IN CONVERSATION WITH

Dr Robert B Nussenblatt,

Chief of the Laboratory of Immunology at the National Eye Institute, eminent ocular immunologist and expert in clinical research design and conduct

Describe the success or relevance of the SUN project.

The Standardization of Uveitis Nomenclature (SUN) project has been highly successful, is still very much in its infancy but it does represent an important first step. Most, if not all, clinical research in the field of uveitis invariably refers to SUN criteria with regard to evaluation. It has provided the international community with the ability to begin to standardise observations in inflammatory eye disease, and from that perspective the SUN initiative represents a seminal endeavour. But it is by no means the end, simply the beginning.

We were able to demonstrate good inter-observer agreement in clinical grading of vitreous haze using schematic photographs for scoring, for example. The issue, however, is that the vitreous haze grading scheme involves gross changes. It is possible to demonstrate a two-step change in clinical grading; however, in most cases, clinicians would not intentionally allow patients to deteriorate that far. So we do need something moving forward that is more precise and sophisticated. I am optimistic progress will be made and that we can do better. I'd be disappointed if the same standards today were being used 20 years from now.

Key future issues?

There are a number of challenges ahead. One is that the present SUN criteria are based on old observations, and more exacting objective methodologies are needed. We are now treating uveitis patients earlier and the indications for treatment have changed, which influences outcomes observed in clinical trials. This illustrates the point that we need more precise and more sensitive methods to evaluate uveitis patients.

The second area relates to the need to establish guidelines for clinical diagnosis and disease entities, as there is still little consensus with regard to many of the observations seen. It is important I believe that standardisation moves beyond observation of clinical activity toward diagnosis itself. Uveitis represents a heterogeneous group of conditions characterised by intraocular inflammation. With at least 30 different possible diagnoses in uveitis, you cannot assume that each of these entities will invariably have the same presentation.

New and more precise assessment methodologies show promise. One example is the use of optical coherence tomography imaging to measure vitreous cells. Our hope is that we will be able to develop high precision, highly reproducible and more sensitive methods for evaluation of ocular inflammation in uveitis, and vitally gain acceptance by drug regulatory authorities for the use of these newer quantitative techniques in clinical trial designs.

Relevant outcome measures in clinical trials of treatment efficacy for uveitis?

The most common and major clinician-observed measures of disease activity used as primary outcome measures are vitreous haze, presence or absence of inflammatory disease, and for posterior conditions, macular oedema. But there are other important parameters that may be considered, including resolution of retinal vasculitis and change in retinal vascular permeability, for example. Undoubtedly, greater consensus is required in outcome measure selection for clinical trials of treatment efficacy relating to uveitis.

For me, a central issue with regard to therapeutic intervention would be the induction of long-term tolerance and disease control. In the vast majority of cases of inflammatory eye disease, we can control the disease initially. The management issue in uveitis is determining the best way to keep the disease away and achieve a high rate of clinical remission.

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