Comment on: How early is early for JIA? Insights from the infantile-onset juvenile idiopathic arthritis patients of the PERA research group cohort: Reply

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Dear Editor,

We would like to thank Maniscalco et al (1) for their constructive Letter to the Editor in response to our article “How early is early for JIA? Insights from the infantile-onset juvenile idiopathic arthritis patients of the PeRA research group cohort”(2). We read their contribution with great interest and appreciate their effort to expand the scientific discussion on this rare and clinically relevant subset of juvenile idiopathic arthritis (JIA).

Maniscalco et al. present data from their bicentric cohort of 52 patients with infantile-onset non-systemic JIA and compare them with a matched group of patients with onset after 2 years of age. Their findings show higher rates of antinuclear antibody positivity, uveitis, and more intensive treatment requirements in the infantile-onset group. These findings are largely consistent with our results. This concordance across independent cohorts from different geographic regions further supports the concept that infantile-onset JIA may represent a distinct clinical phenotype. A recent multicenter retrospective study has similarly highlighted delayed diagnosis, higher systemic JIA prevalence, and greater disease activity in infants compared with toddlers (3).

We appreciate the authors emphasis on the clinical course and therapeutic burden in this group. Their data showing high rates of conventional and biological disease-modifying antirheumatic drugs (DMARDs) use, as well as lower rates of clinical inactive disease off medication, highlight the therapeutic challenges encountered in infantile-onset patients. Similarly, in our study, more than half of the patients required escalation to biologic DMARDs, and remission off medication was achieved in only 18.1%. These findings collectively underline the need for optimized treatment strategies and closer monitoring in this population.

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The Letter also raises an important point regarding age thresholds. While Maniscalco et al. did not observe significant clinical differences between patients with disease onset before and after 12 months, their subgroup of very early-onset children (n=9) was small. By comparison, our study included a larger early-onset subgroup (n=40), increasing our ability to detect potential differences. In our cohort, patients with onset ≤12 months had significantly higher frequencies of systemic and rheumatoid factor-negative polyarticular JIA, more wrist and small-joint involvement, and a higher rate of uveitis. These findings suggest that the first year of life may represent a particularly distinct window for JIA onset. Differences between the two cohorts therefore seem attributable to sample size rather than conflicting disease patterns.

Overall, their findings, together with ours, contribute to the growing body of evidence indicating that infantile-onset JIA may differ in subtype distribution, joint involvement patterns, uveitis frequency, treatment requirements, and long-term disease outcomes. Additional multicenter studies with standardized data collection will be crucial to refining these observations and informing future modifications of JIA classification criteria. This need is further supported by recent long-term data showing that age at diagnosis is a meaningful prognostic variable, but its impact on remission varies by JIA category (4).

We once again thank the authors for their valuable contribution to this discussion. We believe that the parallel findings from both cohorts strengthen the proposition that the question “How early is early for JIA?” merits renewed attention in future classification and management frameworks.

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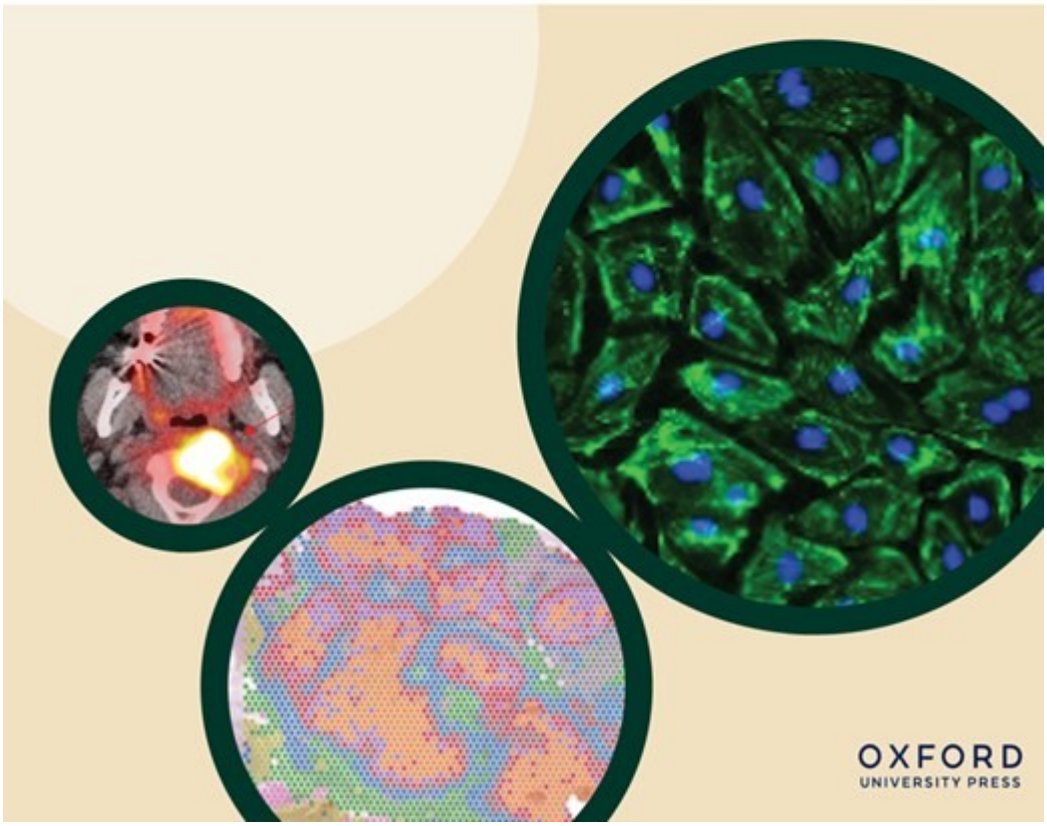
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