Valganciclovir

The potential benefit of valganciclovir in glioblastoma has generated great interest, but efficacy remains to be established in a randomized trial. Also, early stage immunotherapy trials targeting cytomegalovirus (CMV) have shown promise. In the near future we will know more answers to these questions, and although areas of controversy may remain, and the mechanisms and roles of CMV in tumor growth are yet to be clearly defined, this widespread virus may have created important new therapeutic concepts and opportunities for the treatment of glioblastoma [1].

Case series

Forty-two glioblastoma patients were randomized in double-blind fashion to receive Valganciclovir or placebo in addition to standard therapy for 6 months. Magnetic resonance images were obtained before and immediately and 3 and 6 months after surgery to evaluate treatment efficacy by measuring contrast enhancing tumor volume (primary end point). Survival data were analyzed for patients and controls in explorative analyses to aid the design of future randomized trials. Trends but no significant differences were observed in tumor volumes in Valganciclovir and placebo patients at 3 (3.58 vs. 7.44 cm3, respectively, $p = 0.2881$) and 6 (3.31 vs. 13.75 cm3, $p = 0.2120$) months. Median overall survival (OS) was similar in both groups (17.9 vs. 17.4 months, $p = 0.430$). Patients could take Valganciclovir for compassionate use after the study phase. Explorative analyses showed an OS of 24.1 months (95% CI, 17.4-40.3) in patients receiving >6 months of Valganciclovir (Val > 6M) versus 13.1 months (95% CI, 7.9-17.7, $p < 0.0001$) in patients receiving Valganciclovir for 0 or <6 months, and 13.7 months (95% CI, 6.9-17.3, $p = 0.0031$) in contemporary controls. OS at 4 years was 27.3% in Val>6M patients versus 5.9% in controls ($p = 0.0466$). Prolonged OS in Val>6M patients suggest that future randomized trials are warranted and should evaluate whether continuous antiviral treatment can improve outcome in glioblastoma patients [2].

Case reports

Peredo et al. describe a patient with GMB receiving valganciclovir (VGCV) in whom an intracerebral microdialysis catheter was implanted and ganciclovir (GCV) concentrations in brain extracellular fluid (BECF) and serum were monitored. GCV was rapidly absorbed. Cmax values (at 3 h) in serum and BECF were 19.6 and 10.2 µmol/L, T½ values were 3.2 and 4.5 h, and plasma and BECF AUC0-∞ values were 90.7 and 75.9 µmol h/L, respectively. Thus, VGCV treatment results in significant intracerebral levels of GCV that may be sufficient for therapeutic effects. Further studies of this drug in patients with GBM are warranted [3]

1)
Lawler SE. Cytomegalovirus and glioblastoma; controversies and opportunities. J Neurooncol. 2015 Feb 15. [Epub ahead of print] PubMed PMID: 25682092.
2)
Stragliotto G, Rahbar A, Solberg NW, Lilja A, Taher C, Orrego A, Bjurman B, Tammik C, Skarman P, Peredo I, Söderberg-Nauclér C. Effects of valganciclovir as an add-on therapy in patients with cytomegalovirus-positive glioblastoma: a randomized, double-blind, hypothesis-generating study. Int J Cancer. 2013 Sep 1;133(5):1204-13. doi: 10.1002/ijc.28111. Epub 2013 Mar 13. PubMed PMID: 23404447.
3)
Peredo I, Helldén A, Wolmer-Solberg N, Pohanka A, Stragliotto G, Rahbar A, Ståhle L, Bellander BM,

Söderberg-Nauclér C. Ganciclovir concentrations in the cerebral extracellular space after valganciclovir treatment; a case study. BMJ Case Rep. 2015 Dec 15;2015. pii: bcr2014207694. doi: 10.1136/bcr-2014-207694. PubMed PMID: 26670887.