

### 3.0 INTRODUCTION

#### 3.1 Rectal Cancer

Until 1990, it was a controversial issue whether or not high-risk stages of rectal cancer should be treated with adjuvant chemotherapy. The Intergroup – 0035 study published by Moertel et al gave a major impulse for the wide acceptance of adjuvant treatment in patients with high-risk colon cancer. The main compound in rectal cancer therapy is 5-Fluorouracil mostly used in various combinations. In the National Cancer Institute Developmental Therapeutics Program for 5-FU (NCS 19893 –G/10) the dose response curves show inhibition only in 8 human colon cancer cell lines in a Log  $10^{-2.5}$  molar sample concentration. No lethal effects could be achieved with 5-FU on human colon cancer cells with this method, nevertheless the NCI's judged that the anticancer activity of this compound was outstanding. In contrast to this Ukrain has an almost 100% lethal effect on the same 8 human colon cancer cell lines in Log  $10^{-3.5}$  molar sample concentration. Inhibition is reached at Log  $10^{-5.5}$ , that is to say at a 1000-fold lower concentration than 5-FU. This is the main reason for the initiation of a clinical study with Ukrain on rectal carcinoma to evaluate whether these astonishing and unexpected results correlate in the clinic. In contrast to cytostatics which show no pronounced affinity to tumor tissue and are therefore quite uniformly distributed within the body, Ukrain displays strong affinity and selectivity to tumorous tissue and cancer cell nuclei. This has been demonstrated by its fluorescence under UV irradiation. Whereas the dosage of cytostatics will be given according to the square meters of the patients body surface, Ukrain which has an about 1000-fold higher Therapeutic Index than most cytostatics is applicated in 10 mg per injection twice a week. Because of its high selectivity only to cancer cells Ukrain dosage is only based on tumor and metastases volume. Tumor degradation products should not be developed in too high amounts and too quickly (toxification!). Preliminary studies on various oncological diseases have pointed out that this dosage may induce malignotoxic effects and may lead to tumor regression. See Picture 1(next page) for further information, and also Enclosure 1 and Enclosure 2.

Ukrain has proven to be atoxic in therapeutic dosage with a Therapeutic Index of 1250 (in contrast to 5-FU which is approximately 1.4 to 1.8), having high tumorocidal properties in vitro, in vivo and in the clinic together with immunomodulating properties (8, 26). In contrast to the severe toxic effects of chemotherapy schemas using 5-FU, Ukrain shows no adverse effects.

Several in vitro, in vivo and clinical trials have demonstrated the malignotoxic and immunostimulating effects of Ukrain.

Tabelle1 Diagramm 2

UKRAIN. NSC 631570

5-FU. NSC 19893

