# COMBINED USE OF THE BRADYKININ B1R ANTAGONIST R954 AND THE CHEMOTHERAPEUTIC AGENT DACARBAZINE INCREASED GLOBAL SURVIVAL OF MELANOMA BEARING MICE

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Bradykinin receptor subtype 1 (B1R) has been implicated in tumor progression of cancers, including melanoma. Kinins can improve tumor growth either directly, stimulating tumor cell proliferation or indirectly, by inducing angiogenesis. Previous results from our group showed a delay in murine melanoma engraftment in B1R knockout mice. Here we have investigated the effect of the novel and selective B1R antagonist R-954 on anticancer therapy, evaluating its combination with the chemotherapeutic agent dacarbazine. Initial results showed that the administration of the antagonist R-954 caused a significant decrease in melanoma growth in the early phases of tumor implantation (until 10 days) in C57Bl/6 mice. Compound R-954 did not by itself affect the hemorrhagic area, the necrotic area and the number of newly formed blood vessels within tumors as evaluated by histological analyses. However, while the median survival of control groups varied from 28 to 32 days, the median survival of the group receiving both dacarbazine and R-954 increased significantly to 36 days. The results suggest that R-954 concomitant with dacarbazine may have therapeutic potential. Studies on the mechanisms of combined action of these two drugs are warranted. Supported by FAPESP (98/14247-6).