Sorafenib acts synergistically in combination with radiotherapy without causing intestinal damage in colorectal cancer

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ABSTRACT

Aims and background. Colorectal cancer is one of the commonest cancers. Chemoradiotherapy gives better results than radiotherapy or chemotherapy in colorectal cancer. To enhance radiosensitivity of tumor cells for chemoradiotherapy, targeted therapy drugs that act as radiosensitizers can be used. In the present study, we provide a scientific rationale for the clinical application of sorafenib as a radiosensitizer in colorectal cancer, without causing significant adverse effects on normal intestinal tissue.

Methods. Three human colorectal adenocarcinoma cell lines (HCT116, HT-29, and SW480) were treated with sorafenib alone, or radiation followed by sorafenib. In vitro tests were performed using colony forming assays, cell cycle analysis, and comet assays. In addition, the effects of sorafenib and radiation therapy on the inhibition HT29 tumor growth and survival of intestinal jejunum crypts were examined in vivo.

Results. Sorafenib increased the radiosensitivity of tumor cells in human colon adenocarcinoma cell lines (HCT116, HT-29, and SW480), as well as in HT-29 xenograft animal models. Sorafenib, in combination with ionizing radiation, induced the accumulation of tumor cells in the G2-M phase and delayed the repair of DNA damage caused by ionizing radiation. The combination of sorafenib and ionizing radiation did not enhance the apoptosis of intestinal crypt cells, compared with the use of radiation alone.

Conclusions. We provide a scientific rationale for the use of sorafenib in combination with radiotherapy in colorectal cancer.