TMS-007

TMS-007, also known as SMTP-7 or BIIB131, is an investigational small-molecule plasminogen activator developed for the acute ischemic stroke treatment. It operates through a novel mechanism that enhances endogenous fibrinolysis by modulating plasminogen conformation and promoting plasminogen-fibrin binding. Additionally, TMS-007 exhibits anti-inflammatory properties via inhibition of soluble epoxide hydrolase.

In a Phase 2a clinical trial, TMS-007 demonstrated a favorable safety profile, with no incidence of symptomatic intracranial hemorrhage. The study also reported positive effects on blood vessel reopening and patient functional recovery, even when administered up to 12 hours after symptom onset.

In May 2021, Biogen exercised its option to acquire TMS-007 from TMS Co., Ltd., based on the promising Phase 2a data. This acquisition included an upfront payment and potential milestone payments, reflecting Biogen's commitment to advancing stroke therapies.

As of November 2024, TMS-007 is undergoing further clinical development to assess its efficacy and safety in treating acute ischemic stroke. The ongoing studies aim to establish its potential as a next-generation thrombolytic agent with an extended treatment window compared to current therapies.

JX10 (formerly TMS-007), a Stachybotrys microspora triprenyl phenol family member, may extend this therapeutic window.

Methods: In this multicenter, randomized, double-blind, placebo-controlled, dose-escalation phase 2a study, JX10 or placebo was administered as a single intravenous infusion to Japanese patients with acute ischemic stroke who were unable to receive tissue-plasminogen activator or thrombectomy within 12 hours of last known normal. The primary endpoint was the incidence of symptomatic intracranial hemorrhage with a worsening National Institutes of Health Stroke Scale score of ≥4 points within 24 hours of drug administration (symptomatic intracranial hemorrhage incidence).

Results: Ninety patients received either placebo (n=38; female 26.3%) or JX10 at 1, 3, or 6 mg/kg (n=6, 18, 28; female 0%, 33.3%, and 42.9%, respectively). Median age (range) and baseline median (range) National Institutes of Health Stroke Scale scores were respectively 76.5 (42-87) and 8 (6-21) for the combined JX10 cohort (JX10 Cohorts) and 75.0 (34-85) and 8 (6-22) for placebo. Median (range) dosing time since last known normal was 9.5 (5.0-12.1) and 10.0 (3.7-12.0) hours for JX10 Cohorts and placebo, respectively. Symptomatic intracranial hemorrhage incidence was 0% (0/52 [95% CI, 0.0-5.6]) for JX10 Cohorts versus 2.6% (1/38 [95% CI, 0.1-13.8]) for placebo (P=0.42). Vessel patency at 24 hours (secondary endpoint) in patients with baseline arterial occlusive lesion score <3 (39/90) improved in 58.3% (14/24) of patients in JX10 Cohorts versus 26.7% (4/15) for placebo (odds ratio, 4.23 [95% CI, 0.99-18.07]). In JX10 Cohorts, a significantly higher proportion of patients had modified Rankin Scale scores of 0 to 1 on day 90 (secondary end point) versus placebo (JX10: 21/52, 40.4% versus placebo: 7/38, 18.4%; P=0.03).

Conclusions: JX10 was well tolerated and may expand the acute ischemic stroke therapeutic window as a novel thrombolytic agent.

Registration: URL: https://rctportal.niph.go.jp/en; Unique identifier: jRCT2080223786 [1)]

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Niizuma K, Nishimura N, Hasegawa K, Moritoyo T, Kudo K, Bell J, Wald M, Umeda Y, Kuribayashi K, Toda Y, Tominaga T, Hasumi K. Anti-Inflammatory Thrombolytic JX10 (TMS-007) in Late Presentation of Acute Ischemic Stroke. Stroke. 2024 Nov 7. doi: 10.1161/STROKEAHA.124.048464. Epub ahead of print. PMID: 39508107.