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SP-0406
SBRT for metastatic disease: how far can and should we go?
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Stereotactic body radiotherapy (SBRT) is attracting substantial interest as a treatment option for selected patients with metastatic disease. It is reasonable to take a step back and take a look at where the field is now and what we can expect from this intervention. This presentation will focus on a number of contemporary clinical issues, including: what can be expected from SBRT at various anatomical sites; definitions of oligo-metastatic disease and their limitations; defining treatment goals in metastatic disease; lessons from published outcome data; a pragmatic approach to decision-making in the clinic; is radiation technology driving the agenda? and; gathering evidence for the future.

SP-0407
Abdominal-pelvic targets
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Patients with oligometastases from colo-rectal carcinoma (CRC) are often considered as candidates for surgical resection, radiofrequency ablation and SBRT and CRC often metastasize to the abdominal organs, especially to the liver. Therefore, abdominal oligo-metastases are often treated with SBRT. A relative large number of publications demonstrate outcome after SBRT for liver metastases that are almost as good as for lung metastases. Local control rates in both lung and liver are most often in the range 70-90% and survival rates are depending on tumor type and the selection of the patients. There are only few publications on SBRT of abdominal, non-liver oligometastases, but the few available publications indicate favourable local control as well for these patients. Most publications on SBRT for abdominal targets report a low risk of morbidity, but there are reports of relatively severe morbidity related to irradiation of the liver and the bowel, most often in terms of severe mucositis or intestinal ulceration. Treatment of abdominal targets is complex due to the multiple organs at risk. Treatment planning is based on a snapshot of the anatomy on a treatment planning CT-scan. 4DCT takes the intrafraction motion motion of the target into account, but we usually do not take the motion of bowel structures into account. CBCT is used to correct for set-up errors of the target, but organs at risk are less often considered. This may lead to unintended high doses to the organs at risk and side effects that were not expected from the treatment planning.

Symposium: Head and neck: state-of-the-art and directions for future research

SP-0408
Molecular targeting with radiotherapy
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Abstract not received

SP-0409
Immunotherapy for HNSCC: an emerging paradigm?
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Recent progress has been made in oncology with new drug targeting immune system. Ipilimumab which targets CTLA-4 has been the first one approved in melanoma. Another way to block the deleterious cascade of T-lymphocyte inhibition is to block an extracellular target, namely Programmed Death Receptor-1 (PD-1). PD-1 is a cell surface receptor expressed by T cells, B cells, and myeloid cells, and member of the CD28 family involved in T cell regulation. PD-1 pathway is activated by receptor binding to ligands (PD-L1 or PD-L2) and its physiological role is to prevent uncontrolled immune activation during chronic infection or inflammation. In cancer, activation of PD-1 pathway can suppress antitumor immunity. In mouse models, antibodies blocking PD-1/PD-L1 interaction lead to tumor rejection. In clinical trials, targeting PD-1 pathway using human monoclonal antibody such as nivolumab, which blocks binding of PD-1 to PD-L1 and PD-L2, showed promising results in metastatic solid tumors with durability of objective responses, and sustained overall survival (Topalian and al, NEJM 2012). Phase I studies showed a potential better safety profile of anti-PD-1/PD-L1 agents in comparison with ipilimumab. Following, anti-PD-1/PD-L1 drugs have been developed at a phenomenal speed, taking just three years from the first clinical trials to approval. At now, anti-PD-1 nivolumab and pembrolizumab are approved in melanoma and NSLCC... There is a strong rationale for using anti-PD-1/PD-L1 agents in HNSCC. Tumor-infiltrating lymphocytes (TILs) which are required for PD-1 blockade, and PD-L1 expression are present in HPV+ and HPV negative HNSCC. There is a correlation between infiltration by CD8 cells and response to CRT, and between PD-L1 expression and survival. The high number of specific mutations observed in HNSCC could be a mechanism of immunogenicity. Results of phase I studies testing anti-PD-1/PD-L1 agents in HNSCC patients have been recently reported with promising results in terms of efficacy with prolonged responses. During ASCO 2014 meeting, Seiwert et al. presented first results of a phase Ib study of pembrolizumab in recurrent/metastatic (R/M) HNSCC patients. Patients ≥1% with PD-L1 immunohistochemistry expression in tumor cells or stroma were enrolled in the study. The anti-tumor effect was observed both in patients with HPV-positive and HPV-negative tumors. The duration of these responses was impressive, some already lasting over one year (Seiwert TY et al., ASCO 2014, CSS 6011). Updated data on a expanded cohort have been presented at last ASCO 2015 meeting. 132 (81 HPV+) R/M HNSCC patients were treated with prembrolizumab 200 mg Q3W regardless of HPV or PD-L1 status. 78% received at least one line of chemotherapy. Tolerance was good (9.8% of grade 3-5 adverse events). Objective response rate was 25%, stable disease rate was 25% with long-lasting responses (Seiwert TY, et al. J Clin Oncol. 2015;33(suppl): LBA6008). First results of a phase I study evaluating the safety and efficacy of an anti-PD-L1 agent, durvalumab (MEDI4736), have been presented at ESMO 2014 congress (M. Fury M et al., abstr 988PD, ESMO 2014). MEDI4736 is a human IgG1 mAb, engineered to prevent ADCC activity, that blocks PD-L1 binding to PD-1 and CD-80. 50 pts with HNSCC, with median 3 prior treatments received median 3 doses of MEDI4736 10 mg/kg q2w. Treatment-related