Title:

Safety, Resistance, and Efficacy Results from a Phase IIIb Study of Conventional- and Double-Dose Oseltamivir Regimens for Treatment of Influenza in Immunocompromised Patients.

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Abstract:

INTRODUCTION: Immunocompromised patients infected with influenza exhibit prolonged viral shedding and higher risk of resistance. Optimized treatment strategies are needed to reduce the risk of antiviral resistance. This phase IIIb, randomized, double-blind study (NCT00545532) evaluated conventional-dose or double-dose oseltamivir for the treatment of influenza in immunocompromised patients.

METHODS: Patients with primary or secondary immunodeficiency and influenza infection were randomized 1:1 to receive conventional-dose oseltamivir (75 mg adolescents/adults [>= 13 years]; 30-75 mg by body weight in children [1-12 years]) or double-dose oseltamivir (150 or 60-150 mg, respectively), twice daily for an extended period of 10 days. Nasal/throat swabs were taken for virology assessments at all study visits. Co-primary endpoints were safety/tolerability and viral resistance. Secondary endpoints included time to symptom alleviation (TTSA) and time to cessation of viral shedding (TTCVS).

RESULTS: Of 228 patients enrolled between February 2008 and May 2017, 215 (199 adults) were evaluable for safety, 167 (151 adults) for efficacy, and 152 (138 adults) for resistance. Fewer patients experienced an adverse event (AE) in the conventional-dose group (50.5%) versus the double-dose group (59.1%). The most frequently reported AEs were nausea, diarrhea, vomiting, and headache. Fifteen patients had post-baseline resistance, more commonly in the conventional-dose group (n = 12) than in the double-dose group (n = 3). In adults, median TTSA was similar between arms, while median TTCVS was longer with conventional dosing.

CONCLUSIONS: Oseltamivir was well tolerated, with a trend toward better safety/tolerability for conventional dosing versus double dosing. Resistance rates were higher with conventional dosing in this immunocompromised patient population.

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