

## Luncheon Seminar 2

June 28 (Friday), 12:40-13:30

Lecture Room: Room 2 (Small Auditorium)

### The concept of therapeutic window of opportunity in initial-onset VKH uveitis and the treatment strategies resulting from it



Chair

**Shigeaki Ohno, MD, PhD**

Honorary Professor, Department of Ophthalmology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University  
Director, Department of Ophthalmology, Aishin Memorial Hospital



Speaker

**Carl P. Herbort Jr, MD, PhD, FMER, FEBO**

Center for Ophthalmic Specialised Care (COS), Lausanne & University of Lausanne, Switzerland  
Visiting Professor, Department of Ophthalmology, Pavlov University, Saint-Petersburg, Russia  
President, Society for Ophthalmology-Immunoinfectiology in Europe (SOIE)

Initial onset Vogt-Koyanagi-Harada (VKH) disease is a bilateral primary autoimmune granulomatous choroidal inflammatory process. The purpose of this presentation is to put forward the concept of "therapeutic window of opportunity", similar to what has been described for rheumatoid arthritis, defined as a time interval following initial onset of disease during which adequate treatment will substantially modify the disease outcome and possibly even lead to cure. The crucial specificity of VKH stromal choroiditis, is the fact that inflammation exclusively originates from one single structure, the uveal tract, starting in the choroid, and from no other structure of the eye, such as the retina or optic disc. Inflammation in other structures (retina, disc) is only the result of a secondary, spill-over process from choroiditis. This means that if therapy is strongly aimed at choroiditis all inflammation in other structures will subside secondarily and the chances that the process can be brought to a halt are substantial. Several conditions (1-4) are however necessary to hope to achieve healing of an acute early onset attack of VKH disease which will otherwise have a great chance to evolve towards chronic VKH disease.

**1. Early treatment has to be initiated within the "therapeutic window of opportunity", estimated to be around 2-3 weeks after initial symptoms.**

The exact timing of the therapeutic window of opportunity is difficult to determine, but it is clear that the earlier appropriate therapy begins, the higher the chances to achieve an optimal outcome. One study defined the therapeutic window at 2 weeks following disease onset. Although each patient is different, it is accurate to conclude that the therapeutic window of opportunity probably closes approximately 3 weeks after initial onset. Later introduction of appropriate treatment still bears chances of success but this may take longer and need higher dosages.

**2. Treatment has to be aggressive**

Convincing evidence has become available so far to be able to say that systemic corticosteroid monotherapy is not sufficient and inappropriate even if given at an early stage of disease to prevent chronic evolution. Therefore, combinations of corticosteroids with first-line (concomitant) non-steroidal immunosuppressive therapies such as cyclosporine, azathioprine, mycophenolate mofetil, anti-tumor necrosis factor- $\alpha$  agents, or others have been proposed to achieve better control of the uveitis, facilitate earlier tapering of corticosteroids, and avoid chronic evolution in acute initial-onset disease. Quickly acting agents such as ciclosporin and/or TNF- $\alpha$ -blockers (adalimumab) are to be preferred.

**3. Monitoring should not only be limited to usual clinical, fluorescein angiographic or optical coherence follow-up of accessible fundus inflammatory involvement but should be aimed at detecting absence of occult inflammatory activity in the choroid using the appropriate monitoring device of indocyanine green angiography (ICGA) complemented by Enhanced-depth-imaging-OCT (EDI-OCT)**

Subclinical choroiditis is the reason for chronic evolution and is clearly identified by ICGA, uncovering active choroidal inflammation in an apparently quiescent eye during follow-up, and explaining the development of sunset-glow fundus, due to the ongoing insufficiently controlled immunological process.

**4. Treatment has to be sufficiently prolonged and should not be stopped when fundus imaging seems to show resolution of all visible, superficial inflammatory activity but should be based on cessation of occult choroidal inflammatory activity.**

It has been shown that the duration of treatment, when applying "zero tolerance" of occult choroidal inflammation as monitored by ICGA results in much longer periods of treatment, situated more between 2 to 3 years, however resulting in a high proportion of long term disease free patients without treatment.

**Conclusion:** We will show that there is a substantial body of evidence in the literature that a "therapeutic window of opportunity" exists for initial-onset VKH disease. The disease outcome can be substantially improved if dual systemic steroidal and non-steroidal immunosuppression is given within 2-3 weeks of the onset of initial VKH disease, avoiding evolution to chronic disease and development of "sunset glow fundus". Several studies additionally report series in which the disease could be cured, using such an approach of timely and adequately monitored treatment, likely due to the fact that the choroid is the sole origin of inflammation in VKH disease.

Co-sponsored by GOIW2019 and Eisai Co., Ltd. and AbbVie GK