pCR had lower T-stage tumours at baseline, which implicates a lower risk of incomplete resection and distant metastases, simply the latter fact might have been the reason for an improved long-term outcome.
In conclusion, rectal cancer patients with a pCR after having undergone combined RCT and surgery have a better long-term prognosis than those with residual disease. Conclusions about the benefit of adjuvant chemotherapy in these patients are difficult to make. Until further evidence is available, the treatment decision should be based on risk factors for local or distant recurrence including pretreatment staging and the response to chemoradiation.

254 INVITED

Tailored Follow-up According to Staging

Abstract not received

Scientific Symposium (Mon, 26 Sep, 09:00−11:00) **Non-Small Cell Lung Cancer − Advanced Disease**

255 INVITED

Targeting Galectin-1, a Hypoxia Induced Protein, in Non-Small Cell Lung Cancers

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Non-small cell lung cancer (NSCLC) is a highly lethal disease. Despite dose escalation with conformal radiotherapy (RT) in combination with modern chemotherapy, there is still a significantly high rate of intrathoracic failure and poor overall survival in patients with locally advanced disease. A novel approach is needed to improve RT and chemotherapy effectiveness in these tumours. We have previously demonstrated that hypoxia does exist in NSCLC though to a lesser extent than head and neck cancer. Using proteomic analysis, we identified Galectin-1 (Gal-1) as a hypoxia-regulated protein at the level of secretion in several cancer cell types, including NSCLC. Galectin-1 (Gal-1) is a secreted carbohydrate binding lectin that is well known for its role in modulating T-cell homeostasis. More recently, it has been shown to play a major role in cancer progression. It is expressed in many cancers, including NSCLC, where increased Gal-1 expression is closely associated with larger tumours, more nodal metastasis and lower overall survival. In human head and neck cancer, expression of Galectin-1 was inversely related to intratumoral T-cell level and correlated with prognosis. Mechanistically, Gal-1 has been implicated in several pathologic processes including tumour proliferation, adhesion, migration, angiogenesis and enhancing T-cell apoptosis, which can, in turn, can confer tumour immunity. In addition to hypoxia, Gal-1 secretion was also enhanced by RT, raising the hypothesis that it may counteract RT effectiveness in cancers.
Applying a combination of down-regulating Gal-1 in a non-NSCLC cell line and knocking-out the gene in host mice, we show that tumour-derived Gal-1 is more important than host-derived Gal-1 in promoting tumour growth and spontaneous metastasis. Further mechanistic studies suggested that Gal-1 mediated its tumour promoting function by enhancing intratumoral T-cell death while protecting hypoxic tumour cells from apoptosis. Clonogenic studies also showed that Gal-1 down regulation increased radiation sensitivity in these cells, especially under hypoxia. Based on these data, it is logical to evaluate Gal-1 as a new target in NSCLC in combination with radiation and chemotherapy.

256 INVITED

Intensity Modulated Radiotherapy: Fixed-Beam and Arc Delivery Techniques for Locally Advanced Disease

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Increasing tumour sizes have long posed a challenge to the delivery of curative irradiation, as large fields increasing the radiation doses to critical normal organs such as the healthy lung. Historically, some European centers consider primary tumours exceeding 6−8 cm in diameter as being 'incurable' by radiation. A previous review considered the following groups of patients as being at high risk for toxicity of concurrent chemo-radiotherapy as their radiotherapy plans would involve excessive lung irradiation [Senan 2005], including patients with metastases in the contralateral hilus, those with peripheral lower lobe lesions with contralateral upper mediastinal nodes and large retro cardiac tumours with nodal metastases. At present, the availability of intensity-modulated radiotherapy (IMRT) routinely allows many such patients to undergo full-dose concurrent chemo-radiotherapy to 66 Gy or higher, while ensuring compliance with normal organ constraints specified in the EORTC recommendations for delivery of high precision thoracic radiotherapy [DeRuysscher 2011].
Intensity-modulated radiotherapy (IMRT) was introduced in the 1990's, and essentially involves dividing each large radiation beam into numerous small beamlets, with adjustments to the intensity of each beamlet individually. IMRT provides greater flexibility in controlling each beam, ultimately improving dose distributions and reducing toxicity. Traditionally, IMRT that is delivered using fixed beams and also requires more beams (5−9) for delivery of each fraction than for conventional radiotherapy. Some IMRT techniques can prolong the time that a patient spends on the radiotherapy machine and decreasing patient throughput. Furthermore, an IMRT can result in a larger volume of normal tissue receiving low doses of radiation. Recently, arc therapy, including Tomotherapy and fast volumetric modulated arc therapy, has emerged as a technique to address some of the limitations of fixed-field treatments. In contrast to fixed-field IMRT, arc therapy incorporates rotation of the beam relative to the patient while the beam is on. In most cases, the patient is treated from all angles, in one or more 360-degree rotations. The major conceptual advantage of arc therapy over standard fixed-field IMRT techniques is that since the radiation source is rotating around the patient, all angles are available to deliver radiation to the target while avoiding critical structures, and time is used efficiently because the radiation delivery does not stop in between different beam angles.
While IMRT clearly represents an improvement radiotherapy delivery, the learning curve has been exposed by reports of fatal lung toxicity in patients whose plans failed to limit volumes of healthy lung receiving doses in the range of 5−15 Gy. Furthermore, IMRT has allowed for increasingly larger tumour volumes to be treated to high doses, leading to concerns about sub-acute and late in-field toxicity, particularly esophageal toxicity. An update of the clinical toxicity data will be provided. As larger tumours are associated with an increased risk of distant metastases, the patterns of disease relapse following such IMRT approaches are of key interest. Finally, it is essential to ensure that all other aspects of target definition using multi-modality imaging, and of the so-called image guided radiotherapy delivery, are optimized when using IMRT. Typical clinical examples of how large stage III NSCLC tumours undergo this treatment scheme used will be provided.

257 INVITED

Integrating Systemic and Radiation Therapy in Locally Advanced Tumours

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Concomitant chemoradiotherapy (CCRT) has been established as the treatment of choice in patients fit to receive it, with a 4.5% survival benefit over sequential chemoradiotherapy (SCRT) at 5 years, and a 5 year survival of 15% in a meta-analysis of 7 trials and over 1200 participants. Current trials addressing ways to improve this outcome include studies of dose escalation, prophylactic cranial irradiation, cetuximab, different chemotherapies, vaccines and technical radiotherapy changes with IMRT, 4D planning and incorporation of CT-PET into radiotherapy planning.
However, these attempts to further intensify an already aggressive treatment will affect only a small proportion of those with stage III NSCLC. In line with a similar review of practice in Maastricht between 2002−5 [1], a review of patients seen in our centre with stage III NSCLC from 2004−8 identified 992 patients with stage III disease, of whom 59 had surgery, 105 radical radiotherapy (RRT), 133 CCRT and 138 SCRT. Two and 5 year survivals were 50% and 22% with CCRT, 30% and 8% with SCRT, and 17% and 3% with RRT. Less aggressive treatment was associated with increasing age (CCRT median 61 years, SCRT median 68 years and RRT median 75 years) and decreasing performance status (CCRT 0% PS 2, SCRT 12% PS2, RRT 29% PS2).
While considerable research continues on patients receiving CCRT, a greater focus is required on those not deemed fit for CCRT. This might include radiotherapy dose escalation where 66 Gy in 24 fractions is known to be safe, a renewed interest in altered fractionation which meta-analysis suggests may confer a small survival benefit, randomised trials of low dose concomitant chemotherapy and trials of targeted agents.
Substantial improvements have been made in those patients with stage III NSCLC fit to receive CCRT, although the large majority will still die from their lung cancer. Those not fit for CCRT have been largely ignored in research and studies are needed. The results for patients with stage III disease unfit for chemotherapy, a group growing because of the aging demography of this disease, have improved little in the last 25 years.

References

[1] de Ruysscher D et al., Ann Oncol. 2009;20:98–102