Tumori, 98: 257-263, 2012

Tamoxifen in trimodal therapy with cytotoxic drugs and hyperthermia *in vivo* significantly enhance therapeutic efficacy against B16-F10 melanoma

Ana Misir Krpan[1], Sinisa Ivankovic[2], Zdenko Krajina[1], Dusica Ivankovic[3], and Ranko Stojkovic[2]

[1]Center of Oncology and Radiotherapy, Clinic of Oncology and Radiotherapy, University Hospital Center Zagreb, Zagreb; [2]Division for Molecular Medicine, Rudjer Boskovic Institute, Zagreb; [3]Division for Marine and Environmental Research, Rudjer Boskovic Institute, Zagreb, Croatia

ABSTRACT

Aims and background. The aim of the study was to investigate whether use of the antiestrogen tamoxifen and heat treatment in combined therapy with the well-known anticancer drugs cisplatin, dacarbazine and cyclophosphamide enhances their therapeutic efficacy on mouse B16-F10 melanoma *in vivo*. The results of systemic melanoma therapy have been mostly disappointing. Therefore, there is still a great need for strategies that can improve existing chemotherapy options.

Methods and study design. The tumor model for the investigation of antitumor activity was a mouse B16-F10 melanoma transplanted into the footpad of C57BL/6 Zgr/Hr mice. Drugs were given intraperitoneally 15 min before the application of local hyperthermia, and tumor growth and mouse survival were followed.

Results. Hyperthermia alone determined a significant delay of tumor growth, but mouse survival was not affected. In bimodal combinations with hyperthermia, all the tested antitumor drugs significantly increased both tumor growth delay and mouse survival. Tamoxifen alone did not show any inhibitory effect on B16-F10 melanoma *in vivo*. However, in the trimodal therapy with a particular drug and hyperthermia, it potentiated the inhibitory effects of the respective bimodal treatments, especially that of cyclophosphamide and hyperthermia.

Conclusions. Our results obtained on the mouse B16-F10 melanoma *in vivo* confirmed the enhanced therapeutic efficacy of the trimodal therapy tamoxifen, hyperthermia and anticancer drug combinations in melanoma treatment. Further studies should optimize the heat-drug time scheduling and drug doses that will result in the best possible therapeutic achievement for these trimodal therapy options.

Key words: B16-F10 melanoma, cyclophosphamide, hyperthermia, tamoxifen.

Correspondence to: Ranko Stojkovic, Division for Molecular Medicine, Rudjer Boskovic Institute, PO Box 180, HR-10002 Zagreb, Croatia.
Tel/fax +385-1-456 0992;
email stojkov@irb.hr

Received January 20, 2011;
accepted November 18, 2011.