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Title: Update on the development of the Idiopathic Multicentric Castleman Disease Symptom BUrden Scale (ISBUS) (NCT5995834)

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Introduction: The diagnostic criteria for idiopathic multicentric Castleman disease (iMCD) were first established in 2017[1]. While these criteria include symptoms, there is currently no disease-specific symptom scale to aid clinical care. Patients with this rare lymphoproliferative disorder experience a significant symptom burden that affects various aspects of daily life, including work, education, social interactions, travel, mobility, personal relationships, and sexual functioning[2].

Given the evolving understanding of iMCD, the development of a novel symptom burden scale is both timely and crucial. A standardised metric for assessing disease progression and treatment outcomes would greatly benefit clinical practice and research. This study aims to develop a patient-reported outcome measure (PROM) to quantify symptom burden in iMCD, facilitating its use in both clinical settings and trials.

Methods: A protocol for developing a novel, patient-reported outcome measure (PROM) for assessing symptom burden in iMCD has been developed and approved by a multi-stakeholder group, including patients, clinicians, industry representatives, and researchers. This international study is registered with ClinicalTrials.gov (NCT05995834).

The development process involves four stages and includes both a patient advisory group and a wider multi-stakeholder advisory group. In stage one, draft PROM content is developed from existing literature and expert opinion. Stage two explores the content validity of the draft PROM through online qualitative interviews with people living with iMCD. In stage three, the revised PROM will be administered quantitatively alongside existing scales to evaluate its psychometric performance and inform decisions on the final PROM. The PROM will be finalized based on qualitative and quantitative evidence generated in consultation with project advisors. Finally, in stage four, the PROM will be re-administered to observe changes in symptom burden over time. This will be complemented by qualitative interviews in a mixed methods design to estimate a minimally clinically important difference for the measure.

Results: Ethics approval for the project has been obtained from Australia, Canada, the United Kingdom, and the United States. Stage One, which involved creating the draft content for the patient-reported outcome measure (PROM), has been completed. The resulting effort consisted of a list of 42 symptoms. Stage two consisted of two parts: reviewing the PROM content and conducting 10 patient interviews, both of which have been completed. The draft scale had two parts: (i) assessing frequency/presence of symptoms over the past week (on a 4-point scale, 'none of the time' to 'most or all of the time'); (ii) assessing impact of the symptom on patients' lives (on a 4-point scale, 'no impact' to 'severe impact'). The draft survey has been completed, and the project is now in stage three, where it is expected that 100 people living with iMCD will be surveyed using the agreed-upon symptoms identified as important during the consultation processes of stages one and two.

Conclusion: A new PROM for assessing symptom burden in iMCD is being developed collaboratively by patients, academics, clinicians, and industry professionals. This measure is being created in accordance with FDA regulatory guidelines, with necessary adjustments for rare diseases. The outcome of this research will be a new, validated symptom burden scale, intended for use in both routine clinical evaluation and clinical trials.

References:

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2. Mukherjee S, Shupo F, Wayi-Wayi G, et al. Symptom burden in patients with idiopathic multicentric Castleman disease and its impact on daily life: an international patient and caregiver survey. EClinicalMedicine 2023; 64: 102192.