Pediatric Residency Program, University of Genoa

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EULAR Center of Excellence in Rheumatology 2018-2023
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Our division of Pediatric Rheumatology, at Giannina Gaslini Institute, hosts the EULAR Center of Excellence in Rheumatology 2018-2023 and the PRINTO International Coordinating Centre, whose main task is to facilitate the flow of logistic and scientific details needed to design, launch and manage multi-centered, multi-national, collaborative studies. You can find details about our current projects on **https://www.printo.it/projects/ongoing**

Additional study proposals would be:

IMPACT ON FLARE-FREE SURVIVAL OF TWO MEDICATION WITHDRAWAL METHODS IN CHILDREN WITH CLINICALLY INACTIVE JUVENILE IDIOPATHIC ARTHRITIS: A PROSPECTIVE RANDOMISED CONTROLLED TRIAL

Abstract

Background: The recent therapeutic advances have increased considerably the potential of achieving disease remission in children with juvenile idiopathic arthritis (JIA). Once complete disease quiescence has been achieved, it would be desirable to discontinue ongoing treatment to avoid prolonged exposure of the child to the potential of adverse effects. This goal should be balanced with the risk of disease flare after withdrawal of therapy. However, currently no guidelines or recommendations are available concerning appropriate discontinuation of medications after attainment of inactive disease status. As a result, treatment practices vary widely and remain empiric and physician-dependent. Several studies and the clinical experience have shown that the risk of disease flare after treatment discontinuation is substantial. Although there is an increasing interest in the role of biomarkers and articular ultrasonography in predicting the risk of flare, the utility of these procedures is still unclear.
Aim: To compare the impact on flare-free survival of two medication withdrawal methods in patients with JIA who have achieved sustained clinical remission. To examine the capacity of immunologic biomarkers and articular ultrasonography to predict disease flare.
Methods: This open, prospective, multicenter, randomized medication-withdrawal trial will enroll patients with oligoarticular and polyarticular JIA who achieve clinical remission on medications (defined as 6 months with clinically inactive disease while receiving anti-rheumatic drugs). Patients will be randomly assigned to either continue the ongoing therapy at unchanged dosage for another 6 months and then to stop (“discontinuation arm”) or to taper gradually the ongoing therapy over 12 months before stopping (“tapering arm”). At randomization, patients receiving combination therapy with MTX and a TNF inhibitor will stop MTX and enter the respective treatment arm with only the TNF inhibitor. This choice is based on the notion that patients on combination therapy are generally those in whom MTX alone was inadequately efficacious and had clinical remission obtained after the addition of an anti-TNF agent. For prediction analyses, blood samples will be obtained at randomization and then after 6 months or at the time of a disease flare. Articular ultrasonography of a predefined set of joints will be performed at randomization, then after 6 months and at the time of disease flare. Statistics will include univariate and multivariate analysis as well as survival analyses.
Expected results and sample size: Expected results and sample size estimates were based on retrospective studies and one prospective analysis published in the literature, which have shown a flare rate ranging from 30% to 50% among clinically inactive JIA patients after treatment discontinuation. For the purposes of the present study, we assume that treatment tapering will lead to a decrease of the rate of disease flare by at least 30% in comparison with abrupt discontinuation. According to these estimates and considering a drop-out rate of 5%, we calculated that 216 subjects (108 per arm) would be needed to show significance. The achievement of this sample size in the study time frame is considered realistic owing to the prevalence of JIA in Italy and the multicenter design of the study. No assumptions could be made regarding the ability of biomarkers or articular ultrasonography to predict the risk of disease flare because the literature is scanty or conflicting. It is expected that the results of the study will help to make more rationale and standardized the approach to treatment withdrawal in clinically inactive JIA in standard clinical practice and to reduce the risk of disease flare. The analysis of the predictive role of biomarkers and imaging may help to define the role of these procedures in future decision-making through the identification of patients who have the greater likelihood of experiencing disease flare after treatment discontinuation.