LITERATURE REVIEW OF CMV AU MANAGEMENT

<table>
<thead>
<tr>
<th>STUDY</th>
<th>Year</th>
<th>Study design</th>
<th>Level of evidence</th>
<th>Number of patients</th>
<th>Type of AU</th>
<th>Control group (mg/ml)</th>
<th>Treatment</th>
<th>Treatment outcome</th>
<th>Treatment outcome definition</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accorinti M, Gladis M, Pirraglia MP, et al. Cytomegalovirus anterior uveitis: long-term follow-up of immunocompetent patients (published correction appears in Graefes Arch Clin Exp Ophthalmol. 2014 Dec;252(12):1817-1824.).</td>
<td>2014</td>
<td>Retrospective observational study</td>
<td>3</td>
<td>15</td>
<td>CMV anterior uveitis: PSS in nine patients (60 %), FHI in three patients (20 %) and chronic anterior uveitis in three cases (20 %)</td>
<td>All patients were treated with topical dexamethasone 0.2 % [4-6 drops daily as loading dose, then gradually reduced] along with topical ganciclovir, five times daily for two weeks and then three times daily for at least four weeks. Two patients also received oral valganciclovir (900 mg twice daily for 21 days, then 450 mg twice daily for the following month), and four patients received chronic oral acyclovir (800 mg/day) for a mean period of 16.5 ± 3 months (range: 12–18 months)</td>
<td>During and after therapy, 23 relapses in 734 months of follow-up, with a mean of 0.002 uveitis recurrences/month of follow-up/patient. The mean number of uveitis relapses significantly decreased, before and after the diagnosis of CMV anterior uveitis and the administration of the specific therapy, from 0.23 ± 0.17 to 0.03±0.03 (4.9±1.95, p&lt;0.001). The mean number of uveitis recurrences/month of follow-up/patient did not differ between patients who received topical and systemic antiviral therapy (0.03 ± 0.02) compared with those who received topical therapy only (0.03 ± 0.01, t = 1.6, p = 1). At the end of follow-up (mean: 62.1 ± 28.5 months) all patients had a quiescent uveitis, with ten of them (66.6 %), under topical low dose steroid therapy, combined in four cases with systemic acyclovir 800 mg/day.</td>
<td>Antiviral therapy can reduce the frequency of relapses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antoun J, Wilkenman Y, Makhou D, Motulsky E, Caspers L, Relvas LJ. Topical Ganciclovir in Cytomegalovirus Anterior Uveitis. J Ocul Pharmacol Ther. 2017;33(4):313‐318.</td>
<td>2017</td>
<td>Retrospective study</td>
<td>4</td>
<td>15</td>
<td>CMV anterior uveitis/endotheliitis: PSS in 24 (93.3%), FHI in 3 (8.7%)</td>
<td>0.15% topical ganciclovir, minimum 5 times a day, tapered based on anterior chamber inflammation over the course of 3 months, and subsequently kept on long-term maintenance therapy (3–4 times/day).</td>
<td>Patients had a significantly lower number of recurrences/year posttreatment (0.76 – 0.57) than in the pretreatment period (3.76 – 2.46) (P&lt;0.001).</td>
<td>Recurrence was defined as the presence of active inflammation, the appearance of new endothelial keratopathy pre-cipitates, with or without elevated IOP.</td>
<td>0.15% topical ganciclovir have a decreased frequency of CMV anterior uveitis recurrences</td>
<td></td>
</tr>
<tr>
<td>Boursier JP, Guesdon-Le Hénaff P, Schwanke N, et al. Cytomegalovirus anterior uveitis: outcome of treatment. Br J Ophthalmol. 2010;94(12):1648‐1652.</td>
<td>2010</td>
<td>Retrospective review</td>
<td>4</td>
<td>71 eyes of 70 patients</td>
<td>CMV anterior uveitis</td>
<td>Systemic ganciclovir was administered intravenously at 5 mg/kg body weight twice a day for 6 weeks, followed by l g and ganciclovir three times a day for another 6 weeks, or - when oral valganciclovir became available: - valganciclovir: 900mg twice a day for 4 weeks, followed by 450 mg twice a day for another 6 weeks. If the patient could not afford the systemic medication or had contraindications to systemic therapy, the other alternatives were intravitreal injections of ganciclovir, topical ganciclovir, ganciclovir implant. Eyes on systemic antiviral therapy also received 0.12% prednisolone acetate twice a day. The eyes that were treated with intravitreal injections or ganciclovir 0.15% gel received either ketorolac tromethamine 0.5% four times a day or prednisolone acetate 0.12% twice a day. In all the patients, the antifungal agents were tapered off as the inflammation resolved.</td>
<td>Thirty and six (75.6%) of 47 treatment episodes resulted in a response to antiviral therapy, but there were 27 (75.5%) episodes of recurrences after stopping the treatment. The systemic ganciclovir and the ganciclovir implant had good response rates, but they also had high recurrence rates after cessation of therapy, and the recurrence rate was just as high with a second course of the treatment. Intravitreal injections had good response rates, but the recurrence rate was high. Although ganciclovir gel had moderate response rates, it also had low recurrence rates. The response to ganciclovir gel was unpredictable. Some eyes that did not initially respond responded to a subsequent course and vice versa.</td>
<td>Response to therapy in eyes with chronic anterior uveitis was defined as the clinical resolution of anterior chamber cells and keratic precipitates (KPs) and good IOP control with or without glaucoma medications while on treatment. In eyes with acute recurrent anterior uveitis, response was defined as absence of recurrence of inflammation and normalisation of IOP without glaucoma medications other than that given during the acute episode while on treatment. Failure of therapy in eyes with chronic anterior uveitis was defined as persistence of anterior chamber cells and keratic precipitates, with or without elevated IOP.</td>
<td>Ganciclovir gel had lower recurrence rates than the systemic ganciclovir and the implant and should be considered as an option for treatment of CMV anterior uveitis.</td>
<td></td>
</tr>
</tbody>
</table>
Intraocular ganciclovir or foscarnet were administered for cases 1–4 at an induction course for at least 2 weeks followed by oral valganciclovir (450 mg twice a day) for a period of 2 months. Case 5 was treated with oral valganciclovir only. Topical corticosteroids were tapered. Oral valganciclovir: 500 mg twice daily, then reduced to 400 mg twice daily. Nine months after therapy was changed from oral valganciclovir to ophthalmic 1% valganciclovir ointment.

In cases 1–4, the frequency of topical corticosteroids followed by oral valganciclovir can control recurrence of CMV anterior uveitis and glaucoma; pt 3 frequent recurrence of endotheliitis was defined as the frequency of steroid eye drops used daily and convenient for hospitals where preservative-free ophthalmic preparations are not available.

Topical 0.5% GCV and corticosteroids as a maintenance regimen without intropulsion effectively preserved long-term corneal endothelial function. Anti-CMV therapy should be reserved for cases with recalcitrant course or secondary complications.

In patients with CMV anterior uveitis, intraocular ganciclovir injection as a loading dose with or without the following oral valganciclovir can control the inflammation and IOP well.

Maintenance regimens of valganciclovir may be necessary to prevent further relapses.
Systemic administration of anti-CMV drugs (either ganciclovir or valganciclovir) was performed in 74 eyes (87.9%), and topical administration of ganciclovir prepared from vials for intravenous infusion was also used in 82 eyes (75.2%). Fifty-two eyes (47.4%) received both systemic and topical anti-CMV treatment.

During the observation period, 39 eyes (38.2%) showed recurrence of inflammation, and anti-CMV treatment was repeated on those eyes. The responses were impressive regarding disease cessation - asymptomatic, no recurrences.

Outcome variables recorded included IOP and aqueous inflammation grading.

In this case of anterior uveitis presumably caused by CMV inducing secondary glaucoma, treatment with ganciclovir led to a decrease of the IOP, normalization of IOP. It appears that continuous anti-CMV management may be required to control the infection in an immunocompetent patient.

This is a report of proven CMV keratoenulitis highly responsive to the recently available 0.15% ganciclovir gel (Vexol®, Allergan, Inc.), with complete control of disease over 2 years and no toxicity despite daily use of the gel.

For the reduction of the systemic antiviral treatment.

Response to valganciclovir therapy was defined as absence of recurrence of inflammation and topical ganciclovir treatment. The responses were impressive regarding disease cessation - asymptomatic, no recurrences.

Combined anti-CMV therapy (systemic and topical) was more effective than systemic or topical anti-CMV treatment alone.


Topical 2% ganciclovir solution in CMV-positive anterior uveitis: a long-term interventional case series. 2014

Primary measurement of efficacy of topical antiviral therapy, without discontinuation.

Response to therapy was defined as remission of anterior chamber inflammation, resolution of corneal edema, and good IOP control without or with minimal antiglaucomatous medications after topical ganciclovir had been received for one month. Late treatment failure was defined as persistence of anterior chamber inflammation, corneal edema, or poor IOP control despite the use of antiglaucomatous medications within the first 3 months of treatment. Late treatment failure was defined as relapse of anterior chamber inflammation, the presence of corneal edema, or elevated IOP after 3 months of treatment.

Ganciclovir treatment was effective for clearing the viral load, aiding in clearing CMV-positive Posner-Schlossman syndrome patients.


Primary measurement of efficacy of topical antiviral therapy, without discontinuation.

Response to therapy was defined as remission of anterior chamber inflammation, resolution of corneal edema, and good IOP control without or with minimal antiglaucomatous medications after topical ganciclovir had been received for one month. Late treatment failure was defined as persistence of anterior chamber inflammation, corneal edema, or poor IOP control despite the use of antiglaucomatous medications within the first 3 months of treatment. Late treatment failure was defined as relapse of anterior chamber inflammation, the presence of corneal edema, or elevated IOP after 3 months of treatment.

Ganciclovir treatment was effective for clearing the viral load, aiding in clearing CMV-positive Posner-Schlossman syndrome patients.

2007 Retrospective observational case series. 4 CMV anterior uveitis no valganciclovir (induction twice daily for 3 weeks, followed by a maintenance dose of 900 mg once daily).

Reduction in inflammation and IOP, thus making it possible gradually to decrease steroids and antiglaucoma medications. An attempt to discontinue valganciclovir after 1 year (patient 1) resulted in a prompt reaction of the uveitis. One patient (patient 4) experienced a reaction of his uveitis under maintenance valganciclovir treatment, but reacted promptly to a renewed induction course.

Main Outcome Measures: Visual acuity, inflammation, and intraocular pressure (IOP).


2016 Retrospective cohort study 331 patients (33 eyes) CMV anterior uveitis no ganciclovir 0.15 % gel - Patients were initially started on topical ganciclovir at an intensive frequency of 3 h (six times per day), tapered based on anterior chamber inflammation over the course of 3 months, and subsequently kept on long-term maintenance therapy (three to four times per day). All patients were concurrently treated with anti-inflammatory eye drops, in the form of topical steroids.

Patients on topical ganciclovir gel had a statistically significant fewer episodes of uveitis flare per person-year (median −0.66 episodes/person years, p = 0.029). The time-to-quiescence was not significantly affected by topical ganciclovir use (median −1.25 days, p = 0.630). In the survival analysis using the Cox regression model, the use of topical ganciclovir was associated with a lower risk of recurrence, but this was not statistically significant (hazard ratio = 0.857, 95 % CI 0.543–1.36, p = 0.511). The overall median time-to-recurrence was 290 days (95 % CI 113 to 274 days) and 164 days (125 to 404 days) (p = 0.492), with and without topical ganciclovir, respectively.

Compared the disease course of each eye inflicted with CMV anterior uveitis before and after ganciclovir 0.15 % gel was added to the treatment regime. Response to treatment or quiescence was defined as the reduction in anterior chamber (AC) inflammation to nil, with no episodes of flare-up of uveitis, which was defined as an increase in AC activity by one step. The primary outcome measures were time-to-quiescence, time-to-recurrence, and number of uveitis flare-ups per person year.

Topical ganciclovir may be beneficial in reducing the frequency of recurrence in patients with CMV anterior uveitis, but it was not statistically associated with prolonging the time-to-recurrence. The time-to-quiescence was also not significantly affected by topical ganciclovir.