

## Comment to “Recurrent Glioblastoma Treated with Recombinant Poliovirus”

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The median follow-up of the malignant glioma patients who received surgical resection combined with radiochemotherapy is 16 months. The recurrence of malignant glioma is unavoidable. Although the patient with recurrent glioblastoma has multiple choices of therapy, the 5-year survival rate is still less than 5%, and the average survival time is less than 12 months.<sup>[1]</sup> Currently, there is no single second-line drug can have survival benefits.

Due to the drug distribution in the central nervous system, acute systemic toxic reaction, central nervous system toxic reaction, and bone marrow suppression, the target medicine for recurrent glioma now can only have a very limited application. With the immunotherapy rising up in recent years, especially the immune checkpoint blockade of cytotoxic T-lymphocyte-associated antigen 4, programmed death 1 (PD-1) and others have been encouraging efforts in multiple noncentral nervous system malignant tumors, immunotherapy has been a hot issue of the treatment of glioblastoma once upon a time. However, compared with the use of bevacizumab, the clinical trial has proven that the single use of the PD-1 monoclonal antibody cannot have a vivid survival time benefit for the patient with recurrent glioblastoma.<sup>[2]</sup> The reason why the immune checkpoint inhibitor produces a very little effect is that the T-cells around the tumor to be recruited to kill the glioma cell are insufficient, while the cells and substances to inhibit the immune function are plenty.<sup>[3]</sup> Therefore, designing a T-cell driven immune reaction to kill cancer cells is the key point to solve the glioblastoma immune tolerance.

The research of Duke University makes good use of poliovirus which can kill neurons specifically.<sup>[4]</sup> Based on this mechanism, the poliovirus can be applied to treat glioblastoma. Recombinant nonpathogenic polio-rhinovirus chimera (PVSRIPO) recognizes the CD155 overexpressed by recurrent glioma as its target and attacks glioma cells. However, the interferon-responsive sequence element

component of recombinant virus only aims at the neuron, by which the virus can refrain itself from harming neuron easily and causing recovery difficultly, and also avoids some problems such as the toxicity and side effect of viroimmunotherapy. PVSRIPO recombinant virus can dissolve tumor cells and release antigen to activate an immune response, and it can also infect and arouse the immune cell, such as dendrite cells and macrophages, leading to interferon release and secondary immune responses, which might have crucial effects on eliminating the glioma cells. The dual ability of immune activation deals with the bottleneck of the immunotherapy of recurrent glioma. The results from clinical trials revealed that recombinant poliovirus can significantly prolong the survival time of glioblastoma and the 3-year survival rates rise from 4% to 21%, which is a markable advance of the treatment of glioblastoma. For the clinical safety, about 69% had mild adverse reactions including the symptoms of nervous system such as headache, convulsion, and hemiparesis. Therefore, based on the good data of its metaphase experiment, the American Food and Drug Administration has granted the PVSRIPO breakthrough therapy qualification certification.

There is still a problem existing in the recombinant lentivirus treatment. Not all patients can start the immune response well and benefit from it. Hence, it requires a long way to go to cure the glioblastoma with PVSRIPO therapy radically. In the future, PVSRIPO therapy is expected to combine with other chemotherapies and deal with some aspects of

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**Received:** 09-08-2018 **Edited by:** Peng Lyu  
**How to cite this article:** Wang P, Chen GZ. Comment to “Recurrent Glioblastoma Treated with Recombinant Poliovirus”. Chin Med J 2018;131:2645-6.

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www.cmj.org

**DOI:**  
10.4103/0366-6999.244121

immune tolerance, which will provide some ideas of curing other tumors.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

### REFERENCES

1. Taal W, Oosterkamp HM, Walenkamp AM, Dubbink HJ, Beerepoot LV, Hanse MC, *et al.* Single-agent bevacizumab or lomustine versus a combination of bevacizumab plus lomustine in patients with recurrent glioblastoma (BELOB trial): A randomised controlled phase 2 trial. *Lancet Oncol* 2014;15:943-53. doi: 10.1016/S1470-2045.
2. Gilbert MR, Dignam JJ, Armstrong TS, Wefel JS, Blumenthal DT, Vogelbaum MA, *et al.* *N Engl J Med* 2014;370:699-708. doi: 10.1056/NEJMoa1308573.
3. Nduom EK, Weller M, Heimberger AB. Immunosuppressive mechanisms in glioblastoma. *Neuro-Oncology* 2015;17(suppl 7):vii9-14. doi: 10.1093/neuonc/nov151.
4. Desjardins A, Gromeier M, Herndon JE 2<sup>nd</sup>, Beaubier N, Bolognesi DP, Friedman AH, *et al.* Recurrent glioblastoma treated with recombinant poliovirus. *N Engl J Med* 2018;379:150-61. doi:10.1056/NEJMoa1716435.