

Definitive chemoradiotherapy of locally advanced non-small cell lung cancer (LA-NSCLC) with IGRT technique using TomoTherapy HD – updated analysis

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Background: Concurrent chemoradiotherapy (CCRT) of locally advanced NSCLC is considered a standard of care last two decades without important improvement except of adjuvant check-point inhibitor therapy. We present one-institutional results of chemoradiotherapy of inoperable NSCLC using daily 3D IGRT with TomoTherapy HD unit. In this abstract we present updated results with minimal and median follow-up 26/49 months, respectively.

Methods: A total of 39 patients with inoperable NSCLC staged by UICC7 and treated since April 2015 till September 2018 were included. Clinical data and radiation plans were retrospectively reviewed. Survival was analysed using Kaplan-Meier method, univariate analysis was done using Cox regression model. Our preferential chemotherapy regimen was cisplatin/vinorelbine three-weekly, carboplatin doublet with vinorelbine or paclitaxel was acceptable as well. Standard radiation dose was 66Gy/33fractions/6.5 weeks, daily MVCT was done.

Radiotherapy

Concurrent chemoradiotherapy	Yes	69 %
	No	31 %
Dose RT delivered (Gy)	≥ 66	69 %
	< 66	31 %

Chemotherapy

Patients having chemotherapy		100 %
Number of cycles	4	56 %
	< 4	44 %
Regimen	Cisplatin + vinorelbine	54 %
	Cisplatin + pemetrexed	5 %
	Carboplatin + paclitaxel	23 %
	Carboplatin + vinorelbine	18 %
Interval CT d1 – RT d1	≤ 35	54 %
	> 35	46 %

Results:

Patient characteristics

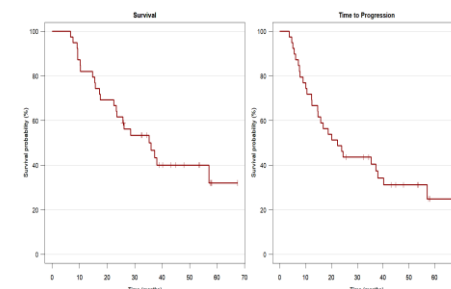
Gender	male	18 / 39 (46.15%)
	female	21 / 39 (53.85%)
Age	Mean ± SD	65.74 ± 7.73
	Median [I.Q.]	68 [61.5;71]
	≤60	9 / 39 (23.08%)
	>60	30 / 39 (76.92%)
Stage UICC 7	IIIA	12 / 39 (30.77%)
	IIIB+IV	13 / 39 (33.33%)
	I+II	5 / 39 (12.82%)
	Recurrence	9 / 39 (23.08%)
Histology	Adenocarcinoma	15 / 39 (38.46%)
	Adenoca + Sarcomatoid	1 / 39 (2.56%)
	NOS	8 / 39 (20.51%)
	Squamous	15 / 39 (38.46%)
Localization	Left lower	6 / 39 (15.38%)
	Left upper	11 / 39 (28.21%)
	Non specified	1 / 39 (2.56%)
	Right lower	7 / 39 (17.95%)
	Right upper	13 / 39 (33.33%)
	Right middle	1 / 39 (2.56%)
PTV Volume	≤440	30 / 39 (76.92%)
	>440	9 / 39 (23.08%)

Toxicity

Event	Grade 1-2 (%)	Grade 3-4 (%)
No febrile neutropenia		
Neutropenia	38	18
Anemia	64	0
Nausea + vomiting	20	3
RT esophagitis	64	3
RT pneumonitis	13	0

Survival and progression data

	Median [95% CI], months	3-year, % [95% CI]	5-year, % [95% CI]
Overall survival	36 (23,5;NA)	46,7 [32,9;66,2]	32 [17,6;58,3]
Time to progression	22,3 (14,7;57)	40,5 [27,5;59,5]	24,9 [12,9;48]



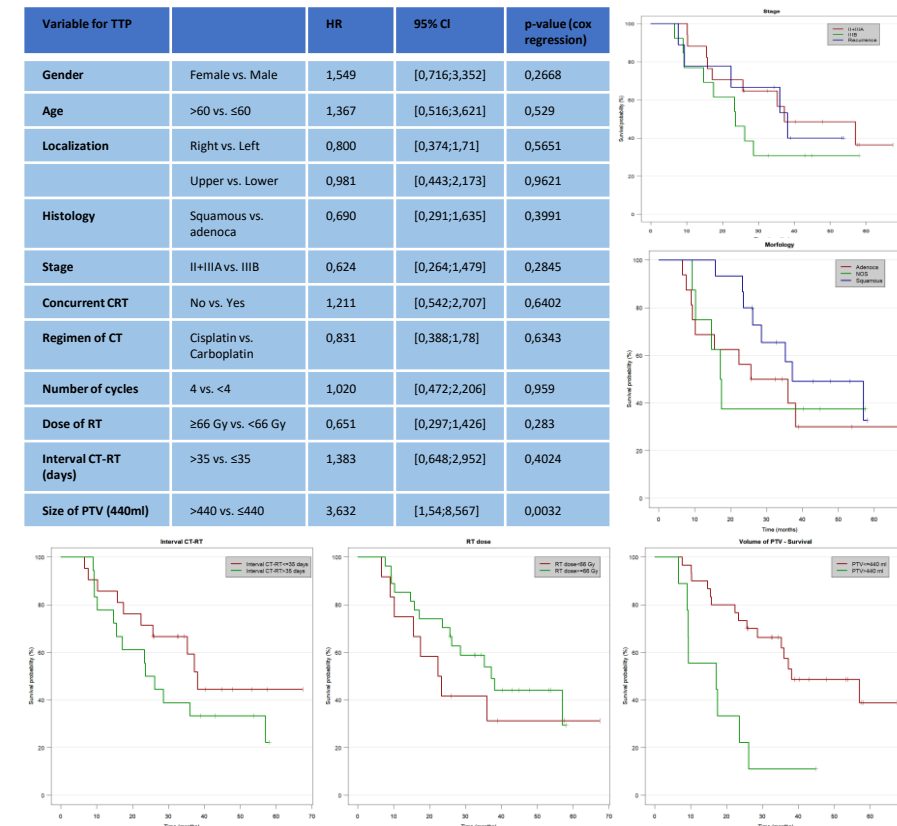
Reasons of progression

Any progression	59 %
Local progression only	15 %
Local + distant progression	18 %
Distant progression only	26 %
No progression	41 %

Analysis for prognostic variables

Univariate analysis did not find any difference in survival or TTP by age, gender, tumour location, SUVmax, regimen and length of chemotherapy, or concurrent treatment delivery. Non-significant trend of better outcome of stage II+IIIA, squamous cancer, higher dose of radiation and shorter interval between chemotherapy and radiotherapy observed in first analysis was not confirmed. Only significant variable was size of PTV. With cut-off 440ml the patients having greater size of PTV had significantly worse TTP in compare with those with smaller one (HR 3.63, 95%CI: 1.54;8.56).

Variable for TTP		HR	95% CI	p-value (cox regression)
Gender	Female vs. Male	1,549	[0,716;3,352]	0,2668
Age	>60 vs. ≤60	1,367	[0,516;3,621]	0,529
Localization	Right vs. Left	0,800	[0,374;1,71]	0,5651
	Upper vs. Lower	0,981	[0,443;2,173]	0,9621
Histology	Squamous vs. adenoca	0,690	[0,291;1,635]	0,3991
Stage	II+IIIA vs. IIIB	0,624	[0,264;1,479]	0,2845
Concurrent CRT	No vs. Yes	1,211	[0,542;2,707]	0,6402
Regimen of CT	Cisplatin vs. Carboplatin	0,831	[0,388;1,78]	0,6343
Number of cycles	4 vs. <4	1,020	[0,472;2,206]	0,959
Dose of RT	≥66 Gy vs. <66 Gy	0,651	[0,297;1,426]	0,283
Interval CT-RT (days)	>35 vs. ≤35	1,383	[0,648;2,952]	0,4024
Size of PTV (440ml)	>440 vs. ≤440	3,632	[1,54;8,567]	0,0032



Conclusion: Chemoradiation of inoperable NSCLC with IGRT technique using TomoTherapy HD has excellent results with 67% of durable local control and 3-year median survival. Only negative prognostic factor was higher size of PTV.