Oligonucleotide

Oligonucleotides are short DNA or RNA molecules, oligomers, that have a wide range of applications in genetic testing, research, and forensics. Commonly made in the laboratory by solid-phase chemical synthesis, these small bits of nucleic acids can be manufactured as single-stranded molecules with any user-specified sequence, and so are vital for artificial gene synthesis, polymerase chain reaction (PCR), DNA sequencing, library construction and as molecular probes. In nature, oligonucleotides are usually found as small RNA molecules that function in the regulation of gene expression (e.g. microRNA), or are degradation intermediates derived from the breakdown of larger nucleic acid molecules.

Immunostimulating oligodeoxynucleotides containing unmethylated cytosine-guanosine motifs (CpG-ODN) have shown a promising efficacy in several cancer models when injected locally. A previous phase II study of CpG-ODN in patients with recurrent glioblastoma (GBM) has suggested some activity and has shown a limited toxicity. This multicentre single-blinded randomised phase II trial was designed to study the efficacy of a local treatment by CpG-ODN in patients with de novo glioblastomas.

Patients with a newly diagnosed glioblastoma underwent large surgical resection and CpG-ODN was randomly administrated locally around the surgical cavity. The patients were then treated according to standard of care (SOC) with radiotherapy and temozolomide. The primary objective was 2-year survival. Secondary outcomes were progression free survival (PFS), and tolerance.

Eighty-one (81) patients were randomly assigned to receive CpG-ODN plus SOC (39 patients) or SOC (42 patients). The 2-year overall survival was 31% (19%; 49%) in the CpG-ODN arm and 26% (16%; 44%) in the SOC arm. The median PFS was 9 months in the CpG-ODN arm and 8.5 months in the SOC arm. The incidence of adverse events was similar in both arms; although fever and post-operative haematoma were more frequent in the CpG-ODN arm.

Local immunotherapy with CpG-ODN injected into the surgical cavity after tumour removal and followed by SOC, although well tolerated, does not improve survival of patients with newly diagnosed GBM [1].

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Ursu R, Carpentier A, Metellus P, Lubrano V, Laigle-Donadey F, Capelle L, Guyotat J, Langlois O, Bauchet L, Desseaux K, Tibi A, Chinot O, Lambert J, Carpentier AF. Intracerebral injection of CpG oligonucleotide for patients with de novo glioblastoma-A phase II multicentric, randomised study. Eur J Cancer. 2017 Jan 28;73:30-37. doi: 10.1016/j.ejca.2016.12.003. [Epub ahead of print] PubMed PMID: 28142059.