



2020 World Conference
on Lung Cancer Singapore

wclc2020.IASLC.com | [#WCLC20](https://twitter.com/WCLC20)

CONQUERING THORACIC CANCERS WORLDWIDE

Stage III NSCLC: Surgical/Combined Modality

Leah Backhus, MD MPH

Associate Professor

Division of Thoracic Surgery

Department of Cardiothoracic Surgery

Stanford University Cancer Institute

JANUARY 28-31, 2021 | WORLDWIDE VIRTUAL EVENT



2020 World Conference
on Lung Cancer Singapore

wclc2020.IASLC.com | [#WCLC20](https://twitter.com/WCLC20)

CONQUERING THORACIC CANCERS WORLDWIDE

DISCLOSURES

I do not have any relevant financial relationships to disclose



2020 World Conference
on Lung Cancer Singapore

wclc2020.IASLC.com | [#WCLC20](https://twitter.com/WCLC20)

CONQUERING THORACIC CANCERS WORLDWIDE

Neoadjuvant Therapy

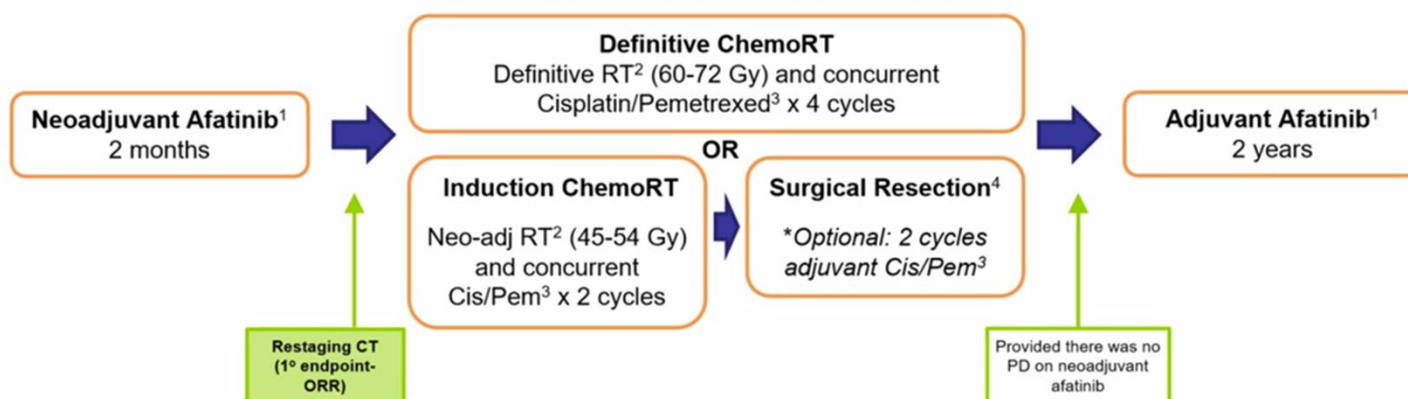
JANUARY 28-31, 2021 | WORLDWIDE VIRTUAL EVENT



FP01.05 - The ASCENT Trial: A Phase II Study of Neoadjuvant/Adjuvant Afatinib, Chemoradiation +/- Surgery for Stage III EGFR-Mutant NSCLC

Presenting Author(s): [Andrew Piper-Vallillo](#)

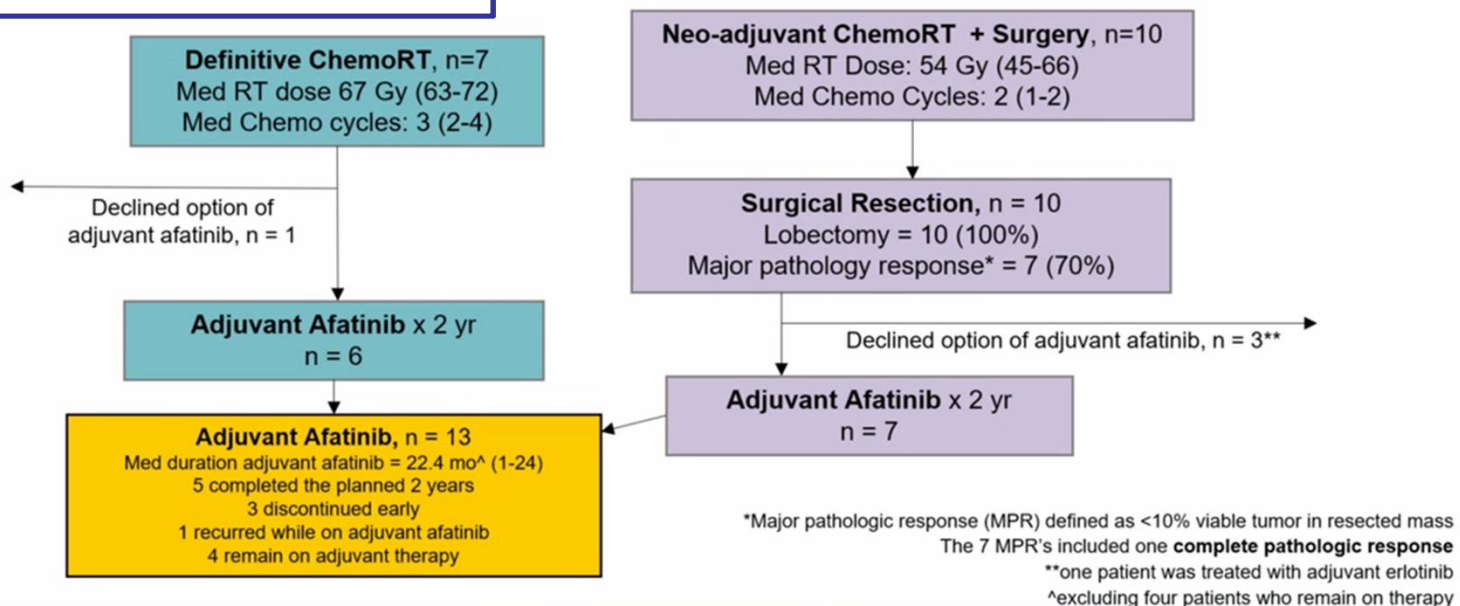
ASCENT: Study Schema



1. Afatinib dose: 40mg QD for neoadjuvant. Adjuvant dose was equal to patients' final neoadjuvant dose
2. Radiation: Dose ranges provided to allow for provider optimization and personalization
3. Chemotherapy: Cisplatin 75 mg/m² + Pemetrexed 500 mg/m² every 21 days
4. Surgery: Lobectomy or Pneumonectomy allowed



ASCENT TRIAL: DISPOSITION



- Planned for n=30 but closed early for slow accrual (n=19)
- STAGE IIIA = 13 STAGE IIIB = 6



Primary Outcome: ORR 11/19 (58%; 95% CI, 33-80%)

Key secondary outcomes, ITT population n=19

Outcome Measure	Median (95% CI)
Median PFS, months	34.6 (16.9 – 66.1)
Median OS, months	69.1 (29.4 – NR)
2-year OS	88% (59 – 97)

Outcome Measure	Number (%)
Recurrent tumor	9 (47)
CNS-only recurrence	5 of 9 (55)
Recurrence post-surgery	3 of 10 (30)
Recurrence post-definitive CRT	5 of 7 (71)

Median follow-up 30.6 months (range 3.1 – 96.3 months);
PFS, progression free survival; OS, overall survival

CONCLUSIONS:

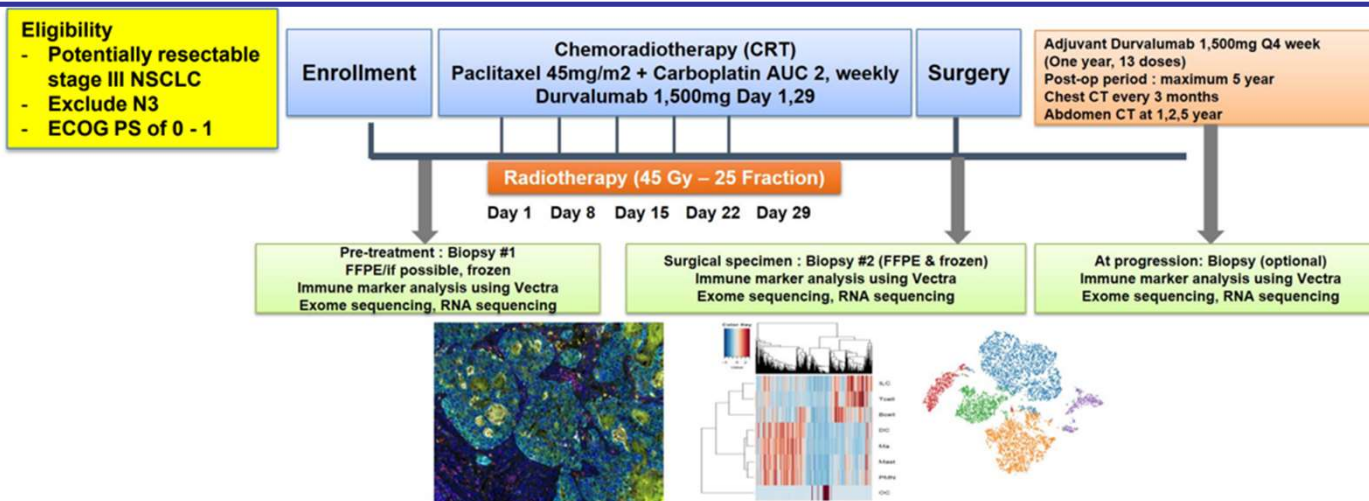
- In stage III EGFRm NSCLC, 2 months of neoadjuvant afatinib is associated with an ORR comparable to that seen in advanced disease and does not impair receipt of chemoradiotherapy ± surgery.
- PFS and OS are favorable in this single-arm study. High rate of CNS-only recurrence highlights a potential for improved outcomes with more CNS-penetrant EGFR TKIs.
- Along with the interim results of ADAURA, these results support genotype-directed therapies in stage III EGFRm NSCLC, though the optimal sequence of TKI therapy will need to be defined.



FP03.02 - Interim Analysis of Neoadjuvant Chemoradiotherapy and Durvalumab for Potentially Resectable Stage III Non-Small Cell Lung Cancer (NSCLC)

Presenting Author(s): [Min Hee Hong](#)

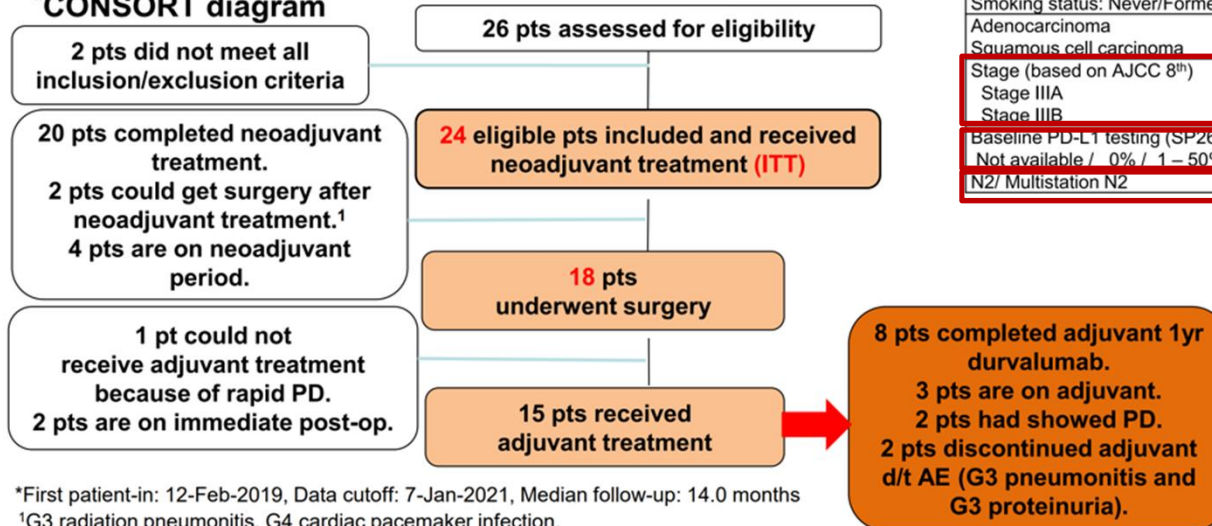
ACTS-30 Study Design: Examine for synergistic effects of combined PD-1/PD-L1 blockade to CRT via two-stage phase Ib clinical trial (ACTS-30) for safety and feasibility of the combination of N-CRT with durvalumab (PD-L1 inhibitor) in potentially resectable stage III NSCLC





FP03.02

*CONSORT diagram



Characteristics	n (%)
Age (year), median (range)	66 (41 – 76)
Male	20 (83.3%)
ECOG Performance status	
0	10 (41.7%)
1	14 (58.3%)
Smoking status: Never/Former/Current	1 (4.2%) / 11 (45.8%) / 12 (50.0%)
Adenocarcinoma	12 (50.0%)
Squamous cell carcinoma	12 (50.0%)
Stage (based on AJCC 8 th)	
Stage IIIA	14 (58.3%)
Stage IIIB	10 (41.7%)
Baseline PD-L1 testing (SP263)	
Not available / 0% / 1 – 50% / 50% or more	5 (20.8%) / 4 (16.7%) / 8 (33.3%) / 7 (29.2%)
N2/ Multistation N2	20 (83.3%) / 10 (41.7%)

*First patient-in: 12-Feb-2019, Data cutoff: 7-Jan-2021, Median follow-up: 14.0 months
¹G3 radiation pneumonitis, G4 cardiac pacemaker infection.



2020 World Conference on Lung Cancer Singapore

wclc2020.IASLC.com | #WCLC20

CONQUERING THORACIC CANCERS WORLDWIDE

FP03.02

Surgery

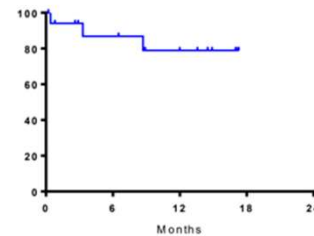
- Currently, 18 patients underwent surgery and all were R0 resection.
- 16 lobectomy, 1 bilobectomy, 1 pneumonectomy
- No in-hospital, 90-day postoperative mortality, or major post-operative morbidity were reported.

Pathologic responses, n (%) *MPR: defined as viable tumor cell of 10% or less

Total patients who underwent surgery	n = 18
Major pathologic response (MPR)*	14 (77.8% , 95% CI: 54.3% - 91.5%)
Pathological complete response (pCR)	7 (38.9% , 95% CI: 20.2% - 61.5%)
Patients without genetic alterations (2 EGFR mutations, 1 KRAS G12C)	n = 15
Major pathologic response (MPR)	14 (93.3% , 95% CI: 68.2% - 100%)
Pathological complete response (pCR)	7 (46.6% , 95% CI: 24.8% - 69.9%)

Considering the radiologic response rate of 40%,
the RECIST criteria dose not capture the effect of neoadjuvant immunotherapy and CRT.

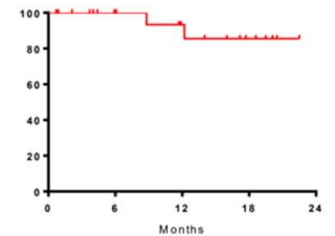
Disease-free survival (n = 18)



Disease-free survival at 6 months: 88.9%
Disease-free survival at 12 months: 83.3%

Disease-free survival: defined from surgery to progression or any cause of death
Overall survival: defined from enrollment of the study to any cause of death

Overall survival (n = 24)



Overall survival at 6 months: 100%
Overall survival at 12 months: 95.8%



FP03.02

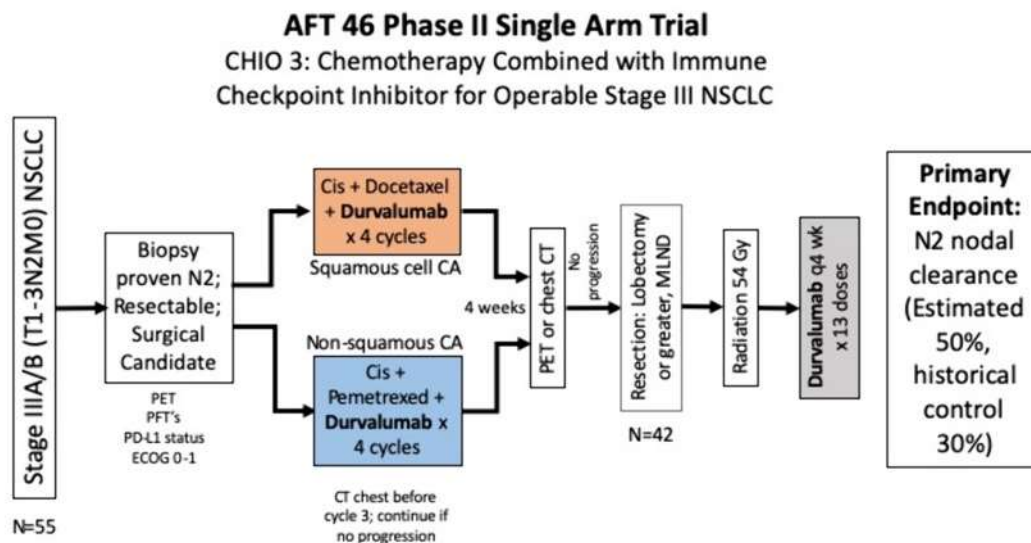
Conclusion

- ✓ In this interim analysis, neoadjuvant concurrent chemoradiotherapy (N-CRT) with durvalumab in stage III NSCLC resulted in no new or unexpected safety data and was not associated with increased peri-operative morbidity or mortality.
- ✓ Among 30 planned patients, 24 patients were enrolled and 18 patients underwent surgery at the data cutoff.
- ✓ N-CRT with durvalumab demonstrated very promising results.
- ✓ The MPR rate and pCR rate were 77.8% and 38.9%, respectively in total resected patients and the MPR rate and pCR rate were 93.3% and 46.6%, respectively in patients without actionable genetic alterations.
- ✓ The pathologic response to patients with actionable genetic alteration seems to be limited. The radiologic RECIST criteria does not capture the effect of N-CRT with immunotherapy.
- ✓ The trial is ongoing and the biomarker analyses will be conducted with PD-L1 assessment, WES, RNAseq, and so on.



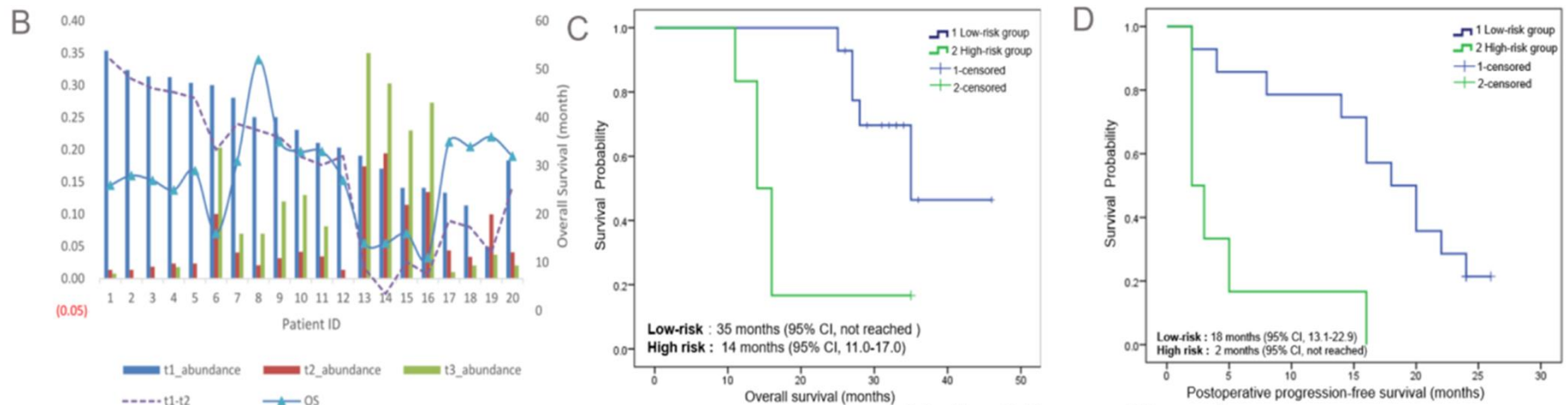
P79.06 - CHIO3: Chemotherapy Combined with Immune Checkpoint Inhibitor for Operable Stage IIIA/B Non-Small Cell Lung Cancer (AFT-46)

Presenting Author(s): [Linda W Martin](#)



Methods

- Resectable Stage IIIA/B (T1-3 N2) **Target enrollment 55 patients** (anticipate 42 will undergo resection)
- Primary Outcome: N2 nodal clearance (N2NC) (H0: >50% for neoadjuvant chemo + durvalumab c/w historical 30% for chemotherapy alone)
- Secondary Outcomes: pathologic response, safety and tolerability, and OS



Median follow-up: 34 months

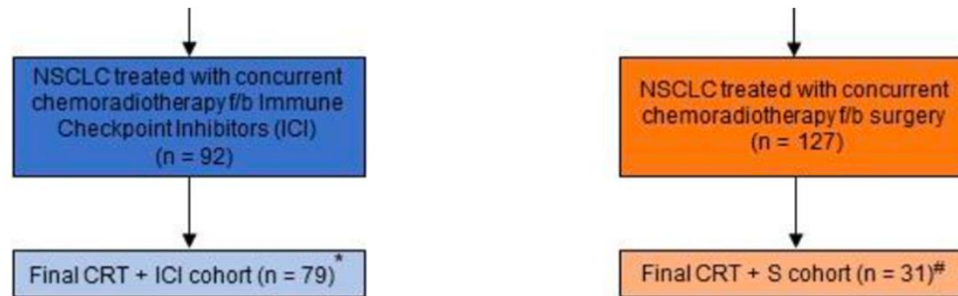
Figure (B) Abundance of mutated genes before targeted therapies, pre-operation or post-operation. (C) Survival curves of OS. (D) Survival curves of postoperative PFS.

- Patients with unchanged or increased abundance of mutated genes after targeted therapy had a poorer prognosis.
- Patients in low-risk group had significantly longer post-mPFS (18 vs. 2 months, $p=0.004$) and mOS (35 vs. 14 months, $p=0.001$) than patients in high-risk group.
- Multivariate analysis: efficacy of targeted therapy and proportional change in genetic abundance were independent prognostic factors for overall survival.



P21.04 - Comparing Outcomes for Patients Receiving Chemoradiation Followed by Surgery vs. Immune Checkpoint Inhibitors in Non Small Cell Lung Cancer

Presenting Author(s): [Turja Chakrabarti](#)



Retrospective review; Single institution
Stage III-N2
Received definitive CRT
Comparing +ICI vs Surgical Resection

CONCLUSIONS

- Lower risk of death among patients receiving CRT +S (HR = 0.162, $p=.02$).
- Lower risk of disease progression among patients receiving CRT +S (HR = 0.411, $p=0.0296$).

Figure 1: Overall Restricted Mean Survival Time

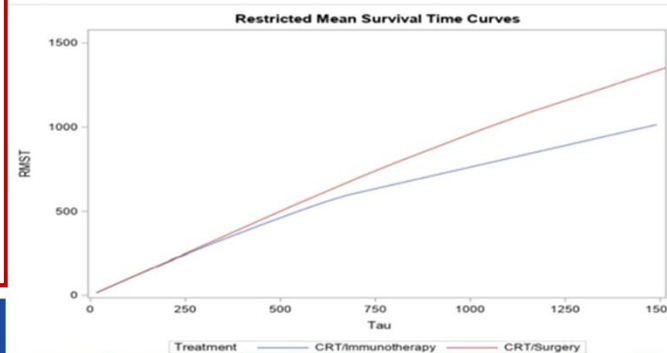
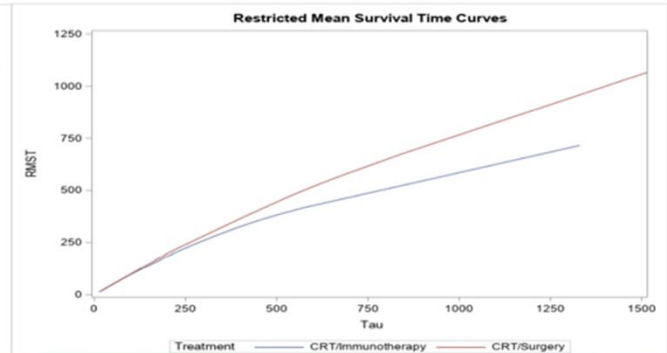


Figure 2: Progression Free Restricted Mean Survival Time





2020 World Conference
on Lung Cancer Singapore

wclc2020.IASLC.com | [#WCLC20](https://twitter.com/WCLC20)

CONQUERING THORACIC CANCERS WORLDWIDE

Health Services

JANUARY 28-31, 2021 | WORLDWIDE VIRTUAL EVENT



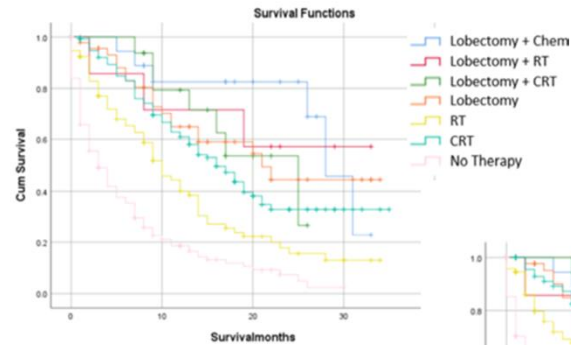
P02.10 - Patterns of Care for Elderly Patients over Age 80 with Stage IIIA-N2, IIIB, and IIIC NSCLC

Presenting Author(s): [Yajie Yin](#)

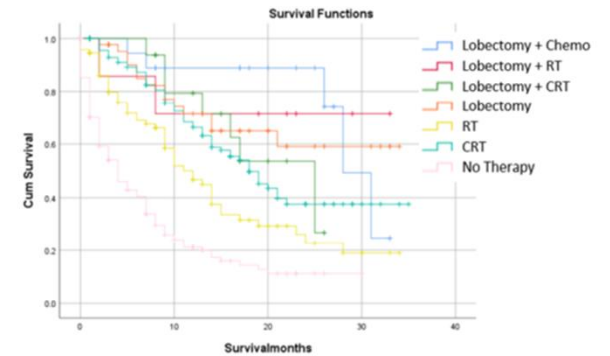
NSCLC patients > 80 years SEER, Stage IIIA-N2, IIIB, IIIC
N=467 patients

1-year outcomes for IIIA-N2 NSCLC

IIIA-N2	n	Median OS (mo)	p value	Median CSS (mo)	p value
Lobectomy + Chemo	20	28.00	<0.001	28.00	<0.001
Lobectomy + RT	7	.		.	
Lobectomy + CRT	17	25.00		25.00	
Lobectomy	50	21.00		.	
RT	93	10.00		12.00	
CRT	124	16.00		18.00	
No Therapy	156	3.00		4.00	



IIIA-N2 OS



IIIA-N2 CSS



2020 World Conference
on Lung Cancer Singapore

wclc2020.IASLC.com | #WCLC20

CONQUERING THORACIC CANCERS WORLDWIDE

Multivariate Model for CSS in IIIA-N2 and IIIB/C NSCLC									
IIIA N2	p value.	HR	95.0% CI		IIIB/C	p value	HR	95.0% CI	
			Lower	Upper				Lower	Upper
Lobectomy+RT vs Lobectomy+Chemo	0.995	0.995	0.191	5.189	CRT vs RT	<0.001	0.314	0.184	0.536
Lobectomy+CRT vs Lobectomy+Chemo	0.182	2.199	0.692	6.992	Lobectomy+Chemo vs RT	0.264	0.318	0.043	2.369
Lobectomy vs Lobectomy+Chemo	0.41	1.537	0.553	4.276	No Therapy vs RT	0.004	1.773	1.205	2.61
RT vs Lobectomy+Chemo	0.015	3.161	1.246	8.021					
CRT vs Lobectomy+Chemo	0.157	1.95	0.774	4.918					
No Therapy vs Lobectomy+Chemo	<0.001	7.857	3.151	19.59					

Conclusion:

- Similar to results from INT0139, IIIA-N2 disease was associated with improved survival after lobectomy
- For Stage IIIB/IIIC disease the addition of chemotherapy to RT was associated with a survival benefit



**P04.03 Patient characteristics and clinical outcomes of stage III NSCLC in a real-world setting: KINDLE
Korean subset data**

Presenting Author(s): [Byoung Chul Cho](#)

KINDLE:

international, multicenter, real-world study, was conducted across 3 non-European and non-North American regions

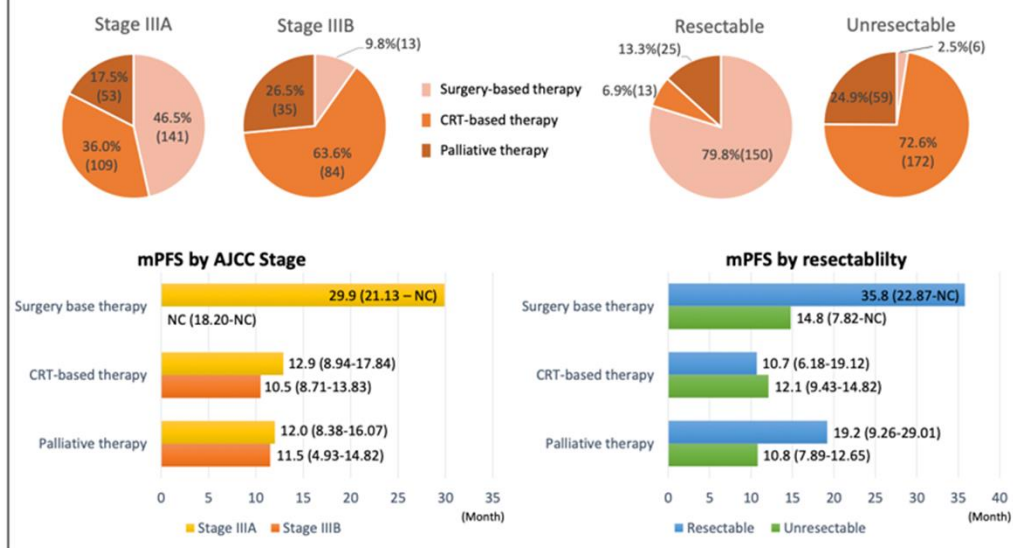
Aims to characterize:

- Treatment patterns
- Demographic and clinical characteristics
- Survival estimates – OS, PFS

Category	Treatment modality	N(%)
CRT-based therapy (44.6%)	CCRT	153 (34.5%)
	SCRT	16 (3.6%)
	CCRT+Chemotherapy	14 (3.2%)
	Other CCRT*	14 (3.2%)
	Other SCRT*	1 (0.2%)
Surgery- based therapy (35.1%)	Surgery+Chemotherapy	41 (9.2%)
	Other Surgery*	37 (8.3%)
	Surgery+SCRT	33 (7.4%)
	Surgery alone	12 (2.7%)
	Surgery+CCRT	10 (2.3%)
	CCRT+Surgery+Chemotherapy	10 (2.3%)
	Radiotherapy+Surgery	8 (1.8%)
	Surgery+Radiotherapy	5 (1.1%)
Palliative therapy (20.3%)	Chemotherapy	51 (11.5%)
	Radiotherapy	19 (4.3%)
	Targeted Therapy	15 (3.4%)
	Radiotherapy+Targeted Therapy	3 (0.7%)
	Radiotherapy+Immunotherapy	1 (0.2%)
	Chemotherapy+Immunotherapy	1 (0.2%)
Total		444

Note: Different orders are considered as different treatment modalities.

Figure 2. Summary of Treatment Modalities and their mPFS by AJCC Stage and resectability



- ### Results
- Surgery-based therapy most common (46.5%) in stage IIIA
 - CRT-based therapy preferred in stage IIIB (63.6%)
 - OS at 1-year and 5-year was 90% (89 to 92) and 67% (64 to 70) for resectable patients c/w 86% (85 to 88) and 54% (51 to 57) for unresectable patients
 - In stage IIIA, the longest mPFS was observed for surgery-based therapy (29.9 months, 21.13 to NC), (CRT 12.9 months, 8.94 to 17.84)

	Overall [N=435]	By AJCC 7 th stage		By Resectability	
		Stage IIIA [N=303]	Stage IIIB [N=132]	Resectable [N= 188]	Unresectable [N=237]
mPFS (months) median (95% CI)	15.2 (13.14 to 17.97)	18.0 (14.72 to 21.72)	12.2 (9.66 to 14.98)	26.3 (20.17 to 39.95)	11.1 (9.43 to 13.14)
Overall Survival rate, % (95% CI)					
1Y	88 (87 to 89)	87 (86 to 89)	87 (86 to 90)	90 (89 to 92)	86 (85 to 88)
3Y	68 (66 to 69)	69 (67 to 71)	64 (61 to 68)	76 (73 to 78)	60 (58 to 63)
5Y	59 (57 to 61)	59 (57 to 62)	59 (55 to 63)	67 (64 to 70)	54 (51 to 57)



2020 World Conference
on Lung Cancer Singapore

wclc2020.IASLC.com | [#WCLC20](https://twitter.com/WCLC20)

CONQUERING THORACIC CANCERS WORLDWIDE

Surgical Outcomes/Local Consolidation Therapy

JANUARY 28-31, 2021 | WORLDWIDE VIRTUAL EVENT



P19.03 - Operative Outcomes of Local Consolidation with Cytoreductive Surgery for Oncogenic-Driven Advanced NSCLC

Presenting Author(s): [Byung Jo Park](#)

METHODS

44 patients
2018.3~2020.7
Stage IIIB/C or IV
NSCLC after targeted
therapy
(ECOG 0~1)
Remnant metastatic
lesions are non-
progressing after
surgery

Variable	Median (IQR) / Number (%)
Age	59 (53.8-65.3)
Male	15 (34.1%)
Initial stage	
IIIB	4 (9.1%)
IIIC	1 (2.3%)
IVA	15 (34.1%)
IVB	24 (54.5%)
Mutation	
EGFR	32 (72.7%)
ALK	11 (25.0%)
ROS	1 (2.3%)
From Dx to Op (mo)	10.9 (8.5-18.2)
From the initiation of TKI immediately prior to surgery to Op (mo)	9.8 (7.8-12.9)

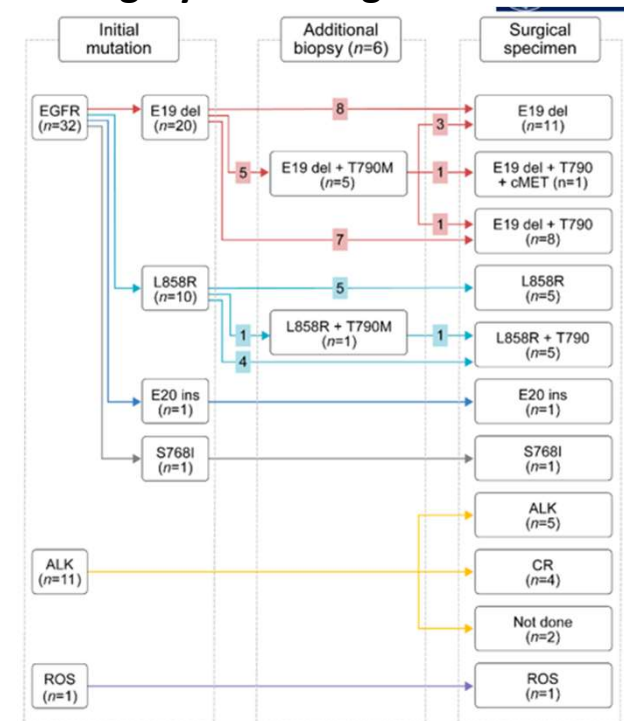
93% R0 Resection

Variable	Median (IQR) / Number (%)
Duration of surgery, min	108.5 (92.0-136.3)
Estimated blood loss, ml	50 (50-102.5)
ICU stay / duration	1 (2.3%) / 1 day
Chest tube duration, day	4 (3.0-5.3)
Postop hospital stays, day	5 (4.0-7.3)
Complication	15 (34.1%)
Prolonged air leak (>5days)	5 (11.4%)
Chyle leakage	3 (6.8%)
Vocal cord palsies	2 (4.5%)
Broncho-pleural fistula	1 (2.3%)
Acute kidney injury	1 (2.3%)
Acute lung injury	1 (2.3%)
Pneumonia	1 (2.3%)
Pneumothorax	1 (2.3%)
In-hospital mortality	0 (0.0%)

P19.03 - Operative Outcomes of Local Consolidation with Cytoreductive Surgery for Oncogenic-Driven Advanced NSCLC

Presenting Author(s): [Byung Jo Park](#)

Variable	Median (IQR) / Number (%)
Additional mutations in surgically resected EGFRm	12 (27.3%)
T790M	11 (25.0%)
MET+	1 (2.3%)

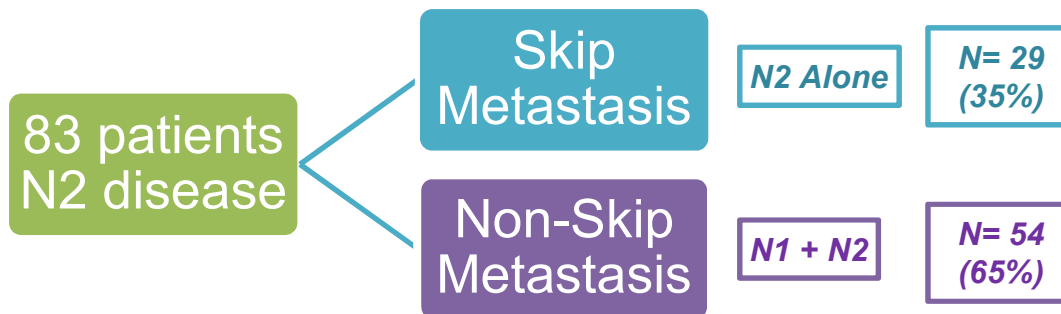


- **EGFR:** Additional T790M mutation, n=11
 - Post op drug change, n=3 / Drug change after progression, n=6 (→ Osimertinib)
 - Gefitinib maintenance due to no progression, n=2
- **ALK**
 - Complete response, n=4, → No progression (TKI maintenance)
- **ROS**
 - Primary site: complete response / Metastatic LN: viable tumor → No progression (TKI maintenance)



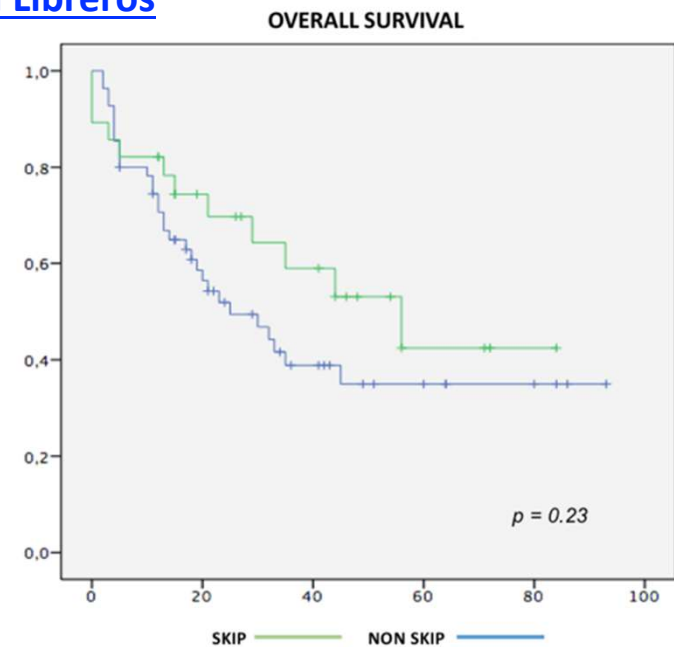
P21.16 - Do patients who underwent lung resection for Non-Small Cell Lung Cancer and Skip-N2 metastases show better survival?

Presenting Author(s): [Alejandra Libreros](#)



CONCLUSIONS

- Female gender associated with increased incidence of skip metastases
- Trend for improved survival associated with skip metastases





2020 World Conference
on Lung Cancer Singapore

wclc2020.IASLC.com | [#WCLC20](https://twitter.com/WCLC20)

CONQUERING THORACIC CANCERS WORLDWIDE

Adjuvant Therapy

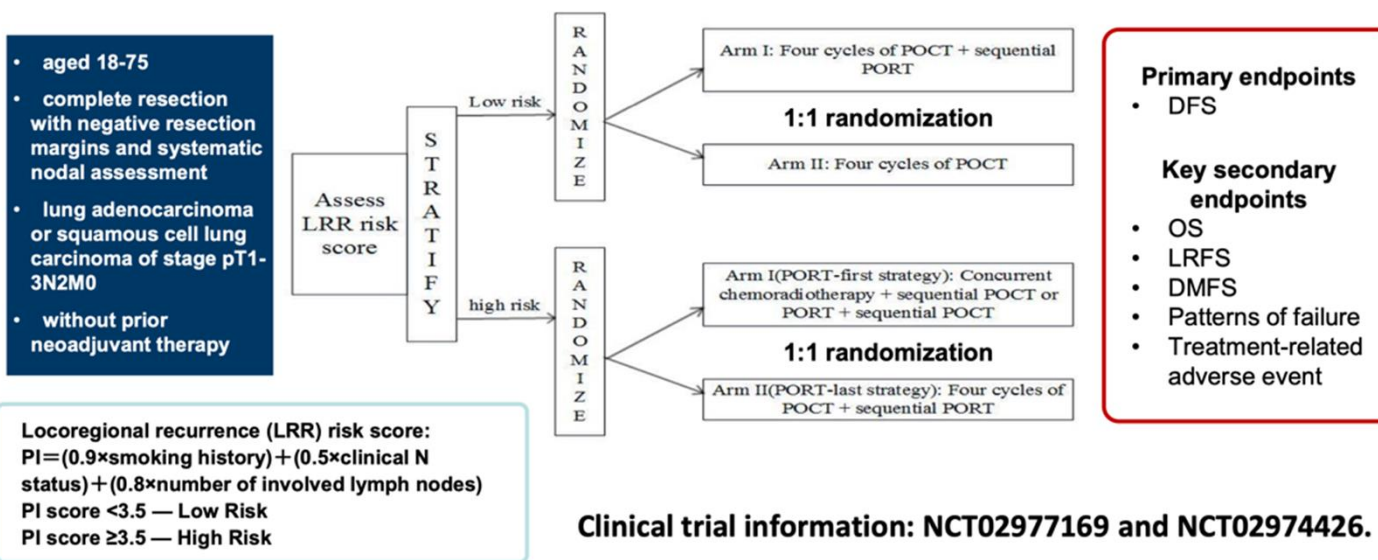
JANUARY 28-31, 2021 | WORLDWIDE VIRTUAL EVENT



P20.02 - To Evaluate the Efficacy and Optimal Timing of Postoperative Radiotherapy in Completely Resected stage IIIA(N2) Non-Small Cell Lung Cancer

Presenting Author(s): [Wen Feng](#)

Study Design Phase II/III Randomized, Multicenter, Study (Recruiting)





CONCLUSIONS

Neo-Adjuvant Systemic Therapy

- Neoadjuvant afatinib and durvalumab show favorable ORR in advanced disease and do not impair receipt of chemoradiotherapy \pm surgery.
- PFS and OS are favorable in this single-arm study. High rate of CNS-only recurrence

Local Consolidative Therapy

- Surgical resection for advanced NSCLC after targeted therapy feasible and be used for further planning of targeted therapy.

Adjuvant Therapy