Cytomegalovirus Disease

Updated: July 14, 2025
Reviewed: March 16, 2026

Epidemiology

Cytomegalovirus (CMV) is a double-stranded DNA virus in the herpesvirus family that can cause disseminated or localized end-organ disease in people with HIV. CMV infection is common in the general population, but CMV prevalence differs by geography, socioeconomic status, and race or ethnicity.[1] In the U.S. National Health and Nutrition Examination Survey 1999–2004, overall CMV seroprevalence for individuals aged 6 to 49 years in the United States was 50.4%. Higher CMV seropositivity was associated with older age; being female; foreign birthplace; and markers of lower socioeconomic status, such as low household income, low education, and high household crowding.[1] CMV seroprevalence is generally higher among developing countries, with seroprevalence between 40% to 70% of adults in most high-income countries,[2] compared with 80% to 100% in several low-income countries.[2-4] Few studies have evaluated CMV seroprevalence among people with HIV, but data reported from Africa suggests CMV seroprevalence is similar or slightly higher among adults with HIV versus adults without HIV.[3,5,6]

CMV is acquired through contact with CMV-infected body fluids. CMV can be transmitted in several ways, including through breastfeeding, perinatally, sexually, viral shedding in bodily fluids (saliva, urine, or tears), and through blood products (transfusions, transplantation).[7,8] After primary infection, CMV establishes a lifelong latent infection that can reactivate and cause clinical disease, particularly in persons with compromised immune systems.[9] End-organ disease caused by CMV occurs in people with HIV— especially those with advanced disease and typically among those with CD4 T lymphocyte (CD4) cell counts <50 cells/mm^3—who are not receiving, adherent to, or responding to antiretroviral therapy (ART).[10-12] Among those treated with ART who have achieved virologic suppression, a new diagnosis of CMV end-organ disease is exceedingly rare.

Before potent ART, an estimated 30% of people with advanced HIV experienced CMV retinitis, the most common CMV end-organ disease in people with HIV.[10-12] The incidence of new cases of CMV end-organ disease has declined by ≥95% with the advent of potent ART.[13,14] The incidence rate of CMV retinitis in individuals with HIV since the introduction of effective ART has been reported to be 0.36 per 100 person-years, with those with a CD4 count below 50 cells/mm^3 accounting for the majority of cases.[15] For people with established CMV retinitis, recurrence of active lesions occurs at a rate substantially lower than that seen in the era before potent ART. Nevertheless, even for those with retinitis whose immune recovery is sufficient to warrant discontinuation of anti-CMV therapy (i.e., CD4 counts ≥100 cells/mm^3), relapse at a rate of 0.03 per person-year has been documented.[16] CMV is the most common cause of vision loss in people with HIV, even in the era of effective ART; therefore, regular ophthalmologic follow-up is needed regardless of whether anti-CMV therapy is continued.[15] See CMV Retinitis Monitoring below for more information.

Clinical Manifestations

CMV Retinitis

Retinitis is the most common clinical manifestation of CMV end-organ disease in people with HIV. It presents as unilateral disease in two-thirds of cases, but ultimately progresses to bilateral in most affected people in the absence of therapy or immune recovery.[16]

Peripheral retinitis (i.e., outside the major vascular arcades, not involving the macula or optic disc) may be asymptomatic or present with floaters, scotomata, or peripheral visual field defects. Posterior retinal lesions, especially those impinging on the macula or optic disc, are associated with decreased visual acuity or central visual field defects.

CMV retinitis is a full-thickness necrotizing retinal infection that typically produces fluffy, yellow-white retinal lesions, with or without intraretinal hemorrhage.[17,18] The most typical feature is the lesion border, which has tiny, dry-appearing, granular, dot-like "satellites" at the interface between infected and normal retina. Vitreous humor inflammation is unlikely unless immune recovery with ART occurs.[10] Blood vessels near the lesions may appear to be sheathed. Occasionally, CMV retinitis lesions, particularly peripheral lesions, may have only a granular appearance throughout the lesion.

In the absence of effective ART or specific anti-CMV therapy, retinitis lesions invariably enlarge. Untreated lesions in severely immunodeficient individuals will involve the entire retina within 6 months. Movement of lesion borders occurs at variable rates in different directions,[19] causing a characteristic "brushfire" pattern, with the granular, leading edges advancing before an atrophic gliotic scar.[20]

CMV Colitis and Esophagitis

Colitis occurs in 5% to 10% of people with advanced HIV.[11] The most frequent clinical manifestations are weight loss, fever, anorexia, abdominal pain, diarrhea (often bloody), and malaise. In the colon, and especially in the cecum, CMV can cause perforation and present as an acute abdomen. Computed tomography (CT) may show colonic thickening or a colonic mass that may be mistaken for malignancy or other opportunistic infections (OIs). Hemorrhage and perforation can be life-threatening complications.

Esophagitis and occasional oral ulcers occur in a small percentage of people with advanced HIV, leading to odynophagia, nausea, mid-epigastric or retrosternal discomfort, and fever.

CMV Pneumonia

In contrast to other severely immunosuppressing conditions, CMV pneumonitis is uncommon in people with advanced HIV. CMV is detected frequently in the bronchoalveolar lavage (BAL) using DNA–specific polymerase chain reaction (PCR), but it is usually a bystander and should trigger a search for a more likely causative pathogen.

CMV of the Central Nervous System

CMV neurologic disease includes dementia, ventriculoencephalitis, central nervous system vasculitis, and polyradiculomyelopathies.[21] People with dementia caused by CMV encephalitis

typically are lethargic or confused, with or without fever. People with ventriculoencephalitis have a more acute course, with focal neurologic signs, often including cranial nerve palsies or nystagmus, and rapid progression to death. Periventricular enhancement on imaging (CT or magnetic resonance) highly suggests CMV ventriculoencephalitis rather than HIV-associated neurocognitive disorder. CMV polyradiculomyelopathy and transverse myelitis cause a Guillain-Barré–like syndrome characterized by radicular back pain, urinary retention, and progressive bilateral weakness in the lower extremities. Clinical symptoms usually progress over several weeks to include loss of bowel and bladder control and flaccid paraplegia. Additionally, spastic myelopathy and sacral paresthesia may occur.

Diagnosis

The diagnosis of CMV end-organ disease is typically based on the clinical presentation and, when possible, evidence of the virus in tissue. CMV is often present in end-organ disease and can be detected by PCR, antigen assays, or culture. Detection of CMV in blood has limited utility in diagnosing CMV end-organ disease in people with HIV. A negative serum or plasma PCR assay does not rule out CMV end-organ disease, and CMV viremia may be present in the absence of end-organ disease, particularly in those with low CD4 cell counts.[21-26]

The presence of CMV serum antibodies does not establish the presence of CMV disease, because a large proportion of the general population has been exposed to CMV and is seropositive. However, a negative immunoglobulin G antibody level indicates that CMV is unlikely to be the cause of the disease process.

CMV Retinitis

CMV retinitis is usually diagnosed based on recognition of characteristic retinal changes observed through a dilated pupil during an ophthalmoscopic examination performed by an experienced ophthalmologist. Nearly all cases can be diagnosed clinically. In rare cases, the diagnosis may be unclear, and PCR of aqueous or vitreous humor specimens for CMV and other pathogens—especially herpes simplex virus, varicella-zoster virus, and *Toxoplasma gondii*—can be useful for establishing the diagnosis. Detection of CMV DNA in cerebrospinal fluid (CSF) or vitreous or aqueous humor specimens is highly suggestive that CMV is the cause of ocular disease. In one study, CMV DNA was detected in 82% of vitreous specimens collected at diagnosis of CMV retinitis, 77% of relapsed retinitis, and 23% of quiescent retinitis.[27] Therefore, failure to detect CMV DNA in vitreous specimens does not rule out the presence of CMV retinitis. A response to empiric anti-CMV therapy also can be an important diagnostic indicator.

CMV Colitis and Esophagitis

CMV colitis is usually diagnosed based on demonstration of mucosal ulcerations on endoscopic examination, combined with histopathologic demonstration of characteristic intranuclear and intracytoplasmic inclusions on hematoxylin and eosin stains.[11,28] Similarly, CMV esophagitis is diagnosed by the presence of ulcers of the distal esophagus together with biopsy evidence of intranuclear inclusion bodies in the endothelial cells with an inflammatory reaction at the edge of the ulcer.[11] The number of inclusion bodies in specimens can vary widely and may be rare. Immunohistochemistry can also be used to detect CMV in tissue. In the absence of histopathologic changes, culturing CMV and detection of CMV DNA by PCR from a biopsy or cells brushed from the colon or the esophagus are insufficient to diagnose of CMV colitis or esophagitis, because a

substantial number of patients with low CD4 cell counts may shed CMV in in the gastrointestinal tract in the absence of clinical disease.[26]

CMV Pneumonia

The diagnosis of CMV pneumonitis, a rare entity in people with HIV, requires consistent clinical and radiological findings (e.g., diffuse pulmonary interstitial infiltrates, fever, and cough or dyspnea), identification of multiple CMV inclusion bodies in lung tissue or cytology, and the absence of any other pathogens that are more commonly associated with pneumonitis.[24,29,30] CMV PCR from the BAL has not been shown to have diagnostic value in people with HIV. Detection of CMV in the lungs in the absence of these criteria typically represents viral shedding, rather than clinical disease.

CMV of the Central Nervous System

CMV neurologic disease is diagnosed based on a compatible clinical syndrome and the presence of CMV in CSF or brain tissue, most often evaluated with PCR.[12,22,25] The CSF in CMV encephalitis typically demonstrates lymphocytic pleocytosis, low-to-normal glucose levels, and normal-to-elevated protein levels, although normal CSF findings do not rule out the diagnosis of CMV encephalitis. The CSF in CMV polyradiculopathy usually demonstrates neutrophilic pleocytosis (usually 100–200 neutrophils/µL and some erythrocytes) accompanied by low glucose levels and elevated protein levels.

Preventing Exposure

CMV infection is common in the general U.S. population, with higher seroprevalence among older individuals, women, people born outside of the United States, and people with lower socioeconomic status.[1] However, in people with HIV, CMV seropositivity cannot be assumed. Limited options exist to prevent exposure to CMV among adults with HIV, but condoms may reduce sexual transmission of CMV.[31,32]

Preventing Disease

Recommendations for Preventing CMV Disease
• To prevent CMV end-organ disease, administer ART to maintain the CD4 count ≥100 cells/mm^3 (AI).

Key: ART = antiretroviral therapy; CD4 = CD4 T lymphocyte; CMV = cytomegalovirus

CMV end-organ disease is best prevented using ART to maintain a CD4 count ≥100 cells/mm^3 **(AI).** A randomized, placebo-controlled trial failed to show benefit for the use of valganciclovir prophylaxis (the current standard oral agent for treatment of CMV disease) combined with ART as preventive therapy for CMV end-organ disease in people at high risk (CD4 count <100 cells/mm^3 and CMV viremia detected by plasma CMV DNA PCR assay).[33] Therefore, valganciclovir primary prophylaxis **is not recommended** to prevent CMV end-organ disease in people with HIV, even among patients who have CMV viremia **(AI),** and monitoring of CMV viremia **is not recommended**.

The primary method for preventing severe CMV disease is recognizing the early manifestations of the disease and instituting proper therapy. People who have a low CD4 cell count (<100 cells/mm^3) and are not on ART should be made aware of how to recognize floaters in the eye and their

implication. Development of floaters or changes in visual acuity should prompt an urgent referral to ophthalmology **(AIII).** The Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV (the Panel) recommends a baseline ophthalmologic examination for people with HIV and CD4 counts <100 cells/mm^3, with counseling about the potential symptoms of CMV retinitis **(CIII).** In the premodern ART era, it was common for follow-up ophthalmologic examinations to be performed every 3 to 4 months for persons with CD4 counts <50 cells/mm^3 (the range associated with most cases of CMV retinitis), because early CMV retinitis may be asymptomatic. The same follow-up schedule is appropriate in the era of effective ART if CD4 counts fall below 50 cells/mm^3 for any reason, including treatment failure **(CIII).** Individuals with CMV retinitis and ART failure are more likely to be asymptomatic than were individuals in the premodern ART era.[18]

Treating Disease

Recommendations for Treating Cytomegalovirus Infections

Treating CMV Retinitis

General Considerations

- CMV retinitis should be treated with the active participation of an ophthalmologist who is familiar with CMV retinitis diagnosis and management.
- See CMV Retinitis Monitoring below for ophthalmic monitoring recommendations for people on treatment for CMV retinitis and after discontinuation of maintenance therapy.

Induction Therapy Followed by Maintenance Therapy

Preferred Therapy

- Valganciclovir[a] 900 mg PO every 12 hours for 14–21 days, then maintenance therapy with valganciclovir 900 mg PO once daily (AI), *or*
- Ganciclovir[a] 5 mg/kg IV every 12 hours for 14–21 days, then maintenance therapy with valganciclovir 900 mg PO once daily (AI), *or*
- Ganciclovir[a] 5 mg/kg IV every 12 hours for 14–21 days, then maintenance therapy with ganciclovir 5 mg/kg IV daily (AI)

Notes

- Many clinicians prefer the IV formulation when retinitis is more central and sight-threatening or when adequate GI absorption is a concern; transition to oral valganciclovir can be considered when there is evidence of clinical response.
- PO valganciclovir is the preferred maintenance regimen as it is the easiest and least toxic to administer to an outpatient population, provided that GI absorption is adequate.

Alternative Therapy

- Foscarnet[a] 60 mg/kg IV every 8 hours or 90 mg/kg IV every 12 hours for 14–21 days, then maintenance therapy with foscarnet 90 mg/kg or 120 mg/kg IV every 24 hours (BI) *or*
- Cidofovir[a,b] 5 mg/kg IV every week for 2 weeks, then maintenance therapy with cidofovir 5 mg/kg IV every other week. Administer 1 L of normal saline before and, if additional fluid load can be tolerated, administer another 1 L of normal saline after each cidofovir infusion. Administer probenecid 2 g PO 3 hours before each cidofovir dose followed by 1 g PO 2 hours after the dose, and 1 g PO 8 hours after the dose (total of 4 g) (CI).
  - Note: Cidofovir should be avoided in patients with sulfonamide allergy because of cross-hypersensitivity with probenecid.

If Immediate Sight-Threatening Lesions (within 1,500 microns of the fovea or optic disc)

- Add intravitreal injections of ganciclovir (2 mg/injection) or foscarnet (2.4 mg/injection), repeated weekly during the induction period until lesion inactivity is achieved (BIII), then systemic treatment alone is considered to be adequate for maintenance therapy.
  - Note: Intravitreal administration of cidofovir is contraindicated, as it has been associated with uveitis and marked hypotony of the injected eye (AIII).

Peripheral Lesions

- Valganciclovir[a] 900 mg PO every 12 hours for 14–21 days, then maintenance therapy with valganciclovir 900 mg PO once daily (AI)

Duration of Induction Therapy for CMV Retinitis

- Minimum 14–21 days; duration determined by clinical response based on retinal examination
- Note: Many clinicians continue induction-level treatment until retinal lesion opacity is resolved or markedly reduced, indicating virus inactivity (BIII).

Starting Maintenance Therapy for CMV Retinitis

- Maintenance therapy is started after induction has achieved control of retinitis. Regimens are as detailed above.

Immune Recovery Uveitis

- The Panel favors the use of both corticosteroids and anti-CMV therapy for active intraocular inflammation at the onset of IRU and the use of corticosteroids for cystoid macular edemas, a late complication of IRU (CIII).
- Corticosteroids can be administered by oral, periocular, or intravitreal routes.
  - Prednisone 1 mg/kg PO daily (maximum dose of 60–80 mg/day) until clinical response, but for no longer than 1 month, followed by tapering and discontinuation over 2 to 3 months (BIII)
  - Periocular or intravitreal corticosteroid injections can be repeated after the expected duration of effect if there is evidence of incomplete clinical response and no treatment complications (BIII).

Stopping Maintenance Therapy for CMV Retinitis

- CMV treatment for at least 3 months, and lesions are inactive, and CD4 count ≥100 cells/mm^3 for at least 3 months in response to ART (AII)
  - Note: In all people for whom anti-CMV maintenance therapy has been discontinued, ophthalmologic monitoring for early detection of CMV relapse and IRU should be performed at least every 3 months and then yearly after immune reconstitution (AIII). Monitoring CMV viral load in blood has poor positive predictive value for relapse of retinitis and, therefore, is not recommended for people with HIV (AII).

Restarting Maintenance Therapy for CMV Retinitis

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

Treating CMV Colitis or Esophagitis

Preferred Therapy

- Ganciclovir[a] 5 mg/kg IV every 12 hours (AI); may switch to valganciclovir 900 mg PO every 12 hours once the patient can absorb and tolerate PO therapy (AIII)
- Valganciclovir[a] 900 mg PO every 12 hours can be used in patients with mild disease (AIII).

Alternative Therapy

- Foscarnet[a] 60 mg/kg IV every 8 hours or 90 mg/kg IV every 12 hours (BIII)—for patients with treatment-limiting toxicities to ganciclovir or with ganciclovir resistance; *or*
- Cidofovir[a,b] 5 mg/kg/week IV for 2 weeks, then 5 mg/kg IV every other week. Administer 1 L of normal saline before and, if additional fluid load can be tolerated, administer another 1 L of normal saline after cidofovir infusion. Administer probenecid 2 g PO 3 hours before each cidofovir dose followed by 1 g PO 2 hours after the dose and 1 g PO 8 hours after the dose (total of 4 g) (CI).
  - Note: Cidofovir should be avoided in patients with sulfonamide allergy because of cross-hypersensitivity with probenecid.

Duration of Anti-CMV Therapy

- 21–42 days or until signs and symptoms have resolved (AIII)

Note: After resolution of acute disease, maintenance therapy is not routinely recommended for CMV GI disease unless there is concurrent retinitis, there have already been recurrent infections, or severe disease was present initially.

Treating CMV Pneumonia

Preferred Therapy

- Ganciclovir[a] 5 mg/kg IV every 12 hours (BIII)

Alternative Therapy

- Foscarnet[a] 60 mg/kg IV every 8 hours or 90 mg/kg IV every 12 hours (BIII)

Note: Transition to valganciclovir 900 mg PO twice daily can be considered if CMV pneumonia is not life-threatening and oral medications can be absorbed (BIII).

Duration of Anti-CMV Therapy

- ≥21 days or until signs and symptoms have resolved (CII)

Note: After resolution of acute disease, maintenance therapy is not routinely recommended for CMV pneumonia unless there is concurrent retinitis, there have already been recurrent infections, or severe disease was present initially.

Treating CMV Neurological Disease

Preferred Therapy

- Ganciclovir[a] 5 mg/kg IV every 12 hours plus foscarnet[a] (60 mg/kg IV every 8 hours or 90 mg/kg IV every 12 hours) (BIII)
- The role of oral valganciclovir has not been established.

Duration of Anti-CMV Therapy

- ≥21 days based on clinical response (AIII)

Note: After resolution of acute disease, maintenance therapy is not routinely recommended for CMV CNS disease unless there is concurrent retinitis, there have already been recurrent infections, or severe disease was present initially.

Pregnancy Considerations

- During pregnancy, indications for treatment of CMV infection are the same as for other people with HIV (AIII).
- Valganciclovir is the preferred treatment for maternal CMV disease during pregnancy (BIII).
- Foscarnet and cidofovir are not recommended in the absence of resistance or toxicity with ganciclovir/valganciclovir (AIII); use of foscarnet and cidofovir should only be done in consultation with a maternal–fetal medicine specialist, and additional fetal surveillance may be recommended in the setting of maternal renal insufficiency (BIII).

- In pregnant women diagnosed with primary CMV infection, the fetus should be monitored by periodic ultrasound after 20 weeks gestation (CIII).

Key: ART = antiretroviral therapy; CD4 = CD4 T lymphocyte; CMV = cytomegalovirus; CNS = central nervous system; GI = gastrointestinal; IRU = immune recovery uveitis; IV = intravenously; the Panel = the Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV; PO = orally

[a] Renal dose adjustment required in patients with chronic renal insufficiency and/or acute renal failure

[b] Contraindicated for serum creatinine >1.5 mg/dL or creatinine clearance <55 mL/min

CMV Retinitis

The therapeutic approach to CMV retinitis should be individualized based on tolerance of systemic medications, prior exposure to anti-CMV drugs, and the location of lesions. CMV retinitis should be treated with the active participation of an ophthalmologist who is familiar with the diagnosis and management of this retinal disease.

The Panel recommends the following as first-line therapies for treating CMV retinitis: oral valganciclovir **(AI),** intravenous (IV) ganciclovir **(AI),** or IV ganciclovir induction followed by oral valganciclovir maintenance **(AI);** other effective treatments, such as IV foscarnet **(BI)** and IV cidofovir **(CI),** are not routinely recommended due to substantial toxicities, including nephrotoxicity.[20,34-41] Systemic therapy has been documented to reduce CMV involvement in the contralateral eye,[34] reduce CMV visceral disease, and improve survival.[35,42] Given the evident benefits of systemic anti-CMV therapy, treatment regimens for CMV retinitis should include a systemic component as recommended in the table above. Few trials have compared regimen efficacy during the past 15 years. None of the listed regimens have been proven in clinical trials to be more effective in protecting vision.[36-40]

The Panel recommends IV ganciclovir **(AI)** or oral valganciclovir **(AI)** for an induction period lasting at least 14 to 21 days, with the duration determined by clinical response based on retinal examination. Many clinicians continue induction-level treatment until retinal lesion opacity is resolved or markedly reduced, indicating virus inactivity **(BIII).**[20] Many clinicians prefer the IV formulation for induction when retinitis is more central and sight-threatening or when adequate gastrointestinal (GI) absorption is a concern. In such cases, transition to oral valganciclovir can be considered when there is evidence of clinical response. In cases where toxicity of ganciclovir and valganciclovir (e.g., severe cytopenias) is a concern or there is concern for ganciclovir-resistant CMV, IV foscarnet should be used **(BI).** If both ganciclovir and foscarnet should be avoided or cannot be used, IV cidofovir should be used **(CI).** Cidofovir administration is complicated by the need to coadminister IV saline hydration and probenecid with each dose to counter the nephrotoxicity of the drug. In addition, IV cidofovir is associated with an increased risk of intraocular inflammation, hypotony, and neutropenia.[43-46]

In the presence of immediately sight-threatening retinal lesions (those within 1,500 microns of the fovea or optic disc) at presentation, the Panel recommends supplementing systemic therapy with intravitreal injections of ganciclovir or foscarnet, at least initially, to provide immediate, high intraocular levels of the drug and presumably faster control of the retinitis **(BIII).** Injections are continued on a weekly basis during induction therapy until lesion inactivity is achieved, at which time systemic treatment alone is adequate for maintenance therapy. The recommendation to supplement systemic therapy with intravitreal injections is based both on the experience of ophthalmologists who saw considerable disease early in the HIV epidemic, and pharmacokinetic

considerations, but the clinical benefit of such supplementation has not been confirmed in clinical trials. Although intravitreal injections deliver high concentrations of the drug to the target organ immediately while steady-state concentrations in the eye are being achieved over time with systemically delivered medications,[34] such injections can be complicated by bacterial or fungal infections, hemorrhage, or retinal detachment.

Intravitreal cidofovir is associated with hypotony and uveitis—and a substantially increased risk of immune recovery uveitis—and **is not recommended (AIII).**[39,47] The ganciclovir implant, a reservoir device for the slow release of drug into the eye, previously used for local therapy, is no longer manufactured. Intravitreal drug injections are not necessary for people with peripheral retinal lesions; oral valganciclovir alone will be adequate **(AI).**

After completing induction therapy, patients should be transitioned to a maintenance regimen. See When to Start Maintenance Therapy below.

CMV Disease Other Than Retinitis

CMV Colitis and Esophagitis

For patients who have colitis or esophagitis, anti-CMV therapy for 21 to 42 days is recommended until resolution of signs and symptoms **(AIII),** based on data that CMV persists with only 14 days of treatment for CMV colitis in people with HIV.[48] IV ganciclovir is the therapy of choice **(AI)** and can be switched to oral valganciclovir once the person can tolerate and absorb oral medications, extrapolated from randomized, clinical trial data showing non-inferiority of oral valganciclovir for treatment of CMV disease in people receiving a solid organ transplant (SOT) **(AIII).**[49] Oral valganciclovir can be used in patients with mild disease **(AIII).** Foscarnet with IV hydration should be used as an alternative if ganciclovir-related toxicity is treatment-limiting or in cases of ganciclovir-resistant virus **(BIII).** Cidofovir, administered with saline hydration before and after therapy, can be used as an alternative **(CI).**

CMV Pneumonia

Experience treating well-documented CMV pneumonia in people with HIV is limited and anecdotal. Treatment with IV ganciclovir or, alternatively, with foscarnet, is recommended **(BIII).** The optimal duration of therapy is a minimum of 21 days (extrapolated from SOT data) **(CII).** The role of oral valganciclovir has not been established, but based on clinical experience with SOT, transition to oral valganciclovir can be considered if CMV pneumonia is not life-threatening and oral medications can be absorbed **(BIII).**

CMV of the Central Nervous System

Therapy for neurologic disease has not been extensively studied. Given the poor outcomes in many patients with CMV-related neurologic disease, the Panel recommends initiating therapy with both IV ganciclovir and IV foscarnet, despite the substantial toxicities associated with such an approach **(BIII).**[50] The role of oral valganciclovir has not been established. The optimal duration of therapy has not been established, but a minimum duration of 21 days is recommended, with extension based on clinical response **(AIII).**

After resolution of acute disease, chronic maintenance therapy is not routinely recommended for CMV GI disease, pneumonia, or central nervous system disease. See When to Start Maintenance Therapy for exceptions.

Special Considerations Regarding IRIS and Antiretroviral Therapy Initiation

Immune recovery uveitis (IRU) is an ocular form of immune reconstitution inflammatory syndrome (IRIS) characterized by inflammation in the anterior chamber or vitreous body. It is presumed to be prompted by immune recovery with ART. IRU can occur both in the context of active CMV retinitis and in persons who have previously had CMV retinitis. IRU is usually observed in patients with a substantial rise in CD4 cell count in the first 4 to 12 weeks after ART initiation.[51-55] The estimated incidence of IRU is 0.02 per person-year after immune recovery.[56] Ocular complications of IRU include macular edema and the development of epiretinal membranes, which can cause loss of vision. Although the inflammatory reactions seen at the onset of IRU can be transient as immune reconstitution occurs, the complications may persist, permanently compromising vision.

Treatment of IRU usually consists of corticosteroid therapy, but the benefit of anti-CMV therapy is unclear.[51,57] The Panel favors the use of both corticosteroids and anti-CMV therapy for active intraocular inflammation at the onset of IRU and the use of corticosteroids for cystoid macular edemas, a late complication of IRU **(CIII).** Data are insufficient upon which to base a recommendation regarding the preferred route of corticosteroid administration; periocular, intravitreal, and oral administration all have been reported to be potentially successful.[52,58-61] Although specific oral corticosteroid regimens for the treatment of CMV as a complication of IRU have not been studied in prospective clinical trials, it is reasonable to follow guidelines for use of oral prednisone in other inflammatory eye diseases.[62] In general, prednisone 1 mg/kg/day, with a maximum adult oral dose of 60 mg/day to 80 mg/day, should be administered until there is a clinical response, but for no longer than 1 month, followed by a tapering regimen and discontinuation over 2 to 3 months **(BIII).** Periocular or intravitreal corticosteroid injections can be repeated after the injection's expected duration of effect if there has been an incomplete clinical response and there have been no treatment complications **(BIII).**

One study demonstrated a substantial increase in IRU associated with immediate, as opposed to deferred initiation, of ART (71% vs. 31%).[63] However, in the current era, the rate of clinically significant IRU following initiation of ART appears to be low (approximately 0.02 per person-year).[56] Delaying ART until retinitis is controlled may reduce the likelihood or severity of IRU; however, this strategy must be weighed against the potential for a worsened immunocompromised state and the occurrence of other OIs.

As CMV replication usually declines within 1 to 2 weeks after anti-CMV therapy is initiated, ART should be initiated no later than 1 to 2 weeks after starting anti-CMV therapy for retinitis, esophagitis, colitis, or other end-organ diseases caused by CMV **(BIII).** IRIS is a particular concern with any neurologic disease, including CMV encephalitis, ventriculitis, and radiculitis. In these cases, however, the Panel recommends initiating ART within 2 weeks, although clinical judgment based on the individual case is needed **(BIII).**

Monitoring of Response to Therapy and Adverse Events

CMV Retinitis Monitoring

Indirect ophthalmoscopy of both eyes through dilated pupils should be performed at the time of diagnosis of CMV retinitis, 2 weeks after initiating therapy, and monthly thereafter while the patient is on anti-CMV treatment **(BIII).** The purpose of such examinations is to evaluate treatment efficacy, identify second eye involvement in cases of unilateral disease, and detect IRU or complications such as retinal detachment. Monthly fundus photographs, using a standardized technique that documents the appearance of the retina, provide the optimum method for following patients and detecting early lesion reactivation.

For people who have experienced immune recovery (CD4 count ≥100 cells/mm^3 for ≥3 months), the frequency of ophthalmologic follow-up can be decreased to every 3 months. Individuals should be examined at least yearly when CD4 counts stabilize and remain above 100 cells/mm^3, HIV RNA blood levels remain undetectable, and existing CMV retinitis lesions have remained clinically inactive for an extended period; however, examinations should be repeated if laboratory values suggest loss of immune reconstitution (CD4 count <100 cells/mm^3) **(AIII).** Clinicians should be aware that lesion reactivation and retinal complications still occasionally occur in patients with immune reconstitution, and regular ophthalmologic follow-up as noted above is needed whether anti-CMV therapy is continued.[15]

Monitoring CMV viral load in blood has poor positive predictive value for detecting relapse of retinitis and **is not recommended** for people with HIV **(AII).**[64]

People with CD4 counts below 100 cells/mm^3 who have no visual changes or evident CMV-related retinal pathology remain at risk for CMV retinitis prior to immune reconstitution after initiation of ART.[65,66] Development of CMV retinitis in the setting of recent ART initiation is not IRIS and should be treated with systemic anti-CMV therapy, similar to any person with CMV retinitis, and the ART regimen should be continued **(AII).** Corticosteroids are not recommended in people with initial CMV retinitis after initiating effective ART **(AIII).**

In addition, in the absence of IRU, corticosteroids should not be used in people undergoing treatment for CMV retinitis who have worsening retinitis upon ART initiation; however, anti-CMV therapy and ART regimens should be continued **(AIII).** IRU can occur months or years after successful treatment of CMV retinitis in a person with a history of CMV retinitis whose immune function is deteriorating and who subsequently starts taking ART or has such therapy optimized.

Drug Adverse Effects

Adverse effects of ganciclovir/valganciclovir include anemia, neutropenia, thrombocytopenia, nausea, diarrhea, and renal dysfunction. Ganciclovir-related neutropenia can often be reversed with granulocyte colony-stimulating factor.[67,68] In people receiving ganciclovir or valganciclovir, complete blood counts (CBC) and renal function should be monitored twice weekly during induction and at least once weekly during maintenance therapy, or more frequently if indicated **(AIII).**

Adverse effects of foscarnet include nephrotoxicity and electrolyte abnormalities, seizures that occur characteristically in the context of renal insufficiency, and anemia. Foscarnet should be administered with intravenous hydration. Genital ulcers also can occur during foscarnet administration in people

with urinary incontinence due to the toxic effects of excreted drug on exposed skin. Foscarnet is typically given in the inpatient setting because of the intensity of monitoring and need for hydration. Serum electrolytes (including potassium, magnesium, calcium, and phosphorus), renal function tests and CBC should be closely monitored **(AIII).** In people who receive foscarnet as maintenance therapy in the outpatient setting, serum electrolytes, renal function tests, and CBC should be performed at least weekly, if stable **(AIII).** Foscarnet treatment should be stopped if the treating physician determines that there has been a substantial worsening of renal function or there is a severe electrolyte imbalance when compared to pre-treatment values **(AIII);** no definitive laboratory profile exists to prompt treatment discontinuation.

Adverse effects of cidofovir include dose-related nephrotoxicity, neutropenia, uveitis, and hypotony (low intraocular pressure). The risk of severe renal injury from IV cidofovir can be reduced by pre- and post-hydration and oral probenecid before cidofovir administration. Serum creatinine, urinalysis, and CBC should be analyzed within 48 hours of each IV cidofovir infusion. Drug administration is contraindicated if renal dysfunction or substantial proteinuria is detected (see Table 6 for renal dosing information). Particular attention is needed for patients receiving other potentially nephrotoxic medications, including tenofovir disoproxil fumarate. Periodic ophthalmologic examinations are needed to monitor for cidofovir-associated uveitis or hypotony, even when CMV disease does not include retinitis.

Managing Treatment Failure

Failure of therapy for CMV retinitis or reactivation of lesions is most likely in patients who do not experience substantial immune reconstitution after initiation or optimization of ART.[18] Treatment failure may also result from inadequate anti-CMV intraocular drug levels, CMV drug resistance, or nonadherence to CMV treatment or ART. Many experts believe that early progression of disease (enlargement of lesions or new lesions) is most often caused by the limited intraocular penetration of systemically administered drugs.[57,69,70] Data are limited on treatment failure for CMV disease other than retinitis, but the potential mechanisms and management strategies for treatment failure are likely similar to those seen in the setting of retinitis.

When lesions reactivate in patients receiving maintenance therapy, a round of treatment induction with the current maintenance therapy is recommended, followed by reinstitution of maintenance therapy **(BIII).**[71] Ganciclovir and foscarnet in combination appear to provide superior efficacy than either agent alone, and their combination is recommended for people whose disease does not respond to single-drug therapy or if there is continued progression or multiple reactivations of retinitis **(CIII).**[71] Notably, this drug combination is associated with substantial toxicity.

Drug resistance can occur in patients receiving long-term anti-CMV therapy.[72-75] Drug resistance developed at a rate of approximately 25% per person-year in the pre-ART era[72,76,77] for ganciclovir, foscarnet, and cidofovir.[72,73] In the ART era, the 1-year incidence of resistance appears to be lower (approximately 5% per person-year).[78] Low-level resistance to ganciclovir occurs through mutations in the CMV UL97 (phosphotransferase) gene, and high-level resistance to ganciclovir typically occurs because of mutations in both the CMV UL97 and UL54 (DNA polymerase) genes.[74,79-83] Resistance to foscarnet or cidofovir occurs because of mutations in the CMV UL54 gene. High-level resistance to ganciclovir often is associated with cross-resistance to cidofovir[81] and occasionally to foscarnet.[82] Although early progression of CMV disease (within 2 months) in patients who recently started anti-CMV drug treatment is typically not a result of drug resistance, late CMV reactivation after many months of treatment may be due to resistance.[40] By themselves, peripheral blood CMV

viral load measurements have poor positive predictive value for treatment failure.[64] Maribavir has recently been approved by the U.S. Food and Drug Administration for treatment of posttransplant refractory CMV but has not been studied extensively in people with HIV.

Ganciclovir resistance in patients who fail therapy can be detected by CMV DNA PCR of blood specimens followed by detection of UL97 mutations by DNA sequencing or by a point mutation assay.[84,85–86] Sequencing the UL97 gene from PCR-amplified specimens from blood can be accomplished in less than 48 hours and correlates well with conventional drug susceptibility testing and clinical outcomes.[86] A comparison of circulating CMV in blood and vitreous fluid showed identical UL97 sequences in more than 90% of cases;[27] therefore, evaluating the blood for resistance is reasonable, and detection of resistance in the blood or urine correlates with the clinical behavior of retinitis in most cases.[87] Viral culture and susceptibility testing and viral DNA sequencing often are not available in clinical laboratories because they are too time-consuming or costly. UL97 mutants usually respond to foscarnet, as do some UL54 mutants.[88] The Panel recommends treating ganciclovir-resistant CMV with a series of intravitreal injections of foscarnet and/or IV foscarnet or IV cidofovir **(CIII).** Intravitreal administration of cidofovir **is not recommended,** as it has been associated with uveitis and marked hypotony of the injected eye **(AIII).**[55,89]

Preventing Recurrence

When to Start Maintenance Therapy

After induction therapy for CMV retinitis is completed, chronic maintenance therapy should be started **(AI).**[21,25,34,37,90] Maintenance therapy is started after induction has achieved control of retinitis, as evidenced by resolved or markedly reduced retinal lesion opacity. Oral valganciclovir is the preferred regimen as it is the easiest and least toxic to administer to an outpatient population, provided that GI absorption is adequate. Alternative regimens for chronic suppression include parenteral ganciclovir, parenteral foscarnet, and parenteral cidofovir. Systemic therapy must be administered to prevent disease in the contralateral eye until immune reconstitution has occurred. Repeated intravitreal injections of ganciclovir or foscarnet alone have appeared to be effective for maintenance therapy of CMV retinitis in uncontrolled case series,[91] but this strategy should be reserved for those individuals who cannot be treated with systemic therapy.

The choice of regimen—including drug type and administration route—should be made in consultation with an ophthalmologist. Considerations should include the anatomic location of the retinal lesion, vision in the contralateral eye, and the individual's immunologic and virologic status, comorbidities, concomitant medications, and response to ART. Ocular complications, such as IRU and retinal detachment, are related to lesion size; therefore, the retinitis should be controlled with anti-CMV therapy to minimize lesion size until immune recovery is sufficient. Furthermore, evidence from both the pre-ART and ART eras demonstrates that specific anti-CMV therapy decreases mortality among immune-compromised patients with CMV retinitis.[26,35,41,92]

After resolution of the acute non-ocular CMV disease and initiation of effective ART, chronic maintenance therapy is not routinely recommended for CMV GI disease, pneumonia, and central nervous system disease unless there is concurrent retinitis, there have already been recurrent infections, or severe disease was present initially.

When to Stop Maintenance Therapy

Based on the experience of multiple investigators and following guidelines published by the U.S Public Health Service and the Infectious Diseases Society of America, the Panel recommends treatment with systemic anti-CMV therapy for at least 3 months, maintaining a sustained (at least 3 months) increase in CD4 count ≥100 cells/mm^3 while on ART, and ensuring CMV retinitis lesions are inactive before stopping maintenance therapy **(AII).**[13,93-101] Such decisions should be made in consultation with an ophthalmologist.

Retinitis relapse[102,103] occurs at a rate of 0.03/person-years in people with CD4 counts ≥100 cells/mm^3 and has been documented in people with CD4 counts >750 cells/mm^3. Therefore, in all people for whom anti-CMV maintenance therapy has been discontinued, ophthalmologic monitoring for early detection of CMV relapse and IRU should be performed at least every 3 months and then yearly after immune reconstitution **(AIII).** Monitoring CMV viral load in blood has poor positive predictive value for relapse of retinitis and, therefore, **is not recommended** for people with HIV **(AII).**[64]

Reactivation of CMV retinitis occurs frequently in people whose CD4 cell counts have decreased to <50 cells/mm^3 and whose anti-CMV maintenance therapies have been discontinued.[104] Therefore, for people with CMV retinitis, reinstitution of maintenance therapy should occur if the CD4 cell count has decreased to <100 cells/mm^3 after prior successful immune reconstitution **(AIII).**

Special Considerations During Pregnancy

During pregnancy, diagnostic considerations and indications for treatment are the same as for other people with HIV **(AIII).** Active CMV retinitis or other end-organ CMV disease during pregnancy is uncommon in the ART era. Suspected or confirmed fetal CMV infection is not an indication for the treatment of the mother in the absence of maternal disease (see below).[105] If anti-CMV treatment is required during pregnancy because of active maternal CMV disease, ART should be given as soon as possible and no longer than 2 weeks after initiating anti-CMV therapy to prevent transmission to the fetus and to limit other complications of immune compromise, balancing concerns about the possible development of IRIS. Duration of anti-CMV therapy should follow guidance for nonpregnant adults.

Based on limited data (case reports only), toxicity reports, and ease of use of the various drugs, valganciclovir is considered the best choice of treatment for maternal CMV disease requiring treatment during pregnancy **(BIII).** Ganciclovir is embryotoxic among rabbits and mice and teratogenic (e.g., cleft palate, anophthalmia, aplastic kidney and pancreas, and hydrocephalus) in rabbits.[106-108] As a prodrug with conversion to ganciclovir for activity, valganciclovir is expected to have similar reproductive toxicity. However, safe use of valganciclovir in all trimesters of human pregnancy after organ transplantation and in other patient populations has been reported.[106,107,109,110] Valganciclovir use during pregnancy may result in fetal anemia. Additional fetal surveillance may be considered if maternal CMV treatment is required.

For retinal disease in pregnancy, the use of intravitreal ganciclovir injections as local therapy that is not systemically absorbed should pose no risk to the fetus.[111] People with inactive retinal disease who achieved immune reconstitution before pregnancy do not require treatment with an anti-CMV agent.

Foscarnet is associated with an increase in skeletal anomalies or variants in rats and rabbits.[112,113] No experience with use early in human pregnancy has been reported. A single case report of use in the

third trimester described a normal infant outcome.[114] Cidofovir is embryotoxic and teratogenic (e.g., meningomyelocele and skeletal abnormalities) in rats and rabbits.[115] No experience with use of cidofovir in human pregnancy has been reported. Based on these concerns, foscarnet or cidofovir use in pregnancy **is not recommended** in the absence of resistance or toxicity with ganciclovir/valganciclovir **(AIII);** if either agent is used, this should be done in consultation with a maternal–fetal medicine specialist. Use of either drug may result in maternal renal toxicity and/or insufficiency. Additional fetal surveillance may be recommended in the setting of maternal renal insufficiency **(BIII).**[105,116-120]

Suspected or Confirmed Fetal CMV

Primary infection, reactivation, or reinfection with CMV during pregnancy (non-primary infection)[121] can lead to *in-utero* transmission and congenital CMV disease. Maternal CMV infection and fetal congenital CMV infection have been associated with an increased risk of perinatal HIV transmission among pregnant women who have not received ART.[122] Maternal ART to prevent perinatal HIV has been associated with decreased rates of perinatal/early postnatal CMV and decreased CMV-related clinical symptoms among infants exposed to or infected with HIV.[123] Studies indicate the prevalence of congenital CMV disease among infants in the United States who are exposed to HIV is 1.2% to 1.3%.[124] Risk factors for congenital CMV include mothers with CD4 <200 cells/mm^3, mothers with urinary CMV shedding,[125] and perinatal HIV infection.[90]

In women diagnosed with primary CMV infection in pregnancy, the fetus should be monitored by periodic ultrasound after 20 weeks gestation **(CIII).**[126] In studies in populations without HIV, about 5% to 25% of newborns infected with CMV had ultrasound evidence of congenital infection (e.g., cerebral calcifications, abdominal and liver calcifications, hydrops, microcephaly, ventriculomegaly, ascites, and echogenic fetal bowel).[126] Any ultrasound findings suspicious of congenital CMV infection should prompt consideration of invasive testing (i.e., amniocentesis) for definitive diagnosis.[118] Referral to a maternal–fetal medicine specialist for evaluation, counseling, and potential further testing is recommended. Potential noninvasive biomarkers for predicting congenital CMV infection are under study.[127]

If fetal CMV infection is confirmed, there is no standard maternal or fetal therapy that can prevent congenital CMV.[105,126] Although several observational studies reported the possible effectiveness and safety of hyperimmune globulin (HIG) in pregnancy for the treatment of congenital CMV,[128-131] two large, randomized, placebo-controlled trials demonstrated that HIG is not effective at decreasing the risk of congenital CMV in the setting of maternal primary infection.[132-134] Thus, HIG administration **is not recommended** during pregnancy **(AI).** Limited recent data exist for use of oral valacyclovir in the setting of maternal primary CMV infection that occurs close to the time of conception or in the first trimester of pregnancy to reduce neonatal CMV infection.[135-139] Additional studies are needed to validate this strategy and it has not been endorsed by the Society of Maternal-Fetal Medicine nor the American College of Obstetricians and Gynecologists.

References

1. Bate SL, Dollard SC, Cannon MJ. Cytomegalovirus Seroprevalence in the United States: The National Health and Nutrition Examination Surveys, 1988–2004. *Clinical Infectious Diseases*. 2010;50(11):1439-1447. Available at: https://doi.org/10.1086/652438.

2. Fowler K, Mucha J, Neumann M, et al. A systematic literature review of the global seroprevalence of cytomegalovirus: possible implications for treatment, screening, and vaccine development. *BMC Public Health*. 2022;22(1):1659. Available at: https://www.ncbi.nlm.nih.gov/pubmed/36050659.

3. Bates M, Brantsaeter AB. Human cytomegalovirus (CMV) in Africa: a neglected but important pathogen. *J Virus Erad*. 2016;2(3):136-142. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27482452.

4. Zuhair M, Smit GSA, Wallis G, et al. Estimation of the worldwide seroprevalence of cytomegalovirus: A systematic review and meta-analysis. *Rev Med Virol*. 2019;29(3):e2034. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30706584.

5. Mhandire D, Duri K, Kaba M, et al. Seroprevalence of Cytomegalovirus infection Among HIV-infected and HIV-uninfected pregnant women attending antenatal clinic in Harare, Zimbabwe. *Viral Immunol*. 2019;32(7):289-295. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31347990.

6. Hoehl S, Berger A, Ciesek S, Rabenau HF. Thirty years of CMV seroprevalence-a longitudinal analysis in a German university hospital. *Eur J Clin Microbiol Infect Dis*. 2020;39(6):1095-1102. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31989374.

7. Centers for Disease Control and Prevention. Clinical overview of CMV and congenital CMV. 2024. Available at: https://www.cdc.gov/cytomegalovirus/hcp/clinical-overview/index.html

8. Gupta M, Shorman M. Cytomegalovirus infections. StatPearls. Treasure Island (FL). StatPearls Publishing. 2025. Accessed: July 2,2025. https://pubmed.ncbi.nlm.nih.gov/29083720/.

9. Griffiths P, Baraniak I, Reeves M. The pathogenesis of human cytomegalovirus. *J Pathol*. 2015;235(2):288-297. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25205255.

10. Jabs DA, Van Natta ML, Kempen JH, et al. Characteristics of patients with cytomegalovirus retinitis in the era of highly active antiretroviral therapy. *Am J Ophthalmol*. 2002;133(1):48-61. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11755839.

11. Dieterich DT, Rahmin M. Cytomegalovirus colitis in AIDS: presentation in 44 patients and a review of the literature. *J Acquir Immune Defic Syndr*. 1991;4 Suppl 1:S29-35. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1848619.

12. Arribas JR, Storch GA, Clifford DB, Tselis AC. Cytomegalovirus encephalitis. *Ann Intern Med*. 1996;125(7):577-587. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8815757.

13. Jabs DA, Van Natta ML, Holbrook JT, et al. Longitudinal study of the ocular complications of AIDS: 1. Ocular diagnoses at enrollment. *Ophthalmology*. 2007;114(4):780-786. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17258320.

14. Schwarcz L, Chen MJ, Vittinghoff E, Hsu L, Schwarcz S. Declining incidence of AIDS-defining opportunistic illnesses: results from 16 years of population-based AIDS surveillance. *AIDS*. 2013;27(4):597-605. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23079812.

15. Sugar EA, Jabs DA, Ahuja A, et al. Incidence of cytomegalovirus retinitis in the era of highly active antiretroviral therapy. *Am J Ophthalmol*. 2012;153(6):1016-1024 e1015. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22310076.

16. Jabs DA, Van Natta ML, Thorne JE, et al. Course of cytomegalovirus retinitis in the era of highly active antiretroviral therapy: 2. Second eye involvement and retinal detachment. *Ophthalmology*. 2004;111(12):2232-2239. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15582079.

17. Holland GN, Vaudaux JD, Jeng SM, et al. Characteristics of untreated AIDS-related cytomegalovirus retinitis. I. Findings before the era of highly active antiretroviral therapy (1988 to 1994). *Am J Ophthalmol*. 2008;145(1):5-11. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18154750.

18. Holland GN, Vaudaux JD, Shiramizu KM, et al. Characteristics of untreated AIDS-related cytomegalovirus retinitis. II. Findings in the era of highly active antiretroviral therapy (1997 to 2000). *Am J Ophthalmol*. 2008;145(1):12-22. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18154751.

19. Holland GN, Shuler JD. Progression rates of cytomegalovirus retinopathy in ganciclovir-treated and untreated patients. *Arch Ophthalmol*. 1992;110(10):1435-1442. Available at: https://www.ncbi.nlm.nih.gov/pubmed/1329703.

20. Holland GN. AIDS and ophthalmology: the first quarter century. *Am J Ophthalmol*. 2008;145(3):397-408. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18282490.

21. Arribas JR, Clifford DB, Fichtenbaum CJ, Commins DL, Powderly WG, Storch GA. Level of cytomegalovirus (CMV) DNA in cerebrospinal fluid of subjects with AIDS and CMV infection of the central nervous system. *J Infect Dis*. 1995;172(2):527-531. Available at: http://www.ncbi.nlm.nih.gov/pubmed/7622897.

22. Dodt KK, Jacobsen PH, Hofmann B, et al. Development of cytomegalovirus (CMV) disease may be predicted in HIV-infected patients by CMV polymerase chain reaction and the antigenemia test. *AIDS*. 1997;11(3):F21-28. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9147416.

23. Zurlo JJ, O'Neill D, Polis MA, et al. Lack of clinical utility of cytomegalovirus blood and urine cultures in patients with HIV infection. *Ann Intern Med*. 1993;118(1):12-17. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8093214.

24. Rodriguez-Barradas MC, Stool E, Musher DM, et al. Diagnosing and treating cytomegalovirus pneumonia in patients with AIDS. *Clin Infect Dis*. 1996;23(1):76-81. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8816133.

25. Wolf DG, Spector SA. Diagnosis of human cytomegalovirus central nervous system disease in AIDS patients by DNA amplification from cerebrospinal fluid. *J Infect Dis*. 1992;166(6):1412-1415. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1331254.

26. Deayton JR, Prof Sabin CA, Johnson MA, Emery VC, Wilson P, Griffiths PD. Importance of cytomegalovirus viraemia in risk of disease progression and death in HIV-infected patients receiving highly active antiretroviral therapy. *Lancet*. 2004;363(9427):2116-2121. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15220032.

27. Hu H, Jabs DA, Forman MS, et al. Comparison of cytomegalovirus (CMV) UL97 gene sequences in the blood and vitreous of patients with acquired immunodeficiency syndrome and CMV retinitis. *J Infect Dis*. 2002;185(7):861-867. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11920309.

28. Laine L, Bonacini M, Sattler F, Young T, Sherrod A. Cytomegalovirus and Candida esophagitis in patients with AIDS. *J Acquir Immune Defic Syndr*. 1992;5(6):605-609. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1316961.

29. Poh KC, Zheng S. A rare case of CMV pneumonia in HIV-infection. *Respir Med Case Rep*. 2019;28:100945. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31709138.

30. Jabbehdari S, Marjani M, Moniri A, et al. Cytomegalovirus pneumonia in HIV-infected patients: case series from Iran. *HIV & AIDS Review*. 2022;21(4):327-331. Available at: https://hivaids.termedia.pl/Cytomegalovirus-pneumonia-in-HIV-infected-patients-case-series-from-Iran,146650,0,2.html.

31. Drew LW. Condoms and the transmission of cytomegalovirus. *Sexually Transmitted Diseases*. 1998;25(9):481-482. Available at: https://journals.lww.com/stdjournal/fulltext/1998/10000/condoms_and_the_transmission_of_cytomegalovirus.7.aspx.

32. Katznelson S, Drew WL, Mintz L. Efficacy of the condom as a barrier to the transmission of cytomegalovirus. *J Infect Dis*. 1984;150(1):155-157. Available at: https://www.ncbi.nlm.nih.gov/pubmed/6086770.

33. Wohl DA, Kendall MA, Andersen J, et al. Low rate of CMV end-organ disease in HIV-infected patients despite low CD4+ cell counts and CMV viremia: results of ACTG protocol A5030. *HIV Clin Trials*. 2009;10(3):143-152. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19632953.

34. Martin DF, Kuppermann BD, Wolitz RA, Palestine AG, Li H, Robinson CA. Oral ganciclovir for patients with cytomegalovirus retinitis treated with a ganciclovir implant. Roche Ganciclovir Study Group. *N Engl J Med*. 1999;340(14):1063-1070. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10194235.

35. Kempen JH, Jabs DA, Wilson LA, Dunn JP, West SK, Tonascia J. Mortality risk for patients with cytomegalovirus retinitis and acquired immune deficiency syndrome. *Clin Infect Dis*. 2003;37(10):1365-1373. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14583871.

36. Studies of Ocular Complications of ARGTACTG. The ganciclovir implant plus oral ganciclovir versus parenteral cidofovir for the treatment of cytomegalovirus retinitis in patients with acquired immunodeficiency syndrome: The Ganciclovir Cidofovir Cytomegalovirus Retinitis Trial. *Am J Ophthalmol*. 2001;131(4):457-467. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11292409.

37. Musch DC, Martin DF, Gordon JF, Davis MD, Kuppermann BD. Treatment of cytomegalovirus retinitis with a sustained-release ganciclovir implant. The Ganciclovir Implant Study Group. *N Engl J Med*. 1997;337(2):83-90. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9211677.

38. Martin DF, Sierra-Madero J, Walmsley S, et al. A controlled trial of valganciclovir as induction therapy for cytomegalovirus retinitis. *N Engl J Med*. 2002;346(15):1119-1126. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11948271.

39. Kempen JH, Jabs DA, Wilson LA, Dunn JP, West SK, Tonascia JA. Risk of vision loss in patients with cytomegalovirus retinitis and the acquired immunodeficiency syndrome. *Arch Ophthalmol*. 2003;121(4):466-476. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12695243.

40. Studies of Ocular Complications of AIDS Research Group in collaboration with the AIDS Clinical Trials Group. Foscarnet-Ganciclovir Cytomegalovirus Retinitis Trial. 4. Visual outcomes. Studies of Ocular Complications of AIDS Research Group in collaboration with the AIDS Clinical Trials Group. *Ophthalmology*. 1994;101(7):1250-1261. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8035989.

41. Bowen EF, Wilson P, Cope A, et al. Cytomegalovirus retinitis in AIDS patients: influence of cytomegaloviral load on response to ganciclovir, time to recurrence and survival. *AIDS*. 1996;10(13):1515-1520. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8931786.

42. Jabs DA, Ahuja A, Van Natta M, Dunn JP, Yeh S, Studies of the Ocular Complications of ARG. Comparison of treatment regimens for cytomegalovirus retinitis in patients with AIDS in the era of highly active antiretroviral therapy. *Ophthalmology*. 2013;120(6):1262-1270. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23419804.

43. Davis JL, Taskintuna I, Freeman WR, Weinberg DV, Feuer WJ, Leonard RE. Iritis and hypotony after treatment with intravenous cidofovir for cytomegalovirus retinitis. *Arch Ophthalmol*. 1997;115(6):733-737. Available at: https://www.ncbi.nlm.nih.gov/pubmed/9194724.

44. Long-term follow-up of patients with AIDS treated with parenteral cidofovir for cytomegalovirus retinitis: the HPMPC Peripheral Cytomegalovirus Retinitis Trial. The Studies of Ocular Complications of AIDS Research Group in collaboration with the AIDS Clinical Trials Group. *AIDS*. 2000;14(11):1571-1581. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10983644.

45. Labetoulle M, Goujard C, Frau E, Offret H, Delfraissy JF, Gasnault J. Cidofovir ocular toxicity is related to previous ocular history. *AIDS*. 2000;14(5):622-623. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10780729.

46. Lampinen TM, Critchlow CW, Kuypers JM, et al. Association of antiretroviral therapy with detection of HIV-1 RNA and DNA in the anorectal mucosa of homosexual men. *AIDS*. 2000;14(5):F69-75. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10780708.

47. Taskintuna I, Rahhal FM, Rao NA, et al. Adverse events and autopsy findings after intravitreous cidofovir (HPMPC) therapy in patients with acquired immune deficiency syndrome (AIDS). *Ophthalmology*. 1997;104(11):1827-1836; discussion 1836-1827. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9373113.

48. Dieterich DT, Kotler DP, Busch DF, et al. Ganciclovir treatment of cytomegalovirus colitis in AIDS: a randomized, double-blind, placebo-controlled multicenter study. *J Infect Dis*. 1993;167(2):278-282. Available at: https://www.ncbi.nlm.nih.gov/pubmed/8380610.

49. Asberg A, Humar A, Rollag H, et al. Oral valganciclovir is noninferior to intravenous ganciclovir for the treatment of cytomegalovirus disease in solid organ transplant recipients. *Am J Transplant*. 2007;7(9):2106-2113. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17640310.

50. Anduze-Faris BM, Fillet AM, Gozlan J, et al. Induction and maintenance therapy of cytomegalovirus central nervous system infection in HIV-infected patients. *AIDS*. 2000;14(5):517-524. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10780714.

51. Nguyen QD, Kempen JH, Bolton SG, Dunn JP, Jabs DA. Immune recovery uveitis in patients with AIDS and cytomegalovirus retinitis after highly active antiretroviral therapy. *Am J Ophthalmol*. 2000;129(5):634-639. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10844056.

52. Karavellas MP, Plummer DJ, Macdonald JC, et al. Incidence of immune recovery vitritis in cytomegalovirus retinitis patients following institution of successful highly active antiretroviral therapy. *J Infect Dis*. 1999;179(3):697-700. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9952380.

53. Robinson MR, Reed G, Csaky KG, Polis MA, Whitcup SM. Immune-recovery uveitis in patients with cytomegalovirus retinitis taking highly active antiretroviral therapy. *Am J Ophthalmol*. 2000;130(1):49-56. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11004259.

54. Karavellas MP, Song M, Macdonald JC, Freeman WR. Long-term posterior and anterior segment complications of immune recovery uveitis associated with cytomegalovirus retinitis. *Am J Ophthalmol*. 2000;130(1):57-64. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11004260.

55. Kempen JH, Min YI, Freeman WR, et al. Risk of immune recovery uveitis in patients with AIDS and cytomegalovirus retinitis. *Ophthalmology*. 2006;113(4):684-694. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16581429.

56. Jabs DA, Ahuja A, Van Natta ML, et al. Long-term outcomes of cytomegalovirus retinitis in the era of modern antiretroviral therapy: results from a United States cohort. *Ophthalmology*. 2015;122(7):1452-1463. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25892019.

57. Jabs DA, Wingard JR, de Bustros S, de Miranda P, Saral R, Santos GW. BW B759U for cytomegalovirus retinitis: intraocular drug penetration. *Arch Ophthalmol*. 1986;104(10):1436-1437. Available at: http://www.ncbi.nlm.nih.gov/pubmed/3021090.

58. Rodrigues Alves N, Barao C, Mota C, Costa L, Proenca RP. Immune recovery uveitis: a focus review. *Graefes Arch Clin Exp Ophthalmol*. 2024;262(8):2703-2712. Available at: https://www.ncbi.nlm.nih.gov/pubmed/38381160.

59. El-Bradey MH, Cheng L, Song MK, Torriani FJ, Freeman WR. Long-term results of treatment of macular complications in eyes with immune recovery uveitis using a graded treatment approach. *Retina*. 2004;24(3):376-382. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15187659.

60. Kuppermann BD, Holland GN. Immune recovery uveitis. *Am J Ophthalmol*. 2000;130(1):103-106. Available at: https://www.ncbi.nlm.nih.gov/pubmed/11004267.

61. Holland GN. Immune recovery uveitis. *Ocul Immunol Inflamm*. 1999;7(3-4):215-221. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10611730.

62. Jabs DA, Rosenbaum JT, Foster CS, et al. Guidelines for the use of immunosuppressive drugs in patients with ocular inflammatory disorders: recommendations of an expert panel. *Am J Ophthalmol*. 2000;130(4):492-513. Available at: https://www.ncbi.nlm.nih.gov/pubmed/11024423.

63. Ortega-Larrocea G, Espinosa E, Reyes-Teran G. Lower incidence and severity of cytomegalovirus-associated immune recovery uveitis in HIV-infected patients with delayed highly active antiretroviral therapy. *AIDS*. 2005;19(7):735-738. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15821403.

64. Jabs DA, Martin BK, Forman MS, Ricks MO. Cytomegalovirus (CMV) blood DNA load, CMV retinitis progression, and occurrence of resistant CMV in patients with CMV retinitis. *The Journal of Infectious Diseases*. 2005;192(4):640-649. Available at: https://doi.org/10.1086/432012.

65. Ruiz-Cruz M, Alvarado-de la Barrera C, Ablanedo-Terrazas Y, Reyes-Teran G. Proposed clinical case definition for cytomegalovirus-immune recovery retinitis. *Clin Infect Dis*. 2014;59(2):298-303. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24771331.

66. Jabs DA, Van Natta ML, Holland GN, Danis R, Studies of the Ocular Complications of ARG. Cytomegalovirus retinitis in patients with acquired immunodeficiency syndrome after initiating antiretroviral therapy. *Am J Ophthalmol*. 2017;174:23-32. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27984023.

67. Dubreuil-Lemaire ML, Gori A, Vittecoq D, et al. Lenograstim for the treatment of neutropenia in patients receiving ganciclovir for cytomegalovirus infection: a randomised, placebo-controlled trial in AIDS patients. *Eur J Haematol*. 2000;65(5):337-343. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11092465.

68. Kuritzkes DR, Parenti D, Ward DJ, et al. Filgrastim prevents severe neutropenia and reduces infective morbidity in patients with advanced HIV infection: results of a randomized, multicenter, controlled trial. G-CSF 930101 Study Group. *AIDS*. 1998;12(1):65-74. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9456256.

69. Kuppermann BD, Quiceno JI, Flores-Aguilar M, et al. Intravitreal ganciclovir concentration after intravenous administration in AIDS patients with cytomegalovirus retinitis: implications for therapy. *J Infect Dis*. 1993;168(6):1506-1509. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8245536.

70. Arevalo JF, Gonzalez C, Capparelli EV, et al. Intravitreous and plasma concentrations of ganciclovir and foscarnet after intravenous therapy in patients with AIDS and cytomegalovirus retinitis. *J Infect Dis*. 1995;172(4):951-956. Available at: http://www.ncbi.nlm.nih.gov/pubmed/7561215.

71. Combination foscarnet and ganciclovir therapy vs monotherapy for the treatment of relapsed cytomegalovirus retinitis in patients with AIDS. The Cytomegalovirus Retreatment Trial. The Studies of Ocular Complications of AIDS Research Group in Collaboration with the AIDS Clinical Trials Group. *Arch Ophthalmol*. 1996;114(1):23-33. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8540847.

72. Jabs DA, Enger C, Dunn JP, Forman M. Cytomegalovirus retinitis and viral resistance: ganciclovir resistance. CMV Retinitis and Viral Resistance Study Group. *J Infect Dis*. 1998;177(3):770-773. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9498461.

73. Jabs DA, Enger C, Forman M, Dunn JP. Incidence of foscarnet resistance and cidofovir resistance in patients treated for cytomegalovirus retinitis. The Cytomegalovirus Retinitis and Viral Resistance Study Group. *Antimicrob Agents Chemother*. 1998;42(9):2240-2244. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9736542.

74. Jabs DA, Martin BK, Forman MS, et al. Mutations conferring ganciclovir resistance in a cohort of patients with acquired immunodeficiency syndrome and cytomegalovirus retinitis. *J Infect Dis*. 2001;183(2):333-337. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11120934.

75. Emery VC, Griffiths PD. Prediction of cytomegalovirus load and resistance patterns after antiviral chemotherapy. *Proc Natl Acad Sci U S A*. 2000;97(14):8039-8044. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10859361.

76. Jabs DA, Enger C, Dunn JP, Forman M, Hubbard L. Cytomegalovirus retinitis and viral resistance: 3. Culture results. CMV Retinitis and Viral Resistance Study Group. *Am J Ophthalmol*. 1998;126(4):543-549. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9780099.

77. Weinberg A, Jabs DA, Chou S, et al. Mutations conferring foscarnet resistance in a cohort of patients with acquired immunodeficiency syndrome and cytomegalovirus retinitis. *J Infect Dis*. 2003;187(5):777-784. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12599051.

78. Martin BK, Ricks MO, Forman MS, Jabs DA, Cytomegalovirus Ra, Group VRS. Change over time in incidence of ganciclovir resistance in patients with cytomegalovirus retinitis. *Clin Infect Dis*. 2007;44(7):1001-1008. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17342657.

79. Chou S, Erice A, Jordan MC, et al. Analysis of the UL97 phosphotransferase coding sequence in clinical cytomegalovirus isolates and identification of mutations conferring ganciclovir resistance. *J Infect Dis*. 1995;171(3):576-583. Available at: http://www.ncbi.nlm.nih.gov/pubmed/7876604.

80. Chou S, Guentzel S, Michels KR, Miner RC, Drew WL. Frequency of UL97 phosphotransferase mutations related to ganciclovir resistance in clinical cytomegalovirus isolates. *J Infect Dis*. 1995;172(1):239-242. Available at: http://www.ncbi.nlm.nih.gov/pubmed/7797920.

81. Smith IL, Cherrington JM, Jiles RE, Fuller MD, Freeman WR, Spector SA. High-level resistance of cytomegalovirus to ganciclovir is associated with alterations in both the UL97 and DNA polymerase genes. *J Infect Dis*. 1997;176(1):69-77. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9207351.

82. Chou S, Lurain NS, Thompson KD, Miner RC, Drew WL. Viral DNA polymerase mutations associated with drug resistance in human cytomegalovirus. *J Infect Dis*. 2003;188(1):32-39. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12825168.

83. Chou S, Van Wechel LC, Lichy HM, Marousek GI. Phenotyping of cytomegalovirus drug resistance mutations by using recombinant viruses incorporating a reporter gene. *Antimicrob Agents Chemother*. 2005;49(7):2710-2715. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15980340.

84. Wolf DG, Smith IL, Lee DJ, Freeman WR, Flores-Aguilar M, Spector SA. Mutations in human cytomegalovirus UL97 gene confer clinical resistance to ganciclovir and can be detected directly in patient plasma. *J Clin Invest*. 1995;95(1):257-263. Available at: http://www.ncbi.nlm.nih.gov/pubmed/7814623.

85. Vitravene Study G. Randomized dose-comparison studies of intravitreous fomivirsen for treatment of cytomegalovirus retinitis that has reactivated or is persistently active despite other therapies in patients with AIDS. *Am J Ophthalmol*. 2002;133(4):475-483. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11931781.

86. Jabs DA, Martin BK, Ricks MO, Forman MS, Cytomegalovirus Ra, Group VRS. Detection of ganciclovir resistance in patients with AIDS and cytomegalovirus retinitis: correlation of genotypic methods with viral phenotype and clinical outcome. *J Infect Dis*. 2006;193(12):1728-1737. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16703517.

87. Jabs DA, Martin BK, Forman MS, et al. Cytomegalovirus resistance to ganciclovir and clinical outcomes of patients with cytomegalovirus retinitis. *Am J Ophthalmol*. 2003;135(1):26-34. Available at: http://www.ncbi.nlm.nih.gov/pubmed/12504693.

88. Jabs DA, Martin BK, Forman MS, Cytomegalovirus Ra, Group VRR. Mortality associated with resistant cytomegalovirus among patients with cytomegalovirus retinitis and AIDS. *Ophthalmology*. 2010;117(1):128-132 e122. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19818505.

89. Banker AS, Arevalo JF, Munguia D, et al. Intraocular pressure and aqueous humor dynamics in patients with AIDS treated with intravitreal cidofovir (HPMPC) for cytomegalovirus retinitis. *Am J Ophthalmol*. 1997;124(2):168-180. Available at: https://www.ncbi.nlm.nih.gov/pubmed/9262540.

90. (ACTG) ACTG. Studies of ocular complications of AIDS Foscarnet-Ganciclovir Cytomegalovirus Retinitis Trial: 1. Rationale, design, and methods. AIDS Clinical Trials Group (ACTG). *Control Clin Trials*. 1992;13(1):22-39. Available at: http://www.ncbi.nlm.nih.gov/pubmed/1315661.

91. Young S, Morlet N, Besen G, et al. High-dose (2000-microgram) intravitreous ganciclovir in the treatment of cytomegalovirus retinitis. *Ophthalmology*. 1998;105(8):1404-1410. Available at: https://www.ncbi.nlm.nih.gov/pubmed/9709750.

92. Spector SA, Wong R, Hsia K, Pilcher M, Stempien MJ. Plasma cytomegalovirus (CMV) DNA load predicts CMV disease and survival in AIDS patients. *J Clin Invest*. 1998;101(2):497-502. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9435323.

93. Tural C, Romeu J, Sirera G, et al. Long-lasting remission of cytomegalovirus retinitis without maintenance therapy in human immunodeficiency virus-infected patients. *J Infect Dis*. 1998;177(4):1080-1083. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9534987.

94. Vrabec TR, Baldassano VF, Whitcup SM. Discontinuation of maintenance therapy in patients with quiescent cytomegalovirus retinitis and elevated CD4+ counts. *Ophthalmology*. 1998;105(7):1259-1264. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9663231.

95. Macdonald JC, Torriani FJ, Morse LS, Karavellas MP, Reed JB, Freeman WR. Lack of reactivation of cytomegalovirus (CMV) retinitis after stopping CMV maintenance therapy in AIDS patients with sustained elevations in CD4 T cells in response to highly active antiretroviral therapy. *J Infect Dis*. 1998;177(5):1182-1187. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9593001.

96. Whitcup SM, Fortin E, Lindblad AS, et al. Discontinuation of anticytomegalovirus therapy in patients with HIV infection and cytomegalovirus retinitis. *JAMA*. 1999;282(17):1633-1637. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10553789.

97. Jabs DA, Bolton SG, Dunn JP, Palestine AG. Discontinuing anticytomegalovirus therapy in patients with immune reconstitution after combination antiretroviral therapy. *Am J Ophthalmol*. 1998;126(6):817-822. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9860006.

98. Jouan M, Saves M, Tubiana R, et al. Discontinuation of maintenance therapy for cytomegalovirus retinitis in HIV-infected patients receiving highly active antiretroviral therapy. *AIDS*. 2001;15(1):23-31. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11192865.

99. Walmsley SL, Raboud J, Angel JB, et al. Long-term follow-up of a cohort of HIV-infected patients who discontinued maintenance therapy for cytomegalovirus retinitis. *HIV Clin Trials*. 2006;7(1):1-9. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16632459.

100. Holbrook JT, Colvin R, van Natta ML, et al. Evaluation of the United States Public Health Service guidelines for discontinuation of anticytomegalovirus therapy after immune recovery in patients with cytomegalovirus retinitis. *Am J Ophthalmol*. 2011;152(4):628-637 e621. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21742304.

101. 1999 USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus. U.S. Public Health Service (USPHS) and Infectious Diseases Society of America (IDSA). *MMWR Recomm Rep*. 1999;48(RR-10):1-59, 61-56. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10499670.

102. Jabs DA, Ahuja A, Van Natta M, Lyon A, Srivastava S, Gangaputra S. Course of cytomegalovirus retinitis in the era of highly active antiretroviral therapy: five-year outcomes. *Ophthalmology*. 2010;117(11):2152-2161.e2151-2152. Available at: https://pubmed.ncbi.nlm.nih.gov/20673591/.

103. Komanduri KV, Feinberg J, Hutchins RK, et al. Loss of cytomegalovirus-specific CD4+ T cell responses in human immunodeficiency virus type 1-infected patients with high CD4+ T cell counts and recurrent retinitis. *J Infect Dis*. 2001;183(8):1285-1289. Available at: https://pubmed.ncbi.nlm.nih.gov/11262214/.

104. Torriani FJ, Freeman WR, Macdonald JC, et al. CMV retinitis recurs after stopping treatment in virological and immunological failures of potent antiretroviral therapy. *AIDS*. 2000;14(2):173-180. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10708288.

105. Practice bulletin no. 151: Cytomegalovirus, parvovirus B19, varicella zoster, and toxoplasmosis in pregnancy. *Obstet Gynecol*. 2015;125(6):1510-1525. Available at: https://pubmed.ncbi.nlm.nih.gov/26000539.

106. Faqi AS, Klug A, Merker HJ, Chahoud I. Ganciclovir induces reproductive hazards in male rats after short-term exposure. *Hum Exp Toxicol*. 1997;16(9):505-511. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9306137.

107. Miller BW, Howard TK, Goss JA, Mostello DJ, Holcomb WL, Jr., Brennan DC. Renal transplantation one week after conception. *Transplantation*. 1995;60(11):1353-1354. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8525535.

108. Pescovitz MD. Absence of teratogenicity of oral ganciclovir used during early pregnancy in a liver transplant recipient. *Transplantation*. 1999;67(5):758-759. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10096536.

109. Adler SP, Nigro G, Pereira L. Recent advances in the prevention and treatment of congenital cytomegalovirus infections. *Semin Perinatol*. 2007;31(1):10-18. Available at: http://www.ncbi.nlm.nih.gov/pubmed/17317422.

110. Seidel V, Feiterna-Sperling C, Siedentopf JP, et al. Intrauterine therapy of cytomegalovirus infection with valganciclovir: review of the literature. *Med Microbiol Immunol*. 2017;206(5):347-354. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28733760.

111. Henry K, Cantrill H, Fletcher C, Chinnock BJ, Balfour HH, Jr. Use of intravitreal ganciclovir (dihydroxy propoxymethyl guanine) for cytomegalovirus retinitis in a patient with AIDS. *Am J Ophthalmol*. 1987;103(1):17-23. Available at: https://www.ncbi.nlm.nih.gov/pubmed/3026186.

112. FOSCAVIR ® (foscarnet sodium) injection 2011.

113. Mathias CV, Simões MJ, Amed AM, et al. Foscarnet effects on the rat pregnancy outcome. *Int J Morphol*. 2005;23(2):137-140. Available at: https://www.scielo.cl/pdf/ijmorphol/v23n2/art08.pdf.

114. Alvarez-McLeod A, Havlik J, Drew KE. Foscarnet treatment of genital infection due to acyclovir-resistant herpes simplex virus type 2 in a pregnant patient with AIDS: case report. *Clin Infect Dis*. 1999;29(4):937-938. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10589917.

115. De Clercq E. Therapeutic potential of Cidofovir (HPMPC, Vistide) for the treatment of DNA virus (i.e. herpes-, papova-, pox- and adenovirus) infections. *Verh K Acad Geneeskd Belg*. 1996;58(1):19-47; discussion 47-19. Available at: https://www.ncbi.nlm.nih.gov/pubmed/8701600.

116. Indications for Outpatient Antenatal Fetal Surveillance: ACOG Committee Opinion, Number 828. *Obstet Gynecol*. 2021;137(6):e177-e197. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34011892.

117. Khalil A, Sotiriadis A, Chaoui R, et al. ISUOG Practice Guidelines: role of ultrasound in congenital infection. *Ultrasound Obstet Gynecol*. 2020;56(1):128-151. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32400006.

118. Enders M, Daiminger A, Exler S, Ertan K, Enders G, Bald R. Prenatal diagnosis of congenital cytomegalovirus infection in 115 cases: a 5 years' single center experience. *Prenat Diagn*. 2017;37(4):389-398. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28207161.

119. Hughes BL, Gyamfi-Bannerman C. Diagnosis and antenatal management of congenital cytomegalovirus infection. *Am J Obstet Gynecol*. 2016;214(6):B5-b11. Available at: https://pubmed.ncbi.nlm.nih.gov/26902990/.

120. Boppana SB, Hui L. Cytomegalovirus infection in pregnancy. 2024. Available at: https://www.uptodate.com/contents/cytomegalovirus-infection-in-pregnancy

121. Yamamoto AY, Mussi-Pinhata MM, Boppana SB, et al. Human cytomegalovirus reinfection is associated with intrauterine transmission in a highly cytomegalovirus-immune maternal population. *Am J Obstet Gynecol*. 2010;202(3):297 e291-298. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20060091.

122. Adachi K, Xu J, Ank B, et al. Congenital cytomegalovirus and HIV perinatal transmission. *Pediatr Infect Dis J*. 2018;37(10):1016-1021. Available at: https://pubmed.ncbi.nlm.nih.gov/30216294/.

123. Frederick T, Homans J, Spencer L, et al. The effect of prenatal highly active antiretroviral therapy on the transmission of congenital and perinatal/early postnatal cytomegalovirus among HIV-infected and HIV-exposed infants. *Clin Infect Dis*. 2012;55(6):877-884. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22675157.

124. Purswani MU, Russell JS, Dietrich M, et al. Birth prevalence of congenital cytomegalovirus nfection in HIV-exposed uninfected children in the era of combination antiretroviral therapy. *The Journal of Pediatrics*. 2020;216:82-87.e82. Available at: https://www.sciencedirect.com/science/article/pii/S0022347619311618?via%3Dihub.

125. Adachi K, Xu J, Ank B, et al. Cytomegalovirus urinary shedding in HIV-infected pregnant women and congenital cytomegalovirus infection. *Clin Infect Dis*. 2017;65(3):405-413. Available at: https://pubmed.ncbi.nlm.nih.gov/28369278/.

126. Society-for-Maternal-Fetal-Medicine, Hughes BL, Gyamfi-Bannerman C. Diagnosis and antenatal management of congenital cytomegalovirus infection. *Am J Obstet Gynecol*. 2016;214(6):B5-B11. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26902990.

127. Tanimura K, Yamada H. Potential biomarkers for predicting congenital cytomegalovirus infection. *Int J Mol Sci*. 2018;19(12):3760. Available at: https://www.mdpi.com/1422-0067/19/12/3760/htm#.

128. Kagan KO, Enders M, Schampera MS, et al. Prevention of maternal-fetal transmission of cytomegalovirus after primary maternal infection in the first trimester by biweekly hyperimmunoglobulin administration. *Ultrasound Obstet Gynecol*. 2019;53(3):383-389. Available at: https://pubmed.ncbi.nlm.nih.gov/29947159/.

129. Nigro G, Adler SP, La Torre R, Best AM, Congenital-Cytomegalovirus-Collaborating-Group. Passive immunization during pregnancy for congenital cytomegalovirus infection. *N Engl J Med*. 2005;353(13):1350-1362. Available at: http://www.ncbi.nlm.nih.gov/pubmed/16192480.

130. Nigro G, Torre RL, Pentimalli H, et al. Regression of fetal cerebral abnormalities by primary cytomegalovirus infection following hyperimmunoglobulin therapy. *Prenat Diagn*. 2008;28(6):512-517. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18509871.

131. Nigro G, Adler SP, Congenital-Cytomegalic-Disease-Collaborating-Group. High-dose cytomegalovirus (CMV) hyperimmune globulin and maternal CMV DNAemia independently predict infant outcome in pregnant women with a primary CMV infection. *Clin Infect Dis*. 2020;71(6):1491-1498. Available at: https://pubmed.ncbi.nlm.nih.gov/31628849/.

132. Hughes B. LB17. Randomized trial to prevent congenital cytomegalovirus (CMV). *Open Forum Infectious Diseases* 2019;6:S1000-S1001. Available at: https://academic.oup.com/ofid/article/6/Supplement_2/S1000/5603805.

133. Revello MG, Lazzarotto T, Guerra B, et al. A randomized trial of hyperimmune globulin to prevent congenital cytomegalovirus. *N Engl J Med*. 2014;370(14):1316-1326. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24693891.

134. Hughes BL, Clifton RG, Rouse DJ, et al. A trial of hyperimmune globulin to prevent congenital cytomegalovirus infection. *N Engl J Med*. 2021;385(5):436-444. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34320288.

135. Egloff C, Sibiude J, Vauloup-Fellous C, et al. New data on efficacy of valacyclovir in secondary prevention of maternal-fetal transmission of cytomegalovirus. *Ultrasound Obstet Gynecol*. 2023;61(1):59-66. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35900718.

136. Shahar-Nissan K, Pardo J, Peled O, et al. Valaciclovir to prevent vertical transmission of cytomegalovirus after maternal primary infection during pregnancy: a randomised, double-blind, placebo-controlled trial. *Lancet*. 2020;396(10253):779-785. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32919517.

137. Chatzakis C, Sotiriadis A, Dinas K, Ville Y. Neonatal and long-term outcomes of infants with congenital cytomegalovirus infection and negative amniocentesis: systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2023;61(2):158-167. Available at: https://www.ncbi.nlm.nih.gov/pubmed/36412976.

138. Faure-Bardon V, Fourgeaud J, Stirnemann J, Leruez-Ville M, Ville Y. Secondary prevention of congenital cytomegalovirus infection with valacyclovir following maternal primary infection in early pregnancy. *Ultrasound Obstet Gynecol*. 2021;58(4):576-581. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33998084.

139. Zammarchi L, Tomasoni LR, Liuzzi G, et al. Treatment with valacyclovir during pregnancy for prevention of congenital cytomegalovirus infection: a real-life multicenter Italian observational study. *Am J Obstet Gynecol*. 2023;5(10):1-10. Available at: https://www.ajogmfm.org/article/S2589-9333(23)00243-4/fulltext.