local control (LC), regional control (RC) and metastasis-free survival (MFS).
A strong correlation between total lymph node tumour volume and N-stage was found (Rs=0.93, P<0.01). MFS was worse with involvement of the lower neck levels (Rs=0.345, P<0.01). Patients with larger total lymph node tumour volumes had poorer RC and MFS rates, independent of treatment regimen. For total lymph node volumes up to 3.5 cm^3, MFS can be improved by ARCON (P<0.01).
Conclusions: The strong prognostic value of T-stage and primary tumour volume, observed in retrospective analyses was not confirmed in patients treated in a prospective randomised trial with accelerated radiotherapy with or without carbogen breathing and nicotinamide. Results of this study indicate that (biological) factors other than primary tumour volume and T-stage are needed to select patients with laryngeal cancer for treatment intensification.

PD-0094
EGFR inhibition radiosensitizes NSCLC cells via permanent G1 arrest but only when p53/p21 signaling is intact
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Purpose/Objective: Radiotherapy combined with targeting of the epidermal growth factor receptor (EGFR) is considered to be a promising new tool to increase tumor control. However, the data available so far, indicate that probably only a subgroup of patients may actually benefit from this new treatment. In order to identify these patients the mechanisms of EGFR targeting has to be known. We asked whether cell cycle effects as caused by EGFR targeting may play a critical role when combined with irradiation and whether biomarkers can be established for this interaction.
Materials and Methods: Study was performed with cell lines differing in p53 status (A549, H1299, H460, H3122, HCT116, FaDu) as well as in A549 grown as xenografts. Cell cycle analysis was measured via FACScan and kinetics of G1 population was followed using colcemid assay. Protein expression was determined via Western, p21 was knocked down via siRNA; cell survival by colony assay, for xenograft model tumor control probability was determined after conventional fractionation.
Results: Targeting of EGFR alone by tyrosine kinase inhibitors (Erlotinib and BIBX1382BS) was able to induce a strongly pronounced accumulation of cells in G1. But this effect was mostly transient. In combination with X-irradiation both TK inhibitors were found to enhance the radiation-induced permanent G1 arrest to a great extant. This effect, however, only occurred in cells with intact p53/p21 signaling. No such an effect was seen in tumor cells mutated in p53 or deleted in p21 or when p21 was knocked down via siRNA. For tumor cell lines showing this increase in permanent G1 arrest, TK inhibitors were always found to result in a moderately enhanced cellular radiosensitivity and vice versa. In a xenograft model, blockage of EGFR was also found to result in a trend towards higher local control.
Conclusions: Overall these data suggest that both *in vitro* as well as *in vivo* EGFR inhibition may lead to a moderately increased radiosensitivity but only when p53/p21 signaling is intact. In order to increase these effects on tumors, radiation and EGFR targeting need to be combined with agents specifically affecting the permanent G1 arrest.

PD-0095
Dosimetric parameters predictive for radiation pneumonitis after SABR for high-risk lung tumors
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Purpose/Objective: Treatment of larger and more centrally located lung tumors with SABR results in high local control, but higher rates of radiation pneumonitis (RP) have been reported. We studied predictors of RP in high-risk patients treated with SABR, to optimize treatment planning objectives.
Materials and Methods: A review was performed of 79 SABR patients at high risk for RP, due to either a PTV>100cc (n=69) or prior pneumonectomy or bi-lobectomy (n=13). All were treated using RapidArc with risk-adapted fractionation schedules. Volume of the total lung(TL), ipsi-(IL) and contralateral lung (CL) receiving 5Gy (V5) to 50Gy (V50) with 5Gy increments were calculated after converted dose to biologically equivalent doses (α/ß 3). These factors, mean lung dose (MLD) and clinical parameters were included in univariable and multivariable logistic regression to identify predictors of CTCAE v4.03 grade ≥3 RP. Concordance-statistics (C-statistic) were used to quantify the degree of association of the factors with high grade RP.
Results: Median follow-up of patients alive was 12.6 months (2.5-32.5). Median PTV was 150cc (13-411cc). Grade≥3 RP was observed in 8 patients (10.1%), at a median time to onset of 6.1 months. In univariable analysis, CL-MLD, CL-V5-15,TL-MLD, TL-V5 and V10 as well as the ITV volume were all related with RP (all p-values <0.05). Multivariable analysis showed contralateral MLD (p=.007) and ITV (p=.063) to best predict grade ≥3 RP, and the model achieved excellent discrimination with a C-statistic of 0.87. The highest risk for RP was found if the contralateral MLD was ≥ 3.6Gy (for 3 out of 8 patients) or if ITV size was ≥ 145cc (2 out of 7 patients). Lowest risk (1 case out of 54) was found for patients outside these two groups.
Conclusions: The contralateral MLD and ITV strongly correlated with risk of Grade≥3 pneumonitis after SABR. New strategies are needed to minimize this risk.

PD-0096
Contralateral hilar or supraclavicular lymph nodes do not impact OS in PET-staged patients with stage I-III SCLC.
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Purpose/Objective: Traditionally patients with contralateral hilar or supraclavicular lymph nodes are often denied curative treatment for stage III small cell lung cancer (SCLC). We hypothesized that the prognostic impact of these lymph nodes is less pronounced in PET-staged SCLC patients due to more accurate staging.
Materials and Methods: Analysis of 111 patients in our prospective database with stage I-III SCLC referred for concurrent chemo-radiotherapy. All patients received a PET-scan as part of their staging work-up. Standard treatment was 45 Gy in 1.5 Gy fractions twice daily concurrently with carboplatin-etoposide, followed by prophylactic cranial irradiation (PCI) in case of non-progression. Only PET-positive or pathologically proven lymph nodes were included in the Gross Tumor Volume (GTV). Survival was calculated from pathologic diagnosis (Kaplan-Meier method).
Results: Out of 111 patients, 10 (9%) had contralateral hilar and 29 (26%) had supraclavicular lymph nodes. Median overall survival for the entire cohort was 20 months (95% CI 17.8-22.1 months), 2-year survival 39%. In univariate analysis neither having supraclavicular nodes (p= 0.675) or contralateral hilar nodes (p=0.536) significantly impacted survival. Median survival was 19 months (95% CI 16-21.9 months) for stage III patients with contralateral hilar and/or supraclavicular lymph nodes and 21 months (95% CI 16-25.9 months) for other patients with stage I-III disease.
In a multivariate Cox regression analysis including WHO-PS, age, gender, LDH, PCI, time between start of any treatment and the end of radiotherapy (SER), GTV, stage and having supraclavicular or contralateral hilar lymph nodes only WHO-PS (p=0.011), GTV (p=0.025) and delivery of PCI (p<0.001) reached significance. Patients with supraclavicular (p=0.997) or contralateral hilar lymph nodes (p=0.749) did not have a significantly worse prognosis.
Conclusions: In stage I-III SCLC staged with PET and treated with modern concurrent chemo-radiation, the presence of supraclavicular or contralateral hilar lymph nodes does not have a significant impact on overall survival. These patients should therefore be offered treatment with curative intent.

PD-0097
Impact of new Dutch guideline on patient selection for WBRT in a large lung cancer cohort
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