ADVANCED GLAUCOMA INTERVENTION STUDY (AGIS)

Between April, 1988 and November, 1992, AGIS enrolled 789 eyes (591 patients) needing surgery after failure of medical treatment for open-angle glaucoma. Enrolled eyes were randomly assigned to one of two sequences of intervention, one starting with argon laser trabeculoplasty (ALT) and the other with trabeculectomy, to test the hypothesis that initiating surgical treatment with ALT was superior to starting with trabeculectomy. Abbreviating ALT as A, and trabeculectomy as T, the two sequences are ATT and TAT. After initial surgery, subsequent interventions in a sequence were offered to the patient upon failure of the previous intervention. The main goal of AGIS was to assess visual function outcomes and course of disease.

Patient follow-up ended in March 2001, when duration of follow-up ranged from 8½ to 13 years. The following table presents the number of active and inactive patients and deaths as of March 31, 2001. Note that inactive patients are living patients who missed the two most recent consecutive scheduled six-month study visits; inactive status began at the second consecutive missed visit.

<table>
<thead>
<tr>
<th></th>
<th>All Patients</th>
<th>Both eyes enrolled</th>
<th>One eye enrolled</th>
<th>ATT</th>
<th>TAT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>All patients</td>
<td>591</td>
<td>100.0</td>
<td>19</td>
<td>100.0</td>
<td>206</td>
</tr>
<tr>
<td>Living</td>
<td>422</td>
<td>71.4</td>
<td>128</td>
<td>64.6</td>
<td>149</td>
</tr>
<tr>
<td>Deaths</td>
<td>169</td>
<td>28.6</td>
<td>70</td>
<td>35.4</td>
<td>57</td>
</tr>
<tr>
<td></td>
<td>All living patients</td>
<td>422</td>
<td>100.0</td>
<td>128</td>
<td>100.0</td>
</tr>
<tr>
<td>Active</td>
<td>328</td>
<td>77.7</td>
<td>102</td>
<td>79.7</td>
<td>114</td>
</tr>
<tr>
<td>Inactive</td>
<td>86</td>
<td>20.4</td>
<td>23</td>
<td>18.0</td>
<td>31</td>
</tr>
</tbody>
</table>
PRINCIPAL AGIS RESULTS ARE:

Interaction between race and treatment sequence. For the main visual field and visual acuity outcomes, the difference between the treatment sequences ATT and TAT differed between black and white patients. This race-treatment interaction mandated separate analyses of black and white patients. For the main vision outcomes, eyes of black patients did better with the ATT sequence, while eyes of white patients eventually did better with the TAT sequence (AGIS Reports No. 4, 9, and 10-year results paper--submitted to *Ophthalmology*).

A relationship between IOP and VF stability. Intraocular pressure during 6 follow-up years was positively associated with progression of glaucomatous visual field defects. Eyes with IOP consistently <18 mm Hg had, on average, minimal long-term progression of visual field defects. (AGIS Report No. 7).

Visual function improved after cataract surgery in AGIS. Visual field and visual acuity improved after cataract surgery, with the amount of improvement greater in white than in black patients. In black and white patients, the worse the presurgical visual acuity, the greater the expected improvement in visual field. (AGIS Report No. 6).

More cataracts after trabeculectomy. After adjusting for age and diabetes, we found that trabeculectomy increased the risk of cataract formation by 78%. ALT before trabeculectomy did not change the risk of cataract after trabeculectomy (AGIS Report No. 8).
• **Race differences in the progression of advanced glaucoma.** In the TAT sequence, blacks were at greater risk than whites of IOP≥18 mm Hg and of visual field loss. Black patients were at lower risk than white patients of failing initial ALT and at greater risk than white patients of failing initial trabeculectomy. In both treatment sequences, on average, the effort to control disease progression resulted in a greater number of medications prescribed for eyes of black than white patients (AGIS Report No. 9).

AGIS has developed a detailed database, currently residing at The EMMES Corporation, in Rockville, MD, of observations related to the long-term outcome of management of open-angle glaucoma after medical treatment has failed to adequately control disease progression. The AGIS investigators have published 12 papers, and additional results from ongoing analyses are expected to appear in the literature in the near future.

**AGIS BIBLIOGRAPHY**


The following manuscripts are in draft format and are planned for submission by the AGIS investigators:

1. AGIS Report No. 14: Complications of AGIS surgical interventions and their effects
2. A statistical methods paper reporting a new approach to assess outcome interactions in data sets with paired measurements.
3. An assessment of increases in visual field defect to determine how large and for how long sustained they need to be to provide a reliable indication of actual visual field deterioration.

A database of nearly all the visual field test results from the AGIS participants has been assembled at the Jules Stein Eye Institute, UCLA, by the AGIS investigators working with J. Caprioli, MD and his coworkers. Analyses of these field test series are leading to reports concerning validity and utility of alternative methods of identifying visual field deterioration.

Blood samples for genetic analysis from AGIS patients have been submitted to a glaucoma genetic analysis center at the University of Michigan. Analysis of AGIS samples, along with samples collected in the NEI-sponsored Collaborative Initial Glaucoma Treatment Study, and a matched group of normal controls, will provide a unique opportunity to study the role of genetic risk factors in glaucoma.