Letters

**Table. Characteristics of Subjects**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Usual Care (n = 49)</th>
<th>Medication Management (n = 48)</th>
<th>Behavioral Management (n = 50)</th>
<th>Medication and Behavioral Management Combination (n = 47)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, No.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>48</td>
<td>45</td>
<td>50</td>
<td>43</td>
</tr>
<tr>
<td>Female</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Race, No.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>23</td>
<td>20</td>
<td>23</td>
<td>25</td>
</tr>
<tr>
<td>Nonwhite*</td>
<td>26</td>
<td>28</td>
<td>27</td>
<td>32</td>
</tr>
<tr>
<td>Follow-up, mean (SD), d</td>
<td>1265 (385)</td>
<td>1219 (368)</td>
<td>1245 (311)</td>
<td>1292 (309)</td>
</tr>
<tr>
<td>Diabetic retinopathy in either eye, No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence at baseline*</td>
<td>15 (31)</td>
<td>16 (33)</td>
<td>16 (32)</td>
<td>11 (23)</td>
</tr>
<tr>
<td>Progression, No. (%)*</td>
<td>20 (41)</td>
<td>11 (23)</td>
<td>22 (44)</td>
<td>12 (26)</td>
</tr>
</tbody>
</table>

Diabetes was defined as self-reported history of diabetes or diagnosis of diabetes listed in the medical record.

Two subjects in the nonwhite category self-identified as American Indian and the remainder identified as African American.

Defined as documented before or within 2 months of study enrollment.

Defined as progression from absence to presence or less severe to more severe from the time of enrollment to the most recent follow-up 365 days or later following enrollment.

Long-term Suppression of Multidrug-Resistant Cytomegalovirus Retinitis With Systemically Administered Leflunomide

Cytomegalovirus (CMV) infection continues to affect outcomes in transplant recipients. Typical CMV antivirals, including ganciclovir sodium and its oral prodrug valganciclovir hydrochloride, foscarnet sodium, and cidovir, are DNA polymerase inhibitors. Resistance of CMV to this class of drugs is an ongoing challenge. Alternative CMV antivirals include leflunomide and cytomegalovirus immunoglobulin.1-3

We report the follow-up of a renal transplant recipient who developed bilateral ganciclovir-resistant CMV retinitis that has been treated with leflunomide since July 2004.4

**Report of a Case |** In March 2002, a 43-year-old CMV IgG-negative woman underwent cadaveric renal transplantation from a CMV IgG-positive donor. Despite ganciclovir prophylaxis, she developed CMV viremia with retinitis. She was placed on treatment doses of ganciclovir and was stable for 14 months. At month 18 following transplantation, she developed bilateral uveitis and reactivation CMV retinitis.

She was referred to the infectious diseases clinic at the University of Colorado and was initially treated with intravenous ganciclovir and CMV immunoglobulin. Intravenous foscarnet, oral valganciclovir, and weekly CMV immunoglobulin were initiated, with remission of the retinitis. Subsequent reactivation retinitis was treated with ganciclovir implantation4 without response. Weekly bilateral intraocular foscarnet injections were successful in the right eye only. Genotyping of the

**References**

5. Hayden B. Bosworth, PhD

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**Trial Registration:** clinicaltrials.gov Identifier: NCT00129103

CMV showed UL97 and UL54 mutations, indicating resistance to ganciclovir, foscarnet, and cidofovir.6

The patient was placed on oral leflunomide, 20 mg/d, with persistent CMV retinitis in the left eye. The leflunomide dosage was increased to 40 mg/d, and fomivirsen sodium injections were administered in the left eye and continued weekly intravitreal foscarnet injections were administered in the right eye. Random serum and vitreous leflunomide levels were measured, at 24.2 and 4.1 μg/mL, respectively. She ultimately responded to leflunomide, 60 mg/d, with no further progression of CMV retinitis.

Weekly intravitreal foscarnet injections into her right eye and intravenous CMV immunoglobulin continued until May 2006, with resolution of retinitis. The leflunomide dosage was decreased to 40 mg/d. She underwent an uneventful cataract extraction in the right eye.

In September 2006, the patient presented with ocular inflammation that manifested as anterior chamber reaction and
macular edema, thought to be immune recovery uveitis in the absence of CMV retinitis. She was treated with topical steroid eye drops twice daily, an increased prednisone dosage to 60 mg/d, and an increased leflunomide dosage to 60 mg/d.

In April 2007, she developed an acute decrease in visual acuity of the right eye without floaters or pain. Her visual acuity without correction was 20/200 OD. Optical coherence tomography demonstrated an increase in macular edema on the right. The leflunomide dosage was increased to 80 mg/d and eventually 100 mg/d without improvement in macular edema, so the leflunomide dosage was decreased back to 60 mg/d.

In April 2010, she developed an acute decrease in visual acuity of the right eye from 20/200 to 20/400 due to an inferiorly dislocated intraocular lens. She underwent intraocular lens surgery and had stable vision as of April 2011 and no CMV reactivation or recurrent inflammation.

Discussion | Multidrug-resistant CMV infection is a significant cause of morbidity and mortality among transplant recipients. Leflunomide has demonstrated activity against CMV, and is also an immunosuppressive agent that may prevent solid-organ rejection. Leflunomide inhibits viral nucleocapsid and tegument development, suggesting that it is unlikely to share cross-resistance with DNA polymerase antivirals. Adverse reactions to leflunomide include hepatotoxic effects and immunosuppression. Our patient has tolerated this drug well with no reactivation of CMV retinitis for a 7-year period. The Table provides details of her clinical course.

Leflunomide monitoring is essential owing to significant variation in the terminal half-life of the active metabolite (A77 1726). Recommended serum levels range from 25 mg/mL to 80 μg/mL. We were able to demonstrate vitreous leflunomide levels correlating with suppression of CMV retinitis.

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Author Contributions: Study concept and design: Weinberg, Chan, Mandava, Levi. Acquisition of data: Dunn, Weinberg, Chan, Levi. Analysis and interpretation of data: Dunn, Weinberg, Chan, Levi, Olson. Drafting of the manuscript: Dunn, Weinberg, Chan, Levi. Critical revision of the manuscript for important intellectual content: Dunn, Chan, Mandava, Levi, Olson. Statistical analysis: Chan. Administrative, technical, and material support: Mandava, Olson. Study supervision: Mandava, Levi.

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Sclerchoroidal Calcification Is Primarily a Scleral Condition Based on Enhanced Depth Imaging Optical Coherence Tomography

Sclerchoroidal calcification (SC) is found in elderly white individuals with calcium pyrophosphate deposition in the sclera and/or choroid, appearing as a typical yellow subretinal mass usually along the retinal vascular arcades. Most cases are idiopathic, but some have a systemic relationship. We review multimodal imaging findings of SC.

Methods | Clinical and imaging data of 17 SC lesions in 13 eyes of 9 patients diagnosed at the Ocular Oncology Service, Wills Eye Institute, Philadelphia, Pennsylvania, were analyzed retrospectively. Institutional review board approval was obtained, and all patients provided written informed consent.

All patients underwent ocular examination, fundus photography, B-scan ultrasonography, fundus autofluorescence imaging using the Topcon TRC-50DX Retinal Camera (Topcon America; excitation light bandwidth, 580 nm; barrier filter bandwidth, 695 nm), infrared reflectance imaging, and enhanced depth imaging optical coherence tomography (EDI-OCT) using the Heidelberg Spectralis HRA + OCT (Heidelberg Engineering Inc). Analysis of the imaging was performed by 2 independent observers (A.T.F. and J.D.A.), with consensus used to resolve disagreements.

Results | There were 17 SC lesions in 13 eyes of 9 patients (5 male), 5 of whom had unilateral SC. All patients were white, and the mean age was 74 years (median, 73 years; range, 60-88 years). The referring diagnoses were SC (n = 3), choroidal tumor (n = 3), choroidal nevus (n = 1), choroidal melanoma (n = 1), and choroidal metastasis (n = 1). The mean best-corrected visual acuity was 20/33 (median, 20/25; range, 20/20-20/150). All lesions were postequatorial and most were superotemporal (n = 12). The shapes of the lesions were geographic (n = 9), circular (n = 4), ill-defined (n = 3), and annular (n = 1). All lesions were more severe at the fovea. The mean greatest basal diameter was 3.5 mm (range, 1.0-7.0 mm), and the mean thickness on B-scan ultrasonography was 1.6 mm (range, 1.0-3.5 mm). All lesions were acoustically solid with shadowing suggestive of calcification. Orbital computed tomography performed on...