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A randomized, placebo-controlled phase III trial of an autologous, formalin-fixed tumor vaccine for newly diagnosed glioblastoma: trial protocol

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Abstract

This multi-institutional, double-blind, randomized, placebo-controlled phase III trial was designed to evaluate the efficacy and safety of Cellm-001, an autologous formalin-fixed brain tumor immunostimulant, for newly diagnosed glioblastoma with gross total resection to prolong overall survival (OS) and prevent recurrence after surgery. One hundred twelve patients are to be randomized 1:1 to either Cellm-001 with standard chemoradiotherapy (CRT) or saline solution with standard CRT. Randomization is based on the following stratified randomization criteria: age, Karnofsky Performance Status, and the presence or absence of photodynamic therapy (PDT). The primary endpoint is OS and secondary outcomes are progression-free survival (PFS), OS and PFS with and without radiographically residual lesions as subgroups, OS and PFS with and without PDT, p53-negative OS and PFS, high Cluster of Differentiation-8 score OS and PFS, OS associated with death in primary disease, and 24-month OS and PFS rates. All institutions received ethical committee approval and patient enrollment began in 2021.

Importance of the study: Given the growing interest in immunotherapy (IMT), we developed an autologous formalin-fixed tumor vaccine (AFTV) manufactured from the patient's own glioblastoma multiforme (GBM) tissue in paraffin-embedded blocks made from the resected tumor and a double-blind, randomized phase IIB trial of AFTV with temozolomide in newly diagnosed GBM was conducted. The 3-year progression-free survival (PFS) rate for patients with gross total resection (GTR) on imaging tended toward improvement: 81% in the AFTV group versus 46% in the placebo group (P = .067). Based on these IIB results, the feasibility of conducting a phase III trial was confirmed for IIB-eligible patients with total resection. We here plan to conduct the world's first double-blind, randomized, placebo-controlled phase III trial using Cellm-001 to demonstrate autologous tumor immunostimulant efficacy. This IMT, in combination with sub-analyses (GTR, P53 status, CD8 score, and other factors) to be validated, is expected to be a breakthrough in effective standards of care for the treatment of GBM.

Trial registration: Registry number: jRCT2031200153; Date of Registration: 20 /October, /2020; Date

of First Patient Enrollment: 14 /January/, 2021.

Keywords: glioblastoma; immunotherapy; randomized controlled trial; temozolomide; tumor immunostimulant.