

EXTENDED REPORT ON THE LONG-TERM PROGNOSTIC EVALUATION SUBSEQUENT TO A CLINICAL TRIAL OF TOCILIZUMAB AS FIRST-LINE BIOLOGIC THERAPY IN PATIENTS WITH REFRACTORY SYSTEMIC ONSET JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: In 2008, Tocilizumab (TCZ) was approved for systemic juvenile idiopathic arthritis (sJIA) as an intravenous formulation after its efficacy and safety were demonstrated in a clinical trial conducted in Japan between 2002 and 2008.

Objectives: This study aimed to comprehend the long-term prognosis of patients who participated in phases II (MRA011JP), III (MRA316JP), and III/IV (MRA324JP) of the clinical trial. A total of 149 participants were included in the study.

Methods: The primary endpoint of this study was the sustained frequency of TCZ administration throughout the prolonged observation period of sJIA. Secondary endpoints encompassed additional long-term prognostic determinants, such as therapeutic conditions, disease status including remission rate and clinical phenotype, complications, social adaptation, employment status, and quantification of health-related quality of life (HRQOL).

Results: Results were collected for 147 cases by April 2023. Among the 135 patients (61 male and 74 female) whose medical records were available and final diagnosis was sJIA, the median age of the study participants was 26.7 years at the time of the study, 4.3 years at the onset of sJIA, 9.2 years at the first administration of TCZ, 4.0 years from the onset to the first TCZ administration, and 9.8 years from the initiation of TCZ (all median values). Thirty-four (25.2%) were in medication-free remission, and 97 (71.9%) continued therapy. Of the 97 patients, 91 were treated with b/ts-DMARDs. Tocilizumab was continued in 83 patients (61.5%), and six were switched to canakinumab (CAN) due to TCZ failure, side effects, or other reasons. Except for an isolated incident of sudden death, three cases resulted in a fatal outcome. Specifically, the causes of mortality were macrophage activation syndrome, sJIA-associated interstitial pneumonia, and disseminated aspergillosis. Forty-four (32.6%) transitioned from acute febrile sJIA to chronic arthritic sJIA, in which chronic arthritis was the primary pathology without systemic inflammation. Macrophage activation syndrome was developed in 33 patients (24.4%) during the clinical course. The most commonly observed complications were osteoporosis in 74 (54.8%), infection requiring hospitalization in 43 (31.8%), and hypertension in 28 (20.7%). The EQ-5D-5L score was 0.89 (mean). The final mean height was 156.6 cm for males and 144.0 cm for females, showing a

significant short stature. The college/university enrollment rate was as high as 65.4%, and all but five students were employed.

Conclusion: After approximately a decade of observation, 71.9% of the patients remained under treatment, with 61.5% electing to receive TCZ. Conversion to chronic arthritic sJIA was detected in 32.6% of the patient population. Despite the presence of primary disease activity and associated complications, the level of social adjustment observed was satisfactory, implying a favorable impact of the administered treatment.

Patient Consent: Yes, I received consent

References: Yokota S, et al. Efficacy and safety of tocilizumab in patients with systemic-onset juvenile idiopathic arthritis: a randomized, double-blind, placebo-controlled, withdrawal phase III trial. *Lancet*. 2008 Mar 22;371(9617):998-1006.

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