Proceedings Paper:
Hanna, G., McDonald, F., Greystoke, A. et al. (7 more authors) (2017) EP-1228 : UK NCRI CTRad consensus on drug and radiotherapy combination platform studies in NSCLC. In: Radiotherapy and Oncology. ESTRO 36 - European Society for Radiotherapy & Oncology, 05-09 May 2017, Vienna, Austria. Elsevier , S662-S663.

https://doi.org/10.1016/s0167-8140(17)31663-8

total BED10Gy (a/b = 10) prescribed dose as treatment related factors were analysed using log-rank test to determine their impact on outcome.

Results

Between 05/2010 and 03/2016, 131 patients with 164 lesions were irradiated. Treatments were delivered 3x/week in a median of three fractions. According to the RECIST criteria a complete or partial response were observed in 86 and 27 lesions, while 12 remained stable. After mean follow-up of 14 months, the 1 and 2-year LC/lung PFS/DPFS/OS were 85.0/62.2/82.6/91.3% and 69.0/44.8/69.8% and 77.9% respectively. Age (>65 years) and controlled primary tumour influenced DPFS (p=0.017) and OS (p=0.02) respectively, while LC and OS differed significantly for BED10Gy (>120 vs. <=120 Gy, p<0.001 and p =0.016) and primary histology (adenocarcinoma or others, p=0.003 and p=0.006) (Figure 1 and 2). Grade 1/2/3/4 fatigue, chest pain and dyspnoea were present in 77/3/0/0, 20/0/0/0 and 26/1/1/0 treatments as acute, while 22/0/0/0, 14/37/0/0 and 18/2/3/1 as late toxicity. One patient died due to RT-induced pulmonary haemorrhage.

Figure 1: Kaplan-Meier curves and log-rank test for LC

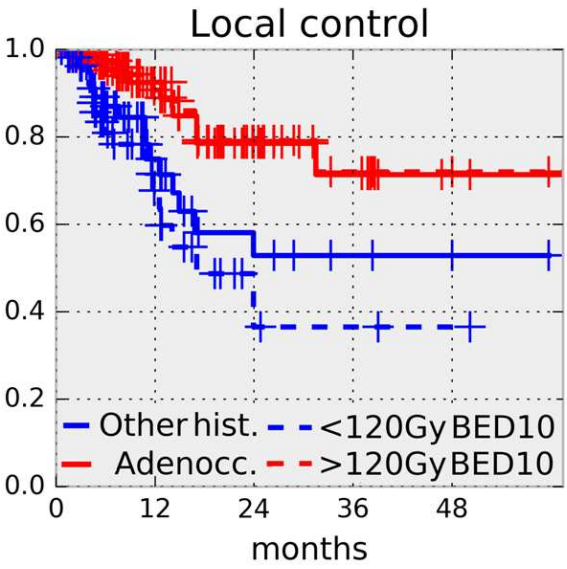
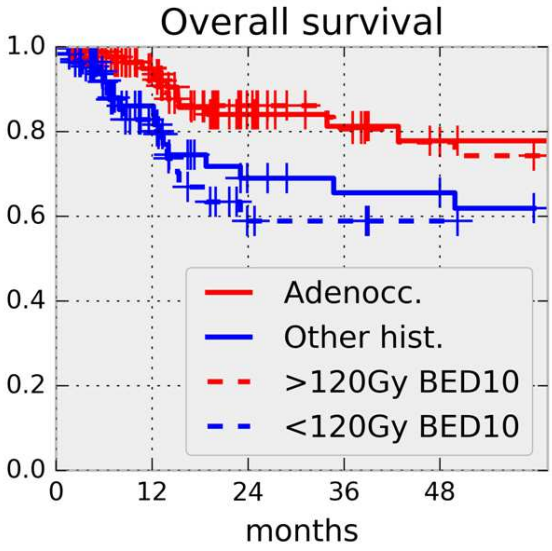


Figure 2: Kaplan-Meier curves and log-rank test for OS



Conclusion

Our favourable outcome data reinforces the paradigm shift of SBRT in oligometastatic pulmonary disease. Longer follow-up is required especially concerning patient selection and fractionation schedules to secure adequate dose and to further strengthen the position of this treatment option.

EP-1227 Neutrophil-lymphocyte ratio and a dosimetric

Y.H. Lee[1], H.S. Choi[1], H. Jeong[1], K.M. Kang[1], J.H. Song[2], W.S. Lee[3], G.W. Lee[3], H.N. Song[3], H.G. Kim[4], M.H. Kang[4], D.Y. Rhee[5], B.K. Jeong[1]

[1]*Gyeongsang National University Hospital, Radiation Oncology, Jinju-si, Korea Republic of*

[2]*Gyeongsang National University Changwon Hospital, Radiation Oncology, Changwon-si, Korea Republic of*

[3]*Gyeongsang National University Hospital, Internal Medicine, Jinju-si, Korea Republic of*

[4]*Gyeongsang National University Changwon Hospital, Internal Medicine, Changwon-si, Korea Republic of*

[5]*Gyeongsang National University Hospital, Emergency Medicine, Changwon-si, Korea Republic of*

Purpose or Objective

To identify the predictive factors for pr ogression of radiological radiation pneumonitis (RP) to symp tomatic RP and to evaluate the usefulness of the neutrophil-lymphocyte ratio (NLR) as a severity and prognosis marker of RP in stage III non-small-cell lung cancer (NSCLC) patients treated with definitive concurrent chemoradiotherapy (CCRT).

Material and Methods

The study included 61 patients treated between January 2010 and December 2015. The patient char acteristics, tumor factors, laboratory findings, and treatment parameters were recorded. Among patients with radiological RP, the predictive factors associated with progression to symptomatic RP were assessed.

Results

Of the 61 patients, 47 (77%) showed radiological RP at a median of 78 days after radiation therapy (RT) completion, and of these, 15 patients (32%) developed symptomatic RP. The interval between RT completion and radiological RP was shorter in patients with progression than in those without progression (p=0.001), and in the latent period within 2 months, progression was highly probable (p=0.002). Stage and the RT technique were related to symptomatic RP (p=0.046 and p=0.046, respectively). Among dosimetric factors, lung volume receiving ≥20 Gy (V_{20}) of >30% was the most significant factor for symptomatic RP (p=0.001). The NLR (NLR_R) and C-reactive protein level at radiological RP were higher in patients with symptomatic RP than in other patients (p=0.012 and p=0.067, respectively). In multivariate analysis, V_{20}>30% and NLR_R>6 were associated with symptomatic RP development. In receiver operating characteristic curve analysis, the combination of NLR_R>6 and V_{20}>30% improved the predictive power for symptomatic RP.

Conclusion

The NLR at radiological RP is a useful biomarker for predicting symptomatic RP development after CCRT in stage III NSCLC patients. Patients showing early appearance of radiological RP along with the combination of a high NLR and V_{20}>30% should be managed with caution as there is a high risk of symptomatic RP.

EP-1228 UK NCRI CTRad consensus on drug and radiotherapy combination platform studies in NSCLC

G. Hanna[1], F. McDonald[2], A. Greystoke[3], M. Forester[4], S. Brown[5], E. Hall[6], C. Faivre-Finn[7], S. Harrow[8], M. Hatton[9], A. Chalmers[10]

[1]*Queen's University Belfast, Centre for Cancer Research and Cell Biology, Belfast, United Kingdom*

[2]*Royal Marsden Hospital- NHS Foundation Trust, Department of Clinical Oncology, London, United Kingdom*
[3]*Newcastle University, Northern Institute for Cancer Research, Newcastle-Upon-Tyne, United Kingdom*
[4]*UCL Cancer Institute- University College London, Department of Medical Oncology, London, United Kingdom*
[5]*University of Leeds, Leeds Institute of Clinical Trials Research, Leeds, United Kingdom*
[6]*The Institute of Cancer Research- London, Clinical Trials and Statistics Unit-, London, United Kingdom*
[7]*University of Manchester, Division of Molecular and Clinical Cancer Sciences, Manchester, United Kingdom*
[8]*Beatson West of Scotland Cancer Centre, Department of Clinical Oncology, Glasgow, United Kingdom*
[9]*Weston Park Hospital, Department of Clinical Oncology-, Sheffield, United Kingdom*
[10]*University of Glasgow, Institute of Cancer Sciences, Glasgow, United Kingdom*

Purpose or Objective
Local control and systemic control need to be improved for patients with locally advanced and metastatic non-small cell lung cancer (NSCLC) and novel mechanism based therapies (MBT) drug and radiotherapy (RT) combinations have the potential to achieve this. Current models of early phase clinical trials for these combinations are developed in a piecemeal fashion leading to inefficiency and slow progress. We describe a joint UK National Cancer Research Institute Clinical and Translational Radiotherapy Research Working Group (NCRI CTRad) and Lung Clinical Studies Group (NCRI Lung CSG) initiative to develop two platform studies of MBT/RT combinations in the treatment of NSCLC.
Material and Methods
NCRI CTRad and the NCRI Lung CSG held a two-day consensus meeting in Glasgow in February 2016 to consider the optimal approach in the development of MBT/RT combinations. Invited participants included UK clinical and medical oncologists, statisticians, methodologists and industry partners active in NSCLC research. The consensus achieved is presented.
Results
It was agreed to establish 2 platform studies which will run in parallel. In patients with locally advanced NSCLC, a phase 1 study will test novel MBT agents, such as DNA damage repair inhibitors, in combination with curative intent RT in patients with stage 3 NSCLC. We agreed to use conventional fractionation to a dose of 60-66 Gray in 30-33 fractions. In patients with metastatic disease, a phase 2 study will investigate RT in combination with immunomodulating agents. It will investigate the use of RT under two scenarios: 1) palliative radiotherapy delivered for the purpose of symptomatic control; 2) radiotherapy delivered for the purpose of immune stimulation. Both platform studies will involve significant pre-clinical and translational components, will have Patient/Consumer involvement at the core of study development and seek to follow the recent NCRI CTRad Academia-Pharma Joint Working Group consensus for the clinical development of new drug-radiotherapy combinations.
Conclusion
The UK consortium establishing two platform studies of novel MBT/RT combinations offers a unique opportunity to rapidly improve outcomes for patients with NSCLC in a collaborative fashion.

EP-1229 Phase II trial of concurrent erlotinib in locally advanced non-small cell lung cancer (LA-NSCLC)
O. Hansen[1], M. Knap[2], A. Khalil[2], C. Nyhus[3], C. Brink[4], L. Hoffmann[5], T. Schytte[1]

[1]*Odense University Hospital, Oncology, Odense, Denmark*
[2]*Aarhus University Hospital, Oncology, Aarhus, Denmark*
[3]*Vejle Hospital, Oncology, Vejle, Denmark*
[4]*Odense University Hospital, Laboratory of Radiation Physics, Odense, Denmark*
[5]*Aarhus University Hospital, Medical Physics, Aarhus, Denmark*

Purpose or Objective
The survival of patients with LA-NSCLC treated with concurrent chemo-radiation (CRT) remains poor. We have performed a phase II study using the tyrosine kinase inhibitor, erlotinib, as radiosensitizer. Due to slow accrual, the study was terminated prematurely. We here report survival and toxicity data from the study.
Material and Methods
The main inclusion criteria were histological or cytological proven stage IIB-IIIAB NSCLC, PS 0-2. The patients were not candidate for CRT. The prescribed dose was 66 Gy/33F, 5F/week. The radiation technique was IMRT or ARC-therapy. No elective lymph nodes were treated. During RT, oral erlotinib was administered 150 mg daily. No chemotherapy was applied concurrent with RT.
The endpoints included overall survival (OS). The results were compared with the survival data from 48 patients treated for LA-NSCLC within the same period and in the same centers in a phase II study using oral vinorelbine (Vino) as radiosensitizer together with radiation 66 Gy/33F. However, the inclusion criteria for this study excluded patients in PS 2, and FEV1<1.

Pt. characteristics		Present study N=15	Vino-study N=48	P-value
Age	Median (range)	75.3 (49.1; 85.0)	64.8 (44.4; 79.4)	0.000
Gender	Male/Female	9/6	27/21	ns
Performance status	0/1/2	3/8/1	28/20	0.000
Histology	Squam/Adeno/NOS	8/6/1	17/32/10	ns
Stage	**2B/3A/3B**	2/10/3	3/35/10	ns

Results
From July 2009-August 2013, 15 patients from 3 centers entered the study.

The median OS was 16.9 months; the 1- and 2-year survival was 53% and 40%. In comparison, the survival data from the vino-trial was 21.0 months, 79% and 46% (P=0.11), see Fig 1. However, the patients in the vino-study were younger, and had better PS, see Table 1.
In the erlotinib study, 3 patients (20%) developed pneumonitis grade 3. In the vino-study, 8 patients (17%) developed grade 3 pneumonitis (p=ns).
Conclusion
This phase II study was prematurely closed. A trend for inferior survival was observed using erlotinib compared to vinorelbine as radiosensitizer, but the small number of patients and differences between the populations treated made the result inconclusive. However, the regimen erlotinib-RT was well tolerate

EP-1230 Post-operative radiotherapy (PORT) in patients with resected non small cell lung cancer (NSCLC)
T. Schimek-Jasch[1], M. Kuppler[1], S. Adebahr[1,2], A.L. Grosu[1], U. Nestle[1,2]

[1]*Uniklinik Freiburg, Department of Radiation Oncology, Freiburg, Germany*
[2]*German Cancer Consortium DKTK, Heidelberg, Partner Site Freiburg, Germany*