(W11) DECIDE RATIONALE/DESIGN: DACLIZUMAB HIGH-YIELD PROCESS MONOTHERAPY IN RELAPSING-REMITTING MULTIPLE SCLEROSIS

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Background: The phase 2 CHOICE trial demonstrated that, in multiple sclerosis (MS) patients on a background of interferon beta-1a (IFNβ-1a) therapy, daclizumab was well tolerated and caused a dose-dependent reduction in new/enlarged gadolinium-enhancing (Gd+) lesions of 72% compared with IFNβ-1a alone. Clinical efficacy was associated with a marked expansion of immunoregulatory CD56bright natural killer (NK) cells. These data and ongoing studies support investigation of daclizumab high-yield process (DAC HYP) in the clinical management of MS. Objectives: To test the superiority of DAC HYP, a humanized monoclonal anti-CD25 antibody, as compared with IFNβ-1a in preventing relapses and slowing disability in subjects with relapsing-remitting MS, and to identify predictive biomarkers of treatment response. Methods: The DAC HYP Efficacy Compared to Interferon Beta 1a StuDy for Multiple SclErosis (DECIDE) trial is a global, phase 3, double-blind active comparator study. Eligible subjects (N = 1500) are randomized 1:1 to receive either 150 mg of subcutaneous DAC HYP every 4 weeks or 30 g intramuscular IFNβ-1a once per week for a minimum of 96 weeks. Results: The effects of DAC HYP will be assessed via annualized relapse rate (primary efficacy end point), brain magnetic resonance imaging (MRI) (T2-hyperintense and T1-hypointense lesions, Gd+ lesions, brain atrophy), sustained disability progression, Multiple Sclerosis Functional Composite scores, cognitive testing, and visual function. Safety and tolerability throughout the study and follow-up will be evaluated by a battery of physical, neurologic, and psychological examinations. Further, pharmacodynamic and pharmacogenetic analyses of prospectively collected samples will be performed to identify potential biomarkers that predict clinical responses to DAC HYP. Conclusions: The DECIDE trial is designed to provide a definitive assessment of the efficacy and safety of DAC HYP in comparison with an established standard of MS care and a confirmatory assessment of CD56bright NK cell expansion as a marker of optimal response to DAC HYP.

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