prognostic effect. CEA and PLUNC expression provides a tool for selecting high-risk p considered for adjuvant therapies

6544 POSTER

Individualized high-dose continuous hyperfractionated accelerated radiotherapy (HI-chart) of non-small cell lung cancer (NSCLC) based on normal tissue constraints: a prospective clinical trial

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Background: Local recurrence is a major problem after (chemo-)radiation for NSCLC. We hypothesized that for each individual patient the highest therapeutic ratio could be achieved by increasing the total tumor dose (TTD) to the limits of normal tissues, delivered within 5 weeks. In a theoretical model this resulted in an increase in tumor control probability from approximately 5% for a classical scheme (60 Gy in 6 weeks) to 25% for the study scheme. Here, we report the first results of a prospective clinical trial.
Materials and Methods: Twenty-nine patients with medically inoperable (stage I, n = 2) or locally advanced NSCLC (stage III, n = 27), in a good general condition (WHO-PS 0−1) and with a reasonable lung function (FEV1 >50% of predicted) were included. Most patients (25/29) received induction chemotherapy. All patients were irradiated using an individualized prescribed TTD, based on normal tissue constraints (mean lung dose 19 Gy, maximal spinal cord dose 54 Gy, no esophageal constraints) up to a maximal TTD of 79.2 Gy in 1.8 Gy fractions, twice daily. Toxicity was scored using the CTCAE-criteria. A FDG-PET-CT scan (n = 27) was performed to evaluate (metabolic) response 70 days after radiotherapy according to EORTC-criteria (PET) and RECIST-criteria (CT). The Kaplan-Meier method was used to compute overall survival.
Results: The mean delivered dose was 62.7 Gy (range 46.8−79.2 Gy), equivalent to a biological dose of approximately 80 Gy. Most patients experienced mild acute toxicity, while only 2 patients (7%) developed acute grade 3 toxicity (n = 1 dysphagia, n = 1 cough). Concerning late toxicity, 93% of patients (n = 25) showed radiographic changes (75% in <25% and 18% in >25% of the lungs), while 12 out of 28 patients (43%) had clinical symptoms (⩾gr 2 pneumonitis). One patient (3%) died 51 days after radiotherapy due to pneumonitis (treatment related mortality). The post-radiotherapy PET-CT showed in 18 patients a metabolic response (41% complete metabolic response, 26% partial metabolic response), whereas only in 9 patients (33%) a response was seen on CT (p = 0.01). Seventeen patients (59%) showed progressive disease, consisting of loco-regional progression (n = 6), metastases (n = 6) or a combination of both (n = 5). With a median FU of 16 months the median overall survival was 19.6 months and a 1-yr and 2-yr survival of resp. 59% and 45%.
Conclusions: Personalized HI-CHART radiation prescription based on normal tissue constraints is tolerable and initial results are promising.

6545 POSTER

Clinical significance of serum TERTmRNA detection in lung cancer patients

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Background: Using a newly developed assay of telomerase reverse transcriptase (hTERT) mRNA in serum by real-time RT-PCR, we previously reported this assay to be superior to other tumor markers for hepatoma. In this study, we attempted to clarify its clinical significance as a biomarker for lung cancer.
Materials: In 89 patients with lung cancer and 27 individuals without it, we measured serum hTERT mRNA and epidermal growth factor receptor (EGFR) mRNA levels, using a quantitative one-step real-time RT-PCR assay. We examined its sensitivity and specificity in lung cancer diagnosis, its clinical significance in comparison with other tumor markers, and its correlation with the clinical parameters using multivariate analyses and correlation relative test.
Results: The copy number of serum hTERT mRNA was independently correlated with tumor size, tumor number, the presence of metastasis and recurrence, and smoking ($P < 0.05$, each). EGFR mRNA correlated with tumor size, tumor number, recurrence, and clinical stage ($P < 0.05$, each). The sensitivity/specificity in lung cancer diagnosis were 71.8%/72.5% for hTERT mRNA, 60.8%/62.5% for EGFR mRNA, respectively. hTERT mRNA was superior to other tumor markers in lung cancer diagnosis. Both mRNAs in serum were significantly correlated with those in lung cancer tissues ($P < 0.05$ for hTERT, $P < 0.05$ for EGFR, respectively). The copy number of hTERT mRNA significantly decreased after the surgical treatment.
Conclusions: The combination of both mRNAs improved the sensitivity/specificity to 82.8%/77.7%, thus suggesting that hTERT mRNA, especially when combining with EGFR mRNA, is a novel and excellent biomarker for pulmonary malignancies to diagnose and assess the clinical stage and effects of treatments.

6546 POSTER

Postoperative 3D conformal radiation therapy with dose-volume histogram assessment in non small-cell lung cancer

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Background: Despite many randomized trials, the indication of postoperative radiation therapy (PORT) in non small cell lung cancer (NSCLC) is controversial. Involved-field conformal (3D) RT has never been studied prospectively. In this study, we aim to assess the outcome of patients treated with involved-field 3D PORT with or without chemotherapy in locally advanced NSCLC.
Materials and Methods: From 1990 to 2006, data from 75 consecutive patients treated with curative surgery and PORT for NSCLC were retrospectively analyzed. Male to female ratio was 57/18, and median age was 58 years (38−76). There were 5 patients with stage I, 22 with stage II, and 48 with stage III disease. Pneumonectomy or lobectomy was realized in 24 and 51 patients, respectively. Mediastinal lymphadenectomy was performed in all patients. PORT indications were positive margins and/or positive mediastinal lymph nodes. Cisplatinbased chemotherapy was given in 15 patients. All patients had 3D conformal planning. Median RT dose was 60 Gy using at least 6-MV photons in 6 weeks, and CTV included bronchial stump and only positive nodal areas. Dose-volume histograms (DVH) assessing the pulmonary volume receiving 20 Gy (V20 Gy) were used in all patients.
Results: Compliance to PORT was 100%. In a median follow-up period of 55 months, 26 (35%) patients are alive without disease. Median overall survival time was 24 months, with survival rate of 35% at 5 years. The 5-year locoregional control and distant disease-free rates were 80% and 57%, respectively. Patients treated with pneumonectomy and those treated with at least 60-Gy PORT had better outcome. Grade 3 or more CTC v3.0 toxicity was observed only in 4 (5%) patients. No lethal toxicity was observed.
Conclusions: We conclude that involved-field 3D conformal 60-Gy PORT tailored with DVH V20 Gy assessment improves locoregional control without increasing lethal toxicity. Prospective studies using the above-mentioned criteria are warranted.

6547 POSTER

SNS-595: Preliminary results of 2 phase 2 second line studies in lung cancer

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SNS-595 is a novel cell-cycle inhibitor that induces DNA damage responses, G2 arrest, and apoptosis. SNS-595 currently is being tested clinically in AML, ovarian cancer, and SCLC.

Objectives: To assess the response rate (RR), using RECIST criteria, patient safety, and time to progression (TTP), duration of response (DOR), and overall survival (OS) in patients (pts) with refractory (Ref) and sensitive (Sen) SCLC and advanced NSCLC treated with SNS-595.
Methods: In both studies, SNS-595 was given q21-days at a dose of 48 mg/m^2 IV bolus for up to 8 cycles. Both studies used a 2-stage Fleming design. The SCLC study had 2 strata, refractory (Ref = relapsed <90 days after end of initial therapy or never responded) and sensitive (Sen = relapse >90 days after response to initial therapy). The SCLC study was powered to distinguish between 4% and 18% RR for the Ref and 11% vs 30% RR for the Sen strata. The study enrolled 20 pts in stage 1 for both strata and required at least 1 response in the Ref and 2 responses in the Sen for continuation to stage 2 and enrollment of 20 more pts in each stratum.
The NSCLC study was powered to distinguish between an RR of disinterest of 3% and one of interest at 15%. The study required a minimum of 1 response in the first 25 pts for study continuation to study stage 2 with 25 more pts.
Results: See the table.

Patient demographics, outcomes, Gr 3 or 4 AEs (>10%).

# Eval	SCLC-Sen 11	SCLC-Ref 20	NSCLC 25
Age (yrs) (med, range)	56, 46−65	60, 46−81	60, 35−76
Sex (M/F)	6/9	11/6	16/9
Race (Cauc, Afr-Amer)	15/0	17/0	22/3
# cycles (median, range)	4, 2−5	2, 1−6	2, 2−6
Best response			
Complete resp (CR)	0	0	0
Partial resp (PR)	2	0	0
Stable dis (SD)	7	5	14
Progressive dis (PD)	2	15	11
# (%) Pts with Gr 3 or AEs	2 (14%)	9 (45%)	8 (32%)
Neutropenia	2	3	2
Febrile neutropenia	0	2	1
Pneumonia	0	2	3

Conclusions: SNS-595 demonstrates clinical activity as single agent 2nd-line therapy in SCLC-Sen and NSCLC. For SCLC-Sen pts, overall RR is 2/11 (18%), with 9/11 (82%) showing SD or better. For NSCLC pts, over 50% show SD. SNS-595 is well tolerated with neutropenia being the main Grade 3 or 4 AE that occurred in 8−18% of pts. SNS-595 met the pre-determined RR for 14 pts in the SCLC-Sen cohort warranting expansion of this cohort to additional patients. Further accrual and follow-up continues.

6548 POSTER

Phase II study of sunitinib malate (SU) as consolidation therapy in patients (pts) with locally-advanced or metastatic non-small cell lung cancer (NSCLC)

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Background: SU is an oral, multitargeted tyrosine kinase inhibitor of VEGFRs, PDGFRs, KIT, RET, and FLT3, approved for the treatment of advanced RCC and imatinib-resistant or -intolerant GIST. An earlier phase II study of sunitinib monotherapy in treatment-refractory NSCLC reported an 11.1% response rate. This study has been evaluating the activity of SU in NSCLC pts when used as consolidation therapy following standard first-line therapy.
Materials and Methods: Pts are treated with up to 4 cycles of carboplatin (AUC=6 mg·min/mL) plus paclitaxel (175–225 mg/m^2) (CP), followed by up to 9 cycles on study of SU (50 mg/d in 6-wk cycles: 4 wks on treatment, followed by 2 wks off) in this ongoing open-label, uncontrolled, multicenter, phase II trial. The efficacy and safety of single-agent SU following CP was assessed in adult pts with locally advanced or metastatic NSCLC, with no prior systemic or antiangiogenic therapy for NSCLC, ECOG PS 0/1, and adequate organ function. The primary endpoint is 1-year survival. Secondary endpoints include objective response rate, progression-free survival, overall survival, and safety measures.
Results: 84 pts have been enrolled (81 pts treated), and data on 76 pts are reported. Baseline characteristics have included: mean age 61 yrs (range 30–81); male 61%; ECOG PS 0/1/2 36%/63%/1%; smoker 89%; adenocarcinoma 36%, squamous cell carcinoma 21%, large cell carcinoma 21%, other 22%. Median number of CP cycles was 4 (range 1–4); median number of SU cycles was 2 (range 1–5+) with 52 pts starting 4 cycles of CP and 64 pts receiving at least 1 dose of sunitinib. At completion of CP, there were 13 PR, 44 SD and 9 PD as best response (n = 68). To date, of pts receiving SU, 1 initial PR became a CR, and 1 SD converted to PR. 92% of pts in the CP treatment phase and 89% in the consolidation phase experienced an adverse event (AE). The most common AEs in SU-treated pts were fatigue (38%), diarrhea (36%), nausea (23%), the majority of which were mild-to-moderate in severity. The most common grade 3/4 AE with SU was fatigue (13%/2%). 13 pts discontinued SU due to an AE.
Conclusions: SU is associated with acceptable safety when used following first-line carboplatin/paclitaxel therapy in adult pts with locally advanced or metastatic NSCLC. The preliminary confirmed response rate to CP of 19% (13/68) is similar to that expected for this pt population; additional tumor reduction may occur in some pts with early SU treatment following chemotherapy.

6549 POSTER

Treatment of recurrent or progressive brain metastases with patupilone in patients with non-small cell lung cancer (NSCLC): results of a multicenter, open-label phase II study

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Background: Advances in chemotherapy and delivery of radiation therapy have improved overall survival for patients with advanced non-small cell lung cancer (NSCLC); however, central nervous system (CNS) metastases occur in ⩾50% of patients with NSCLC and limits the survival benefits of current therapies. The novel epothilone patupilone has shown antitumor activity, in contrast to taxanes, in preclinical brain tumor models and in patients with NSCLC. The current study evaluated the activity of patupilone for the treatment of recurrent or progressive brain metastases in patients with NSCLC. All of these patients progressed after previous chemotherapy, surgery, and/or radiation to the brain.
Material and Methods: This was an open-label, multicenter, phase II, single-arm, multinomial, 2-stage study (25 patients per stage). Patients had histologically confirmed NSCLC and ⩾1 recurrent, bidimensionally measurable intracranial lesion ⩾2 cm. Patupilone was administered as a 10 mg/m^2 single IV infusion over 20 minutes every 3 weeks until disease progression (PD), satisfactory response, or unacceptable toxicity. Safety was assessed by adverse event (AE) reporting. Early progression (PD or death before cycle 1, day 21) and response rate (alive without PD at cycle 4, day 1) were the primary efficacy endpoints.
Results: The clinical review of emerging data consisted of 15 patients with a median age of 59 years (range, 40 to 67 years). The most commonly reported AEs related to the study drug were National Cancer Institute Common Toxicity Criteria grade 1/2 diarrhea (7/15 patients; 47%), nausea (4/15 patients; 27%), and fatigue (3/15 patients; 20%). There were 6 grade 3 AEs reported: 4 events related to study drug (3 cases of diarrhea, 1 additional case of diarrhea and neutropenia) and 2 events not related to study drug (confusion, dementia). There were 3 grade 4 AEs reported but not related to study drug (colitis, pulmonary embolism, headache). Five (33%) patients experienced early progression and 6 (40%) patients responded to therapy (without progression by cycle 4, day 1) for a median of 8 cycles (range, 5 to 13 cycles). The remaining 4 patients had stable disease or have not reached cycle 4 at the time of the clinical review.
Conclusions: Patupilone was well tolerated and has shown activity in patients with CNS metastases from advanced NSCLC. Further studies warrant investigation of patupilone as a treatment for brain metastases from NSCLC.