Temozolomide

- TRIM22 promotes glioblastoma development by ubiquitinating Bcl-2
- Clinical outcome and deep learning imaging characteristics of patients treated by radio-chemotherapy for a "molecular" glioblastoma
- Efficacy of individualized orelabrutinib-based regimens in relapsed or refractory central nervous system lymphoma
- Novel desensitization protocol utilizing conventional formulations to mitigate Temozolomide-Related skin hypersensitivity
- Bufalin enhanced temozolomide efficacy by promoting EGFR protein degradation in glioblastoma
- Nimotuzumab Combined With Chemoradiation Therapy in Newly Diagnosed Pediatric Diffuse Intrinsic Pontine Glioma
- [¹⁸F]FET PET-Guided management of pseudoprogression in glioblastoma (FET POPPING): the study protocol for a diagnostic randomized clinical trial
- Radio-chemotherapy and metformin selectively modulate the heterogeneous landscape of glioma with ribosome biogenesis, long non coding RNA and immune-escape markers as major player

Temozolomide (Temodar®), an oral alkylating agent, is a derivative of Dacarbazine (DTIC®). It is a prodrug that undergoes rapid non-enzymatic conversion at physiologic pH to the active metabolite monomethyl triazenoimidazole carboxamide (MTIC). The mutagenic/cytotoxic effect of MTIC is associated with alkylation (adding an alkyl group, the smallest of which is a methyl group) to DNA at various sites primarily at the O6 and N7 positions on guanine.

Cells can repair this damage via O6- methylguanine-DNA methyltransferase (MGMT), a protein which may be deficient to some degree in various tumors (especially astrocytomas, IDH-mutant which renders them more susceptible to temozolomide

Indications

Temozolomide Indications.

Resistance

see Temozolomide resistance.

Rechallenge

Temozolomide rechallenge is a treatment option for MGMT promoter-methylated Glioblastoma recurrence. Alternative strategies need to be considered for patients with progressive glioblastoma without MGMT promoter methylation [1)].

Temozolomide dosage

Temozolomide (TMZ) for malignant gliomas is traditionally dosed in 5 out of a 28-day cycle, however alternative regimens exist, including dose-dense. Continuous daily dosing is available, but the acceptable dose and duration of therapy is unknown.

Zhou et al. document a 40-year-old male with recurrent anaplastic astrocytoma, IDH mutant and MGMT promotor methylation negative, who has well-tolerated continuous daily TMZ for 20 months at 100 mg per day for nearly the length of this period. A trial at 80 mg per day demonstrated disease progression with response upon return to 100 mg per day. Prior to the daily TMZ, the patient underwent three surgical resections, radiation therapy with concurrent TMZ according to the EORTC NCIC protocol, and subsequently bevacizumab in combination with use of the Optune device. Long-term survival of patients with recurrent malignant gliomas is uncommon, and currently no standard treatment strategies exist for these patients. We present this case to demonstrate the tolerability and dose dependency of prolonged daily TMZ dosing as a therapeutic option for recurrent anaplastic astrocytomas [2].

Adverse effects

Temozolomide adverse effects.

1)
Weller M, Tabatabai G, Kästner B, Felsberg J, Steinbach JP, Wick A, Schnell O, Hau P, Herrlinger U, Sabel MC, Wirsching HG, Ketter R, Bähr O, Platten M, Tonn JC, Schlegel U, Marosi C, Goldbrunner R, Stupp R, Homicsko K, Pichler J, Nikkhah G, Meixensberger J, Vajkoczy P, Kollias S, Hüsing J, Reifenberger G, Wick W; DIRECTOR Study Group. MGMT Promoter Methylation Is a Strong Prognostic Biomarker for Benefit from Dose-Intensified Temozolomide Rechallenge in Progressive Glioblastoma: The DIRECTOR Trial. Clin Cancer Res. 2015 May 1;21(9):2057-64. doi: 10.1158/1078-0432.CCR-14-2737. Epub 2015 Feb 5. PubMed PMID: 25655102.
2)
Zhou Z, Howard TA, Villano JL. Long-term daily temozolomide with dose-dependent efficacy in MGMT promotor methylation negative recurrent high-grade astrocytoma. Cancer Chemother Pharmacol. 2017 Aug 8. doi: 10.1007/s00280-017-3415-5. [Epub ahead of print] PubMed PMID: 28791452.