INTRODUCTION. Chemotherapy for cancer often has severe side effects. Dexamethasone is frequently used as co-treatment to prevent nausea and other symptoms. Clinical trials evaluating the impact of dexamethasone on tumor control and survival of cancer patients never have been performed.

METHOD. Several carcinoma cell lines and freshly isolated carcinomas from resected tumors of patients were treated with a variety of chemotherapeutic drugs or $\gamma$-irradiation in the presence or absence of glucocorticoids. Apoptosis was analyzed by flow cytometry, viability by the MTT-assay and protein expression by Western blot analysis or in vivo tumor growth analyzed using xenografts on nude mice.

RESULTS. By measuring apoptosis and viability we found induction of therapy-resistance by DEX in cervical, ovarian, pancreatic, lung, prostate, colorectal and hepatocellular carcinomas and liver metastases. This was shown in freshly isolated tumor cells from patient’s carcinomas or established cell lines. DEX-mediated resistance occurred in response to diverse cytotoxic drugs or radiation. DEX diminished the cytotoxic effect in all examined tumor cells independently of the p53 status or of BAG-1 expression suggesting other underlying molecular mechanisms. Resistance was due to blockade of several key elements within the apoptosis programme. Resistance was detected by measuring apoptosis and viability in vitro or by measuring the size of tumor xenografts on nude mice in vivo (Fig.1). DEX was used in concentrations corresponding to those found in plasma of cancer patients but it induced resistance also in higher or lower...
concentrations. Resistance was longlasting since recovery of full chemosensitivity of DEX pre-treated cervix carcinoma cells needed more than 10 days upon removement of DEX. Other steroids such as hydrocortisone, betamethasone and prednisolone had the same effect. In contrast, non-steroidal anti-emetic agents used in cancer therapy such as serotonin-receptor antagonists or the new NK1 receptor antagonists did not induce therapy resistance.

Fig. 1 Human solid tumors grow faster in the presence of DEX despite chemotherapy

**DISCUSSION.** Glucocorticoids are known to exert pro-apoptotic and anti-proliferative effects in lymphoid cells. Hence, these agents are widely used in cancer therapy. However, our data demonstrate induction of resistance towards cytotoxic therapy by co-treatment with DEX in several carcinomas. These data therefore rise concern about the widespread combined use of steroids with anti-neoplastic drugs and radiation in the clinical management of patients with solid tumors. However, although we confirmed our data by in vitro, ex vivo and in vivo assays, prospective clinical trials are missing as yet.

**REFERENCES.**