60 INVITED

The Tipping Point for Combination Therapy − Cancer Vaccines With Radiation

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Local radiation is an established therapy for human tumours. Radiation may also act synergistically with immunotherapy to enhance immune responses, inhibit immunosuppression, and/or alter the phenotype of tumour cells, thus rendering them more susceptible to immune-mediated killing. As monotherapies, both immunotherapy and radiation may be insufficient to eliminate tumour masses. However, following immunization with a cancer vaccine, the destruction of even a small percentage of tumour cells by radiation could result in cross-priming and presentation of tumour antigens to the immune system, thereby potentiating antitumour responses. This talk will discuss a) mechanisms by which many forms of radiation therapy can induce or augment antitumour immune responses, b) preclinical systems that demonstrate that immunotherapy can be effectively combined with radiation therapy, and c) current clinical trials where standard-of-care radiation therapy is being combined with immunotherapy. Capitalizing on the immunological effects induced by radiation treatment by adding potent antitumour vaccines may lead to synergistic approaches to cancer management that offer feasible, well-tolerated therapeutic options for cancer patients.

Special Session (Sat, 24 Sep, 14:15−15:15)
Monitoring Tumour Response to Therapy − What Do the Images Tell Us?

61 INVITED

PET/CT for Tumour Response Assessment

Abstract not received

62 INVITED

Functional MRI of Therapy Response

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Learning objectives:

1. To approach functional MRI via the depiction of biological information of relevance to cancer
2. To learn the biological basis for commonly available functional MRI techniques such as diffusion MRI, dynamic susceptibility and relaxivity contrast enhanced MRI, and proton spectroscopy. For each techniques to demonstrate how measurements are acquired, the quantification process, and show biological/clinical validation
3. To show the added value of the multiparametric approach for depicting biology, disease characterization and therapy monitoring
4. To show how multiparametric functional MRI can use for medicines development and in the clinic.

Take home points:

1. Multiparametric MRI is potentially important development for non-invasive biological exploration of cancer because of its multidimensional (multispectral, multispatial and temporally resolved) nature
2. Multiparametric MRI can be used for improving tumour characterization as well as for monitoring therapy response
3. Multiparametric MRI allows us to understand how therapies affect tumours and tissue microenvironments
4. Sophisticated, user-friendly software workspaces need to be developed urgently, in order to be able to integrate/cross-correlate data analyses

63 INVITED

Monitoring Effect of Antiangiogenic Treatments by Dynamic Contrast Enhanced Ultrasonography

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New treatments based on antiangiogenic substances are developed in order to destroy tumour vessels and are the object of promising clinical research for cancer treatment. Considering the large number of new targeted drugs under development, there is a great need for early reliable imaging indicators of tumour responses, and identification of a recommended modality of drug administration to guide further steps in the clinical development. The response rate remains the best objective parameter of efficacy of the treatments tested in clinical trials but this parameter is obtained very late in the clinical development, while the effect on the tumour must be determined as soon as possible in order to optimise the schedule and the dose to be recommended for the late clinical development stage. The early functional evaluation of new treatments is a main goal.

At present, technical advances in DCE-US using bolus contrast agent (SonoVue®, Bracco) and perfusion software allow the detection of microvascularization and perfusion for superficial and deep malignant tumours. Thus, it becomes possible to early evaluate the efficiency of antiangiogenic or anti-vascular molecules. Treatment response can be early predicted according to modifications of this vascularization before any volume modification. The acquisition of raw linear data affords the precise quantification (peak intensity, time to peak intensity, sloap of wash-in, and area under the curve. . .) of the perfusion after contrast uptake curves modelization, in particularly using time tracking of region of interest. The results will be focused on GIST, RCC, HCC, and melanoma with different molecules including 117 patients.

Reduction in tumour vascularization can easily be detected in responders after 2 weeks and is correlated with progression-free survival and overall survival in RCC or HCC.

DCE-US is supported by the French National Cancer Institute (INCa), which is currently studying the technique in metastatic breast cancer, melanoma, colon cancer, gastrointestinal stromal tumours and renal cell carcinoma, as well as in primary HCC, to establish the optimal perfusion parameters and timing for quantitative anticancer efficacy assessments. 539 patients with a follow-up of 1 year are included in 19 centers and the preliminary results including 1950 DCE-US demonstrated that AUC could be a robust parameter to predict response.

References

Lassau et al. Metastatic Renal Cell Carcinoma Treated with Sunitinib: Early Evaluation of Treatment Response Using Dynamic Contrast-Enhanced Ultrasonography Clin Cancer Res. 2010

Lassau et al. Advanced Hepatocellular Carcinoma: Early Evaluation of Response to Bevacizumab Therapy at Dynamic Contrast-enhanced US with Quantification–Preliminary Results. Radiology. 2011

Lassau at al. Dynamic contrast-enhanced ultrasonography (DCE-US) and anti-angiogenic treatments. Discov Med. 2011

Scientific Symposium (Sat, 24 Sep, 16:00−18:00)
Optimal Treatment for a 72-Year-Old Patient With Stage III-N2 Non-Small Cell Lung Cancer

64 INVITED

Stage III-N2 Non-Small Cell Lung Cancer − Identifying Patients Subgroups and the Need to Tailor Therapy

Abstract not received

65 INVITED

Evidence to Support Definitive Chemo-Radiotherapy

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Stage III NSCLC is a heterogeneous disease: see www.predictcancer.org. However, phase III trials have mostly included all stage III patients that were in a good general condition with adequate organ function. From a meta-analysis based on individual patient data, it was clear that the concurrent administration of chemotherapy and radiotherapy resulted in a significant improvement of the 5-year survival. Most of these patients had multi-level N2 or N3 disease and had bulky nodes. There is thus level I evidence that if our 72-year old patient is in a good general condition and has adequate organ functions, the first choice treatment is concurrent chemo-radiation.

Patients with resectable N2 disease were randomized between surgery and definitive chemo-radiation after induction concurrent chemo-radiation in the Lung Intergroup Trial 0139. 75% of the patients had single nodal station NSCLC. There was no difference in survival between the two arms. Although the study has often been criticised because of the high rate of pneumonectomies and toxic deaths in the surgery arm, the overall median survival as well as the 5-year survival, about 24 months and 25%, respectively, is at least as good as single-institutional surgical series that reported on an intention to treat basis. Indeed, a major caveat in surgical series is beside patient selection that often only patients that indeed went on to surgery are reported, which is mostly only 70−80% of the initial population that initiated therapy. In the same trial, a hypothesis-generating non-planned subgroup analysis was performed of patients that were treated with concurrent chemo-radiation (45 Gy) followed by