Background Standard aggressive therapy of glioblastoma (GBM), which includes maximum safe resection, concurrent radiation therapy and temozolomide chemotherapy (RT/TMZ) followed by maintenance TMZ, is associated with a 25% 2-year overall survival (OS). Adding treatment with AV-GBM-1, a vaccine consisting of autologous dendritic cells (DC) pulsed with autologous tumor antigens (ATA) may improve OS by inducing and/or enhancing the host anti-GBM immune response. Methylation of the O-6-methylguanine-DNA methyltransferase (MGMT) gene promoter, and mutation of the gene for isocitrate dehydrogenase (IDH) are favorable prognostic markers in newly diagnosed GBM. An objective of a multicenter phase II clinical trial was to determine whether these markers were still prognostic for OS in patients treated with adjunctive AV-GBM-1.

Methods Key eligibility criteria for intent-to-treat (ITT) enrollment were: (1) confirmation of primary GBM, (2) successful GBM cell culture, (3) collection of sufficient numbers of monocytes (MC) by leukapheresis, (4) Karnofsky Performance Status 70 or greater after recovery from surgery, and (5) plan to treat with concurrent RT/TMZ. AV-GBM-1 was manufactured while patients were being treated with RT/TMZ. Interleukin-4 and granulocyte-macrophage colony stimulating factor (GM-CSF) were used to differentiate DC from MC. Each vaccine consisted of autologous DC incubated with ATA from the lysate of irradiated cultured GBM cells grown in serum-free media with factors that favor survival and proliferation of stem cells and early progenitor cells (tumor-initiating cells). After recovery from RT/TMZ, intent was to vaccinate for up to six months with cryopreserved AV-GBM-1 admixed with 500 mg GM-CSF. All patients had testing for MGMT-methylation and IDH-mutation. OS was calculated from date of ITT enrollment.

Results 60 patients were enrolled during August 2018 to January 2020. MGMT promoter methylation was detected in 21 (35%), mutated IDH in 7 (12%), and one or both in 25 (42%). At a minimum follow-up of 15 months, median OS had not been reached for patients with a methylated MGMT promoter, IDH mutation, or one or both, compared to 14.6 months for 38 with unmethylated MGMT promoter (p=0.026), 14.7 months for 53 with IDH wild-type (p=0.044), and 14.6 months for 35 who had neither (p=0.017). 18-month OS rates were 59% vs 35% for MGMT promoter methylation, 71% vs 40% for IDH mutation and 58% vs 32% for either.

Conclusions Both MGMT promoter methylation and IDH mutation were associated with a substantial and similar survival benefit in primary GBM patients treated with AV-GBM-1 in addition to standard aggressive therapy.

Trial Registration ClinicalTrials.gov NCT03400917

Ethics Approval This study was approved by the Western IRB, approval number 20182582; all participants gave written informed consent before taking part

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