ATPS-39. COMBINATORY EFFECT OF A NEWLY DESIGNED BIGUANIDE (HL156A) AND TEMOZOLOMIDE AGAINST GLIOBLASTOMA TUMORSHHERE

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BACKGROUND: Glioblastoma (GBM) is a lethal disease in spite of recent therapeutic progress and new treatment strategies are being required. Recently, biguanide-derived compounds with better pharmacokinetics are being suggested as new therapeutic agents for malignant tumor and their effect against the tumorsphere (TS) were reported. In the present study, effect of a newly designed biguanide, HL156A against glioblastoma tumorsphere (GBM-TS) is assessed. METHODS: We assessed an effect of HL156A, alone or combined with conventional treatment agent temozolomide (TMZ), on the stemness and invasive properties of GBM-TS and survival of orthotopic xenograft animals. RESULTS: HL156A, TMZ and combination, exhibited an inhibitory effect on the stemness of GBM-TS, proven by the sphere formation assay and the assessment of surface marker expression, without affecting viability of cells. The invasive property of GBM-TS was inhibited by HL156A, TMZ and the combination treatment in 3-dimentional collagen matrix invasion assay, but the effect was most prominent in combination treatment. Treatment of the HL156A, alone and with TMZ, repressed epithelial-mesenchymal transition (EMT) related gene expression. Gene ontology class comparison of TMZ and combination treatment groups reveals altered expression of gene sets involving cellular adhesion and migration. The combined treatment of HL156A and temozolomide showed most prominent survival benefits in the orthotopic xenograft mouse model compared with HL156A and TMZ alone. CONCLUSION: Targeting of GBM-TS by a combination of a newly designed biguanide HL156A and TMZ through the inhibition of stemness and invasion properties of GBM-TS, can be a novel strategy for the treatment of GBM.