Dr. Gottlieb et al reply

To the Editor:

We thank the author for their reply and appreciate the approach of having clear terminology and standard definitions within clinical practice guidelines or recommendations, that are applicable across specialist groups. A definition of controlled anterior uveitis or quiescent disease is important for treatment decisions, particularly when classifying a patient’s disease as failing current therapy and making decisions for escalating therapy.

The author correctly points out that the Canadian Rheumatology Association (CRA) recommendations did not define an anterior chamber cell grade for quiescent or controlled disease in uveitis in the referenced paper. The goal of the Canadian recommendations was to use an algorithm based on the 2019 American College of Rheumatology/Arthritis Foundation (ACR/AF) guidelines to adopt, adapt, and elicit consensus on the previously published guidelines, in the context of the differences across Canadian provinces, including cost/resource considerations and feasibility of implementation. The terms, definitions, medication interventions, and critical/important outcomes as defined by the ACR/AF guidelines were used during the development of the CRA recommendations. This includes the ACR/AF expert panel definition of “controlled uveitis” as inactive or grade < 1+ anterior chamber cells without new complications due to active inflammation, according to Standardisation of Uveitis Nomenclature (SUN) criteria, found in Table 1 of the guideline. We agree that tight disease control is a central paradigm for the management of juvenile idiopathic arthritis (JIA). Having an endpoint for a definition of uveitis activity or inactivity is desired by all groups of specialists who treat patients with JIA-associated uveitis and is important for communication among specialists making treatment decisions. The lack of consensus among groups of international experts is likely multifactorial and standard definitions remain unresolved.

We concur with the author, who points out the absence of an international consensus on defining inactive disease. Neither the ACR/AF, Single Hub and Access point for pediatric Rheumatology in Europe (SHARE) group, nor the Australian and New Zealand Juvenile Idiopathic Arthritis-Uveitis Working Group could reach a consensus on threshold for inactive disease. The author relays that lack of consensus may reflect the shortcomings of the current method of quantifying disease; however, it is also due to the lack of clinical trial evidence linking the incidence of specific complications of uveitis to the number of cells in the anterior chamber (or SUN grade) and duration of active inflammation.

Inactive disease (with or without identifiable cells in the anterior chamber) would be the state of inflammation where complications never occur and there was no structural damage or consequences to the eye or the patient. If the minimum anterior chamber cell grade and duration of these cells could accurately predict each JIA-associated uveitis complication, a clear and specific definition of inactive disease could be identified, underpinned by scientific data.

Presently, in the absence of validated biomarkers or objective data to support one or more clinical signs defining disease activity/inactivity, clinicians are left to apply published guidelines and recommendations with variations in definitions and to determine when therapy for uveitis must be increased for any specific patient. Older published guidelines have generally relied on 0 cells as a treatment goal. More recent guidelines have introduced 0.5 cells or < 1+ anterior chamber cells as a definition of “controlled disease” and inactive uveitis. This later proposition not only takes into consideration the potential of disease activity to result in ocular complications but also tries to balance this concept with the risk of iatrogenic complications, increased costs of therapy, and treatment burden for patients and their families. One of these more recently published guidelines used an interesting argument to justify their recommendation: “We agreed with the consensus that although 0.5+ [anterior chamber] cells is considered ‘active’ by SUN criteria, we would not necessarily escalate therapy based on the presence of 0.5+ cells.”

A 2023 update to the SHARE recommendations by the Multinational Interdisciplinary Working Group for Uveitis in Childhood (MIWGUC) defined inactive uveitis as “both eyes fulfilling the following conditions at a specific assessment: slit lamp total number of AC cells: 0 inflammatory cells (in aphakia patients some cells may be present in the anterior vitreous); absence of optic disc edema; absence of macular edema; absence of vitreous haze (< 0.5+); ophthalmologist global assessment of uveitis activity on [visual analog scale] score (range 0-100 mm) must be 0.” Although this becomes the most stringent published definition of inactive uveitis using several clinical findings in combination, it is understood that a clinical care plan formulated in the patient context does not always align with the treatment goal of achieving the stringent definition of disease inactivity in research studies. Clinical guidelines and recommendations by expert panels are the important bridge between research and clinical care. As a result, definitions may vary among guidelines for uveitis that is active, inactive, controlled, and in remission.

With the available evidence, the expert panel of Canadian pediatric rheumatologists and ophthalmologists had no issues with adopting the ACR/AF definition of no cells or < 1+ anterior chamber cells. We feel it is important to highlight that the publication’s purpose was to apply recommendations on treatment decisions to the Canadian context, where equity in terms of access to care, access to medications, and access to specialists is variable, with limitations geographically and in some patient populations. The best care for each patient remains patient centered. Patient-centered care takes into consideration uveitis activity, JIA activity, and disease severity (presence of complications), balanced by tolerance of medications, risks of side effects, risk of iatrogenic complications, costs, patient effort, and the
risk of over- or undertreatment as our definition of disease quiescence becomes more or less stringent.

In summary, we thank the author¹ for raising these critical data that underpins treatment decisions in the care of patients with JIA-associated uveitis, and we would like to thank the CRA JIA-associated uveitis working group for their effort in using the adolopment process to develop the recommendations.

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REFERENCES