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Penile Cancer − Chemotherapy

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Penile cancer is a rare disease and accounts for only about 0.5% of all malignancies. Advanced (T3/4) or metastatic disease is even rarer, comprising only 5% of patients in Europe and up to 13% in Brazil.
The role of chemotherapy in the treatment of penile cancer is limited. For patients with fixed or relapsed inguinal nodes upfront combination chemotherapy followed by surgery is recommended. In the adjuvant setting chemotherapy should be considered for patients with pN2/3 disease, although supporting data is scarce. Combination chemotherapy can provide palliation in the case of metastatic disease or relapse.
There are only very small retrospective series and very rare prospetive trials with multiple chemotherapy regimens and partly conflicting results. Since the late 1980-ies the following compounds have been used as single agents, but mostly in combination: methotrexate, bleomycin, cisplatin, 5-fluorouracil (5-FU), vinblastin. More recently the taxanes, irinotecan and ifosfamide have been added to the chemotherapeutic armamentarium. Cisplatin combination chemotherapy is active in penile cancer with response rates of about 20%. The highest response rate of 32% was reported in one of the larger series from the South West Oncology Group with one oft he regimens of the 1990ies (methotrexate, bleomycin, cisplatin). However, toxicity was very high with five treatment related deaths. Cisplatin has become the basis of chemotherapy combinations in more recent series, mostly combined with 5-FU, which is the recommended combination in the European guidelines. The EORTC conducted one of the rare prospective trials and explored the efficacy and safety of cisplatin and irinotecan (Theodore et al, Ann Oncol 2008). The response rate was 31%, including two complete pathologic responses (pCR). Neoadjuvant paclitaxel, ifosfamide, and cisplatin showed an objective response rate of 50%, including three pCR, and acceptable toxicity in a 30 patient prospective trial (Pagliaro et al, J Clin Oncol 2010). The inclusion of the taxanes and contemporary chemotherapy support add to the efficacy of chemotherapy and the reduction of toxicity in the treatment of locally advanced and metastatic penile cancer.

Special Session (Sat, 24 Sep, 14:15−15:15) **Immune System and Tumour Response to Radiotherapy**

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Role of T-Lymphocytes for Tumour Response to Radiotherapy

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Over the past ten years we have developed a clinical translational program based on the rationale of immunizing patients against their own tumour by concomitantly: 1) removing existing “breaks“ in their immune system and 2) harnessing local ionizing radiation (IR) to induce physical and biological perturbations at the irradiated tumour site, to achieve the successful conversion of the original tumour into an immunogenic hub (Formenti, Lancet Oncology 2009). Preclinical investigations have shed some light on the specific role of T cells in these processes. For instance, in the 4T1 syngeneic murine model of metastatic breast cancer targeting regulatory receptors or cells (Treg) by anti-CTLA-4 and anti-CD25 antibodies, respectively, synergized with IR and reduced the number of metastases to the lung (an abscopal effect, defined as a significant growth inhibition of the tumour outside the irradiated field) in a CD8+ T cells dependent way. In the same model IR increased the migration of CD8 CXCR6 activated T cells to tumours. This effect was mediated by IR-enhanced secretion by cancer cells of CXCL16, a chemokine that binds to CXCR6 on Th1 and activated CD8 effector T cells. CXCR6-deficient mice showed reduced infiltration of tumours by activated CD8+ T cells and impaired tumour regression following treatment with local IR + CTLA-4 blockade.
Interestingly, an abscopal effect, occurred only in mice treated with the combination of 9H10 and fractionated radiotherapy, but not when a single dose of 20 Gy was administered ($P < 0.01$), as reflected by the frequency of CD8+ T cells showing tumour-specific IFN-gamma production.
The contribution of invariant natural killer T (iNKT) cells, a subset with unique regulatory functions, in the response to IR and CTLA-4 blockade was also studied. Growth of 4T1 primary tumours and lung metastases was compared in wild type (WT) and iNKT cells-deficient (iNKT−/−) mice. The response to IR+CTLA-4 blockade was markedly enhanced in the absence of iNKT cells: 50% of iNKT−/− compared to none of the WT mice had complete tumour regression, long-term survival, and resistance to a challenge with 4T1 cells.
Finally, intravital microscopy demonstrated that while both IR and CTLA-4 blockade given as monotherapy enhanced the motility of activated CD8 T cells infiltrating 4T1 tumours, IR with anti-CTLA-4 increased the arrest of T cells in contact with tumour cells. The latter required interaction of NKG2D on CD8+ T cells with its ligand retinoic acid early inducible-1 (Rae-1) on the tumour cells, which was up-regulated by IR. Blocking NKG2D-Rae-1 interactions increased markedly the motility of anti-CTLA-4 treated T cells within irradiated tumours inhibiting their contact with tumour cells, and abrogated immune-mediated tumour rejection, suggesting a critical role of radiation-induced NKG2D ligands for the antitumour effects of anti-CTLA-4 in the setting of a poorly immunogenic tumour.

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CD11b Cells Provide Resistance to Radiotherapy

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We are testing a new therapeutic paradigm based on the dual origin of tumour blood vessels: Angiogenesis, the sprouting of endothelial cells from nearby blood vessels, and vasculogenesis, the formation of blood vessels by circulating cells, primarily of bone marrow origin. We have shown that by killing the endothelial cells in and surrounding the tumour, local tumour irradiation abrogates local angiogenesis suggesting that the tumour has to rely on the vasculogenesis pathway for regrowth after irradiation. We have shown that local irradiation of human tumour xenografts in nude mice produces a large influx of bone marrow derived CD11b+ myelomonocytes into the tumours as they begin to regrow following irradiation. We demonostrate that inhibition of this influx using neutralizing antibodies against CD11b inhibits tumour recurrence. Thus the influx of CD11b+ monocytes promotes tumour recurrence after irradiation. The mechanism for this effect could be by their proangiogenic nature or they could be suppressing T-cell immunity by their nature as myeloid-derived suppressor cells (MDSC). The fact that these experiments were performed in T-cell deficient mice does not rule out the MDSC mechanism as we and others have demonstrated that there is residual anti-tumour immunity in nude mice. To distinguish the two mechanisms we also tested anti-Gr1 antibodies and showed no effect on tumour response to irradiation. As MDSC are Gr1+CD11b+ monocytes these data argue for the importance of the proangiogenic properties of Gr1− CD11b+ cells. We are testing other models including immunodeficient SCID mice to further interrogate the mechanism by which CD11b+ myelomonocytes promote tumour recurrence after irradiation.

Special Session (Sat, 24 Sep, 14:15−15:15) **Developments in Surgical Oncology**

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Improving the Diagnostic Pathway for Men With Prostate Cancer

Abstract not received

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Robotic Surgery − Opportunities and Issues for Nursing

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The operating theatre of the 21st century has become a hi-tech environment. Since the early days of laparoscopic surgery, there has been a continuous increase in the number of devices for surgical use thus, crowding of the operating theatre.
Robotic surgery is quickly replacing conventional surgery in several surgical specialties and is not only heralded as the new revolution, but is one of the most talked about subjects in surgery today. Such advances have facilitated significant improvements in the management of the surgical patient effectively cancer patients, minimising open surgical resections.
Results have shown that robotic procedures reduce recovery times in addition to a shorter hospital stay, reduced pain, reduced tissue damage, and scarring. This change bears a significant impact on the clinical practice of surgeons, surgical trainees and operating theatre practitioners.
In September 2000 the da Vinci Robotic System, the first of its kind to be installed in the UK, was introduced to Imperial College St Mary’s Hospital London. The role of the robotics nurse specialist was developed to create