PVSRIPO

PVSRIPO, or PVS-RIPO, is the name of a modified poliovirus that has shown promise for treating cancer. It is the focus of clinical trials being conducted at Duke University.

PVS-RIPO consists of a genetically modified nonpathogenic version of the oral poliovirus Sabin type 1. The internal ribosome entry site (IRES) on the poliovirus was replaced with the IRES from human rhinovirus type 2 (HRV2), to avoid neurovirulence. Once administered, the virus enters and begins replicating within cells that express CD155/Necl5, which is an onco-fetal cell adhesion molecule that is common across solid tumors.

A website at Duke University describes many of properties of PVSRIPO, and historical background about using viruses to oppose cancer.

The FDA approved clinical trials with PVS-RIPO in brain tumor patients recently. Since May 2012, five brain tumor patients have been treated. Remarkably, there have been no toxic side effects with PVS-RIPO whatsoever, even at the highest possible dose (10 billion infectious virus particles).

The potential value of PVSRIPO was the focus of a 2015 story on Newsmax, and a 2015 story on 60 Minutes.

In May 2016 the US FDA granted it Breakthrough therapy designation for Glioblastoma.

Desjardins et al., enrolled consecutive adult patients who had recurrent supratentorial WHO grade IV malignant glioma, confirmed on histopathological testing, with measurable disease (contrast-enhancing tumor of ≥1 cm and ≤5.5 cm in the greatest dimension). The study evaluated seven doses, ranging between 107 and 1010 50% tissue-culture infectious doses (TCID50), first in a dose-escalation phase and then in a dose-expansion phase.

From May 2012 through May 2017, a total of 61 patients were enrolled and received a dose of PVSRIPO. Dose level -1 (5.0×107 TCID50) was identified as the phase 2 dose. One dose-limiting toxic effect was observed; a patient in whom dose level 5 (1010 TCID50) was administered had a grade 4 intracranial hemorrhage immediately after the catheter was removed. To mitigate locoregional inflammation of the infused tumor with prolonged glucocorticoid use, dose level 5 was deescalated to reach the phase 2 dose. In the dose-expansion phase, 19% of the patients had a PVSRIPO-related adverse event of grade 3 or higher. Overall survival among the patients who received PVSRIPO reached a plateau of 21% (95% confidence interval, 11 to 33) at 24 months that was sustained at 36 months.

Intratumoral infusion of PVSRIPO in patients with recurrent WHO grade IV malignant glioma confirmed the absence of neurovirulent potential. The survival rate among patients who received PVSRIPO immunotherapy was higher at 24 and 36 months than the rate among historical controls. (Funded by the Brain Tumor Research Charity and others; ClinicalTrials.gov number, NCT01491893 .) [1)].

In a review, Gromeier et al. explain the mechanisms of recombinant poliovirus, PVSRIPO, which is currently in phase I clinical trials against recurrent glioblastoma. We focus on an unusual host:virus

relationship defined by the simple and cytotoxic replication strategy of poliovirus, which generates inflammatory perturbations conducive to tumor antigen-specific immune priming [2)].

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Desjardins A, Gromeier M, Herndon JE 2nd, Beaubier N, Bolognesi DP, Friedman AH, Friedman HS, McSherry F, Muscat AM, Nair S, Peters KB, Randazzo D, Sampson JH, Vlahovic G, Harrison WT, McLendon RE, Ashley D, Bigner DD. Recurrent Glioblastoma Treated with Recombinant Poliovirus. N Engl J Med. 2018 Jul 12;379(2):150-161. doi: 10.1056/NEJMoa1716435. Epub 2018 Jun 26. PubMed PMID: 29943666; PubMed Central PMCID: PMC6065102.
2)
Gromeier M, Nair SK. Recombinant Poliovirus for Cancer Immunotherapy. Annu Rev Med. 2018 Jan 29;69:289-299. doi: 10.1146/annurev-med-050715-104655. PubMed PMID: 29414253; PubMed Central PMCID: PMC6013836.