Besides the standard therapeutic drug temozolomide (TMZ), quinoline-based antimalarial drugs such as hydroxychloroquine (HCQ) and BH3 mimetics such as AT101 were considered as possible drugs for GBM therapy.

Adamski et al. investigated the effects of sequentially applied single and combined TMZ, HCQ and AT101 treatments in a long-term stimulation GBM in vitro model. We performed all investigations in parallel in human astrocytes and two differentially TMZ-responsive human GBM cell lines and adjusted used drug concentrations to known liquor/plasma concentrations in patients. We determined amounts of dead cells and still remaining growth rates and depicted our results in a heatmap-like summary to visualize which sequential long-term treatment schedule seemed to be most promising.

They showed that sequential stimulations yielded higher cytotoxicity and better tumor growth control in comparison to single TMZ treatment. This was especially the case for the sequences TMZ/HCQ and TMZ + AT101/AT101 which was as effective as the non-sequential combination TMZ + AT101. Importantly, those affected both less and more TMZ-responsive glioma cell lines, whilst being less harmful for astrocytes in comparison to single TMZ treatment.

Sequential treatment with mechanistically different acting drugs might be an option to reduce side effects in long-term treatment, for example in local administration approaches [1].

1)
Adamski V, Schmitt C, Ceynowa F, Adelung R, Lucius R, Synowitz M, Hattermann K, Held-Feindt J. Effects of sequentially applied single and combined temozolomide, hydroxychloroquine and AT101 treatment in a long-term stimulation glioblastoma in vitro model. J Cancer Res Clin Oncol. 2018 Jun 1. doi: 10.1007/s00432-018-2680-y. [Epub ahead of print] PubMed PMID: 29858681.