Tumori, 99: 176-182, 2013

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

Youn Kyoung Jeong[1,2], Mi-Sook Kim[3], Ji Young Lee[1], Eun Ho Kim[4], Wonwoo Kim[1], Hunjoo Ha[2], and Jae-Hoon Jeong[1]

[1]Research Center for Radiotherapy, Korea Institute of Radiological and Medical Sciences; [2]Division of Life and Pharmaceutical Sciences, College of Pharmacy, Ewha Womans University; [3]Department of Radiation Oncology, and [4]Division of Heavy Ion Clinical Research, Korea Institute of Radiological and Medical Sciences, Seoul, South Korea

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 HT-29 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.

Key words: colorectal cancer, G2-M arrest, gamma-radiation, jejunum crypt, radiosensitive effect, sorafenib.

Acknowledgments: The study was supported by a grant (code 50541-2012) from the Ministry of Education, Science and Technology, Republic of Korea.

Financial disclosure and conflict of interest statements: None.

Correspondence to: Mi-Sook Kim, MD, PhD, Department of Radiation Oncology, Korea Institute of Radiological and Medical Sciences, 215-4 Gongneung-Dong, Nowon-gu, Seoul 139-706, South Korea.
Tel +82-2-970-1264;
fax +82-2-970-2412;
email mskim@kcch.re.kr

Received September 27, 2012;
accepted December 4, 2012.