Lung Cancer

Oral presentations (Thu, 3 Nov, 8.30–10.30)
Lung cancer – NSCLC

1119 ORAL

Continuous hyperfractionated accelerated radiotherapy – weekend less (CHARTWEL) versus conventionally fractionated (CF) radiotherapy in non-small-cell lung cancer (NSCLC): first results of a phase III randomised multicentre trial (ARO 97-1)

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Background: Shortening of overall treatment time by accelerated radiotherapy has been shown to improve survival of patients with localised inoperable NSCLC in the CHART trial. This trial compared 54 Gy in 36 fractions of 1.5 Gy in only 12 consecutive days (CHART) with conventional fractionation (CF) to 60 Gy in 6 weeks. However also after CHART more than 80% of the patients developed local recurrences, calling for further intensification of local therapy. CHARTWEL (CHART weekend less) allows to escalate the total dose of highly accelerated radiotherapy. The present randomized phase III trial investigated whether CHARTWEL to 60 Gy improves outcome in patients with localized NSCLC compared with CF to 66 Gy which reflects a widely used standard for 3D conformal radiotherapy.
Patients and methods: 406 patients were randomised by 15 centres in Germany, Poland and Czech Republic between Sept. 1997 and Febr. 2005. Patients with NSCLC localised to the chest, performance status 0–1, with and without prior Chemotherapy (CTx) were included. Stratification criteria for randomisation were UICC stage, histology, prior CTx, and centre. CHARTWEL was applied in fractions of 1.5 Gy given three times per day on 5 days per week to a total dose of 60 Gy in 2.5 weeks. CF was applied in 36 fractions of 2.0 Gy, 5 fractions per week, to a total dose of 66 Gy in 6.5 weeks. All patients were treated using 3D conformal radiotherapy techniques at linear accelerators. Data in this abstract are from prelimary analysis at the end of accrual in February 2005. Formal analysis of the complete data set will be performed after retrieval of missing data in July 2005 and will be reported during the meeting.
Results: The groups were well matched for prognostic factors. Most patients suffered from locally advanced tumours (UICC I 10%, II 6%, IIIA 38%, IIIB 46%). Median follow-up is 47 months. Overall survival rates (main endpoint) at 1, 2 and 3 years were 55%, 32%, and 18% after CF versus 54%, 28%, and 21% after CHARTWEL (HR 0.99 [95% CI 0.79; 1.24]; p = 0.96). Disease free survival and local control (secondary endpoints) were also not significantly different in the treatment arms. Oesophagitis was more pronounced in the CHARTWEL arm but was clinically well manageable and resolved after treatment. Radiological signs of pneumopathy were increased after CHARTWEL, clinical symptoms of pneumonitis are currently being analysed.
Conclusions: Highly accelerated CHARTWEL radiotherapy to 60 Gy in 2.5 weeks was not superior to conventional fractionation to 66 Gy in 6.5 weeks in NSCLC localised to the chest. The data support a small time factor of fractionated radiotherapy in NSCLC since the higher dose in the CF arm was compensated by the shortening of overall treatment time in the CHARTWEL arm. Subgroup analysis awaits longer follow-up.
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1120 ORAL

A randomized trial of radical surgery (S) versus thoracic radiotherapy (TRT) in patients (pts) with stage IIIA-N2 non-small cell lung cancer (NSCLC) after response to induction chemotherapy (ICT) (EORTC 08941)

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Background: The optimal locoregional treatment – TRT or S – following systemic ICT of pts with stage IIIA-N2 NSCLC is unclear. 5-year survival rate in uncontrolled series of either modality varies between 5–25%.
Methods: selected pts with histological or cytological proven stage IIIA-N2 NSCLC were given 3 cycles of platinum-based ICT. Responding pts were then randomized between S: radical resection with lymph node dissection and optional postoperative radiotherapy (PORT), or TRT: at least 40 Gy in 2 Gy daily fractions on the mediastinum with a boost to at least 60 Gy on the involved field (IF). In order to observe an increase of 5-year overall survival (OS) from 15 (TRT) to 25% (S), 292 events out of 358 randomized pts had to be observed (log rank test, power 80%, type I error 5%). Secondary endpoints were progression free survival (PFS) and toxicity.
Results: ICT achieved an average response rate of 62% (95%CI: 58–66) among the 570 registered pts who started protocol treatment. Of these, 332 were randomized (167 to S and 165 to TRT), having the following characteristics: median age 61 years; male 74%; squamous/non-squamous: 40/60%; T1/2/3: 12/68/17%. In the 154 operated S pts, the following rates were observed: exploratory thoracotomy: 14%; radical resection: 50%; pathological downstaging: 42%; pathological complete response: 5%; operative mortality: 4%; PORT 40%. Among 154 pts randomized to TRT and actually irradiated, median total treatment time was 43 days (15–60). CT-scan planning was used in 92%. The median total dose delivered to the normal mediastinum/IF was 40/60 Gy, respectively. A grade 3/4 acute side effect of any kind occurred in 9% of irradiated TRT pts and 1 patient died of radiopneumonitis. With a median follow up of 72 months, median and 5 year OS for pts randomized to S and TRT are 16.4 vs.17.5 months and16 vs. 13%, respectively (HR 1.08, 95% CI 0.84–1.35). Median and 2y PFS for pts randomized to S and TRT are 9.0 vs.11.3 months and 27 vs. 24%, respectively (HR 1.06, 95% CI 0.85–1.33). Subgroupanalysis shows lobectomy and mediastinal downstaging to be linked to better survival.
Conclusion: In selected pts with proven stage IIIA-N2 NSCLC and a response to ICT, S improves neither OS nor PFS in comparison to TRT.

1121 ORAL

The impact of giving neo-adjuvant chemotherapy for patients with non-small cell lung cancer (NSCLC): data from the MRC LU22/NVALT/EORTC 08012 randomised clinical trial

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Background: Patients with resectable NSCLC were randomised to receive either surgery alone (S) or 3 cycles of cisplatin-based chemotherapy followed by surgery (CT-S). On a patient by patient basis, chosen prior to randomisation, clinicians could choose to give MIC, MVP, cisplatin/vinorelbine, carboplatin/paclitaxel, carboplatin/docetaxel or cisplatin/gemcitabine. Using data from the first 500 patients randomised, this paper reports on the impact of neo-adjuvant chemotherapy in terms of its feasibility, toxicity, response rates, downstaging, and extent of resection. Survival endpoints will be reported when the required number of events (233) have been achieved.
Material and methods: Patients (252 S, 248 CT-S) were entered from 66 centres in the UK, the Netherlands, Germany and Belgium from July 1997 to Nov 2004.
Results: The main patient characteristics were well balanced between the 2 treatment groups at randomisation: median age 63 years, male