A phase I trial of carboplatin administered by convection-enhanced delivery to patients with recurrent/progressive glioblastoma multiforme.

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Abstract
Glioblastoma multiforme (GBM) is the commonest primary malignant brain tumour in adults. Standard treatment comprises surgery, radiotherapy and chemotherapy; however this condition remains incurable as these tumours are highly invasive and involve critical areas of the brain making it impossible to remove them surgically or cure them with radiotherapy. In the majority of cases the tumour recurs within 2 to 3cm of the original site of tumour resection. Furthermore, the blood-brain barrier profoundly limits the access of many systemically administered chemotherapeutics to the tumour. Convection-enhanced delivery (CED) is a promising technique of direct intracranial drug delivery involving the implantation of microcatheters into the brain. Carboplatin represents an ideal chemotherapy to administer using this technique as glioblastoma cells are highly sensitive to carboplatin in vitro at concentrations that are not toxic to normal brain in vivo. This protocol describes a single-centre phase I dose-escalation study of carboplatin administered by CED to patients with recurrent or progressive GBM despite full standard treatment. This trial will incorporate 6 cohorts of 3 patients each. Cohorts will be treated in a sequential manner with increasing doses of carboplatin, subject to dose-limiting toxicity not being observed. This protocol should facilitate the identification of the maximum-tolerated infused concentration of carboplatin by CED into the supratentorial brain. This should facilitate the safe application of this technique in a phase II trial, treating patients with GBM, as well as for the treatment of other forms of malignant brain tumours, including metastases.

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