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# Combined administration of imatinib mesylate and ionizing radiation leads to increased radiosensitivity in the human glioblastoma cell line RuSi RS1

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Abstract  
1564

**Background:** The selective tyrosine kinase inhibitor imatinib mesylate (Gleevec) effectively inhibits the activity of the abl, PDGF receptor (PDGFR) and c-kit tyrosine kinases. Because of the specific target profile of this orally available and generally well tolerated drug, imatinib is under intensive investigation for the potential treatment of other diseases. Malignant gliomas frequently show a high expression of PDGF receptor which is involved in tumorigenesis by formation of an autocrine loop. A role in DNA repair carried out through c-abl and c-kit was previously described both for c-abl and c-kit. In this study we address the potential use of imatinib mesylate and concomitant ionizing radiation (IR) to improve the radiosensitivity of the glioblastoma cell line RuSi RS1.

**Methods:** Cells of the primary glioblastoma cell line RuSi RS1, as well as of the colon cancer cell line WiDr and of BT20, a human breast cancer cell line, were incubated with different concentrations of imatinib mesylate 30 minutes prior to irradiation (doses between 0 and 16 Gy). Western blots were done comparing the different expression of c-abl, PDGFR alpha and beta, and c-kit in the different cell lines. Immunoprecipitation was performed to assess inhibition of the different kinases by imatinib mesylate.

**Results:** Under combined treatment with imatinib and IR a significant shift of the IC50 (dose needed to reduce the survival fraction by 50%) was detected in RuSi RS1 compared to IR alone. This effect was not seen in WiDr or BT20. RuSi RS1 showed an overexpression of PDGFR beta. Inhibition of tyrosine kinase phosphorylation by imatinib could be shown for PDGFR beta and c-abl (the IP failed for c-kit).

**Conclusion:** Concomitant administration of imatinib mesylate and ionizing radiation increases the radiosensitivity of the glioblastoma cell line RuSi RS1. This effect might partly be due to disruption of an autocrine loop of the PDGF/PDGFR system. Inhibition of DNA repair mechanisms in which the tyrosine kinase activity of c-abl and c-kit is involved might be important causes of this observed phenomenon as well.

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