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Study of NTx®-265: Human Chorionic Gonadotropin (hCG) and Epoetin Alfa (EPO) in Acute Ischemic Stroke Patients (REGENESIS Trial)

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Introduction: Preclinical studies suggest that certain growth factors given in the early days after stroke can improve long-term behavioral outcome. An earlier study ("BETAS trial") found that 3 doses of b-hCG followed by 3 doses of erythropoietin was safe. The current trial (NCT00938314) examined this sequential growth factor study in a Phase IIa, placebo-controlled, double-blind, randomized trial. **Methods:** Entry criteria included NIHSS 8-20, supratentorial ischemic stroke, 24-48 hr post-stroke at start of therapy; tPA administration was an exclusion criterion. Patients received 3 QD doses of SQ b-hCG (10,000 IU) followed by 3 QOD doses of IV erythropoietin (EPO). There were 3 equally sized cohorts, each randomized to active:placebo in a 3:1 ratio: in Cohort 1, EPO dose=4,000 IU; Cohort 2, 12,000 IU; Cohort 3, 20,000 IU. Primary outcome measure was change in NIHSS from enrollment to d90. Secondary outcome measures included modified Rankin Score (mRS) and Barthel Index at day 90, plus an array of exploratory assessments. Due to financial constraints, enrollment was reduced to 96 patients and moved to India (18 sites). **Results:** A total of 8 patients died during the trial, the distribution of which did not differ by treatment assignment. All but 4 living patients received all 6 study doses as planned. Patients were 65 M/21 F, mean (SD) age = 58 (12) yr. At least one 15 minute session of post-stroke OT was provided to 25% of patients; PT, to 81%; and ST, to 29%. Median NIHSS at baseline, prior to therapy, was 12.7, decreasing to 7.9 at d30 and 6.0 at d90. There was no significant difference between active therapy and placebo in any endpoint, whether the 3 Cohorts were examined separately or together. Among those patients who received OT, both the change in NIHSS and the mRS were significantly better among those receiving active therapy as compared to placebo. **Discussion:** The current trial did not find that sequential growth factor therapy initiated 24-48 hours after stroke onset was associated with improved outcome at 90 days based upon the primary outcome measure. The current trial did demonstrate that, in the setting of moderate to severe acute ischemic stroke, sequential hCG and EPO are safe at the EPO doses examined. Future studies might restrict enrollment to those subjects likely to receive physiotherapy.

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