HIV/AIDS & CMV

Santral Sinir Sistemi ve Göz Tutulumu

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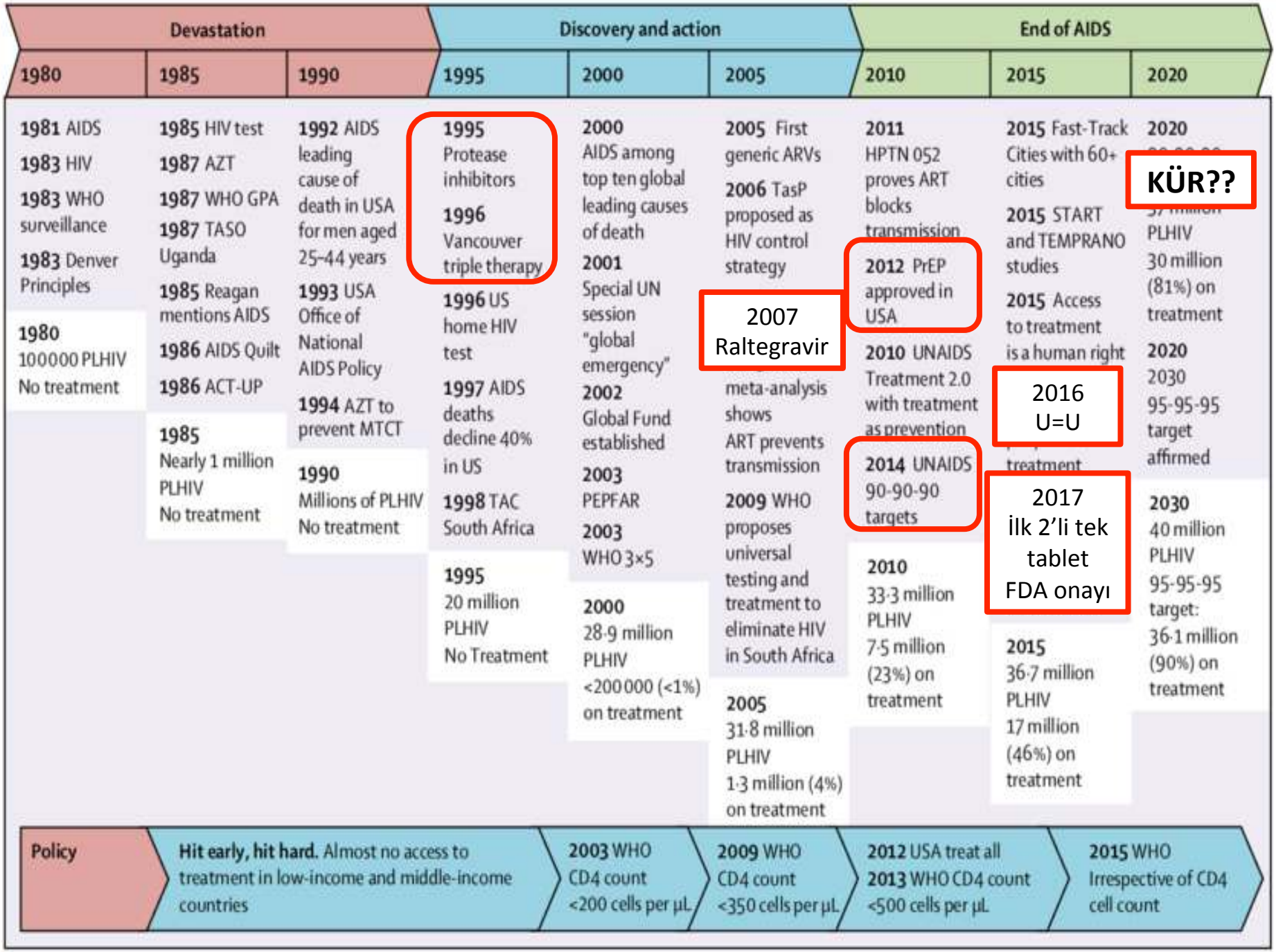
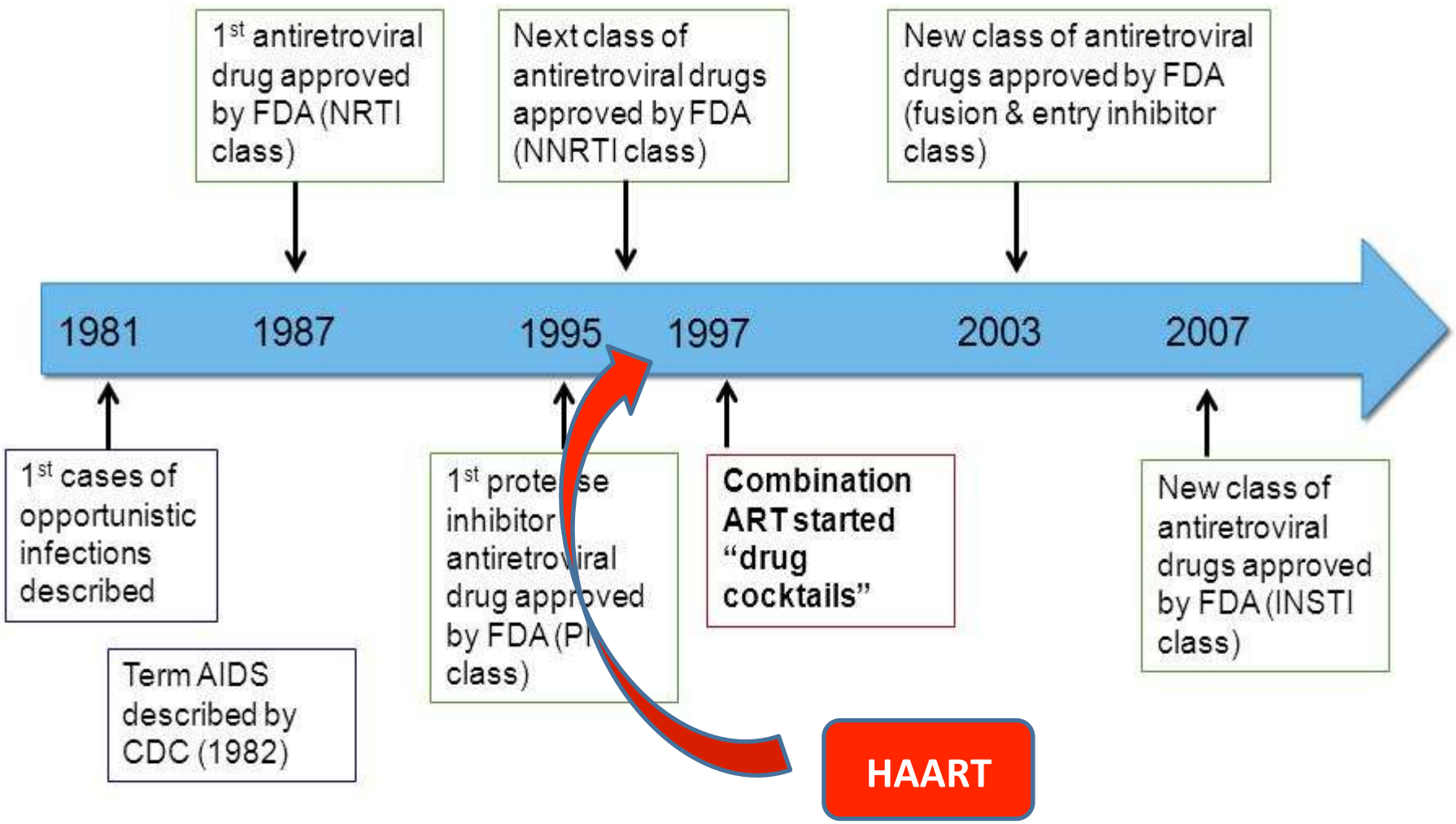
Sunum Planı

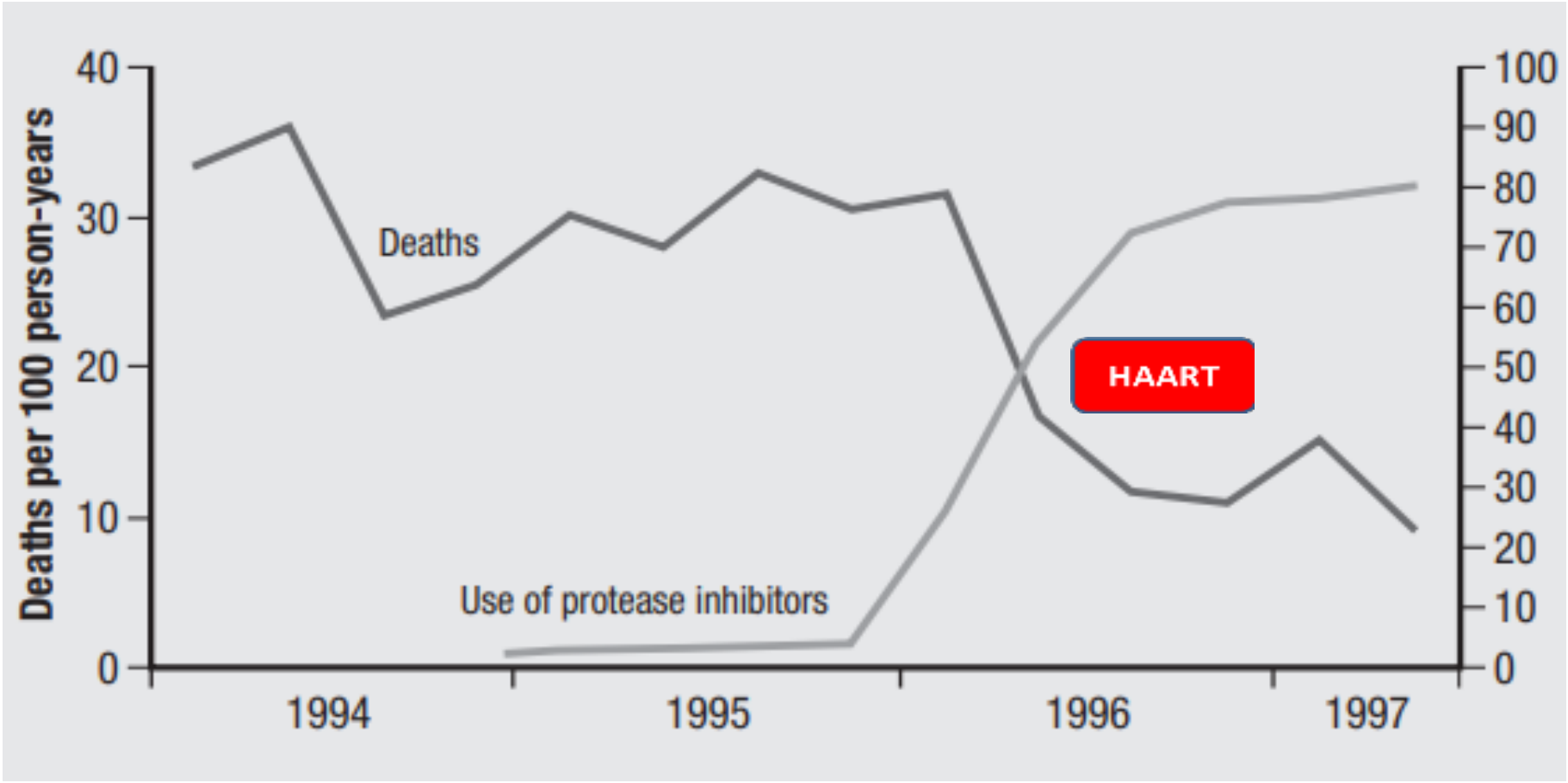
HIV ve MSS enfeksiyonları
CMV: Merkezi sinir sistemi tutulumu

HIV ve Oküler enfeksiyonlar
CMV retinitis

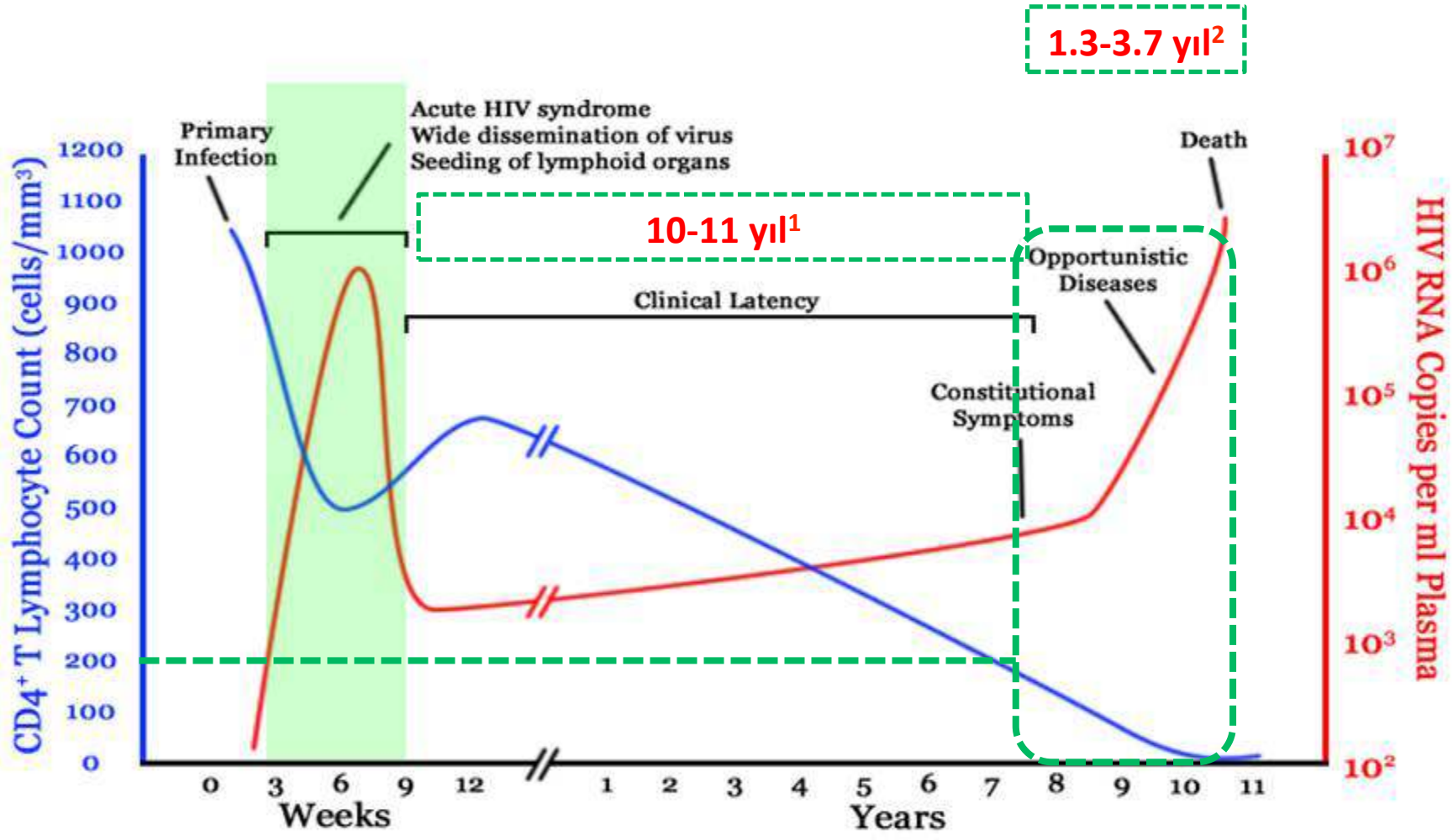

Devastation
Discovery and action
End of AIDS
1980
1985
1990
1995
2000
2005
2010
2015
2020
1981 AIDS
1983 HIV
1983 WHO surveillance
1983 Denver Principles
1980
100000 PLHIV
No treatment
1985 HIV test
1987 AZT
1987 WHO GPA
1987 TASO Uganda
1985 Reagan mentions AIDS
1986 AIDS Quilt
1986 ACT-UP
1985
Nearly 1 million PLHIV
No treatment
1992 AIDS leading cause of death in USA for men aged 25–44 years
1993 USA Office of National AIDS Policy
1994 AZT to prevent MTCT
1990
Millions of PLHIV
No treatment
1995 Protease inhibitors
1996 Vancouver triple therapy
1996 US home HIV test
1997 AIDS deaths decline 40% in US
1998 TAC South Africa
1995
20 million PLHIV
No Treatment
2000 AIDS among top ten global leading causes of death
2001 Special UN session "global emergency"
2002 Global Fund established
2003 PEPFAR
2003 WHO 3×5
2000
28·9 million PLHIV
<200 000 (<1%) on treatment
2005 First generic ARVs
2006 TasP proposed as HIV control strategy
2007 Raltegravir
meta-analysis shows ART prevents transmission
2009 WHO proposes universal testing and treatment to eliminate HIV in South Africa
2005
31·8 million PLHIV
1·3 million (4%) on treatment
2011 HPTN 052 proves ART blocks transmission
2012 PrEP approved in USA
2010 UNAIDS Treatment 2.0 with treatment as prevention
2014 UNAIDS 90-90-90 targets
2010
33·3 million PLHIV
7·5 million (23%) on treatment
2015 Fast-Track Cities with 60+ cities
2015 START and TEMPRANO studies
2015 Access to treatment is a human right
2016 U=U
2017 İlk 2'li tek tablet FDA onayı
2015
36·7 million PLHIV
17 million (46%) on treatment
2020
PLHIV
30 million (81%) on treatment
KÜR??
2020
2030
95-95-95 target affirmed
2030
40 million PLHIV
95-95-95 target:
36·1 million (90%) on treatment
Policy
Hit early, hit hard. Almost no access to treatment in low-income and middle-income countries
2003 WHO CD4 count <200 cells per µL
2009 WHO CD4 count <350 cells per µL
2012 USA treat all
2013 WHO CD4 count <500 cells per µL
2015 WHO Irrespective of CD4 cell count

History of antiretroviral therapy





Palella FJ et al. N Engl J Med. 1998;338:853-60



1. Rutherford GW, Lifson AR, Hessol NA, et al. BMJ 1990; 301: 1183–88.

2. Fauci AS, Pantaleo G, Stanley S, Weissman D. Ann Intern Med 1996; 124: 654–63.

HIV ve MSS enfeksiyonları

Fokal kitle	Beyaz cevher hastalığı	Meningeal hastalık
Toksoplazmoz	HIV ensefalopatisi	HIV meningoensefaliti
TBC	CMV ensefalopatisi	Kriptokokkal menejit
Kriptokokkoz	PML	Tüberküloz menenjit
Primer MSS lenfoması		Bakteriyel – viral menenjit (diğer)
Bakteriyel – fungal abseler		
CMV ensefalit (nadir)		

HIV ve MSS enfeksiyonları

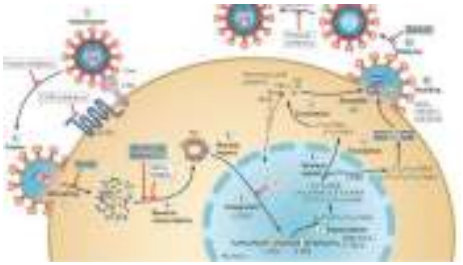
- ART insidansta >10 kat azalma
  - Naif
  - MSS enfeksiyonlarında 2 kat artış[1]

- ART dönemi sonrası kimlerde;
  - HIV durumu bilinmeyen bireyler
  - Direnç
  - Psikoaktif ilaç kullanımı

1. Garvey, L. *et al. Eur. J. Neurol.* 18, 527–534 (2011).

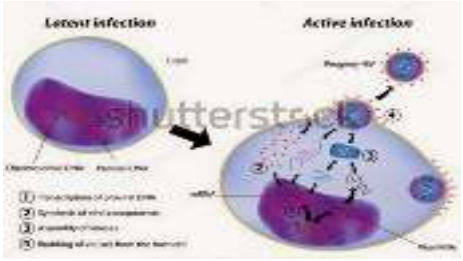
HIV & MSS Patogenez

- Persistan viral replikasyon, kronik immün aktivasyon ve progressif immün sistem harabiyeti



- Hücresel immün sistem fonksiyon kaybı

- MSS içinde yerleşme ve çoğalma



- Latent patojenlerin reaktivasyonu;
  - CMV, toksoplazma, PML, primer MSS lenfoması…

Tan IL. Lancet Neurol. 2012 Jul;11(7):605-17

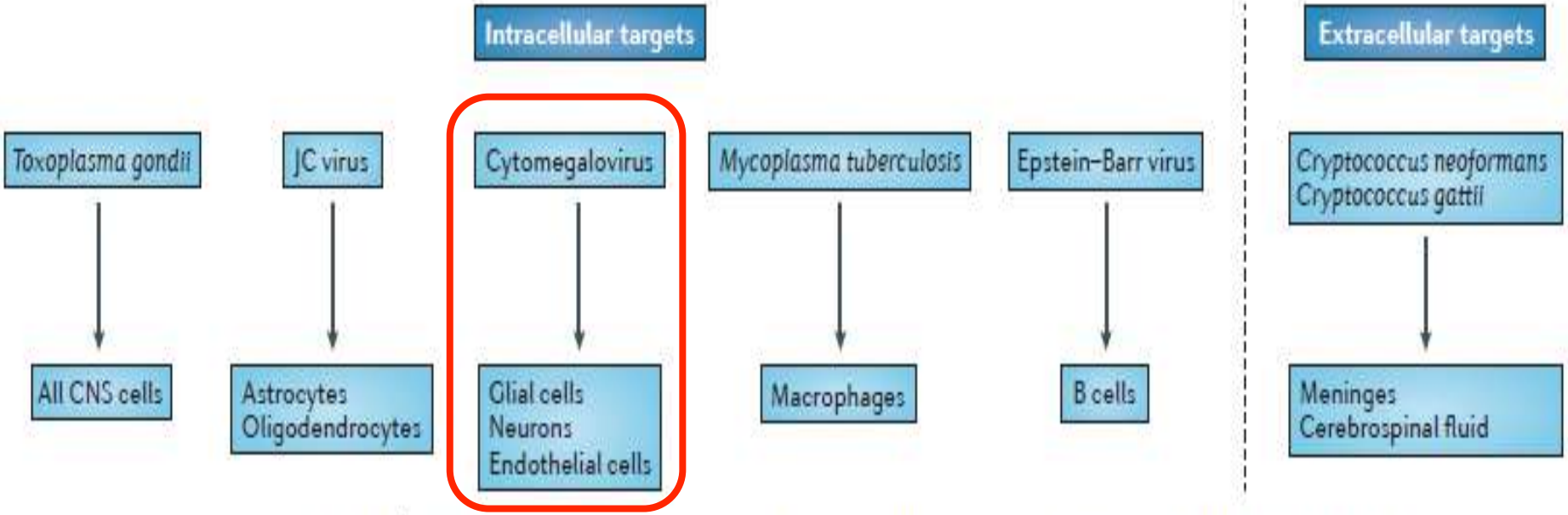


Figure 5 | Cellular tropism of organisms causing opportunistic infections in the CNS. The major HIV-associated opportunistic infections preferentially infect specific cell types in the CNS, a phenomenon referred to as cellular tropism.

Bowen LN *et al.* Nat Rev Neurol. 2016 Oct 27;12(11):662-674

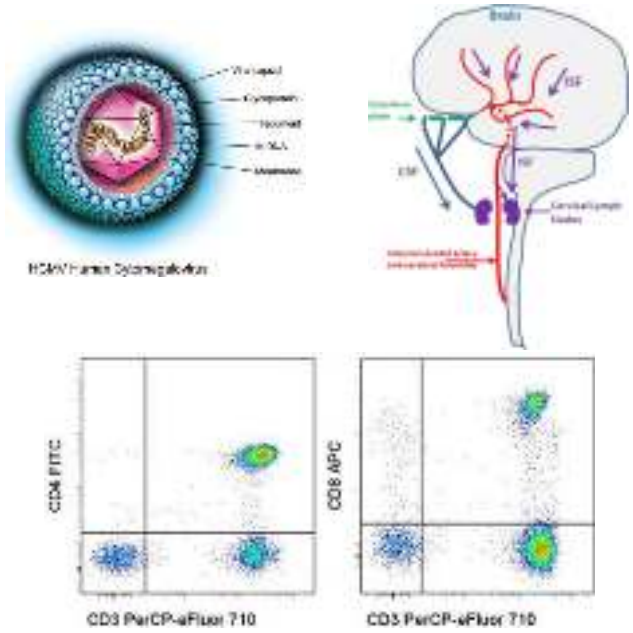
HIV & MSS Enfeksiyonu

- MSS enfeksiyonu HIV ilk bulgu
- ART sonrası IRIS
- %15 eş zamanlı 2. bir MSS enfeksiyonu
- Tanı;
  - Klinik bulgular
  - BOS incelemesi
  - Radyolojik görüntüleme

Tan IL. Lancet Neurol. 2012 Jul;11(7):605-17

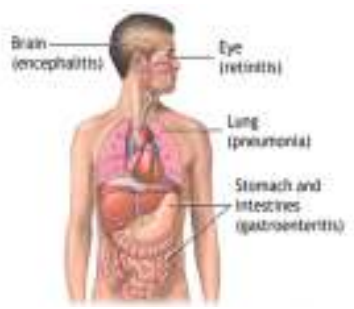
CMV & MSS Tutulumu - Patogenez

- Re-aktive olan virüsün hematojen yolla
- Vakalar CD4 <50 hücre/microL;
- CMV antijen-spesifik sitotoksik T lenfosit aktivitesi

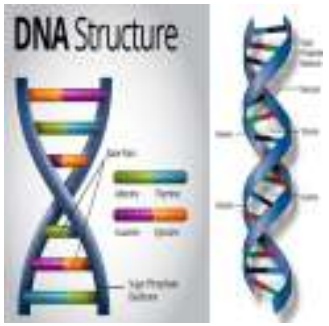


www.uptodate.com Pathogenesis, clinical manifestations, and diagnosis of AIDS-related cytomegalovirus retinitis

CMV & MSS Tutulumu - Patogenez



- CMV end-organ hastalığı öncesi
  - CMV spesifik IFN-gama üreten CD4 + T hücre sayısında azalma



- Genetik faktörler;
  - HLA B44 ve DR7 pozitiflerde daha sık???

www.uptodate.com Pathogenesis, clinical manifestations, and diagnosis of AIDS-related cytomegalovirus retinitis

CMV & MSS Tutulumu - Patogenez

- Beyin, spinal kord, sinir kökleri ve periferal sinir
  - Demans
  - Ventriküloensefalit
  - Poliradikülomiyelopati

- Beyindeki CMV hastalığındaki histolojik paternler;
  - Mikroglial nodüller; gri cevherdeki makrofaj kümeleri
  - Fokal parankimal nekroz
  - Ventriküloensefalit

www.uptodate.com AIDS-related cytomegalovirus neurologic disease

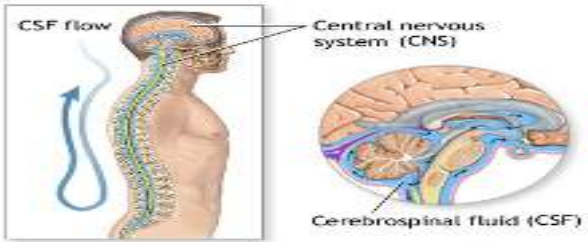
CMV & MSS Tutulumu - Patogenez

- Omurilikte, sinir köklerinde ve periferik sinirlerde;
  - Subpial nekroz
  - Aksonal destrüksiyon
  - Miyelin dejenerasyonu
  - Epinöral arterlerin fokal, polimorfonükleer nekrotizan vasküliti

www.uptodate.com AIDS-related cytomegalovirus neurologic disease

CMV Demansı

- Laterji, konfüzyon ve ateş
- Daha silik klinik tablo
- BOS bulguları;
  - Lenfositik pleositoz
  - Normal-hafif azalmış glukoz
  - Normal-hafif artmış protein



www.uptodate.com AIDS-related cytomegalovirus neurologic disease

CMV Ensefaliti

- CMV ensefalit 676 hasta*
  - %85'inde AIDS
  - % 12'sinde immünsüprese (diğer)
  - % 3'ü immünkompanse

*Arribas JR, Storch GA, Clifford DB, Tselis AC. Cytomegalovirus encephalitis. Ann Intern Med 1996; 125:577.

CMV Ensefaliti - Klinik

- Çoğunlukla subakut-akut

- Fokal belirtiler az, non-spesifik
  - Laterji, konfüzyon
  - Yürüme bozukluğu
  - Baş ağrısı

- Nöbet, kraniyel sinir palsileri veya ataksi

Bowen LN et al. Nat Rev Neurol. 2016 Oct 27;12(11):662-674

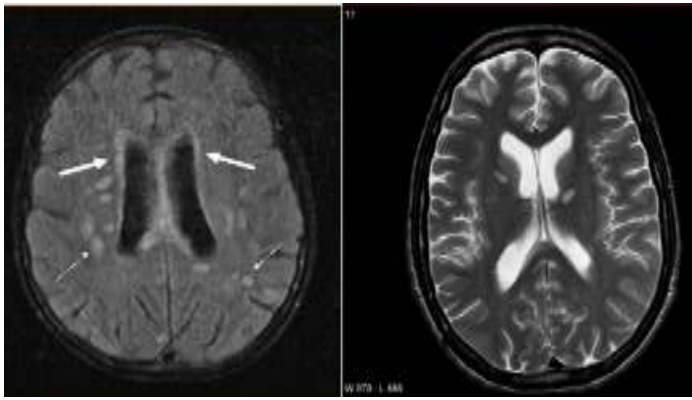
CMV & MSS Enfeksiyonu - Tanı

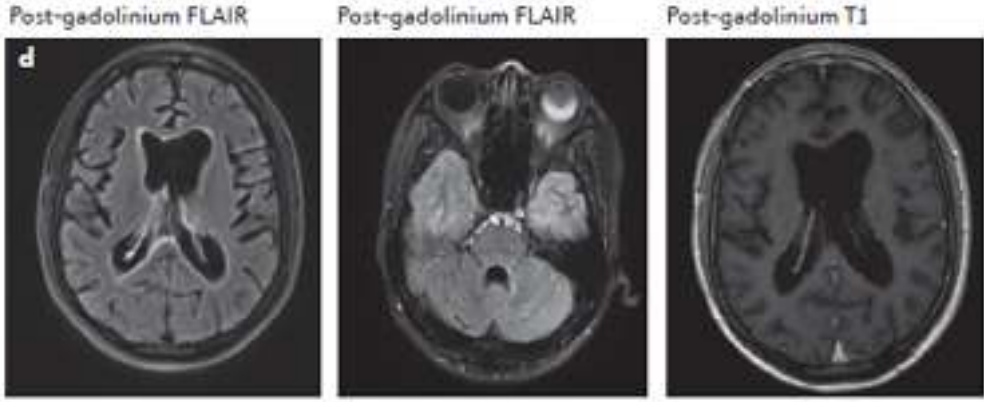
- Viremi olmaması end-organ hastalığını dışlamaz veya tam tersi
- CMV PCR düşük pozitif prediktivitesi rutin tarama önerilmez[1]
- CMV ilişkili nörolojik bulgu varlığı BOS CMV PCR çalışılmalı
- BOS PCR duyarlılığı %95, özgüllüğü %85[2]

1- Marra, C. M. et al. AIDS 16, 1791–1797 (2002). 2- Dodt, K. K. et al. AIDS 11, F21–F28 (1997).

CMV Ensefaliti - Tanı

- BOS bulguları;
  - Nötrofilik pleositoz
  - Normal-hafif azalmış glukoz
  - Normal-hafif artmış protein
- MR görüntüleme;
  - Lineer periventriküler hiperintensite,
  - Simetrik kontrast tululumu
  - Normal MR CMV ensefalitini dışlamaz





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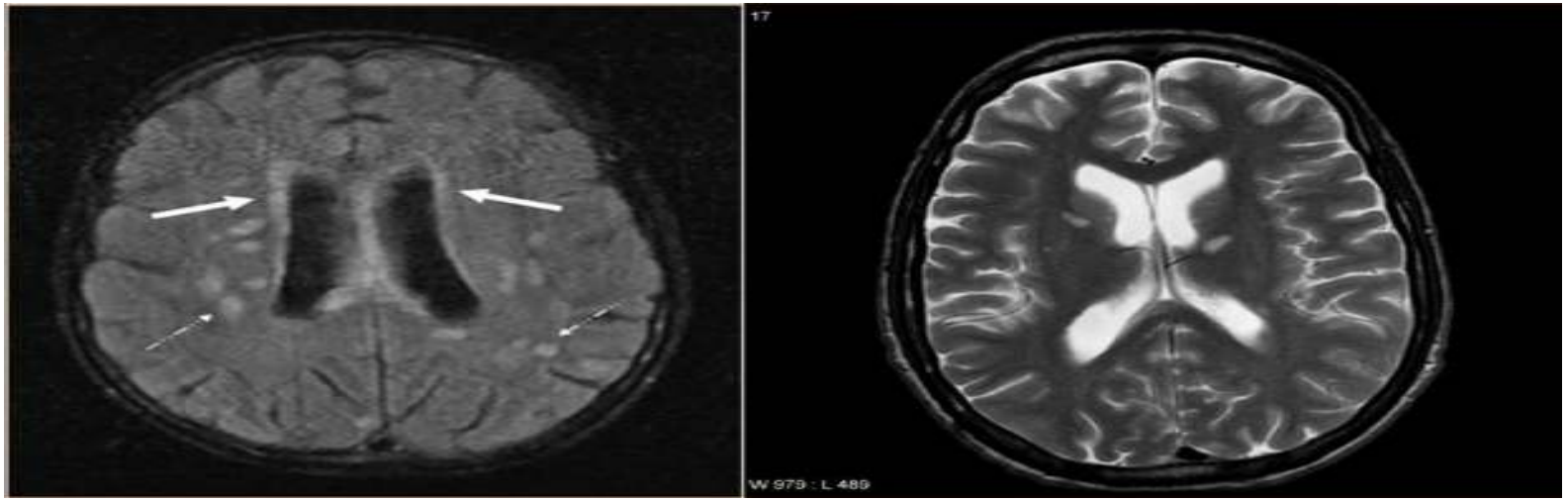
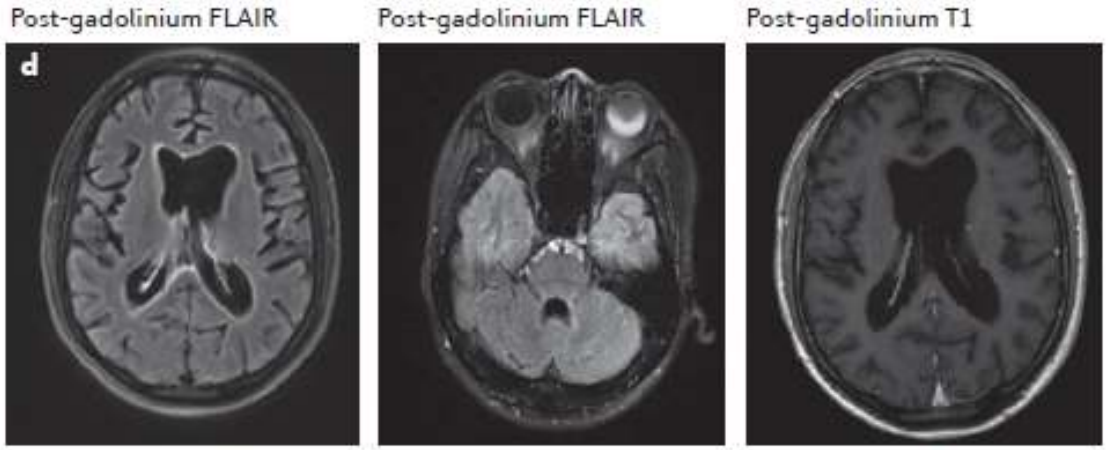
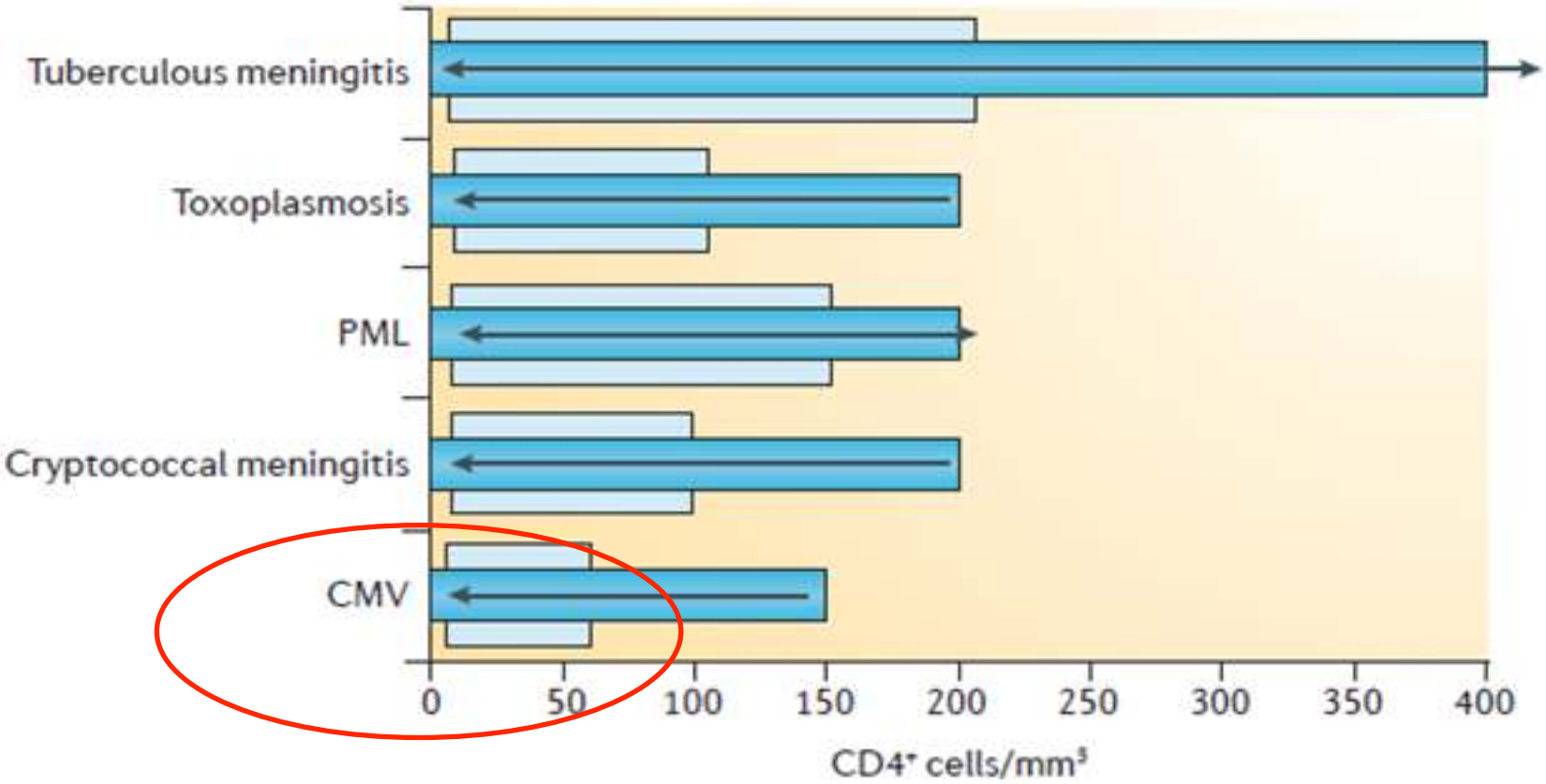




***Cytomegalovirus encephalitis and retinitis.**

FLAIR sekansta periventriküler hiperintens sinyal Post-kontrast FLAIR sekansta CMV retiniti görünümü.

HIV&MSS - Ayırıcı Tanı



Bowen LN et al. Nat Rev Neurol. 2016 Oct 27;12(11):662-674

HIV & MSS – Ayırıcı tanı

	CD4-cell count at presentation (cells per µL)	Time from symptom onset to presentation	Change in mental status	Seizures	Headache	Fever	Focal deficits	Cranial neuropathies
Toxoplasmic encephalitis[21,22]	<200	Days	+to+++	+to++	+++	++to+++	++to+++	+
PML[21,24]	<100, but occasionally higher	Generally weeks to months; sometimes acute, mimicking stroke	++to+++	+	+to++	+	+++	+
Primary CNS lymphoma[25,26]	<100	Weeks	+++	+to++	++to+++	None	++to+++	+
Cytomegalovirus encephalitis[27,28]	<50	Days	+++	++	+to++	++	+	++
Cryptococcal meningitis[29-33]	<50 (rarely, up to 200)	Days	+to+++	+	+++	+to+++	+	+
Tuberculous meningitis[32-34]	Variable, but <200	Days to weeks	++to+++	+	+++	+++	+to++	++to+++
Herpes simplex virus[35]	Variable	Weeks	+++	++	+	+to++	++	+to++

+=uncommon (0–<30%). ++=sometimes (30–<60%). +++=often (>60%). PML=progressive multifocal leukoencephalopathy.

Table 3: Clinical characteristics of HIV-associated CNS opportunistic infections

** Tan IL. et al. HIV-associated opportunistic infections of the CNS. Lancet Neurol. 2012 Jul;11(7):605-17*

	White-blood-cell count	Glucose concentration	Protein concentration	Other
Toxoplasmic encephalitis[21,22,24]	Normal or increased lymphocytes	Decreased or normal	Normal or increased	*Toxoplasma gondii* PCR nearly 100% specific and 50–80% sensitive
PML[23,24]	Normal, rarely increased lymphocytes	Normal	Normal or increased	JC-virus PCR sensitivity variable at 50–90%, but specificity 90–100%
Primary CNS lymphoma[25,26]	Normal or increased lymphocytes	Normal	Normal	Epstein-Barr virus PCR nearly 100% sensitive and about 50% specific
Cytomegalovirus encephalitis[27,28]	Normal, rarely increased neutrophils	Normal	Normal or increased	PCR >90% sensitive and specific and <25% culture positive
Cryptococcal meningitis[29,30,37]	Normal, rarely increased lymphocytes	Decreased or normal	Normal or increased[36]	Opening pressure frequently raised; India ink stain 75% sensitive; CSF cryptococcal antigen sensitivity 92% and specificity 83%; high CSF antigen titre associated with poor prognosis, but change of titre with treatment has little correlation with prognosis
Tuberculous meningitis[33–34]	Increased lymphocytes	Decreased	Normal or increased	*Mycobacterium tuberculosis* culture has variable sensitivity, but use of microscopy for acid-fast bacilli and CSF NAAT can increase sensitivity to >80%
Herpes simplex virus[35]	Usually increased lymphocytes	Normal or increased	Increased	CSF PCR sensitivity 100%, specificity 99·6%

PML=progressive multifocal leukoencephalopathy. NAAT=nucleic-acid amplification test.

Table 4: CSF characteristics of HIV-associated CNS opportunistic infections

** Tan IL. et al. HIV-associated opportunistic infections of the CNS. Lancet Neurol. 2012 Jul;11(7):605-17*

	Mass effect	Proportion of solitary lesions (%)	Typical locations	Enhancement	Other
Toxoplasmic encephalitis[23,27,36]	Frequent	<20%	Frontal, basal ganglia, parietal	Frequent, mainly ring enhancing	Generally 1–2 cm
PML[23,24,35]	Rare	~50%	Subcortical white matter, cerebellum, brainstem	~25% show enhancement, (especially in patients with IRIS)	Hyperintense areas in white matter on T2-weighted, FLAIR MRI and hypointense lesions on T1-weighted MRI, with sparing of cortical ribbon
Primary CNS lymphoma[25,26,38]	Frequent	30–50%	Periventricular, frontal, cerebellum, temporal	Frequent, potentially with heterogeneous enhancement	Generally >3 cm diameter
Cytomegalovirus encephalitis[27,28]	None	NA	Periventricular	<50% show periventricular enhancement	About 50% of cases show normal imaging
Cryptococcal meningitis[29,30]	Communicating hydrocephalus with raised intracranial pressure	Typically multiple	Basal ganglia	Potentially leptomeningeal enhancement, especially in patients with IRIS	Frequently "punched-out" cystic lesions
Tuberculous meningitis[33–34]	Hydrocephalus possible	Mainly ill-defined exudates	Infratentorial with basal ganglia or cortical infarcts	<50% show basilar enhancement on CT	Haemorrhage, tuberculomas, or abscesses possible
Herpes simplex virus[35]	Minimal	NA	Inferomedial temporal lobes	Frequent enhancement	May involve brainstem, cerebellum, diencephalon, and periventricular regions; associated intracranial haemorrhage

PML=progressive multifocal leukoencephalopathy. IRIS=immune reconstitution inflammatory syndrome. FLAIR=fluid-attenuated inversion recovery. NA=not applicable.

Table 5: **Radiographic characteristics of HIV-associated CNS opportunistic infections**

** Tan IL. et al. HIV-associated opportunistic infections of the CNS. Lancet Neurol. 2012 Jul;11(7):605-17*

CMV Poliradikülopati

- Guillain-Barre benzeri
  - Alt ekstremite duyu kaybı
  - Bilateral bacaklarda motor güçsüzlik
  - Arefleksi
  - Üriner retansiyon
  - Flask parapleji
- Poliradikülite miyelopati eşlik ediyorsa canlı refleks
- Klinik tablonun oturması birkaç haftayı bulabilir

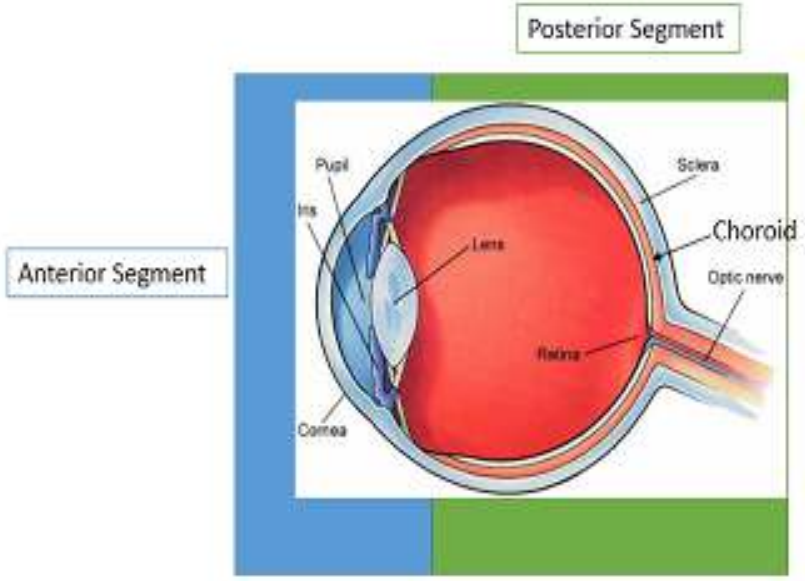
Bowen LN *et al.* Nat Rev Neurol. 2016 Oct 27;12(11):662-674

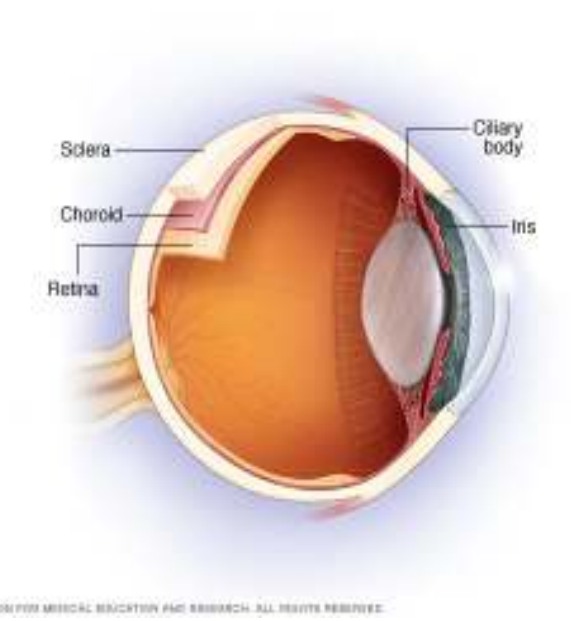
CMV Poliradikülomiyelit

- MR görüntüleme
  - Normal
  - Post-kontrast serilerde sinir köklerinde sinyal artımı
  - Histopatolojik olarak leptomeningeal tutulum
- BOS bulguları;
  - Nötrofilik pleositoz (100–200 nötrofil/µL)
  - Hipoglukoraji
  - Hafif artmış protein

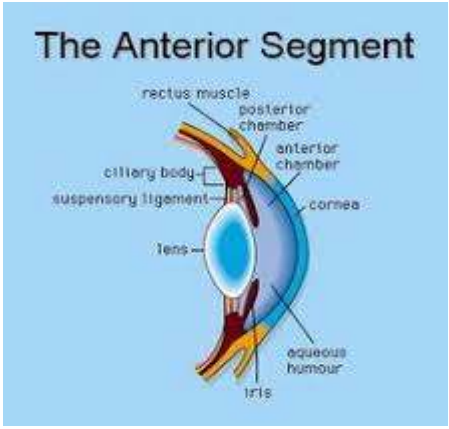
Bowen LN et al. Nat Rev Neurol. 2016 Oct 27;12(11):662-674

HIV & CMV Oküler Tutulum





HIV hastalarında anterior segment ve external göz tutulumu yapan enfeksiyonlar



A. Göz kapağı ve oküler adneksi tutanlar

1. Molluscum contagiosum
2. Herpes zoster ophthalmicus
3. Herpes simplex virus veziküler lezyonlar
4. Tuberculosis (cilt lezyonları)
5. Cryptococcosis (cilt lezyonları)

B. Konjonktivayı tutanlar

1. Molluscum contagiosum (nadir)
2. Gonorrhea
3. Sifilitik şankır
4. Tuberculosis
5. Cryptococcosis
6. Pneumocystosis (nadir)
7. Microsporidiosis

C. Episikera/siklera

1. VZV ilişkili skleritis
2. Tuberculosis

D. Korneayı tutanlar

1. Molluscum contagiosum
2. Varicella-zoster virus-associated keratitis
3. Herpes simplex virus-associated keratitis
4. Cytomegalovirus keratitis
5. Gonorrhea
6. Sifilitik keratitis
7. Tuberculosis
8. Cryptococcosis
9. Microsporidiosis

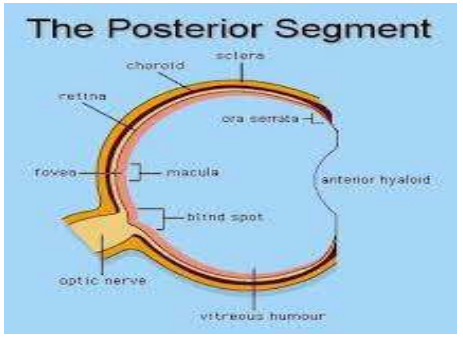
E. Anterior üveayı tutanlar

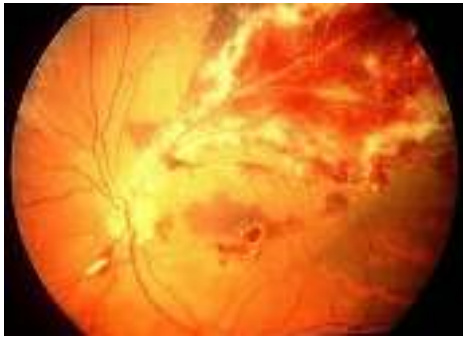
1. VZV ilişkili üveit
2. HSV ilişkili üveit
3. Cytomegalovirus-ilişkili iritis (nadir)
4. HIV ilişkili üveit
5. Sifilitik anterior üveit
6. Tuberculosis
7. Cryptococcosis
8. Toxoplasmic iritis

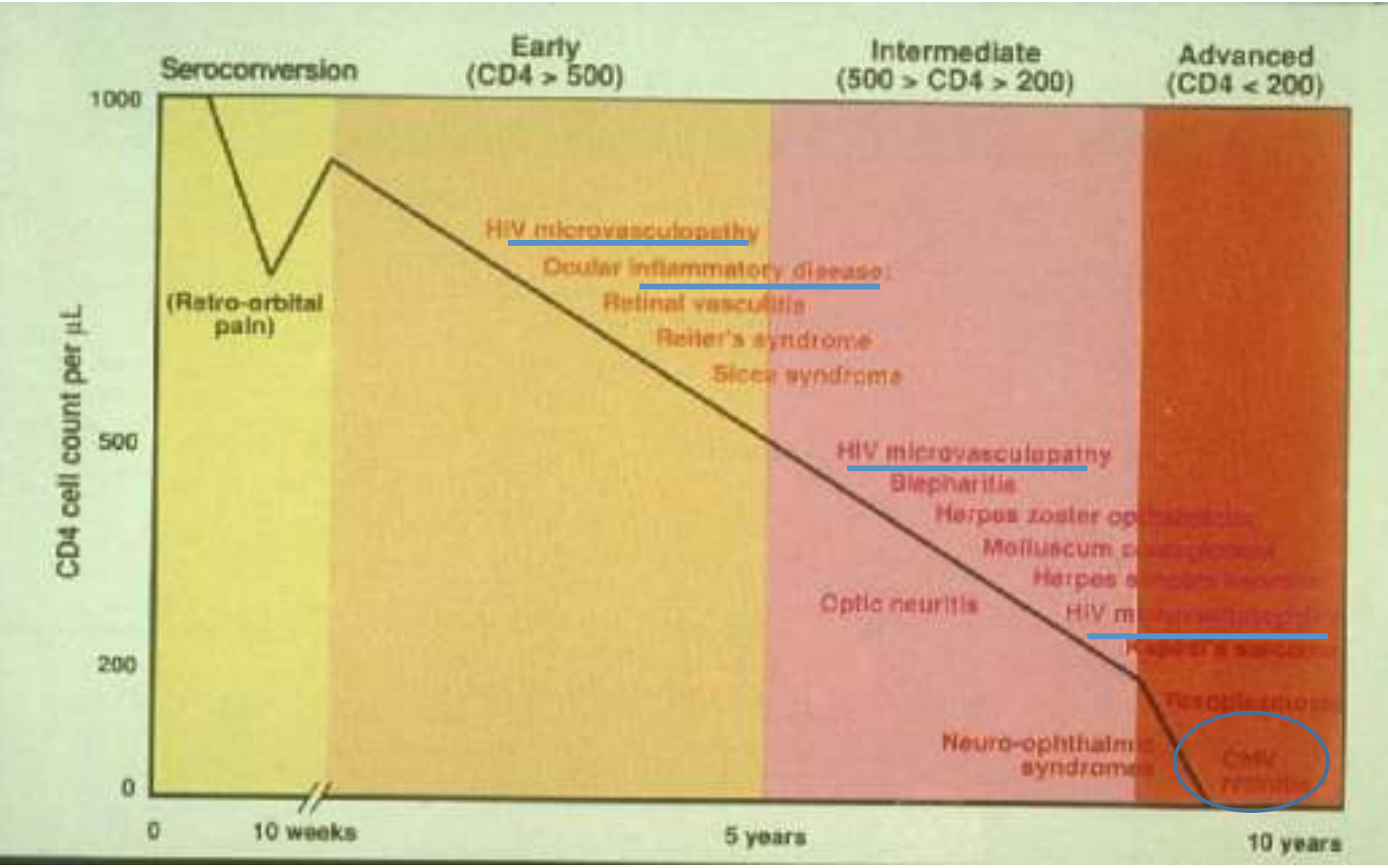
Jeng BH Et al. Surv Ophthalmol. 2007 Jul-Aug;52(4):329-68

Posterior segment tutulumu

- HIV retinopatisi
- HIV ilişkili retinitis
- Toksoplazmozis
- Oküler sifiliz
- Kandidal enfeksiyonlar
- Tüberküloz
- Akut retinal nekroz ve PORN
- CMV retinitis
- Oküler immün rekonstitüsyon inflamatuvar sendrom (IRU)






Seroconversion
Early
(CD4 > 500)
Intermediate
(500 > CD4 > 200)
Advanced
(CD4 < 200)
1000
500
200
0
CD4 cell count per µL
(Retro-orbital pain)
HIV microvasculopathy
Ocular inflammatory disease:
Retinal vasculitis
Reiter's syndrome
Sicca syndrome
HIV microvasculopathy
Blepharitis
Optic neuritis
Neuro-ophthalmic syndromes
0
10 weeks
5 years
10 years

January 2009

International Council of Ophthalmology

ICO International Clinical Guidelines
Ocular HIV/AIDS Related Diseases
(Initial and Follow-up Evaluation)

General - Initial Exam History

- Age **(B:III)**
- Ocular symptoms including laterality **(A:III)**
- Systemic symptoms **(A:III)**
- Complete review of systems **(A:III)**
- Prior ocular history **(A:III)**
- Prior medical history **(A:III)**
- Prior surgical history **(B:III)**
- History of other sexually transmitted diseases **(A:III)**
- History of AIDS-defining illnesses or complications **(A:III)**
- Method of HIV acquisition **(B:III)**
- Duration of HIV infection **(A:III)**
- Past and current risk factors – sexual behavior, intravenous drug abuse, transfusion history **(A:III)**
- Current anti-HIV regimen – duration and compliance **(A:III)**
- Current medications **(A:II)**
- Current CD4 count **(A:II)**
- Current viral load **(A:II)**
- Medication allergies **(B:III)**

General - Initial Physical Exam

- General appearance **(A:III)**
- External examination – face, ocular adnexa **(A:III)**
- Lymphatics – preauricular and submandibular nodes **(A:III)**
- Visual acuity **(A:III)**
- Extraocular motility **(A:III)**
- Confrontation visual fields **(A:III)**
- Eyelids – lid closure, interpalpebral fissure height **(B:III)**
- Lacrimal gland **(B:III)**
- Evaluation of tear film – Schirmer, rose bengal and fluorescein staining **(A:III)**
- Nasolacrimal function **(B:III)**
- Slit-lamp examination
    - Eyelid margins **(A:III)**
    - Conjunctiva **(A:III)**
    - Sclera **(A:III)**
    - Cornea **(A:III)**
    - Anterior chamber **(A:III)**
    - Iris **(A:III)**
    - Lens **(A:III)**
    - Anterior vitreous **(A:III)**
- Dilated ophthalmoscopic examination
    - Vitreous – cell/flare, blood, condensations **(A:III)**
    - Optic disc **(A:III)**
    - Retinal vasculature **(A:III)**
    - Macula/fovea **(A:III)**
    - Peripheral retina with scleral depression **(A:III)**
    - Choroid **(A:III)**

Table 2. Corneal and Anterior Segment Manifestations of HIV/AIDS **(A:III** unless otherwise indicated)

Entity		CD4 count	History	Examination	Key Findings	Diagnostic workup	Management	Follow-up
Keratoconjunctivitis sicca		Any **(A:II)**	• Typical history • History of HIV encephalopathy **(B:III)** • Duration of infection with HIV **(B:III)**	• VA • Periorbita **(B:III)** • Lacrimal gland **(C:III)** • Eyelids **(A:II)** • SLE with fluorescein	• Lagophthalmos and reduced blink rate **(B:II)** • Diminished tear meniscus **(B:III)** • Rapid TBUT **(A:II)** • Interpalpebral staining with rose bengal or fluorescein **(A:II)**	• Clinical examination • Schirmer testing **(A:II)** • TBUT **(B:II)** • Rose bengal or fluorescein staining **(A:II)**	• Artificial tears • Long-acting lubricants • Consider punctual occlusion in resistant cases	• As dictated by examination
Viral keratitis	VZV	Any **(B:II)**	• Reduced vision • Ocular symptoms • Presence or recent history of zoster dermatitis **(A:II)** • Prior history of zoster or herpes infection **(A:II)**	• VA • IOP • Periorbita • Eyelids/lashes • Corneal sensation • SLE with fluorescein • DOE with scleral depression	• Dendritic epithelial keratitis **(A:II)** • Decreased corneal sensation **(A:II)** • Elevated IOP **(B:II)** • Iris atrophy **(B:II)** • May present with a mild conjunctivitis or anterior uveitis **(B:II)** • 1/3 develop stromal involvement **(B:II)**	• Clinical examination • Corneal sensation **(A:II)** • May confirm with viral culture, DFA, PCR **(B:II)**	• Acyclovir 800 mg PO 5 times daily or 10 mg/kg IV tid **(A:II)** • Foscarnet IV for resistant cases **(A:II)** • Consider maintenance dose of acyclovir (600 mg PO tid) **(A:II)** • Infectious dendrites can be treated with oral (as described above) or topical antiviral medications (trifluridine 1% 9 times daily) **(A:II)**	• Every 1 to 7 days until resolution, then every 6 months • Observe for stromal and/or neurotrophic keratitis and postherpetic neuralgia **(B:III)**
	HSV				• Dendritic epithelial keratitis, which may be larger in HIV+ patients **(A:II)** • Limbal involvement **(B:II)**		• Topical trifluridine 1% 9 times daily or Acyclovir ointment 5 times daily **(A:II)** • May treat with oral acyclovir (400-800 mg PO 5 times daily) alone **(A:II)** • Consider lesion debridement **(B:III)** • Long term suppression with acyclovir 400 mg PO bid for 1 year **(A:I)**	• Every 1 to 7 days until resolution • HSV appears to recur more frequently in HIV/AIDS patients **(A:II)**
Bacterial or fungal keratitis	Gonorrhea Syphilis Tuberculosis Cryptococcus	Any **(B:II)**	• Reduced vision • Discharge • Timing of symptom onset **(B:III)**	• VA • SLE with fluorescein • DOE **(C:III)**	• Epithelial defect with stromal infiltrate **(A:II)** • Tend to be more severe and bilateral in HIV+ patients **(A:II)**	• Clinical examination • Culture and gram stain **(A:II)**	• Guided by culture results **(B:II)** • Aggressive treatment with topical fortified antibiotics and/or antifungal agents **(A:II)**	• Daily follow-up until substantial improvement • High risk for corneal perforation **(A:II)**
Microsporidial keratitis		< 100 cells/μl **(A:II)**	• Reduced vision • Ocular symptoms – FBS, irritation, photophobia	• VA • SLE with fluorescein	• Punctate epithelial keratopathy **(A:II)** • Mild papillary conjunctivitis **(A:II)** • Mild AC inflammation **(A:II)**	• Scraping or biopsy of suspicious corneal and conjunctival lesions **(A:II)** • Giemsa stain **(A:II)**	• Immune reconstitution **(A:II)** • Directed treatment options include: topical propamidine isethionate, topical fumagillin, oral albendazole, oral itraconazole **(A:II)** • Consider debulking **(B:III)**	• Serial examinations until resolution
Vortex keratopathy (Phospholipidosis)		Any **(B:II)**	• FBS • Medication history (eg. amiodarone, chloroquine, chlorpromazine, ganciclovir, acyclovir) **(A:II)**	• VA • SLE	• Characteristic whorl-like pattern of gray-white subepithelial corneal deposits **(A:II)**	• History and clinical examination	• Reduce or discontinue offending medication, if possible **(A:II)**	• Lesions resolve slowly
Drug-associated uveitis • Cidofovir • Rifabutin • Terbinafine		Any **(A:II)**	• Reduced vision • Medication history, including daily doses **(A:II)** • Immune status **(B:III)** • Duration on HAART **(B:III)** • History of CMV retinitis **(A:II)**	• VA • SLE • IOP **(B:III)** • DOE **(B:III)**	• AC inflammation **(A:II)** • Rifabutin-associated hypopyon **(A:II)**	• History and clinical examination	• Topical corticosteroids with or without dose reduction of offending medication **(A:II)** • Usually unnecessary to discontinue offending medication **(B:III)** • Mydriatic agent	• Serial every 1 to 2 weeks examinations until resolution

HIV = human immunodeficiency virus, VA = visual acuity, SLE = slit lamp examination, TBUT = tear film breakup time, VZV = varicella zoster virus, HSV = herpes zoster virus, IOP = intraocular pressure, DOE = dilated ophthalmoscopic examination, DFA = direct fluorescent antibody, PCR = polymerase chain reaction, PO = per os (by mouth), IV = intravenous, AIDS = acquired immunodeficiency syndrome, FBS = foreign body sensation, AC = anterior chamber, HAART = highly active antiretroviral therapy, CMV = cytomegalovirus

Table 3. Posterior Manifestations of HIV/AIDS **(A:III** unless otherwise indicated)

Entity	CD4 count	History	Examination	Key Findings	Diagnostic workup	Management	Follow-up
HIV retinopathy	< 50 cells/µl **(A:II)**	• Visual and ocular symptoms (typically asymptomatic) **(B:III)**	• VA • SLE **(B:III)** • DOE **(A:II)**	• Conjunctival microvascular changes **(B:II)** • CWS **(A:II)** • IRH **(A:II)** • MAs **(A:II)** • Retinal ischemia **(A:II)** • CME **(A:II)**	• Clinical diagnosis	• Improve immune status with HAART **(A:II)** • Screen for other infections/illnesses • Consider corticosteroids **(B:III)** or focal laser **(A:II)** for macular edema	• Lesions spontaneously resolve over weeks to months **(A:II)** • DOE every 3 months for CD4 counts persistently < 50 cells/µl **(A:II)**
CMV retinitis	< 50 cells/µl **(A:II)**	• Duration of AIDS **(A:II)** • History of systemic CMV infection **(A:II)** • Ocular symptoms including blurred vision, gradual visual field loss, photopsia, and floaters **(A:II)**	• VA **(A:II)** • SLE **(B:II)** • DOE **(A:II)**	• Geographic thickening and opacification of the retina **(A:II)** • Mild anterior chamber and vitreous inflammation **(B:II)** • Characteristic linear or stellate KP **(B:II)** • 3 main types: granular retinitis with satellite lesions, hemorrhagic retinitis with prominent edema, or perivascular retinitis **(A:II)**	• Primarily a clinical diagnosis • CD4 count **(A:II)** • Rule out syphilis and other causes of retinitis **(A:II)** • Consider vitreous biopsy in challenging cases	• Improve immune status, although consider delay of HAART in HAART-naïve patients until retinitis is improved to reduce the risk of IRU **(A:II)** • Immediate treatment if persistent immune suppression is expected **(A:II)** • Induction followed by maintenance **(A:II)** • Ganciclovir: IV (5 mg/kg every 12 hours for 3 weeks, then 5 mg/kg/day) **(A:I)**; IO (2-2.5mg/0.1ml twice weekly until inactive) **(A:I)**; intraocular implant **(A:I)**, combine with oral anti-CMV medications for systemic coverage **(A:II)** • Foscarnet: IV (60 mg/kg every 8 hours or 90 mg/kg every 12 hours for 14 days, then 90 to 120 mg/kg/day) **(A:I)**; IO (1.2 mg/0.05 ml) **(A:I)** • Valganciclovir: PO (900 mg bid for 2 weeks, then 900 mg daily). Monitor for leukopenia **(A:II)**	• CMV cannot be eliminated from the eye **(A:II)**; patient education for recurrences is crucial • Reevaluate patients monthly while treating with anti-CMV medications **(A:II)** • Extend visit intervals when CD4 counts are elevated, anti-CMV medications are discontinued, and the disease remains inactive in the setting of immune recovery **(A:II)** • Consider serial fundus photography **(B:II)** • Treat recurrences with re-induction of same therapy, unless contraindicated due to side effects or resistance **(A:II)** • May discontinue maintenance therapy in patients without active CMV retinitis and at least 6 months of CD4 cell counts above 150 cells/µl **(A:II)**
Toxoplasmosis	< 200 cells/µl **(A:II)**	• Visual symptoms **(A:II)** • Exposure to undercooked meat or cats **(A:II)**	• VA **(A:II)** • IOP **(B:II)** • SLE **(C:II)** • DOE **(A:II)**	• Moderate-to-severe AC and vitreous inflammation **(B:II)** • Retinochoroiditis with a relative lack of retinal hemorrhage **(A:II)** • Smooth leading edge without satellite lesions **(B:II)** • A rare cause of isolated anterior uveitis **(C:II)**	• Clinical diagnosis • Anti-*Toxoplasma* IgM/IgG **(A:II)** • PCR of aqueous in unclear cases **(B:II)**	• Trimethoprim/sulfamethoxazole (800/160) 500 mg PO bid for 4 to 6 weeks **(A:II)** • Pyrimethamine and sulfamethoxazole for 4 to 6 weeks (option of combination with azithromycin) **(B:II)** • Clindamycin (300 mg PO every 6 hours) for 3 or more weeks **(B:II)** • Atovaquone (750 mg PO qid) for 3 months **(B:II)**	• Initially every 3 to 5 days, then as indicated by examination • Maintenance therapy with at least one medication is recommended for all patients with persistent severe immune deficiency
Tuberculosis	< 200 cells/µl **(A:II)**	• Visual symptoms **(A:II)** • History of *M. Tuberculosis* infection, systemic complications, or exposure **(A:II)**	• VA • External examination **(B:III)** • SLE **(B:III)** • IOP **(B:III)** • DOE **(A:II)**	• Vitritis **(A:II)** • Choroidal tubercles and tuberculomas **(A:II)** • Overlying exudative retinal detachment **(B:II)** • Retinal periphlebitis **(A:II)**	• Presumptive diagnosis combined with PPD skin testing and CXR **(A:II)** • Consider IGRAs (eg. QuantiFERON®-TB Gold; T.SPOT-TB®) **(B:II)** • FA, ICG, and OCT when indicated (see text) **(B:III)**	• Systemic treatment with rifampin (500 mg/day for weight > 50 kg and 600 mg/day for weight < 50 kg), isoniazid (5 mg/kg/day), pyrimethamine (25 to 30 mg/kg/day, and ethambutol (15 mg/kg/day) for 2 months then rifampin and isoniazid for another 4 to 7 months **(A:II)** • PO prednisone (1 mg/kg/day), taper as directed by clinical response **(A:II)** • Immune reconstitution **(A:II)** • Involve an infectious disease specialist	• Monitor all patients for drug toxicity **(A:II)** • Examine patients monthly until a significant improvement

Syphilis	Often < 200 cells/µl, but can vary **(A:II)**	• Visual symptoms **(A:II)** • Sexual history **(B:II)**	• VA **(A:II)** • IOP **(B:II)** • SLE **(B:II)** • DOE **(A:II)**	• Iridocyclitis or diffuse inflammation **(A:II)** • Necrotizing retinitis **(A:II)** • Subretinal plaque **(B:II)** • Papillitis, optic neuritis, or neuroretinitis **(A:II)**	• RPR or VDRL **(A:II)** • FTA-ABS or MH-ATP **(A:II)** • Consider seronegative syphilis **(B:II)** • CSF examination **(A:II)**	• Treat as neurosyphilis **(A:II)** • Involve an infectious disease specialist • IV penicillin G, 18 to 24 million units for 14 days **(A:II)**	• Serial serum and CSF antibody levels – every month for 3 months, then every 6 months until CSF cell count normalizes and CSF VDRL becomes non-reactive **(A:III)** • Maintenance therapy not recommended **(B:II)** • Monitor patients for a Jarish-Herxheimer reaction **(A:II)**
Non-CMV necrotizing herpetic retinitis	PORN: < 50 cells/µl **(A:II)** ARN: > 50cells/µl **(A:II)**	• History of HZO or dermatitis **(A:II)** • History of herpes encephalitis **(B:II)** • Visual symptoms (pain, vision loss, new floaters or scotomata) **(A:II)**	• VA **(A:II)** • IOP **(B:III)** • SLE **(B:III)** • DOE **(A:II)**	• Retinal whitening with occasional hemorrhages **(A:II)** • Multiple large confluent areas of retinitis **(A:II)** • Rapid progression **(A:II)** • Prominent (ARN) or minimal (PORN) vitreal inflammation **(B:II)**	• Clinical diagnosis • Aqueous or vitreous biopsy for PCR-based analysis can aid in diagnosis **(B:II)** • Note location and extent of involved retina	• Induction with high-dose intravenous acyclovir (15 mg/kg q 8 hours) **(A:II)** • Intraocular ganciclovir (2 to 2.5mg/0.1ml twice weekly) or foscarnet (1.2 mg/0.05ml) as indicated **(A:II)** • Maintenance with long term oral valacyclovir or valganciclovir may be considered **(B:II)** • Patients receiving high doses of valacyclovir should be monitored for TTP/HUS **(A:II)** • Patients receiving valganciclovir should be monitored for leukopenia **(A:II)**	• Can progress rapidly **(A:II)** • Daily until significant improvement, then weekly
Immune recovery uveitis	>100 cells/µl or 50 cell/µl increase **(A:II)**	• History/extent of CMV retinitis **(A:II)** • History of cidofovir use **(B:II)**	• VA **(A:II)** • IOP **(B:II)** • SLE **(A:II)** • DOE **(A:II)**	• Panuveitis with vitreous predominance **(A:II)** • May be complicated by TRD, RNV, ERM formation, or CME **(A:II)**	• Diagnosis based on history and clinical examination • Consider FA to rule out CME **(B:III)**	• Topical, periocular, or intraocular corticosteroids **(A:II)** • PPV for VMTS, ERM, cataract, PVR **(A:II)**	• Weekly until resolution
Pneumocystis choroiditis	< 200 cells/µl **(A:II)**	• History of aerosolized pentamidine use **(A:II)**	• VA **(A:II)** • SLE **(C:III)** • DOE OU **(A:II)**	• Multiple well-demarcated yellowish choroidal lesions in the posterior pole **(A:II)** • Lack of iritis, vitritis, or vasculitis **(A:II)**	• Clinical diagnosis • Consider workup for systemic disease, including CXR, ABG analysis, abdominal CT, and liver function testing	• TMP-SMX or pentamidine (4 mg/kg/day) **(A:II)**	• Monthly until resolution – usually 1 to 3 months • Following a 3 week IV induction regimen, maintain on oral prophylactic treatment until immune system recovers (CD4 count above 200 cells/µl) **(A:II)**
Cryptococcus	< 50 cells/µl **(A:II)**	• Visual symptoms including vision loss, diplopia, and new scotomata **(A:II)** • Headache/ meningismus **(A:II)**	• VA • SLE **(B:II)** • EOM **(A:II)** • DOE **(A:II)**	• Signs and symptoms of central nervous system infection **(A:II)** • Papilledema **(A:II)** • Retrobulbar optic neuritis **(B:II)** • Multifocal choroiditis **(A:II)** • Other findings may include iritis, iris mass, vitritis, necrotizing retinitis, and eyelid or conjunctival mass **(B:II)**	• Clinical diagnosis • CNS symptoms – think of cryptococcal meningitis **(A:II)** • Skin lesions – biopsy **(B:II)**	Isolated choroiditis: • IV fluconazole, 400 mg/day and IV flucytosine, 100 to 150 mg/kg/day for 10 weeks **(A:II)** Associated with meningitis: • IV amphotericin B, 0.7 to 1 mg/kg/day and IV flucytosine 100 mg/kg/day for 2 weeks followed by IV fluconazole for at least 10 weeks **(A:II)**	• Weekly until resolution
HIV-associated retinitis	> 120 cells/µl **(A:II)**	• Visual symptoms **(A:II)**	• VA • IOP **(C:II)** • SLE **(C:III)** • DOE **(A:II)**	• Peripheral multifocal retinitis **(A:II)** • Retinal vasculitis **(A:II)** • Mild vitreous inflammation **(B:II)** • Lack of retinal hemorrhage **(B:II)** • Slow progression **(B:II)**	• Clinical diagnosis • Rule out other entities, particularly syphilis **(A:II)**	• Antiretroviral therapy should lead to regression **(A:II)**	• Weekly until resolution

January 2009

International Council of Ophthalmology

ICO International Clinical Guidelines
Ocular HIV/AIDS Related Diseases
(Initial and Follow-up Evaluation)

- İlk tanıda ve rutin oftalmolojik muayene (CD4 bağımsız)***
- Multidisipliner yönetim***

The distribution of patients depending on the specific conditions of the posterior segment of the eye

Specific posterior segment ocular disease	Number of patients
Retinal microangiopathy	31
Retinitis	59
Choroiditis	8
Chorioretinitis	40

Distribution of patients with CMV retinitis depending on the clinical form shown

Clinical form	Number of eyes
Edematous form	29
Indolent form	5
Perivascular form	10
Optic neuropathy	4

48/59 (%81)
CMV retinitis

Immunodeficiency Syndrome) patients.

METHOD: The study is retrospective, condu
during the period 1 August 2007 - 1 August
microscope lens and 20D indirect lens after

RESULTS: 348 patients with HIV/AIDS and
who had eye disorders (194 patients aged t
them had the anterior segment affected. 22.90% of the 131 patients with compromised posterior segment microangiopathy have been diagnosed with HIV / AIDS.

CONCLUSIONS: Doctors should be aware of the existence of ocular damage in HIV / AIDS and to emphasize the importance of regular ophthalmologic examination of patients with HIV / AIDS.

Sitomegalovirüs (CMV) & Retinit

- AIDS en sık ve en ciddi oküler komplikasyon
- HIV en sık CMV end-organ hastalığı
- Büyük oranda latent enfeksiyonun reaktivasyonu
- ART sonrası
  - insidansta %95
  - Oküler komplikasyon belirgin azalma

https://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf

Sitomegalovirüs (CMV) Retiniti

- HAART öncesi;
  - insidans ~ % 30
  - tedavisiz olgularda körlük kaçınılmaz

- Oral gansiklovir proflaksi çalışması [1];
  - CD4<50 veya
  - CD4<100 hc/microL + AIDS fırsatçı enfeksiyon hastalar
  - placebo ve gansiklovir kolunda yıllık CVM retinit insidansı sırasıyla %24, %12

- CD4<200 tedavisiz AIDS olguları [2];
  - 4 yıllık izlemde CMV retiniti görülme oranı %25

1.Spector SA et al. N Engl J Med 1996; 334:1491. 2. Hoover DR, Peng Y, Saah A, et al. Arch Ophthalmol 1996; 114:821.

- 24 ülke
- 39 çalışma Asya kıtasında
- 12.931 hastada
- CMV retinit %14
- 1/3 görme kaybı

CMV Retiniti - Patogenez

- MSS ile benzer
- Tam kat retinal nekroz ve ödemi takiben kalın ve atrofik skar doku
    - Skar dokusu yırtılmaya hassas; retina dekolmanı
- Sentrifugal yayılım
- Retinal doku hasarı geri dönüşümsüz
- Bu nedenle erken tanı en az tedavi kadar önemlidir

www.uptodate.com
Pathogenesis, clinical manifestations, and diagnosis of AIDS-related cytomegalovirus retinitis

CMV Retiniti - Klinik

- Bulanık görme
- Santral görme kaybı
- Kör noktalar
- Uçuşan cisimcikler, noktalar*
- Fotopsi ve ışık çakmaları*
- Asemptomatik

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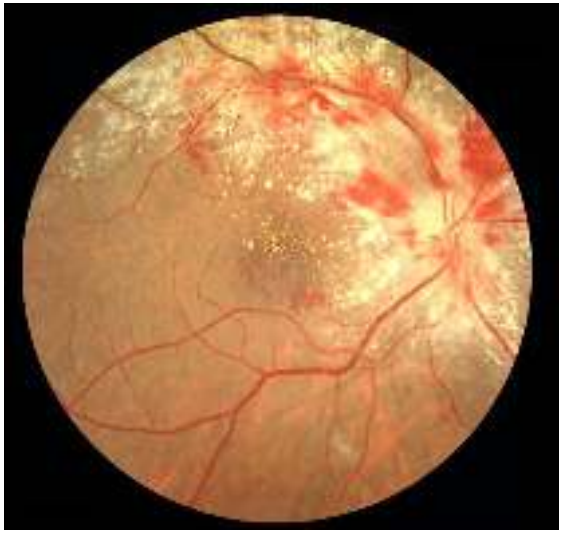
CMV Retiniti – Oftalmolojik Muayene

- Eksüda (cotton wool spots); sarı-beyaz, sınırları keskin olmayan, birleşme eğiliminde
- Retinal nekroz
- Retinal hemoraji
- Çoğunlukla periferik lezyon, ileri dönemde fovea tutulumu
- Retinal dekolman
- Hafif düzeyde vitreus inflamasyonu



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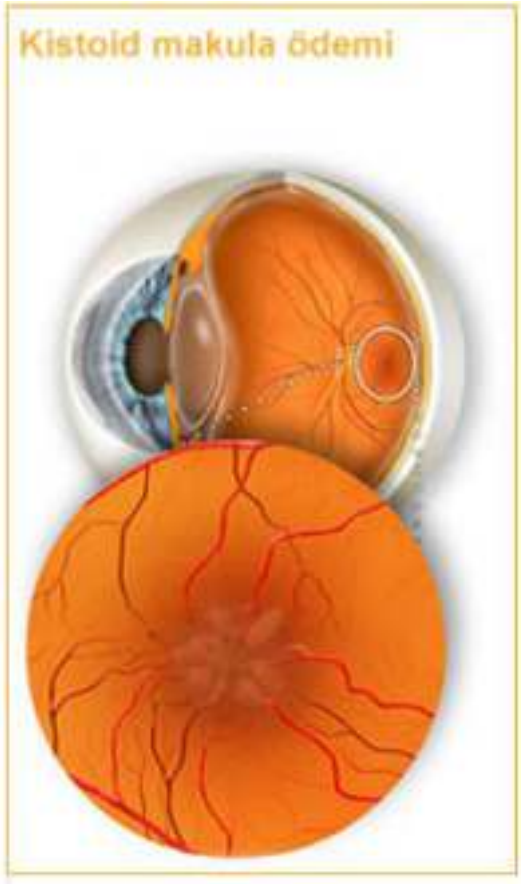
CMV Retiniti – Komplikasyonlar

- Retinal dekolman
- Kontralateral göz tutulumu
- IRIS-immun recovery uveitis***

  Anterior üveitis

  Vitritis

  Kistoid maküla ödemi



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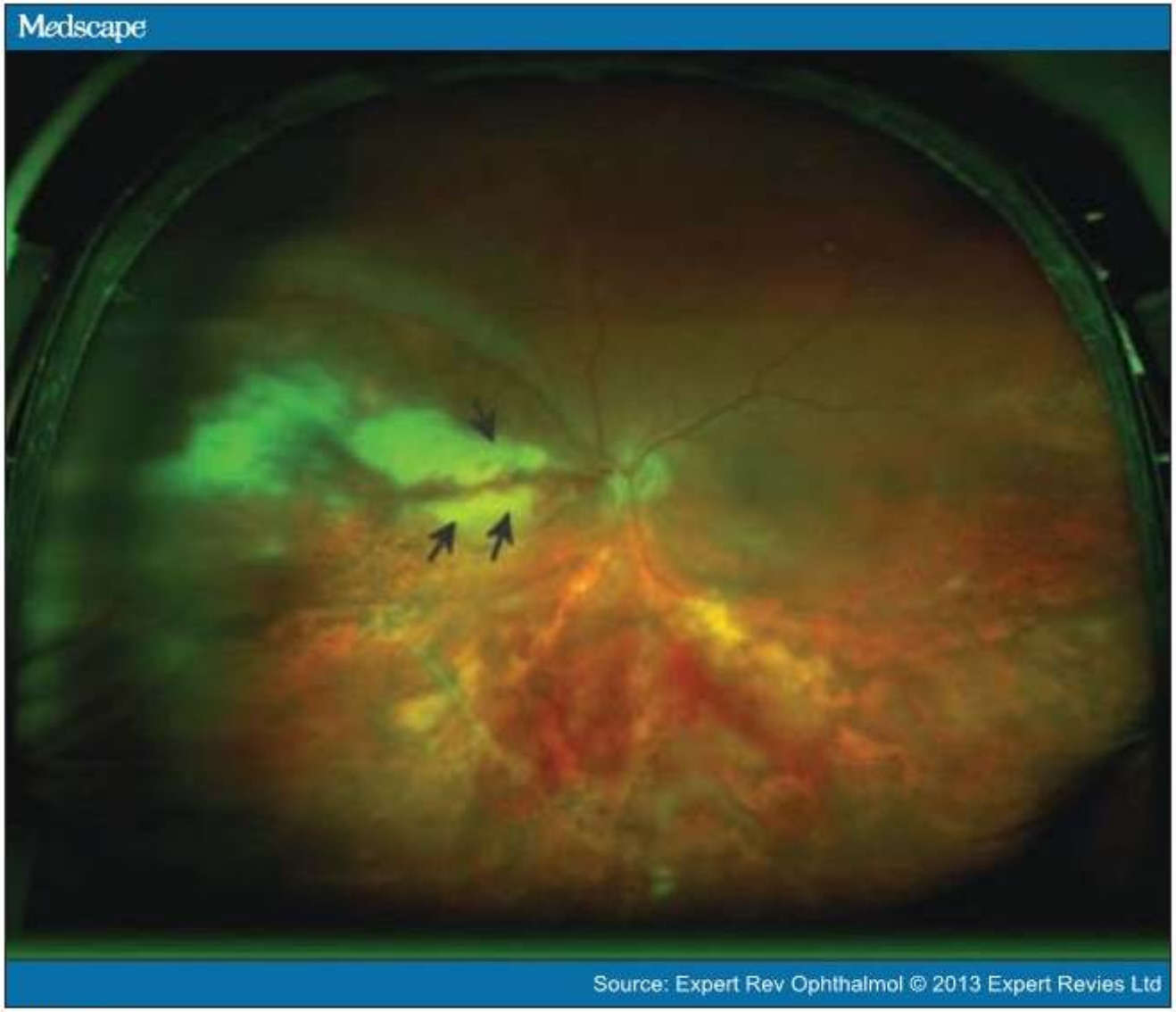
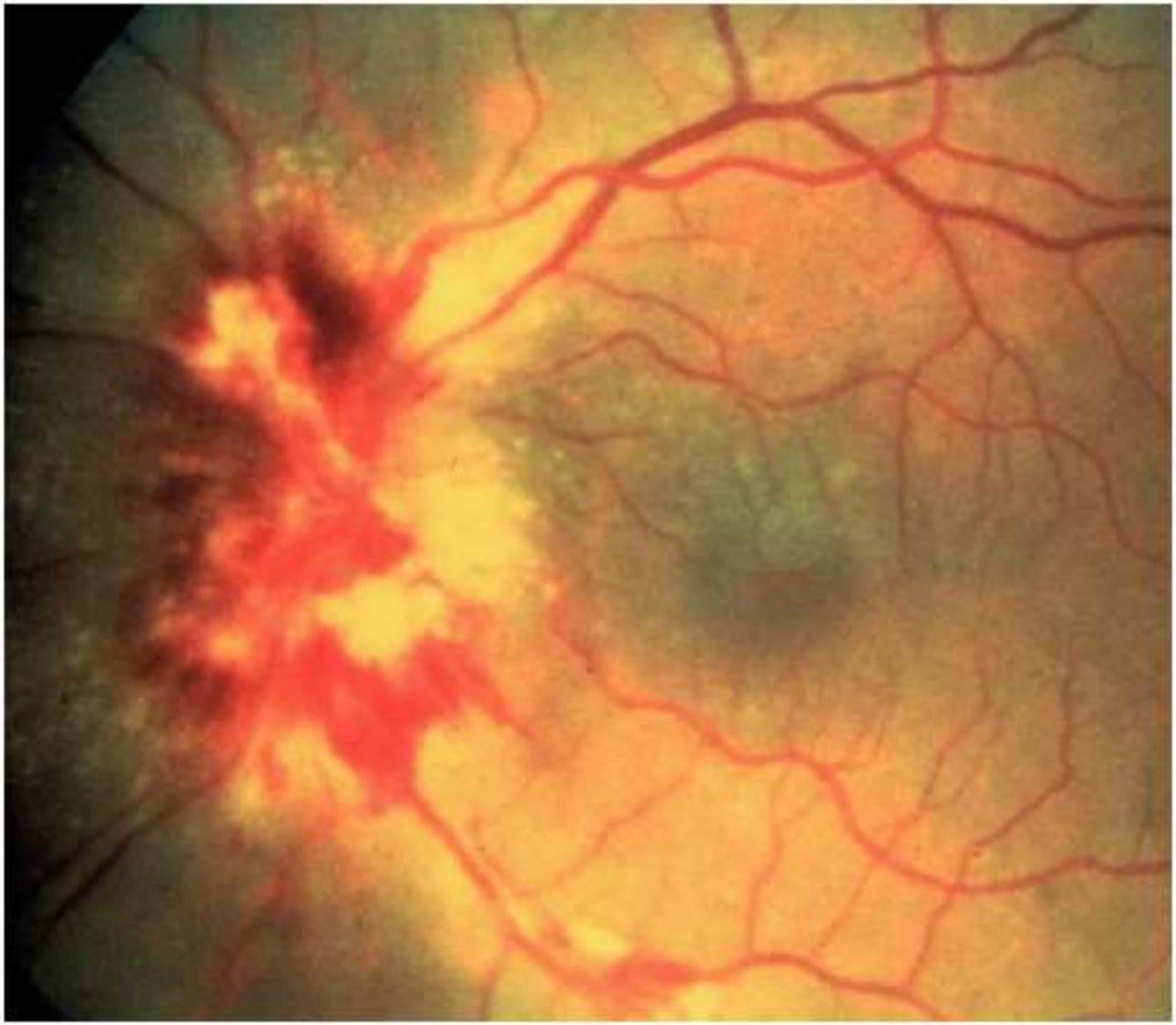
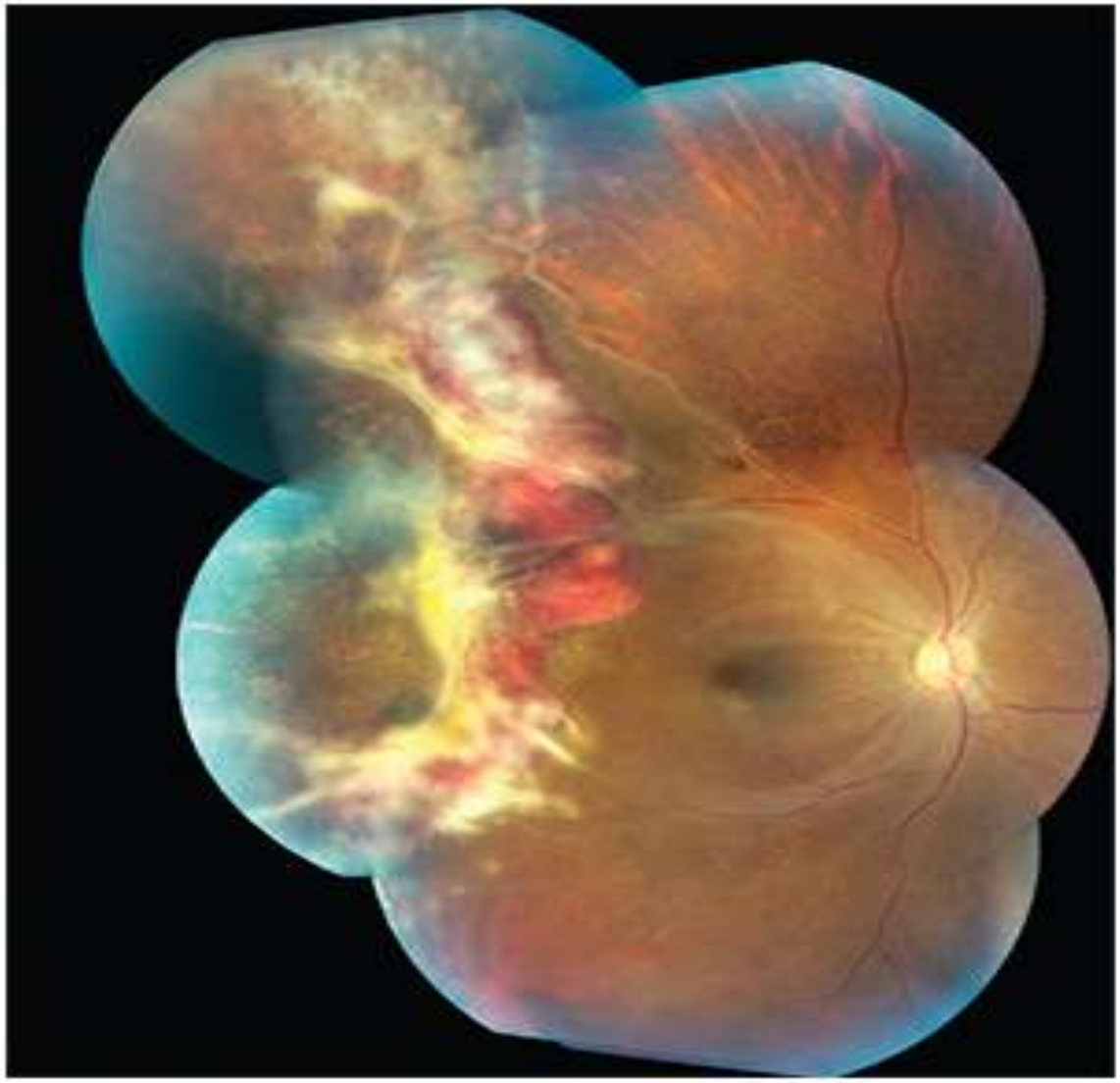


Figure 1.

Optos P200 imaging system (Optos PLC, UK) showing a wide field pseudocolor image of the left eye in a patient with HIV and cytomegalovirus retinitis. Some areas of retinal necrosis and hemorrhage are shown (arrows).



Cytomegalovirus papillitis.



The **hemorrhage** and **vascular sheathing** suggests fulminant CMVR. Encroachment of the CMVR into the superotemporal macular area suggests Zone 1 involvement. The border opacification at 9 o'clock matches the standard peripheral photograph of **severe (4+) border opacification**; this is active retinitis. The CMVR involves approximately 25 percent of the retina surface of the right eye.

CMV Retiniti – Ayırıcı tanı

Table 1. Differential Diagnoses of Cytomegalovirus Retinitis

Infective causes	Non-infective causes
Acute retinal necrosis (ARN)	Behçet's disease
Progressive (outer) retinal necrosis (PORN)	Primary vitreoretinal lymphoma (PVRL)
Herpes simplex virus retinitis	
T oxoplasmosis	
Candida infection	
Syphilis	
Subacute sclerosing panencephalitis (SSPE)	

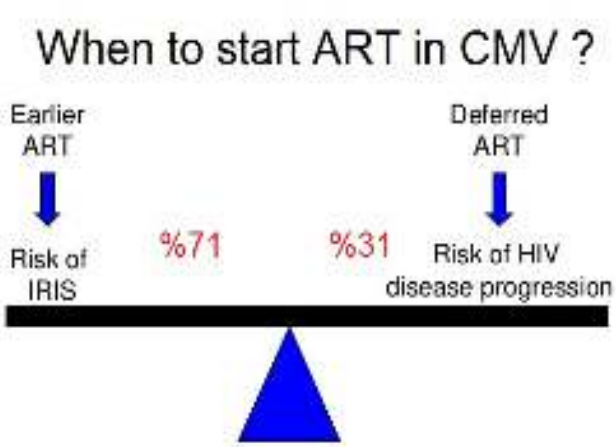
- http://www.reviewofophthalmology.com/article/cmv-retinitis-reduced-incidence-still-a-threat#sthash.jTpWEcbB.dpuf

CMV Retiniti- Tedavi

- Amaç;
  - Klinik süreci kısaltmak
  - Komplikasyon
  - Rekürrens, yayılımı ve latensi azaltmak,
  - Diğer gözü korumak
- Etkin bir ART ile birlikte

HAART
HIV/AIDS Alliance for Region Two, Inc.

1. *Springer KL, Weinberg A. J Antimicrob Chemother. 2004 Sep. 54(3):582-6.*
2. *https://aidsinfo.nih.gov/guidelines*



- CMV enf. ART sonrası IRIS (IRU)
- CMV replikasyonu 1-2 haftalık tedavi
- ART CMV enf. 2 haftadan fazla beklenmez **(CIII)**
- İlk 2-3 hafta indüksiyon, devamında idame tedavisi şeklinde

-Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents
https://aidsinfo.nih.gov/guidelines

	Drug	Dose	Comments
Retinitis, immediate sight-threatening lesions	**ganciclovir**	2 x 5 mg/kg/day iv	21 days, then secondary prophylaxis
	or **foscarnet**	2 x 90 mg/kg/day iv	
Retinitis, small peripheral retinal lesions	**valganciclovir**	2 x 900 mg/day po (with food)	14-21 days, then secondary prophylaxis
	or **foscarnet**	2 x 90 mg/kg/day iv	
	or **cidofovir** **+ probenecid** **+ NaCl 0.9% hydration**	1 x 5 mg/kg/week iv	2 weeks then every 2 weeks. Cidofovir may not be available in all European countries
Oesophagitis/Colitis	**ganciclovir**	2 x 5 mg/kg/day iv	Treat 3-6 weeks, respectively until symptoms resolved
	or **foscarnet**	2 x 90 mg/kg/day iv	
	or **valganciclovir**	2 x 900 mg/day po (with food)	In milder disease if oral treatment tolerated
Encephalitis/Myelitis	**ganciclovir and / or** **foscarnet**	2 x 5 mg/kg/day iv 2 x 90 mg/kg/day iv	Treat until symptoms resolved and CMV replication in CSF has cleared (negative PCR in CSF) Treatment is individualised according to clinical symptoms and response to treatment
Secondary prophylaxis / Maintenance therapy: Cytomegalovirus (CMV) Retinitis			
Stop: if CD4 count > 200 cells/µL and HIV-VL undetectable over 3 months			
Regimens listed are alternatives	**valganciclovir**	1 x 900 mg/day po (with food)	
	or **ganciclovir**	1 x 5 mg/kg/day (x 5 days/ week) iv	
	or **foscarnet**	1 x 90-120 mg/kg/day (x 5 days/ week) iv	
	or **cidofovir** **+ probenecid** **+ NaCL 0.9% hydration**	1 x 5 mg/kg every 2 weeks iv	Cidofovir may not be available in all European countries

Recommendations for Treating Cytomegalovirus Infections (page 1 of 2)

Preventing CMV Disease

- CMV end-organ disease is best prevented by using ART to maintain CD4 count >100 cells/mm^3.

Managing CMV Retinitis

- The choice of initial therapy for CMV retinitis should be individualized, based on location and severity of the lesion(s), the level of immunosuppression, and other factors (e.g., concomitant medications, ability to adhere to treatment) **(AIII)**.
- Given the evident benefits of systemic therapy in preventing contralateral eye involvement, reduce CMV visceral disease and improve survival,whenever feasible, treatment should include systemic therapy.
- The ganciclovir ocular implant, which is effective for treatment of CMV retinitis, is no longer available.

Initial Therapy Followed by Chronic Maintenance Therapy—For Immediate Sight Threatening Lesions (within 1500 microns of the fovea)

Preferred Therapy:

- Intravitreal injections of ganciclovir (2 mg/injection) or foscarnet (2.4 mg/injection) for 1–4 doses over a period of 7–10 days to provide higher intraocular levels of drug and faster control of the infection until steady state intraocular ganciclovir concentrations are achieved **(AIII)**; *plus*
- Valganciclovir 900 mg PO BID for 14–21 days, then 900 mg once daily **(AI)**

Alternative Therapy

- Intravitreal injections as listed above **(AIII)**; *plus* one of the following systemic therapy:
  - Ganciclovir 5 mg/kg IV q12h for 14–21 days, then 5 mg/kg IV daily **(AI)**, *or*
  - Ganciclovir 5 mg/kg IV q12h for 14–21 days, then valganciclovir 900 mg PO daily **(AI)**, *or*
  - Foscarnet 60 mg/kg IV q8h or 90 mg/kg IV q12h for 14–21 days, then 90–120 mg/kg IV q24h **(AI)**, *or*
  - Cidofovir 5 mg/kg/week IV for 2 weeks, then 5 mg/kg every other week with saline hydration before and after therapy and probenecid 2 g PO 3 hours before the dose followed by 1 g PO 2 hours after the dose, and 1 g PO 8 hours after the dose (total of 4 g) **(BI)**.

  Note: This regimen should be avoided in patients with sulfa allergy because of cross hypersensitivity with probenecid

For Peripheral Lesions

- Administer one of the systemic antiviral therapy listed above for the first 3–6 months until ART induced immune recovery **(AII)**.

CMV Retiniti - Tedavi

- İdame tedavi süresi;
  - 3-6 aylık etkin
    - ART sonrası > CD4 100 hc./mm^3 **(AI)**
    - anti-CVM tedavisi sonrası lezyonları gerileyen **(AII)**
  - CD4 > 200 hc/mm^3 + HIV RNA neg. (>3 ay)

AIDSinfo

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

-Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents
https://aidsinfo.nih.gov/guidelines

CMV Retiniti - Tedavi

- Relaps ve IRU açısından tedavi kesildikten sonra 3 aylık kontrol **(AIII)**
- Relaps takibinde serum CMV viral yük takibinin yeri yok **(BII)**
- CD4 <100 hc/mm^3; idame tedavisi tekrardan başlanmalı **(AIII)**

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CMV - MSS Enfeksiyonu - Tedavi

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- Tedavi seçenekleri ve dozları ~ retinit
- Tedaviye yanıtı ve klinik stabilizasyon; gansiklovir + foskarnet **(CIII)**
- Gansiklovir; lökopeni-trombositopeni
- Foskarnet; nefrotoksisite
- Oral valgansiklovir; tedavide etkinliği yeterli veri yok
- Tedavi süresi konusunuda yeterli kanıt yok
- Retinit yoksa kronik idame tedavisi önerilmiyor **(BII)**

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CMV Enfeksiyonu - Korunma

- Etkin ART ile CD4>100 hc/µL***
- Gansiklovir ve valgansiklovir?? Maliyet, yan etki, direnç gelişimi, hastalığı azaltmak için tedavi gereken hasta sayısı…gibi nedenlerden dolayı rutin primer proflakside standart olarak önerilmemektdir **(AI)**
- Hasta bilinçlendirilmesi; retinitin erken belirtileri **(BIII)**
- Rutin göz muayenesi ? **(CIII)**
- Sekonder proflaksi ; uzun süreli immun rekonstitüsyon (CD4>100-150 hc/µL; >6 ay) sağlanana kadar devam edilmeli

https://aidsinfo.nih.gov/contentfiles/lvguidelines/glchunk/glchunk_337.pdf

TEŞEKKÜRLER...