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# Recurrent Glioblastoma Treated With Recombinant Poliovirus

Treating glioblastoma (GBM) with an oncolytic virus (OV) has been an attractive avenue of therapy for over 20 yr. GBM has been particularly suited for OV therapy due to the tumor's confinement to one organ compartment, lack of distant metastases, and growth being surrounded mainly by postmitotic cells, which allows for the use of viruses that require active cells cycles for replication.[1] Recently, in the *New England Journal of Medicine*, Desjardins et al[2] reported a novel technique for convection enhanced delivery (CED) of recombinant poliovirus for patients with recurrent GBM.

The authors evaluated the therapeutic potential of intratumoral CED of the recombinant nonpathogenic polio-rhinovirus chimera (PVSRIPO) in a dose-escalation phase followed by a dose-expansion phase. The agent introduced was a live attenuated poliovirus type 1 vaccine with a modified internal ribosome entry site restricting its neurovirulence due to its inability to recruit host ribosomes for protein synthesis. PVSRIPO subsequently targeted glioma cells through coreceptor CD155, a high-affinity ligand upregulated on malignant cells.[3]

The primary objective of this phase 1 clinical trial was to determine the toxicity profile of the virus. Seven 50% tissue culture infectious doses ($TCID_{50}$) were assessed: $10^7$ to $10^{10}$. A total of 61 patients were assessed and a toxicity dose was determined to be at a dose level of $10^7$ $TCID_{50}$. The most common AEs in the dose-expansion phase included headache (52%), pyramidal tract syndrome (50%), seizure (45%), dysphasia (28%), and cognitive disturbance (25%). A grade 4 intracranial hemorrhage occurred following catheter removal in the last patient who was treated with dose level 5. In total, 2 deaths occurred—one patient (4.8 mo later) who received dose level −2 had a seizure likely relating to tumor progression and a second patient (10.5 mo later) who received dose level −1.

The median survival (OS) of patients who received PVSRIPO (n = 61) vs those in the matched historic control (n = 104) was 12.5 vs 11.3 mo. Overall survival in the PVSRIPO vs historic control at 24 mo was 21% vs 14.4%, and at 36 mo 21% vs 4%.

The authors also investigated if patients with IDH1 R132 mutations influenced the OS data. Survival data were done only on patients with nonmutant IDH1 R132 GBM (n = 45) with a median OS of 12.5 mo, the same as that of all 61 patients who received PVSRIPO. Thus, this trial's survival data showed no influence of IDH1 R132 status on results. Post PVSRIPO administration, 4 patients underwent tumor resection and 34 patients received bevacizumab every 3 wk during the dose-expansion phase. Other chemotherapeutics that were given to certain patients post PVSRIPO included lomustine, CPT-11, marizomib, and carboplatin. Survival among patients who received bevacizumab did not enhance survival data. In fact, PVSRIPO patients who received bevacizumab every 3 wk postinfusion did not differ from those who were not treated with this regimen. Also, survival data on patients who received any type of bevacizumab regimen post PVSRIPO showed significantly worse survival than those who were not administered any bevacizumab.

Desjardins et al[2] report impressive early trial results for the efficacy of utilization of the poliovirus for recurrent GBM. Limitations of the study include the lack of a blinded control group although the authors provided a fairly matched control patient cohort. Neurovirulence was not reported, but there were significant adverse events that require further evaluation to assess whether the risk of the procedure outweigh the survival benefits. Additional clinical investigation in a phase 2 trial is necessary to determine the efficacy of this novel treatment modality.

## Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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## REFERENCES

1. Wollmann G, Ozduman K, van den Pol AN. Oncolytic virus therapy for glioblastoma multiforme: concepts and candidates. *Cancer J*. 2012;18(1):69-81.
2. Desjardins A, Gromeier M, Herndon JE, 2nd, et al. Recurrent glioblastoma treated with recombinant poliovirus. *N Engl J Med*. 2018;379(2):150-161.
3. Merrill MK, Bernhardt G, Sampson JH, Wikstrand CJ, Bigner DD, Gromeier M. Poliovirus receptor CD155-targeted oncolysis of glioma. *Neuro Oncol*. 2004;6(3):208-17.