suggesting that primary TE prophylaxis can be safely discontinued in patients with CD4 counts 100 to 200 cells/mm3 and HIV plasma RNA levels below limits of detection with commercial assays. Similar observations have been made with regard to stopping primary or secondary prophylaxis for PCP.36-38 Data on which to base specific recommendations are inadequate, but one approach would be to stop primary prophylaxis in patients with CD4 counts of 100 to 200 cells/mm3 if HIV plasma RNA levels remain below limits of detection for at least 3 to 6 months **(BII).**

Candida

- The occurrence of oropharyngeal or esophageal candidiasis is recognized as an indicator of immune suppression and is most often observed in patients with CD4 T lymphocyte (CD4) cell counts <200 cells/mm3 , with esophageal disease typically occurring at lower CD4 counts than oropharyngeal disease.1,2
- Esophageal candidiasis generally presents with retrosternal burning pain or discomfort along with odynophagia; occasionally esophageal candidiasis can be asymptomatic. Endoscopic examination reveals whitish plaques similar to those observed with oropharyngeal disease.

- Oropharyngeal candidiasis is usually diagnosed clinically based on the characteristic appearance of lesions. In contrast to oral hairy leukoplakia, the white plaques of oropharyngeal candidiasis can be scraped off the mucosa. If laboratory confirmation is required, scrapings can be examined microscopically for characteristic yeast or hyphal forms, using a potassium hydroxide preparation. Cultures of clinical exudative material yield the species of Candida present.

- Candida organisms are common commensals on mucosal surfaces in healthy individuals. No measures are available to reduce exposure to these fungi.

- Data from prospective controlled trials indicate that fluconazole can reduce the risk of mucosal disease (i.e., oropharyngeal, esophageal, and vulvovaginal) in patients with advanced HIV.11-14 However, routine primary prophylaxis is not recommended because mucosal disease is associated with very low attributable morbidity and mortality and, moreover, acute therapy is highly effective. Primary antifungal prophylaxis can lead to infections caused by drug-resistant Candida strains and introduce significant drug-drug interactions. In addition, long-term oral prophylaxis is expensive. **Therefore, routine primary prophylaxis is not recommended (AIII**). Administration of ART and immune restoration is an effective means to prevent

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Pneumocystis jiroveci pneumonia prophylaxis is not required with a CD4+ T-cell count < 200 cells/microl when viral replication is suppressed.

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Author information

Abstract

OBJECTIVE: To determine the safety of discontinuing Pneumocystis jiroveci pneumonia (PCP) prophylaxis, in patients on effective antiretroviral therapy with CD4+ T-cell counts that have plateaued at < 200 cells/microl.

METHODS: We prospectively evaluated a cohort of HIV infected patients at a multidisciplinary HIV clinic with sustained HIV RNA levels < 50 copies/ml and CD4+ T-cell counts that have plateaued at < 200 cells/microl and who have discontinued PCP prophylaxis.

RESULTS: Nineteen patients fulfilled the above criteria. Eleven had been taking daily trimethoprim-sulfamethoxazole, seven were receiving monthly aerosolized pentamidine, and one patient never received any prophylaxis. The median CD4+ T-cell count at the time of discontinuation and at the most recent determination were 120 (range, 34-184) and 138 (range, 6-201) cells/microl, respectively. To date, patients have been off PCP prophylaxis for a mean of 13.7 +/- 10.6 months and a median of 9.0 (range 3-39) months for a total of 261 patient-months. To date, no patient has developed PCP. This is significantly different from the risk of developing PCP with a CD4+ T-cell count of < 200 cells/microl in untreated HIV infection (rate difference 9.2%; 95% confidence interval, 5.7 to 12.8%; P < 0.05).

CONCLUSION: With sustained suppression of viral replication, PCP prophylaxis may not be necessary, regardless of CD4+ T-cell count. This illustrates a degree of immune recovery that occurs with virologic suppression that is not reflected in absolute CD4+ T-cell count or percentage and suggests that guidelines for P. jiroveci pneumonia prophylaxis may need to be re-evaluated.

N Engl J Med. 1990 Jan 18;322(3):161-5.

The risk of Pneumocystis carinii pneumonia among men infected with human immunodeficiency virus type 1. Multicenter AIDS Cohort Study Group.

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Abstract

We assessed the risk of pneumonia due to Pneumocystis carinii in 1665 participants in the Multicenter AIDS Cohort Study who were seropositive for human immunodeficiency virus type 1 (HIV-1) but did not have the acquired immunodeficiency syndrome (AIDS) and were not receiving prophylaxis against P. carinii. During 48 months of follow-up, 168 participants (10.1 percent) had a first episode of P. carinii pneumonia. The risk was greatly increased in participants with CD4+ cell counts at base line of 200 per cubic millimeter or less (relative risk, 4.9; 95 percent confidence interval, 3.1 to 8.0). Although most participants (60.7 percent) described no HIV-1-related symptoms at the clinic visit at which a CD4+ cell count of 200 per cubic millimeter or less was first noted, this finding during follow-up was also associated with an increased risk of P. carinii pneumonia. The development of thrush or fever significantly and independently increased the risk of P. carinii pneumonia in these patients (adjusted relative risks, 1.86 and 2.15 for thrush and fever, respectively). Most participants with CD4+ cell counts above 200 per cubic millimeter who had P. carinii pneumonia within six months were symptomatic. We conclude that P. carinii pneumonia is unlikely to develop in HIV-1-infected patients unless their CD4+ cells are depleted to 200 per cubic millimeter or below or the patients are symptomatic, and therefore that prophylaxis should be reserved for such patients.