

## PubMed

U.S. National Library of Medicine  
National Institutes of Health



Display Settings:  Abstract

Clin Cancer Res. 2010 Jan 1;16(1):154-63.

# The telomerase antagonist, imetelstat, efficiently targets glioblastoma tumor-initiating cells leading to decreased proliferation and tumor growth.

Marian CO, Cho SK, McEllin BM, Maher EA, Hatanpaa KJ, Madden CJ, Mickey BE, Wright WE, Shay JW, Bachoo RM.

Department of Cell Biology, Annette G Strauss Center for Neuro-Oncology, University of Texas, Southwestern Medical Center, Dallas, Texas 75390-9039, USA.

**PURPOSE:** Telomerase activity is one of the hallmarks of cancer and is a highly relevant therapeutic target. The effects of a novel human telomerase antagonist, imetelstat, on primary human glioblastoma (GBM) tumor-initiating cells were investigated *in vitro* and *in vivo*. **EXPERIMENTAL DESIGN:** Tumor-initiating cells were isolated from primary GBM tumors and expanded as neurospheres *in vitro*. The GBM tumor-initiating cells were treated with imetelstat and examined for the effects on telomerase activity levels, telomere length, proliferation, clonogenicity, and differentiation. Subsequently, mouse orthotopic and subcutaneous xenografts were used to assess the *in vivo* efficacy of imetelstat. **RESULTS:** Imetelstat treatment produced a dose-dependent inhibition of telomerase (IC<sub>50</sub> 0.45 micromol/L). Long-term imetelstat treatment led to progressive telomere shortening, reduced rates of proliferation, and eventually cell death in GBM tumor-initiating cells. Imetelstat in combination with radiation and temozolomide had a dramatic effect on cell survival and activated the DNA damage response pathway. Imetelstat is able to cross the blood-brain barrier in orthotopic GBM xenograft tumors. Fluorescently labeled GBM tumor cells isolated from orthotopic tumors, following systemic administration of imetelstat (30 mg/kg every day for three days), showed approximately 70% inhibition of telomerase activity. Chronic systemic treatment produced a marked decrease in the rate of xenograft subcutaneous tumor growth. **CONCLUSION:** This preclinical study supports the feasibility of testing imetelstat in the treatment of GBM patients, alone or in combination with standard therapies.

PMID: 20048334 [PubMed - in process]

[Publication Types](#), [Grant Support](#)

[LinkOut - more resources](#)