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Hepatic arterial therapy-is the concept dead or alive?

Abstract not received.

935

Intraperitoneal chemotherapy in the management of ovarian cancer

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The intraperitoneal (IP) administration of cytotoxic agents is based on sound anatomic, physiologic and pharmacokinetic considerations. Phase 1 trials have demonstrated the safety of delivering a number of antineoplastic agents by this route, and have confirmed increased exposure for the peritoneal cavity (compared to the systemic compartment) ranging from 10-fold (e.g., cisplatin, carboplatin) to > 1000-fold (e.g., paclitaxel). Phase 2 second-line ovarian cancer studies have documented the ability of regional drug delivery to achieve surgically-documented complete responses, with activity being observed almost exclusively in those patients with microscopic or very small volume macroscopic disease (maximum diameter of residual tumor masses < 0.5-1 cm) when IP therapy is initiated. Two previously reported randomized trials comparing IP cisplatin to intravenous cisplatin as initial chemotherapy of small volume residual advanced ovarian cancer have confirmed a survival advantage associated with this approach. Despite this fact, IP therapy is rarely considered for routine clinical use, possibly due to concerns for technical difficulties associated with regional drug delivery and the apparent (but possibly incorrect) conclusion that cisplatin must be utilized, rather than carboplatin for IP treatment of ovarian cancer. Currently available data strongly supports further exploration of IP drug delivery, both as an initial and second-line treatment strategy for ovarian cancer.

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Intratumoral treatment

Abstract not received.

937

Isolated limb perfusion: Lessons from preclinical models

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Isolated Limb Perfusion (ILP) with melphalan has a more than 30 year tradition as the treatment of choice of multiple melanoma in-transit metastases with overall complete response (CR) rates of about 50%. It has however failed in the treatment of large limb threatening extremity sarcomas. Since the use of Tumor Necrosis Factor-alpha (TNF) this situation has completely changed. Now, ILP with TNF + melphalan is a new, very successful EMEA-approved option in the management of extremity tumors to prevent amputation.

New data from experiments in our laboratory on the effects of TNF in isolation perfusion system has provided new insight in the synergistic antitumor effects that are seen in these systems when TNF is used in combination with melphalan or doxorubicin. A number of crucial observations about prerequisites for optimal effects of TNF have been identified; apart from the vasculotoxic effects on the tumor vasculature which leads to the selective destruction of tumor-associated vessels, a most essential mechanism has been discovered in our animal models: addition of TNF to the perfusate results in a highly significanty increased drug uptake (melphalan or doxorubicin) in tumors (3–6 fold). Similar synergy is observed in the treatment of well vascularized liver metastases by isolated hepatic perfusion with TNF and melphalan. New (vaso-active) drugs and new mechanisms of action are being discovered. We have also demonstrated that ILP is a promising treatment modality for adenoviral vector mediated genetherapy. Many new developments in the field of ILP can be expected for early clinical phase I–II evaluation

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Molecular markers of pancreatic cancer

Abstract not received.

939

Pancreatic cancer surgery – The chance to be cured: Who benefits?

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The prognosis of patients suffering from pancreatic cancer is significantly related to the degree of cancer dissemination; on the basis of histopathological classification patients with pancreatic cancer, tumor size less than 2 cm, without lymph node metastases, without extrapancreatic nerve infiltration, without vessel wall infiltration and with cell differentiation grade I have a 30–50% chance to get cured by an R0-resection. On the basis of the UICC classification only patients with UICC stage I and II are candidates for surgery who have benefits from oncological resection. On the basis of the Ulm experience, 1000 patients with pancreatic cancer were managed surgically (5/1982–3/2001). 2.5% were UICC I, 6.2% UICC II, and 14.6% UICC III. Only 23.3% of the patients had a cancer stage without lymph node metastasation. Hospital mortality in 427 patients after resection was 2.3%. 60% of the patients had an uneventful postoperative course without any local or systemic complications. Patients who had an R0-resection had a 5-year survival chance of 28%. Patients with an R1/R2-resection had an actuarial survival of less than 10%. All patients after pancreatic cancer resection should have adjuvant chemotherapy which leads, on the basis of the ESPAC trial (*Lancet* 2001), to an additional significant survival benefit.

Conclusion: Patients in cancer stages UICC I, II and III have a survival benefit from oncological resection if an R0-resection has been performed: adjuvant chemotherapy is recommended in every case after surgical resection, leading to an additional survival increase.

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ESPAC-1: A European, randomised study to assess the roles of adjuvant chemotherapy and chemoradiation in resectable pancreatic cancer

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Pancreatic cancer affects 8–12 per 100,000 population per year in Europe and North America. Post-resection, long term survival is 10–15%. ESPAC-1 is the largest randomised adjuvant pancreatic study designed to answer: (i) is there a role for chemoradiation (40 Gy + 5-fluorouracil); (ii) is there a role for chemotherapy (5-fluorouracil + folinic acid). 541 patients with pancreatic ductal adenocarcinoma were randomised from 83 clinicians in 11 countries. Presently, 227 patients (42%) are alive with median follow-up of 10 months (inter-quartile range 1–25). Preliminary results show no evidence of a survival benefit for chemoradiation treatment (median survival 15.5 months with chemoradiation vs 16.1 months without, $p = 0.24$). There is evidence of a benefit for patients having chemotherapy (median survival 19.7 months with chemotherapy vs 14.0 months without, $p < 0.001$). Secondary endpoints include QoL which was assessed by patient questionnaires (EORTC QLQ-C30/ESPAC-QLQ32) completed at 3 monthly intervals. The 15 QoL dimensions measured by the questionnaire were analysed. A total of 296 patients have completed 789 questionnaires within 1 year of entry. Changes in dimension scores within 6 months from entry were compared between treatments. Initial analysis suggests that, for 3 of the 15 dimensions (social functioning, appetite and constipation), the change over time differs depending upon treatment.

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Outcomes trial demonstrating a survival advantage of initial chemoradiotherapy for regional pancreatic adenocarcinoma (PCa)

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Background: Resection of PCa, traditionally considered the patient's only chance for cure, is resource-intensive with limited impact on survival.