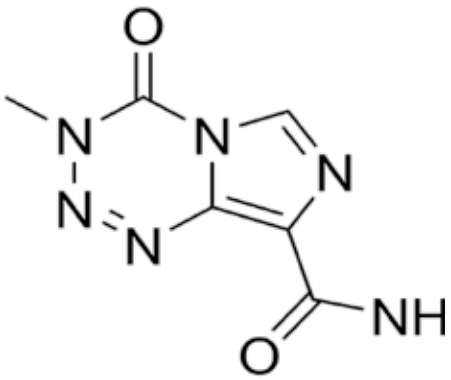
Temozolomide
and MGMT Inhibitors

Temozolomide (T1849) is an alkylating agent used in the treatment of cancers. Like other alkylating agents, temozolomide attaches an alkyl group to DNA at N7 and O6 positions of guanine bases and at the N3 position of adenine bases, interfering with DNA replication[1]. Because cancer cells generally proliferate faster and with less error correcting than normal cells, cancer cells are more susceptible to the effects of these compounds.

Temozolomide has been well studied as a stand-alone therapy and is used to treat oligodendrocytoma, melanoma, and glioblastoma multiforme. Recently, this compound has been studied as a combination therapy. Research suggests additional benefit when temozolomide is co-administered with inhibitors of *O6*-methylguanine DNA methyltransferase (MGMT), an enzyme that repairs alkylations. Compounds that inhibit MGMT include **Lomeguatrib (L5750)** and ***O6*-Benzylguanine (B1855)**[2-3]. In models of glioblastoma, the combination of temozolomide and green tea component **Epigallocatechin Gallate (EGCG, E6234)** improves survival time compared to temozolomide alone[4]. EGCG's inhibition of endoplasmic reticulum chaperone GRP78 is thought to contribute significantly to its anticancer efficacy when administered as a combination therapy with other treatments.



T1849 Temozolomide

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4. Chen TC, Wang W, Golden EB, et al. Cancer Lett. 2011 Mar 28;302(2):100-8.