29th Conference of the European Society for Therapeutic Radiology and Oncology (ESTRO 29)

Highlights of the 29th International Conference of the European Society for Therapeutic Radiology and Oncology, 12th-16th September 2010, Barcelona, Spain

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The 29th conference of the European Society for Therapeutic Radiology and Oncology (ESTRO 29) offered the most relevant and cutting edge in both science and education, not only in the field of radiation oncology, radiation biology, physics and technology, but also oncology. The program was divided into several parallel tracks reflecting the different disciplines and groups within ESTRO. Each track started with a state-of-the-art teaching lecture in the morning followed by symposia and different proferred paper sessions which ensured first hand information on new developments. The importance of multidisciplinary collaboration was emphasized by several joint sessions with other oncological societies, including the European Society of Medical Oncology (ESMO), the European Society of Surgical Oncology (ESSO), the European Association of Urology (EAU), and many more. Furthermore, interesting debates on controversial subjects, multiple award lectures, early morning contouring clinics and over 1,800 selected abstracts allowed for little spare time to enjoy the vibrant Spanish port-town. Considering the amount of different lectures and abstracts presented at the conference, we will mainly focus on the results from the different randomized trials presented at the congress.

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In head and neck cancer (HNC) there was a lot of attention for alternative fractionation schedules and for the importance of human papilloma virus (HPV). Firstly, the results of the RTOG 0129 trial were presented. This study investigated the impact of accelerated radiotherapy (RT) and cisplatin intensity on the outcome in HNC. Apparently both cisplatin dose and RT duration affected outcome significantly. However, in multivariate analysis HPV status emerged as the strongest prognostic factor. Secondly, the results of the DAHANCA 6 and 7 trials were presented in which the influence of HPV-associated p16 expression on response was investigated. The studies confirmed that accelerated radiotherapy (6 fractions per week) significantly improved outcome in head and neck squamous cell carcinoma compared to conventional fractionation (5 fractions per week) for both p16-positive and

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p16-negative tumours.

J. Bourhis later presented the final results of the GORTEC trial on accelerated RT and/or concomitant chemotherapy (CT) in locally advanced HNC. In this trial patients were randomized between 3 groups receiving either conventional RT + CT, accelerated RT + CT or very accelerated RT without CT. After a median follow-up of 5.1 years, there was a significant progression-free survival advantage in favour of the 2 RT + CT arms, as compared to the very accelerated RT arm. In the latter arm, acute toxicity was also more pronounced. It appears that the dose of chemotherapy given concomitantly to radiotherapy has a significant impact on patient outcome and that further acceleration of radiotherapy cannot compensate for the missing dose of chemotherapy.

The effect of hypoxia on treatment outcome was also tackled in a few trials. In a subrandomization trial of the DAHANCA 5 trial the importance of hemoglobin (Hb) level and the effect of transfusion was investigated in HNC patients. Patients with low pre-irradiation Hb values were randomized to receive a transfusion or not. They found that patients with an initially high Hb level had a significant better outcome compared to low Hb patients. However, transfusion prior to treatment was unable to improve outcome in patients with low Hb values. Similarly, the DAHANCA 10 trial tried to improve Hb levels by means of the darbepoetin alpha (Aranesp®). Although it increased Hb levels in more than 81% of the patients, these patients still had a significantly poorer outcome in 5-year locoregional control and disease-specific survival. The treatment principle was abandoned and the difference in outcome is being subjected to further investigation.

The Dutch ARCON trial investigated the use of carbogen and nicotinamide in accelerated RT for laryngeal cancer. A significant gain was seen in regional control in the experimental arm but no benefit was found on local control. The reduced dose in the experimental arm may mask the potential benefit. Using pimonidazole binding, they found that the hypoxic status of the primary tumour might help to select those patients who are most likely to benefit from ARCON. It was generally well tolerated but failed to demonstrate a significant difference in acute side effects, with only a slight increase in median duration of acute confluent mucositis in the experimental arm. Further follow-up is needed to determine its effect on late morbidity.

Several trials were presented aiming to decrease toxicity of radiotherapeutic management of HNC. The long awaited British PARSPORT trial demonstrated that the sparing of the salivary glands using intensity-modulated radiotherapy (IMRT) was able to reduce the incidence of xerostomia and preserve salivary flow compared to conventional RT. Amidst all these novel treatment modalities the results of the headSTART trial, testing the importance of good RT protocol compliance and plan quality when using combined modality treatments, were presented. Patients treated with poor quality RT did significantly worse than patients in the protocol compliant group. Moreover, after further analysis the investigators saw that the potential therapeutic advantage of adding tirapazamine to cisplatinum was masked by poor radiotherapy.

In rectal cancer the main emphasis was on prediction of tumour response to neoadjuvant treatment. A meta-analysis was presented where clinical factors from six European trials were used to develop and validate nomograms for the prediction of local control, distant metastases and survival for locally advanced rectal cancer patients after a long course of chemoradiotherapy. These nomograms were then validated on the pooled data of 3 other trials. Although accuracies were relatively high, the question remains whether this currently presented nomogram is sufficiently accurate to allow for stratification for treatment selection.

The addition of functional imaging modalities and molecular parameters will be essential to increase accuracy, as was demonstrated by M. Janssens in his interesting talk on the use of FDG-PET/CT in prediction and early evaluation of response in rectal cancer. In order to increase the response rate, several possibilities were investigated. The Lyon R96-02 trial opted to deliver an additional RT dose using endocavitary irradiation (CXRT) in the preoperative treatment of low seated rectal cancer patients. Although the rate of local recurrence was not significantly different between both groups, a significantly lower rate of permanent colostomies was found in the experimental arm after 10 years (29 versus 61%).

The French ACCORD 12 trial investigated the effect of a higher RT dose (50 Gy versus 45 Gy) combined with a more intensive CT schedule (capecitabine + oxaliplatin versus capecitabine). They saw a significant increase in grade 3 to 4 toxicity in the more intensive treatment arm, although it did not compromise surgical resectability nor resulted in more surgical complications. The rate of positive circumferential resection margins was significantly higher in the standard arm, although no significant difference was found in pathological response between both groups. The treatment design where the experimental arm received both a higher RT dose and extra chemotherapy, makes it impossible to conclude on the role of oxaliplatin in the neoadjuvant treatment of rectal cancer. An Italian trial presented by L. Ciocini addressed the role of adjuvant 5-FU in rectal cancer. It failed to show a significant difference in overall survival between both arms and did not modify the incidence of distant metastasis, confirming the results the EORTC 22921 trial.

For prostate cancer the question on androgen deprivation was tackled by the RTOG 94-08 trial, where short-term androgen deprivation (STAD) prior to and during radiation for a total period of 6 months was found to provide the greatest clinical advantage in the intermediate-risk subgroup. No apparent benefit was found in the low-risk group. Death and late toxicity rates were similar between both arms. W. Shipley also presented outcome data of the PROG 95-09 trial. With a median follow-up of 8.9 years, the high dose radiation (79 Gy) significantly improved long term cancer control rates when compared to conventional dose radiation (70 Gy) without an increase in grade 3 and 4 late urinary or rectal morbidity. However, it should be mentioned that no overall survival benefit was recorded so far.

Besides dose escalation, hypofractionation is another hot topic in prostate cancer radiotherapy. The 3 year follow-up results of a prospective phase III randomized trial which compared hypofractionation and conventional fractionation in patients with high-risk prostate cancer, demonstrated superiority for the hypofractionated schedule in terms of freedom from biochemical failure. The late toxicity levels were equivalent between both treatment groups. Longer follow-up is essential before altering daily practice. Last but not least, the 10 year follow-up results from the EORT 22911 trial were presented. In this trial immediate postoperative irradiation was compared with wait-and-see-policy, for patients with positive surgical margins or pT3 stage after radical prostatectomy. The trial's primary endpoint was biochemical progression-free survival, which significantly improved when immediate postoperative radiotherapy was applied. Local control rates were also superior in the immediate postoperative radiotherapy treatment arm. However, this did not translate into better overall survival nor had an impact on the incidence of distant metastases. Results were similar in the subgroup with postoperative PSA ≤0.2 ng/ml.

In breast cancer a lot of attention was addressed to partial breast irradiation (PBI) and hypofractionated RT. In an interesting debate R. Orecchia and J.R. Yarnold discussed whether PBI should be considered standard of care in 2010. Although there is strong evidence that PBI might be as efficient as standard RT in early breast cancer, we currently lack a reliable estimate of non-inferiority for local tumour control in a well-designed clinical trial. When considering hypofractionation on the other hand, more evidence is at hand.

J.R. Yarnold presented the updated results of 3 trials concerning fractionation. Updated results of the START A and B trial demonstrated that the estimated α/β for tumour control was 4,6 Gy and the adjusted α/β for photographic breast appearance of 3,1 Gy, which is consistent with the observed relationships between the different regimens. As a result the 15-fraction regimen (40 Gy in 15 fractions of 2,67 Gy) is now standard of care in the United Kingdom. Next to this, the results of the first analysis of the FAST trial were reported. This trial tested 50 Gy in 25 fractions versus 28.5 and 30 Gy in 5 once-weekly fractions in breast cancer patients with a lower-than-average risk of relapse. The primary end point again was change in photographic breast appearance. Considering 2 and 3-year normal tissue effects, the 5 fraction schedule was comparable to the 50 Gy/25 fractions schedule in terms of 2- and 3-year normal tissue effects.

The necessity of giving a boost dose after breast conserving therapy was addressed in a subanalysis of

the EORTC boost no boost trial. In stage I and II breast cancer patients a boost dose of 16 Gy significantly improved local control, irrespective of age and tumour grade. The question whether whole breast dose can be reduced when a boost dose is applied was answered by an Australian trial. After a median follow-up of 8.5 years, the reduced whole breast dose appeared to be associated with inferior local control, despite use of a boost dose. Next to this, the benefit of RT after mastectomy was demonstrated in the long term results of the Stockholm randomized trial in breast cancer. Adjuvant RT decreased locoregional control ($p<0.001$) without an increase in the incidence of secondary malignancies. However, the reduced number of patients after 15 years of follow-up probably does not provide the statistical power to detect such small differences.

Trying to summarize a meeting of this magnitude in a limited number of words implies that many other interesting talks have been omitted from this overview. Novel molecular targeted therapies and their potential use in RT, positron emission tomography in radiotherapy planning, technical advances in image guided radiotherapy, strategies for dose painting, innovations in brachytherapy, developments in radiobiology and radiophysics, education of radiation technologists are only a few extra topics discussed at this meeting. For all those interested, there is good news as the abstract book is freely available at http://www.estro-events.org/Documents/ESTRO29_abstractbook_WEB.pdf