Liv 10

IMMEDIATE RESPONSE DETERMINATION IN VITRO FOLLOWING DRUG EXPOSITION IN VIVO BY REGIONAL CHEMOTHERAPY (RC). K.H.Link, K.R.Aigner.

The immediate response (R) of tumors to a single application of various forms of RC was measured by comparing the growth of tumor biopsies in soft agar (s.a.) immediately before and after intraoperative RC. In addition, the 'Human Tumor Colony-forming Assay' (HTCA) was performed with the 1st (untreated) biopsy to predict the growth delay of the 2nd biopsy after in vivo drug exposure. If possible, the HTCA results were correlated to the clinical R of RC, as well.
19 pts (13 colorectal liver metastases (LM), 2 carcinoid LM, 3 melanoma metastases, 1 adeno-ca. LM) received a single shot of high dose RC by either intraarterial infusion, isolated liver perfusion, chemoembolization, or intraperitoneal instillation. The paired 1st and 2nd biopsies had to be comparable pathologically and the cell suspensions were adjusted to viability by trypan blue exclusion.
In 16/19 pts the growth delay of the intraoperatively treated biopsy exceeded 50% growth inhibition in s.a., compared to the 1st biopsy. This R was predicted correctly in the HTCA with the 1st biopsy in 17/19 (89%) cases and correlated correctly to the clinical R in 13/14 (93%) cases. Predictive accuracy of the HTCA for clinical R was high, as well.
Our results indicate that tumors respond to single high dose RC - shots. In addition, the HTCA seems to be biologically relevant in RC, as drug treatment in vitro induces similar s.a. growth delay as drug exposition in vivo.

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Liv 11

INTRAARTERIAL INFUSION OF MONOCLONAL ANTIBODIES (ANTI-CEA) IN PATIENTS WITH LIVER METASTASES OF COLORECTAL CARCINOMAS
K.H. Muhrer, K. Bosslet, K.R. Aigner, R. Holzheimer, S. Grebe

The conjugation of cytotoxic drugs to monoclonal antibodies (MAB) promisses new possibilities in selective tumor therapy. In this study we tested 12 patients with liver metastases of colorectal carcinomas by intraarterial infusion of radiolabelled monoclonal antibodies.
The patients previously had received a surgically placed hepatic artery catheter for regional chemotherapy. The monoclonal antibody (Tu MAK 431/31) specifically binds to an epitope of the carcinoembryonic-antigen (CEA). We chose intraarterial antibody injection as metastases are supplied arterially allowing optimal MAB-targeting.
For scanning the antibodies were labelled with 131 J.
During the 60-minutes infusion we monitored and documented the antibody distribution in the liver by scintigraphy. One, two and three days after infusion the patients had control scans.
Localisation and extent of the liver metastases were documented by CT-scan or 99 Tc-liver scintigraphy. During antibody infusion in 8 out of the 12 patients there was an immediate MAB-enrichment at the sites of liver metastases. These MAB-radiolabelled areas corresponded to "cold" areas of previously performed 99 Tc-liver scintigrams.
In the control scintigrams the initial activity concentration in the tumor areas was diminished as background activity had increased. In 2 patients there was no distinct imaging of metastases, 2 patients failed.
The high incidence of positive tumor imaging indicates rapid binding of monoclonal antibodies to tumor lesions already during intraarterial infusion.

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Liv 12

CEA AS AN INDICATOR FOR THE EFFICACY OF REGIONAL CHEMOTHERAPY FOR LIVER METASTASES OF COLORECTAL CANCER
A.Quentmeier,P.Hohenberger,H.Feil and P.Schlag

The course of disease of 29 patients undergoing longterm continous intrahepatic chemotherapy with 5-FU or FUDR was observed by serial CEA measurements (RIA/Abbott).The arithmetical mean (CEA-x) of the CEA values before the onset and during the first three courses of chemotherapy (reference time) was taken as the individual basis to analyze the CEA follow-up curve of each patient. Related to this individual score (CEA-x) the CEA curves of all 29 patients could be divided in three groups. In group 1 the CEA-values after the reference time did never fall below CEA-x. The CEA values of group 2 decreased for less than three months and of group 3 for more than three months below CEA-x.The results listed in the table below demonstrate a strong correlation between the course of CEA and the survival time of the patients.

	n	survival time	mean survival time	no.pat.alive
Group 1	7	4-18 mo.	7.9 mo.	0
Group 2	10	5-15 mo.	10.8 mo.	4
Group 3	12	9-24 mo.	15.2 mo.	8

In some patients we found a continous decrease or rise of the CEA curves to be a sign of a successful or failing therapy respectively. In contrast, most of our patients exhibited a nonlinear behaviour of the CEA curves. In these cases the interpretation of the actual CEA value was only possible by using the individual reference score CEA-c.A longterm course of CEA below CEA-x is associated with a more favourable prognosis and an effectiv therapy.

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Liv 13

CHEMOTHERAPY OF METASTASIZED COLO-RECTAL CARCINOMAS WITH FOLINIC ACID AND 5-FLUOROURACIL: RESULTS WITH SYSTEMIC AND INTRA-ARTERIAL CHEMOTHERAPY
T.M. Löffler, T. U. Hausamen

In a pilot-study the efficacy of the combination folinic acid and 5-fluorouracil in the treatment of metastasized colo-rectal carcinomas was investigated. (Cancer Treatment Reports 66:1803, AACR Abstr. 432, 1982)
If there was only liver metastasis an arterial catheter (Implantofix®, Braun-Melsungen) with subcutaneous injection port was implanted.
Method: Systemic therapy: Day 1, 3, 5, 8, 15 folinic acid 100 mg/m² as short time infusion over 15 min, then 5-fu 500 mg/m² as i.v.-injection. Arterial therapy: Day 1, 3, 5, 8, 15 folinic acid 100 mg/m² as i.a.-infusion over 15 min. Therapy was repeated on day 28.
Results: Evaluable are 38 patients, 11 with i.a.-therapy and 27 with systemic chemotherapy.
Intra-arterial therapy: CR 1/11, PR 8/11, NC: 2/11.
Median duration of remission for CR + PR at present time: 10,3 months.
Systemic therapy: CR 0, PR 13/27, NC: 10/27, PD: 4/27.
Median duration of remission for PR at present time: 8,4 months.
I.a. + i.v.therapy: CR + PR 22/38 = 55 % remission rate.
Toxicity: Leukopenia (1500-3000): i.a.-therapy: 3/11, i.v.-therapy 6/27. Diarrhoe: i.a.-therapy: 3/11, i.v.-therapy 14/27.
Conclusions: Our results show a very good remission for hepatic metastases with this combination. At present time there is no difference in efficacy with systemic or arterial chemotherapy. Toxicity with i.a.-therapy is minimal and with i.v.-therapy tolerable. The obtained remission rates show an improvement in the treatment of metastasized colo-rectal carcinomas.

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