PO-0778 New prognostic factors in the SBRT treatment of early stage non-small cell lung cancer

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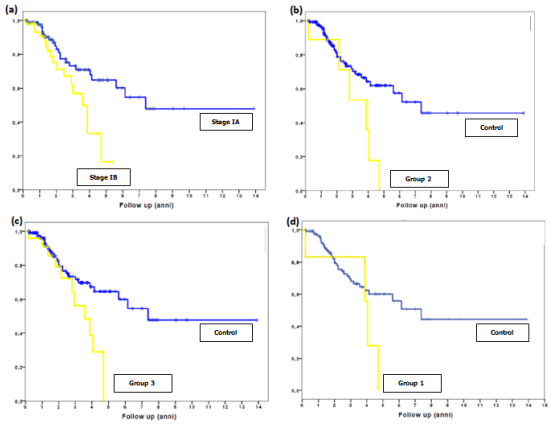
Purpose or Objective
The indication of SBRT in operable patients affected by early stage NSCLC who refuse surgery is always increasing, with the need to identify prognostic factors for disease control. Our study aims to identify histological and molecular biology factors for a prognostic stratification of these patients.

Material and Methods
The database of the radiotherapy institute of the University of Turin was retrospectively reviewed in search of patients underwent SBRT for early stage NSCLC from January 2003 to October 2017. Only patients with histological typing performed at the Pathology Unit of the University of Turin were included in the analysis. Patient and tumor data were collected together with immunohistochemistry and molecular biology data. Molecular biology data detected were EGFR mutation, ALK translocation, KRAS, ROS1 and BRAF mutation. the patients were analysed according to the subdivision into 3 groups. The first with the only KRAS positive, the second (unfavorable) with KRAS positive, ROS1 negative and BRAF positive, the third (very unfavorable) with the presence of the previous factors but EGFR and ALK negative. Total dose of treatment was prescribed at 80% isodose and risk-adapted treatment schedules were used. All patients were treated with a minimum BED of 100 Gy.

Results
142 patients were included in the analysis with a median follow-up of 22 months. Patient characteristics are listed in Table 1. Median progression free survival was 49 months. Stage (p = 0.008) and molecular biology factors (KRAS p = 0.007, unfavorable p = 0.004 and very unfavorable p <0.001) were statistically significant with univariate analysis. Stage (p = 0.02) and the very unfavorable group (p <0.001) were confirmed at the multivariate analysis. Median cancer specific survival was 73.7 months. Stage (p = 0.02) and molecular biology factors (KRAS p = 0.009, unfavorable p = 0.025, very unfavorable p = 0.027) were statistically significant in the univariate analysis as clinical predictors. Stage (p = 0.03) and the unfavorable group (p = 0.06) were confirmed in multivariate analysis. Local control at 12, 24 and 36 months was 95.8%, 83.6%, 80.1%, respectively. Stage (p = 0.005) and the very unfavorable group (p = 0.001) proved to be predictive for univariate analysis. Both factors were confirmed in multivariate analysis (p respectively of 0.01 and 0.008). Systemic control at 12, 24 and 36 months was 90.1%, 72.5% and 67.7%, respectively. Stage (p < 0.001), histology (p = 0.04) and molecular biology factors (KRAS p <0.001, unfavorable p <0.001 and very unfavorable p < 0.001) proved to be predictive for univariate analysis. Only stage and the very unfavorable group were confirmed at the multivariate analysis (p of 0.03 and 0.002, respectively).

Cancer Specific Survival



	Number (%)	Media (range)
Sex		
Male	114 (80,3)	
Female	28 (19,7)	
Age		75 (52 - 86)
Stage		
Ia	88 (62)	
Ib	50 (35)	
PTV Volume		46,6 (4 - 143)
Mean Lung Dose		11,9 (2,50 – 19,80)
BED		114,4 (100 - 151,2)
Diagnosis		
Adenocarcinoma	83 (58,4)	
Squamous cell carcinoma	42 (29,6)	
NSCLC NOS	14 (9,8)	
Others	3 (2,1)	
Pattern		
Papillary	6	
Acinary	8	
Lepidic	2	
Micropapillary	1	
Solid	0	
Mixed	3	
TTF1		
Undeterminated	93 (65,5)	
Negative	15 (10,5)	
Positive	34 (24)	
P40		
Undeterminated	108 (76)	
Negative	13 (9,5)	
Positive	21 (14,5)	
KRAS		
Undeterminated	136 (95,8)	
Mutated	6 (4,2)	
Not Mutated	0 (0)	
EGFR		
Undeterminated	116 (81,7)	
Mutated	23 (16,2)	
Not Mutated	3 (2,1)	
ALK		
Undeterminated	126 (88,7)	
Translocated	1 (10,5)	
Not Translocated	15 (0,7)	
ROS1		
Undeterminated	140 (98,6)	
Mutated	0 (0)	
Not Mutated	2 (1,4)	
B-RAF		
Undeterminated	141 (99,3)	
Mutated	1 (0,7)	
Not Mutated	0 (0)	

Conclusion
Molecular biology and histological parameter, such as KRAS, could select a population of patients with more aggressive tumor. These patients may be deserving of greater personalization of therapy by dose intensification or integration with systemic therapies.

PO-0779 Current management of limited-stage SCLC and CONVERT trial impact: an EORTC LCG survey

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Purpose or Objective
The CONVERT trial (NCT00433563: once-daily (OD) vs. twice-daily (BD) thoracic chemoradiotherapy (CTRT)) confirmed that BD radiotherapy (RT) should continue to be considered the standard of care but impact on CTRT regimens in daily care is unknown. A European survey was launched to evaluate current practice in good performance status (PS) limited-stage small-cell lung cancer (LS-SCLC) patients suitable for chemo-radiotherapy (CTRT) to 1) assess the impact of the CONVERT trial and 2) identify relevant research questions for future clinical trials
Material and Methods
An European Organisation for Research and Treatment of Cancer (EORTC) Lung Cancer Group (LCG) survey containing 28 questions on LS-SCLC was distributed between April 2018 and October 2018 to the EORTC LCG and several European thoracic oncology societies' members.
Results
188 responses were analyzed (radiation oncologists: 50% [n=94], pulmonologists: 15% [n=28], medical oncologists: 23% [n=35]); 84% with >5 years' experience of treating SCLC. Italy (18%, n=34), Spain (16%, n=31), and the UK (15%, n=28) contributed the most. 87% (n=164) were aware of the CONVERT trial and 20% (n=38) included patients in the trial. Concurrent CTRT is favoured (n=169, 90%) compared to sequential treatment. OD is the most commonly used regimen, but the use of BDRT increased after the CONVERT publication (n=120, 64% prior to and n=107, 57% after the publication) (**Table 1**). 60-66 Gy in 30-33 fractions is the most commonly prescribed OD RT regimen (n=73/120, 61%). The main reasons for not implementing BD after the CONVERT publication are logistical issues (n=84, 45%) and inconvenience for patients (n=55, 29%). 139 respondents (74%) deliver 4 cycles of chemotherapy and 45 deliver 6 cycles (24%) routinely in the context of CTRT. G-CSF (granulocyte colony-stimulating factor) is used by 39%, either routinely or as secondary prophylaxis. Prophylactic cranial irradiation (PCI) is routinely used in patients who have not progressed after CTRT (n=178, 95%). The most commonly prescribed PCI dose is 25 Gy in 10 fractions (n=150, 80%) and more than half of respondents do not apply an upper age limit (n=100, 53%). The main research questions of interest for LS-SCLC are 1) integrating novel targeted therapies-immunotherapies (151, 80%) and 2) PCI (+/- hippocampal sparing) vs. MRI surveillance (134, 71%).

Table 1: Type of preferred radiotherapy delivered in the concurrent setting.

	Before CONVERT Total=176* N (%)	After CONVERT Total=180* N (%)
OD	120 (68)	107 (59)
Preferred regimen	60-66 Gy: 73/120 (61)	60-66 Gy: 70 (65)
Preferred regimen	45 Gy: 55/56 (98)	45 Gy: 72 (99)

*excluding respondents that never used concurrent CTRT

Conclusion
Although the CONVERT trial confirmed that BD radiotherapy should be considered the standard of care, OD (60-66 Gy in 30-33 fractions) remains the most prescribed radiotherapy fractionation.

PO-0780 Prognostic value of PD-L1 expression in locally advanced NSCLC treated with chemoradiotherapy

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Purpose or Objective
Immune checkpoint inhibitors (CPIs) are an integral part of multimodal treatment approach in locally-advanced stage non-small cell lung cancer (LA-NSCLC). Purpose of the present study was to investigate prognostic value of PD-L1 expression on tumor cells and tumor-infiltrating lymphocytes (TILs) in a single-center patient cohort treated with chemoradiotherapy.
Material and Methods
We collected tumor tissue samples and clinical characteristics of 37 LA- NSCLC patients treated with chemoradiotherapy between 2000 and 2004. The analyzed tissue was taken before therapy and immunostaining was performed by experienced pathologist. VENTANA PD-L1 (SP263) Rabbit Monoclonal Primary Antibody was used to detect PD-L1 in formalin-fixed, paraffin-embedded tissue through the OptiView CC1.The samples were pretreated for 64 minutes, the antibody incubation time measured 16 minutes. Dilution was not necessary (Ready-to-use, RTU). The histological staining was carried out by the Benchmark Ultra. Tumor cells and lymphocytes were analyzed separately. Based on PD-L1 expression (0%, 1-5%, >5%) 3 groups were defined.
Results
All patients were treated with definitive chemoradiotherapy (CRT). Follow-up data of all patients until death was available. One patient was diagnosed in UICC stage II, 31 patients in stage III and 5 patients in stage IV. Absolute majority (35 patients, 95%) were treated with concurrent cisplatin- and taxane-based CRT. 23 patients (62%) received consolidative chemotherapy. A total of 30 males (81%) and 7 females (19%) were evaluated, 11 of which (30%) were non-smokers, 26 (70%) had at least 20 pack years. Patients without (0%) and very low expression (1-5%) of PD-L1 on tumor cells showed a significantly better overall survival compared to the subgroup showing PD-L1 expression over 5% with 13.8 versus 6.6 months as well as one-year survival rate of 67.7 versus 33.3%, respectively (p=0.039). Expression of PD-L1 on the TILs showed no significant impact on overall survival (p=0.808).
Conclusion
PD-L1 expression on tumor cells correlates significantly with reduced overall survival in patients with LA-NSCLC treated with CRT. In contrast, PD-L1 expression on tumor-infiltrating lymphocytes has no impact on overall survival in our study.

PO-0781 30 Gy single dose SBRT: Outcome in a large series of patients with lung oligometastatic disease

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