Lung Cancer UPDATES
ASCO HIGHLIGTHS
04-08 JUNIO 2021

Iniciativa científica de:
GECP
lung cancer research

CPCP Y OTROS TUMORES TORÁCICOS

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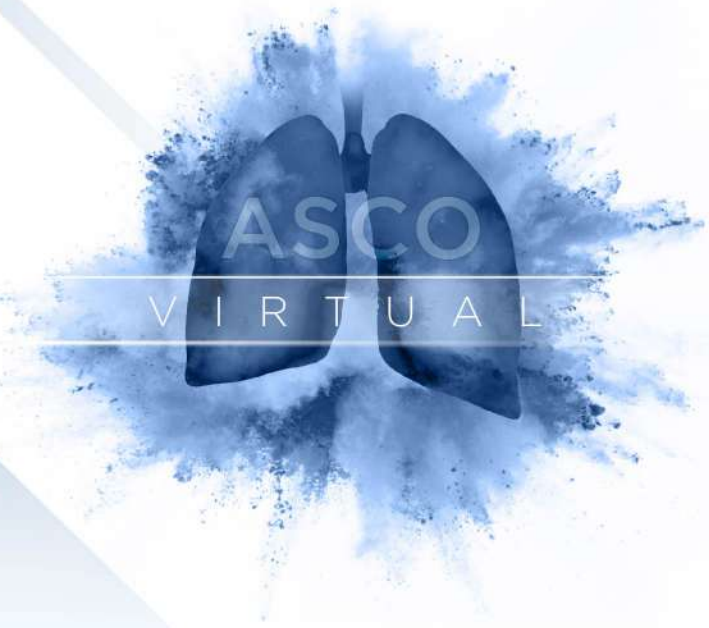

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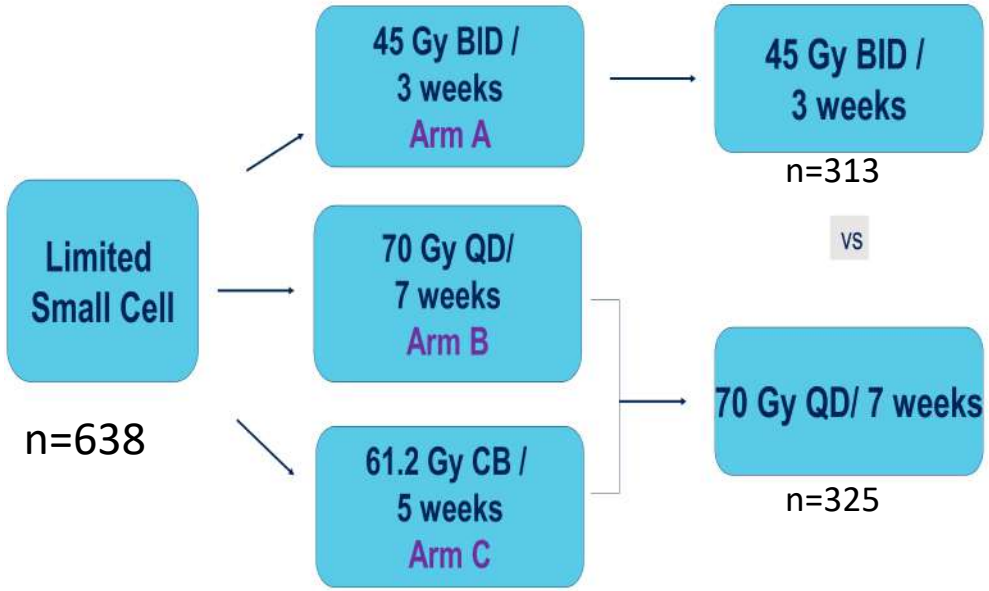
Disclosures

- Advisory and consultancy: Boheringher Inghelheim.
- Speaker honoraria: Roche, Boheringher Inghelheim, BMS, Astra Zeneca, Lilly, Kyowa Kirin.

Phase 3 comparison of high-dose once-daily (QD) thoracic radiotherapy (TRT) with standard twice-daily (BID) TRT in limited stage small cell lung cancer (LSCLC): CALGB 30610 (Alliance)/RTOG 0538. (J.A. Bogart)

Initial Schema



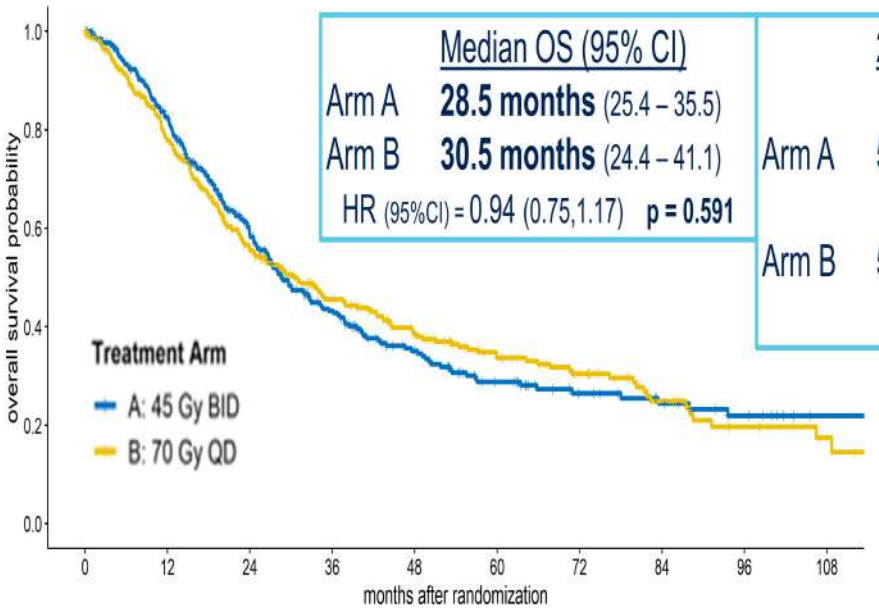
Primary Objective: To determine whether high dose thoracic radiotherapy will improve median and 2-year overall survival compared with standard BID TRT

- Main Eligibility
  - LSCLC and **regional lymph node involvement** excluding contralateral hilar or contralateral supraclavicular nodes
  - ECOG PS 0-2
- Stratification
  - Gender
  - Weight loss prior 6 months
  - ECOG Performance Status
  - TRT technique (3D vs IMRT)

Overall Survival

Median follow-up = 4 years

Figure 1. C30610 Kaplan-Meier Curve for Overall Survival



	Median OS (95% CI)
Arm A	**28.5 months** (25.4 – 35.5)
Arm B	**30.5 months** (24.4 – 41.1)

HR (95%CI) = 0.94 (0.75,1.17) **p = 0.591**

	2-yr OS	5-yr OS
Arm A	**58%** (53, 64)	**29%** (23, 35)
Arm B	**56%** (51, 62)	**34%** (23, 35)

number at risk

Arm A	313	239	150	99	66	44	30	23	16	9
Arm B	325	238	158	111	82	58	45	24	13	6

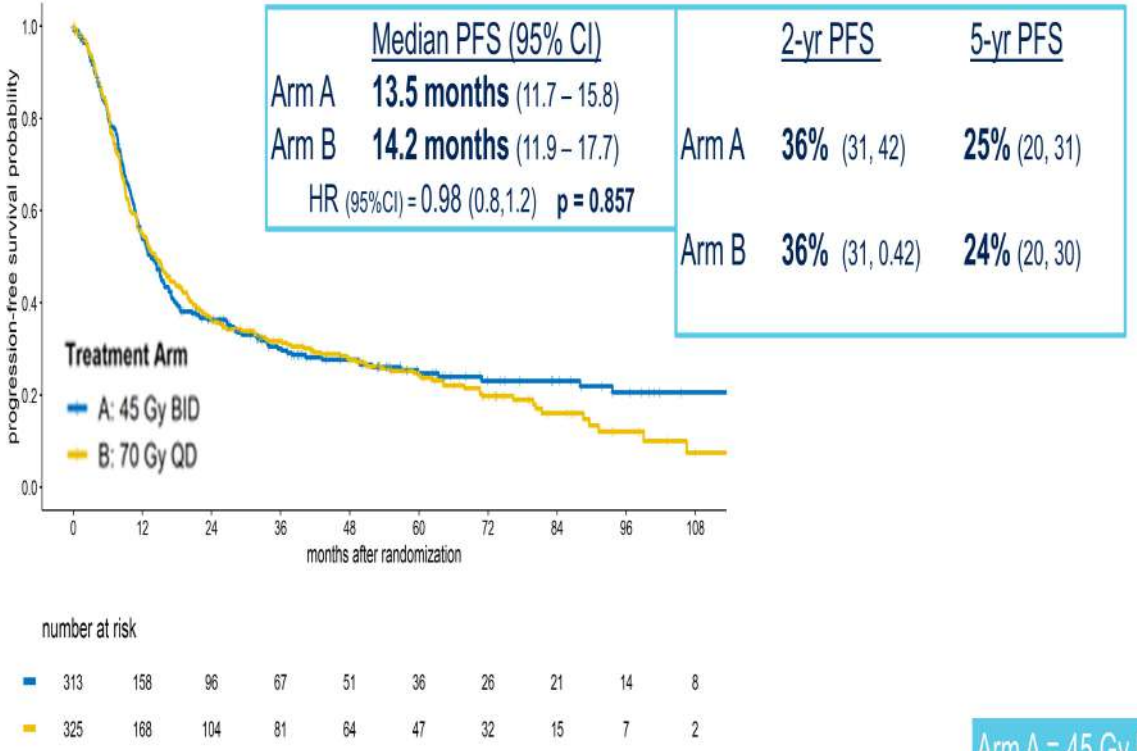
Arm A = 45 Gy BID

Arm B = 70 Gy QD

Phase 3 comparison of high-dose once-daily (QD) thoracic radiotherapy (TRT) with standard twice-daily (BID) TRT in limited stage small cell lung cancer (LSCLC): CALGB 30610 (Alliance)/RTOG 0538. (J.A. Bogart)

Progression-free Survival

Figure 2. C30610 Kaplan-Meier Curve for Progression-Free Survival



	Median PFS (95% CI)	2-yr PFS	5-yr PFS
Arm A	**13.5 months** (11.7 – 15.8)		
Arm B	**14.2 months** (11.9 – 17.7)		
HR (95%CI) = 0.98 (0.8,1.2) **p = 0.857**			
Arm A		**36%** (31, 42)	**25%** (20, 31)
Arm B		**36%** (31, 0.42)	**24%** (20, 30)

Arm A = 45 Gy BID

Arm B = 70 Gy QD

Adverse Events

Pneumonitis G3+: 1% two Arms

Esophagitis: 16.7% (A) vs 18.6 %(B)

Overall Maximum:	Arm	N(%)
Grade 3	A	93 (31.5%)
	B	78 (25.9%)
Grade 4	A	149 (50.5%)
	B	161 (53.5%)
Grade 5	A	**4 (1.4%)**
	B	**11 (3.7%)**

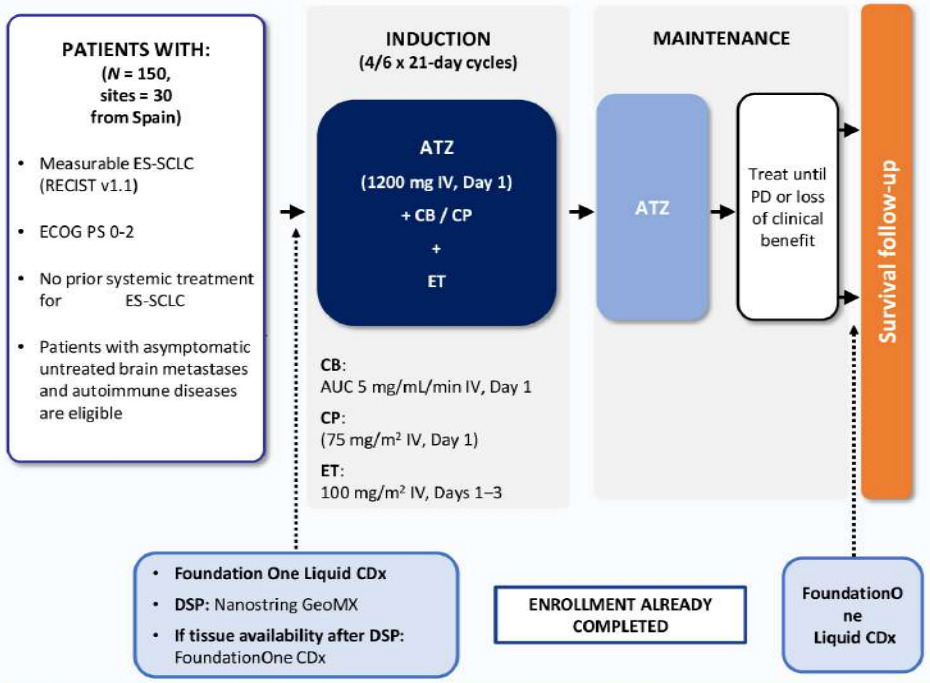
Conclusions

- **CALGB 30610 failed to prove that 70 Gy QD TRT significantly improves OS compared with standard 45 Gy BID TRT**
- **Outcomes in the 70 Gy cohort provide the best evidence available for high dose once - daily TRT in LSCLC**
  - The study was not designed to assess whether 70 Gy QD was non-inferior to 45 Gy BID

Imfirst: A phase IIIb, safety, single arm study of carboplatin (CB) or cisplatin (CP)plus etoposide (ET) with atezolizumab (ATZ) in patients with untreated extensive-stage small cell lung cancer (ES-SCLC) in Spain—Primary safety results of the induction phase. (R. García-Campelo et al.)

STUDY DESIGN

FIGURE 1. PHASE IIIB, OPEN LABEL, SINGLE ARM, MULTICENTER STUDY DESIGNED FOR PATIENTS WITH UNTREATED ES-SCLC



PATIENT POPULATION

- As of Oct 2020, 117 patients had been enrolled, 105 treated with ATZ + CB + ET and 12 with ATZ + CP + ET, with a median number of cycles of study treatment received of 4.
- 81 patients (69.2%) were over 60 years old, 14 patients (12%) had PS2, 94 patients (80.3%) had high tumor burden, 79 patients (67.5%) had comorbidities and 14 patients (12%) presented with CNS metastases (**Table 1**).
- 11 patients (9%) were previously treated with radiotherapy and 25 patients (21.3%) had ongoing steroid treatment at baseline.

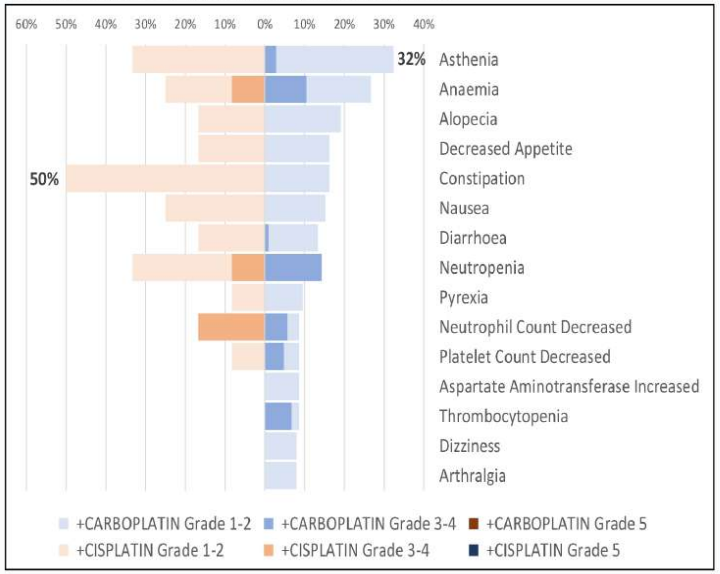
TABLE 1. PATIENT CHARACTERISTICS

	All (*N* = 117)	ATZ + CB + ET (*N* = 105)	ATZ +CP + ET (*N* = 12)
Age (years)			
Mean (SD)	64.7 (9.2)	65.0 (9.1)	62.7 (10.2)
Median	65.0	65.0	66.0
Age (years) [n(%)]			
≤ 60	36 (30.8%)	32 (30.5%)	4 (33.3%)
> 60	81 (69.2%)	73 (69.5%)	8 (66.7%)
Gender			
Male	84 (71.8%)	75 (71.4%)	9 (75.0%)
Female	33 (28.2%)	30 (28.6%)	3 (25.0%)
Tobacco use history			
Never	1 (0.9%)	1 (1.0%)	0 (0.0%)
Current	66 (56.4%)	58 (55.2%)	8 (66.7%)
Previous	50 (42.7%)	46 (43.8%)	4 (33.3%)
Presence of CNS metastases at baseline			
Yes	14 (12.0%)	10 (9.5%)	4 (33.3%)
No	103 (88.0%)	95 (90.5%)	8 (66.7%)
ECOG Performance status			
0	28 (23.9%)	26 (24.8%)	2 (16.7%)
1	75 (64.1%)	65 (61.9%)	10 (83.3%)
2	14 (12.0%)	14 (13.3%)	0 (0.0%)

TABLE 4. AE AND SAES IN SUBGROUPS OF SPECIAL INTEREST

	All (*N* = 117)	
	AEs	SAEs
ECOG Performance status		
0	96.4%	28.6%
1	92.0%	28.0%
2	92.9%	50.0%
Presence of CNS metastases at baseline		
Yes	78.6%	35.7%
No	95.2%	30.1%
Concomitant steroid treatment ongoing at baseline		
Yes	92.0%	44.0%
No	93.9%	27.2%
Age		
≤ 60	94.4%	30.6%
> 60	92.6%	30.9%
Radiotherapy at baseline		
Yes	91.7%	33.3%
No	93.3%	30.5%
Patients with high tumour burden [1]		
Yes	91.5%	33.0%
No	100.0%	21.7%
Co-morbidities [2]		
Yes	93.7%	34.2%
No	92.1%	23.7%

FIGURE 3. MOST FREQUENT ADVERSE EVENTS



IMfirst induction phase analysis confirms the safety profile of ATZ plus C in a broader population of patients. Efficacy, biomarker and further safety analyses will be presented in the future with longer follow up.

Real-world evidence of cancer immunotherapy (CIT) combination treatment in first-line (1L) extensive-stage small cell lung cancer (ES-SCLC). (Eric Nadler et al.)

Poster Session Abstr#8561

OBJECTIVES

This study investigated patient characteristics and treatment patterns for patients with ES-SCLC receiving this regimen in the real-world (RW) community oncology setting.

	Real-World Study	IMpower 133 (Reference)
	Atezo + Chemo (n=267)	Atezo + Chemo (n=201)
Median Age (range) (years)	68 (32, 88)	64 (28, 90)
Gender (n,%)		
Female	146 (54.7)	72 (35.8)
Race (n,%)		
White	195 (73.0)	163 (81.1)
African American	8 (3.0)	1 (0.5)
Other	3 (1.1)	--
Not documented	61 (22.9)	--
ECOG PS Grouped (n,%)		
0	16 (6.0)	73 (36.3)
1	143 (53.6)	128 (63.7)
2+	65 (24.3)	--
Not Documented	43 (16.1)	--
Smoking Status (n,%)		
Current	54 (20.2)	74 (36.8)
Former	63 (23.6)	118 (58.7)
Never	3 (1.1)	9 (4.5)
Not documented	147 (55.1)	--
Brain mets at baseline (n,%)	61 (22.8)	17 (8.5)

N=347

- 267 (76.9%) ATZ+CHT
- 80 (23.1%) CHT

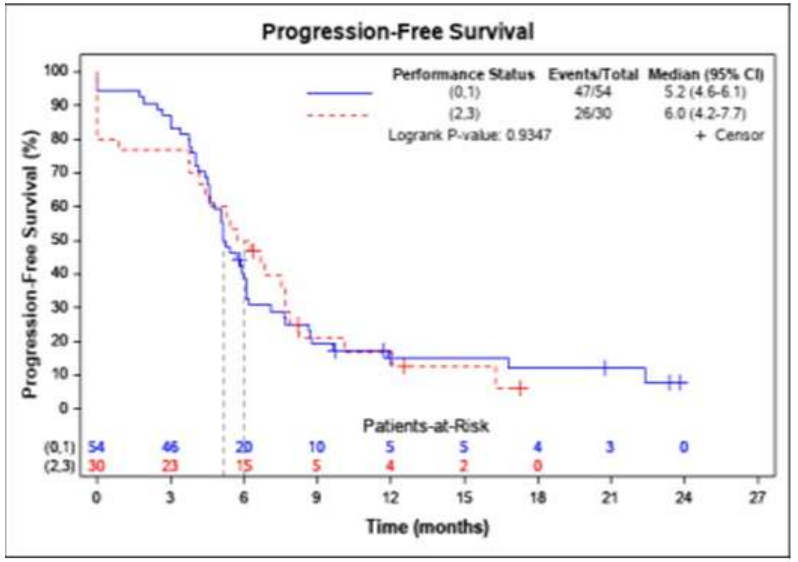
Real-world Study: Atezo + Chemo (n=267)	IMpower 133*: Atezo + Chemo (Reference) (n=201)
Median follow-up (FU): 5.45mo (range 0.72, 14.36)	Median FU 13.9mo (Data cut-off April 24, 2018)
K-M median TTD†: 4.9mo (95% CI 4.2, 5.3)	Median duration of treatment: 4.7mo (range:0, 21) ††
% still on treatment at 6mo (K-M): 35.1% (95% CI 28.4, 41.9)	% still on treatment > 6mo: 31.3%†
K-M median TTNT: 6.9m0 (95% CI 6.4, 8.2)	K-M Median progression-free survival (PFS): 5.2mo (95%CI 4.4, 5.6)
% not initiated on 2L at 6mo: 64.5% (95% CI 56.7, 71.3)	PFS (RECIST criteria) at 6mo: 30.9% (95% CI 24.3, 37.5)

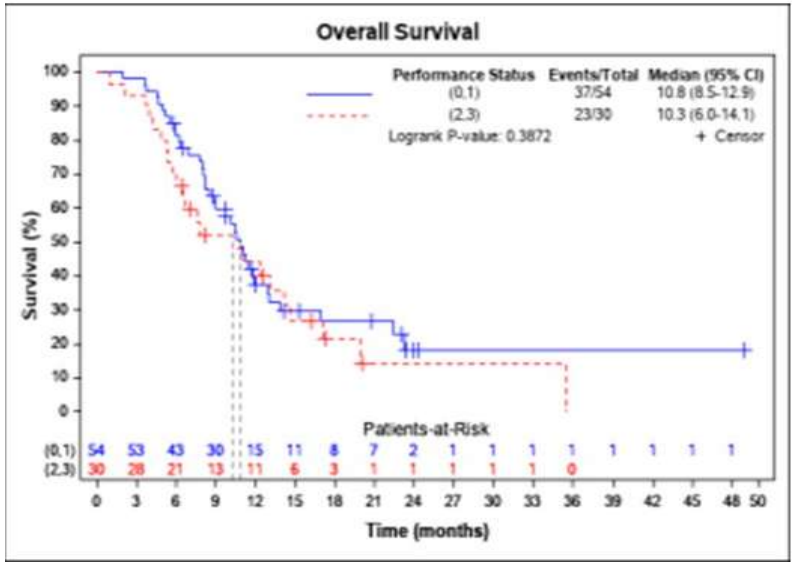
While the follow-up was much shorter (5.45mo vs. 13.9mo) and patients had worse baseline characteristics (age, brain metastases, ECOG) in the RW setting compared to the IMpower 133 trial, the RW median TTD in this descriptive analysis was found to be in line with the median duration of treatment in the trial.

Chemoimmunotherapy for the treatment of extensive-stage small cell lung cancer (ES-SCLC) in patients with an Eastern Cooperative Group (ECOG) performance status (PS) of two or greater. (D. Almquist et al.)

Overall Survival (OS) and progression free survival (PFS) for ECOG-PS 2-3 were compared to patients with an ECOG-PS 0-1. n=84

Characteristic	ECOG PS 0-1 (N=54)	ECOG PS 2-3 (N=30)	P value
Median age (range) — years	67 (48-86)	69 (52-88)	
Male sex — no. (%)	25 (46)	10 (33)	0.35
Female sex—no. (%)	29 (54)	20 (66)	
Smoking status			
Never smoker	0 (0)	2 (7)	0.12
Former smoker or current smoker	54 (100)	28 (93)	
Race — no. (%)			
White	52 (96)	28 (93)	0.61
Non-white	2 (4)	2 (7)	
Brain metastases — no. (%)	29 (53)	16 (53)	>0.99
Liver metastases — no. (%)	35 (65)	21 (70)	0.80
WBRT —no. (%)	10 (18)	5 (17)	>0.99
Chest consolidation — no. (%)	8 (15)	3 (10)	0.73
Second line treatment — no. (%)	21 (39)	5 (17)	**0.04**
Third line treatment — no. (%)	6 (11)	1 (3)	0.41





Conclusions:

- ***No significant difference*** in PFS, OS, and ability to achieve a least a PR in ECOG-PS 2-3 cohort when compared to ECOG-PS 0-1
- Chemoimmunotherapy ***should not be reserved*** for only an ECOG-PS of 0-1 but should be considered for all treatment eligible patients

MAYO CLINIC

Updated results from a phase 1 study of AMG 757, a half-life extended bispecific T-cell engager (BiTE) immuno-oncology therapy against delta-like ligand 3 (DLL3), in small cell lung cancer (SCLC). (T. K. Owonikoko)

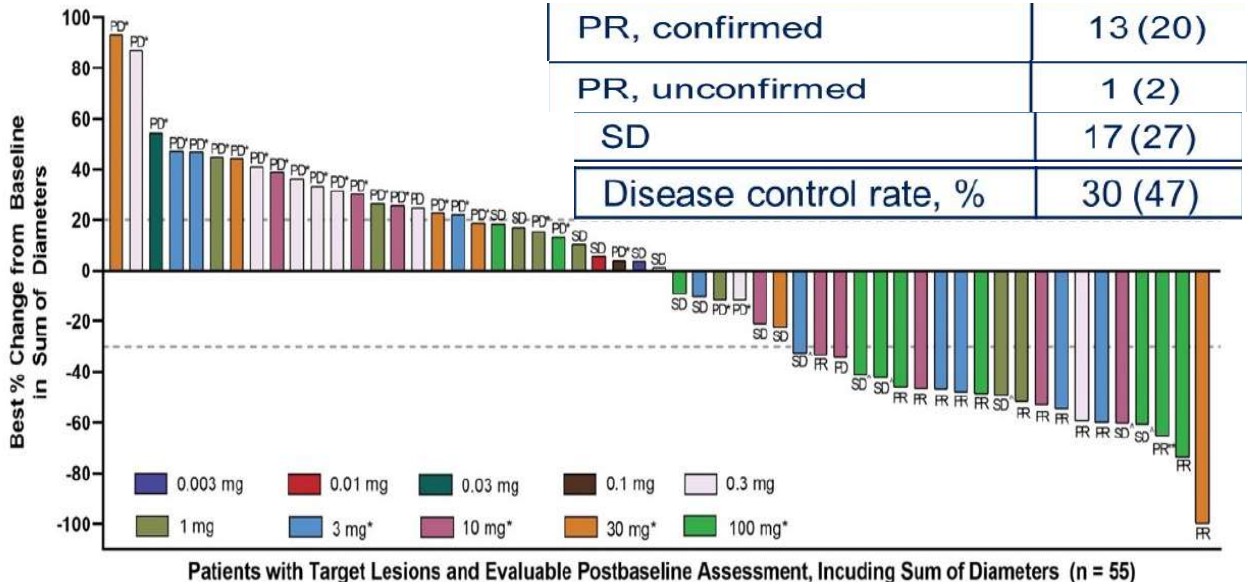
Key Inclusion Criteria

- Histologically/cytologically confirmed SCLC
  - Received ≥ 1 line systemic therapy
  - Progressed/recurred following ≥ 1 platinum-based chemotherapy
- ECOG performance status: 0–2
- ≥ 1 measurable lesion(s)
- Adequate organ function

Key Exclusion Criteria

- Untreated or symptomatic brain metastases
- Prior anti-cancer therapy within 28 days
- Immunodeficiency or systemic steroid use
- Interstitial lung disease

Modified RECIST 1.1 Response, n (%)	Patients† (N = 64)
PR, confirmed	13 (20)
PR, unconfirmed	1 (2)
SD	17 (27)
Disease control rate, %	30 (47)

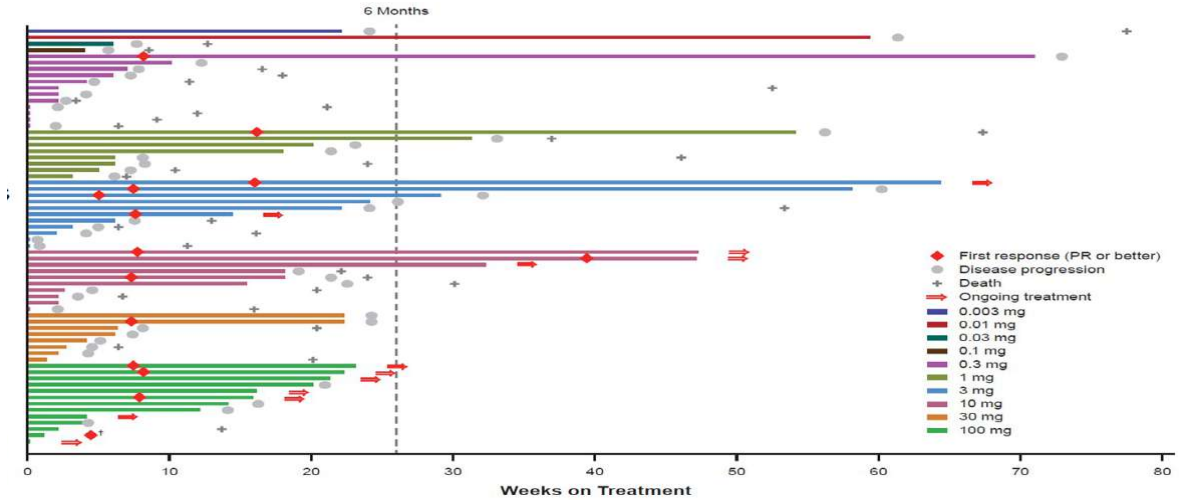


For patients with confirmed PR (n = 13)

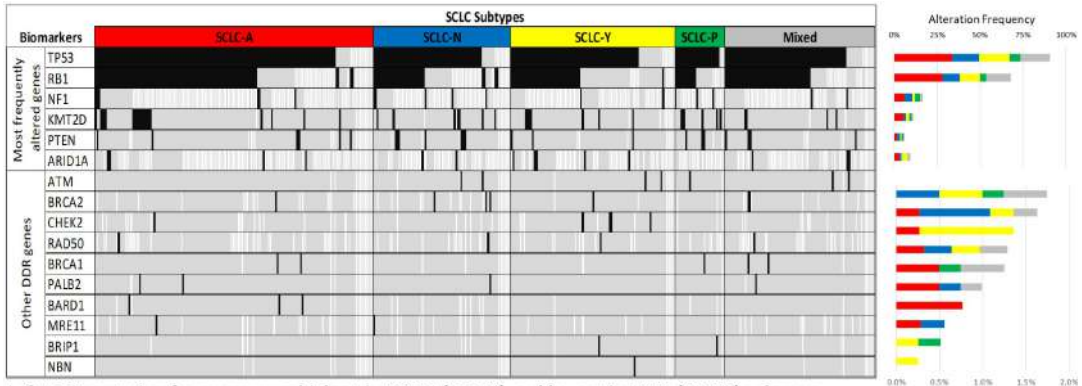
- **Median duration of response was 8.7 months**

10/66 (15%) patients completed ≥ 6 months of treatment

Grade ≥3 TRAEs 18(27%)
Only 3(5%) discontinuation



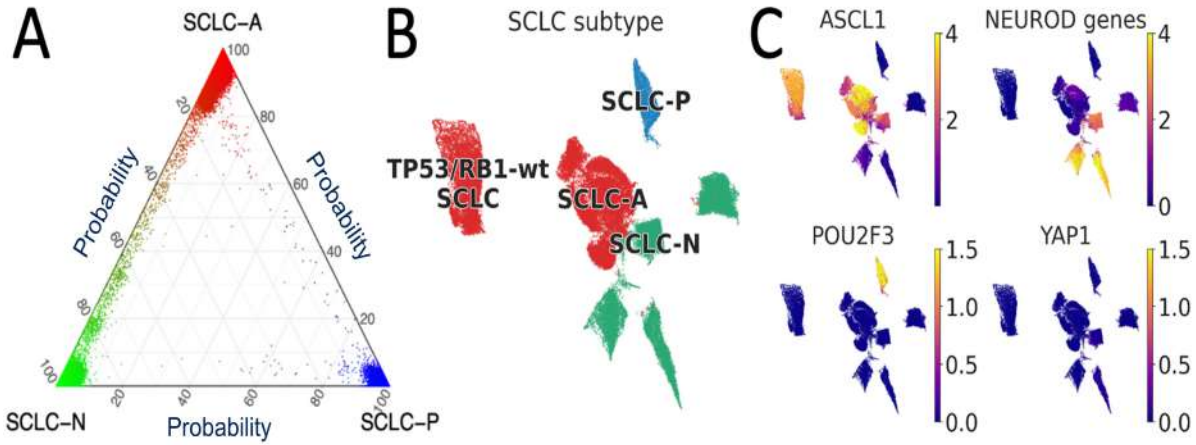
Real-world multiomic characterization of small cell lung cancer subtypes to reveal differential expression of clinically relevant biomarkers.(S. Puri et al) n=437



Left: ***RB1* mutation frequency was highest in ASCL1 (79.2%) and lowest in YAP1 (49.4%) subgroup**
Right: *EGFR*-sensitizing mutations (L858R and Exon 19 deletions) were recurrent (5.2%, n = 4) in the SCLC-N tumor subtype
DDR: DNA damage Repair

- **SCLC-Y** associated with the highest expression of **T-cell inflamed**, NK cell and SITING pathway signatures
- MYC and NOTCH strongly correlated with YAP1 expression
- **EGFR-sensitizing mutations (L858R and EXON 19 del) werer recurrent (5.2% n=4) in SCLC-N**

Signatures of plasticity and immunosuppression in a single-cell atlas of human small cell lung cancer. (J.Minhow Chan et al.) n=21

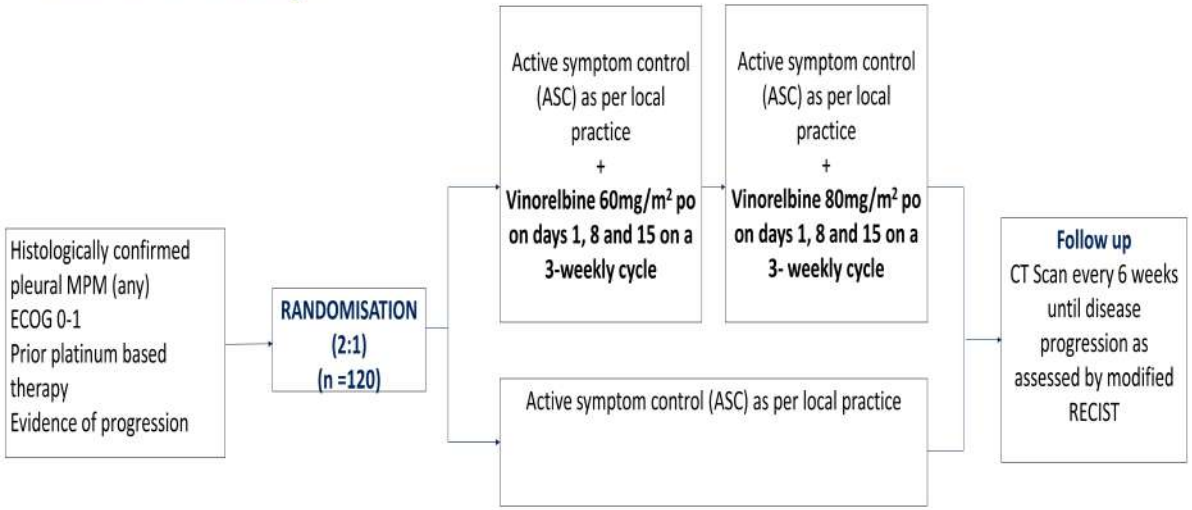


Major SCLC subtype of each tumor (N=21)
*SCLC-A = 14
*SCLC-N = 6
*SCLC-P = 1

- SCLC-A, N and P subtypes have **distinct therapeutic vulnerabilities**
- scRNA-seq can **characterize intratumoral heterogeneity** and the **tumor microenviroment**
- **PLCG2** may be a prognostic marker→worse OS
- PLCG-2 high sub-clone associates with **exhausted CD8+ T-cells→promote metástasis**

A randomized phase II trial of oral vinorelbine as second-line therapy for patients with malignant pleural mesothelioma. (D.A. Fennell)

VIM Trial Design



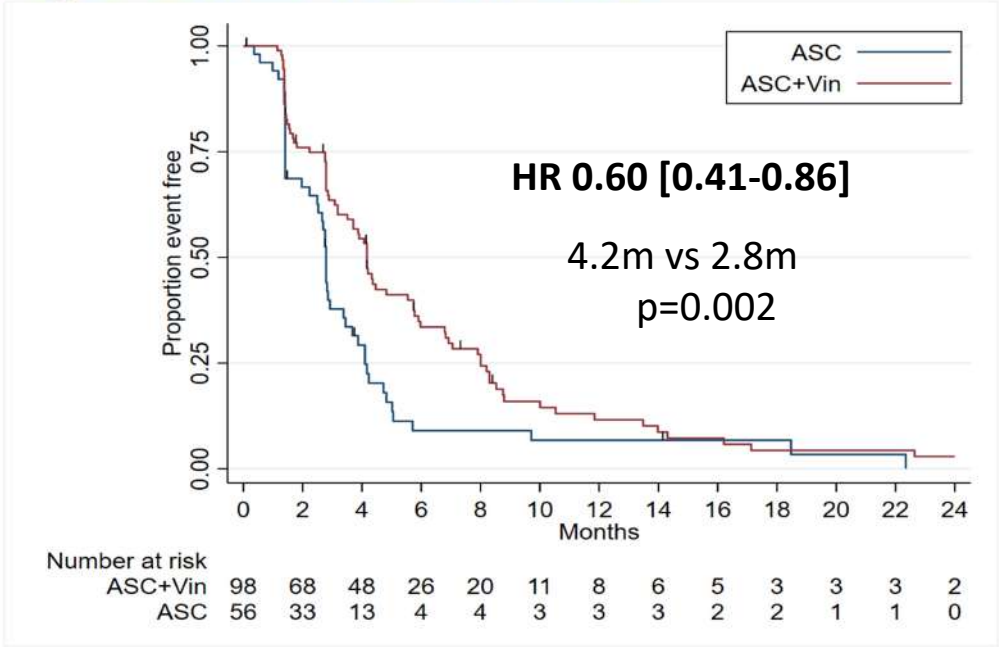
Primary outcome measure: To establish the anti-tumour activity of vinorelbine as measured by progression free survival (PFS)

Secondary Outcome measures:

- PFS by BRCA1 expression Overall survival (OS), & objective response rate (ORR) as assessed by modified RECIST
- Safety, tolerability (side effects) and feasibility of use (number of participants requiring dose delays or reductions and/or treatment withdrawal)

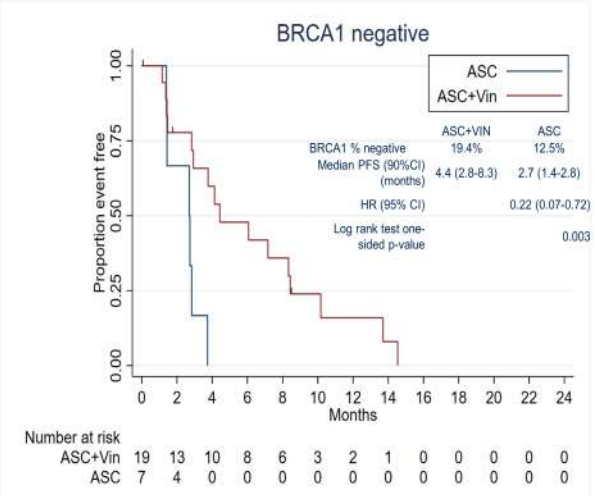
Characteristic	ASC+VIN (N=98)	ASC (N=56)
Age-years (median, IQR)	70.5 (65.4-76.4)	70.7 (66.6-74.2)
Male	80 (81.6%)	45 (80.4%)
ECOG Status 0	26 (26.5%)	12 (21.4%)
Epithelioid	81 (82.7%)	48 (85.7%)
Biphasic or sarcomatoid	13 (13.3%)	3 (5.4%)
BRCA1 positive*	36 (36.7%)	15 (26.8%)
BRCA1 negative	19 (19.4%)	7 (12.5%)

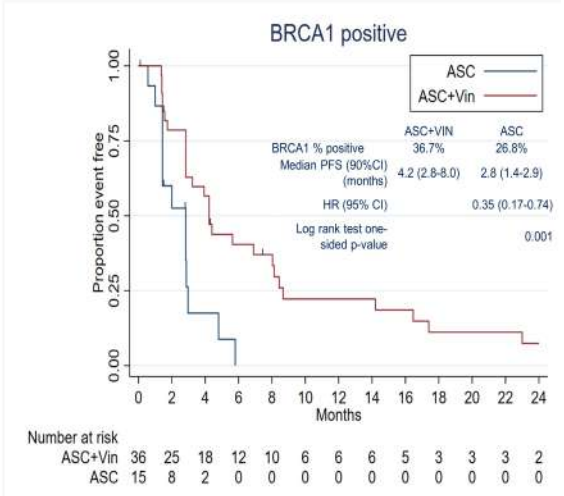
Progression Free Survival



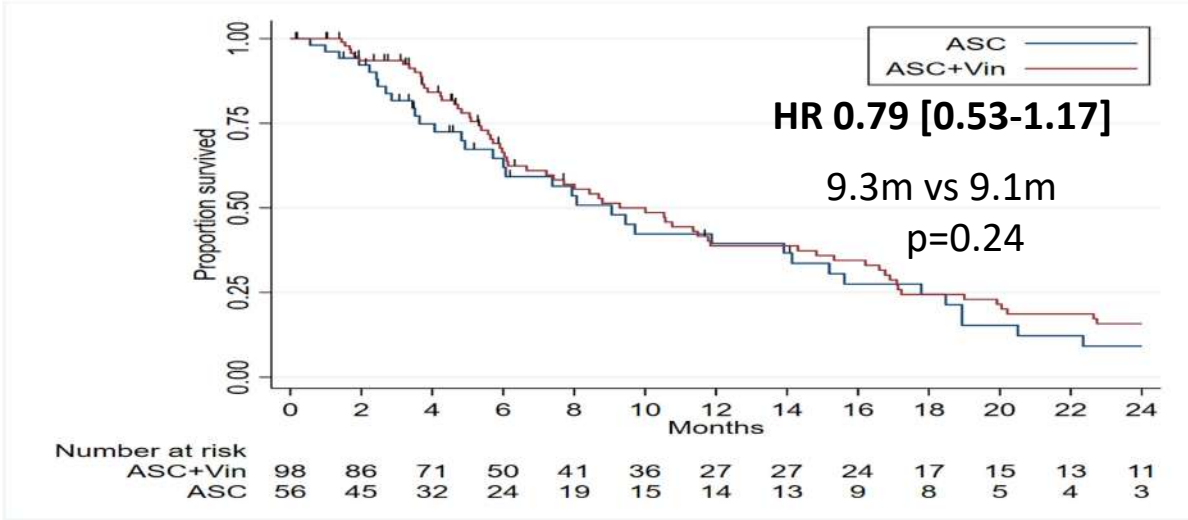
A randomized phase II trial of oral vinorelbine as second-line therapy for patients with malignant pleural mesothelioma. (D.A. Fennell)

Progression Free Survival by BRCA1 expression





Overall Survival



Best response

	ASC+VIN (N=98)	ASC (N=56)
PR rate	3.1%	1.8%
SD rate	62.2%	46.4%
Median duration of response (95%CI) (months)	7.2 (3.1-8.5)	4.2 (4.2-4.2)
Median duration of PR/SD	4.2 (2.8-6.9)	3.7 (2.8-4.2)
PD rate	19.4%	28.6%

22 patients (**39.3%**) in control arm proceeded to another clinical trial -15 (26.8%) went into the CONFIRM trial - Nivolumab vs placebo

CONCLUSIONS

Vinorelbine is a safe and effective treatment and should be considered a treatment option for patients with relapsed mesothelioma

A phase II trial of abemaciclib in patients with p16ink4a negative, relapsed mesothelioma. (D.A. Fennell et al)

Screening
MM with confirmed P16ink4a deficiency was deemed eligible
Screening was completed within 28 days of cycle 1 day1

Treatment:
200mg bd po daily every 21 days for 24 weeks (on study) until disease progression, unacceptable toxicity, withdrawal or death

Disease Progression
Confirmed by CT scan

Withdrawal
Due to unacceptable toxicity, withdrawal or death

Disease control
Remain on treatment (off study)

Post treatment visit and follow-up:
Follow-up at 30 days and 6 months after last dose, up until death or patient withdrawal
CT scans will continue as standard care

Primary Endpoint
Disease control rate (DCR) at 12 weeks assessed by modified RECIST 1.1 criteria

Secondary Endpoints
Safety and toxicity evaluated using NCI CTCAE (v4.03)
Objective response rate (ORR) assessed by modified RECIST 1.1 criteria
Disease control rate at 24 weeks assessed by modified RECIST 1.1

Safety
Treatment related grade 3 or greater adverse events (AEs) occurred in 5.7%, the most common toxicity being vomiting (4%) or diarrhoea (4%)

This phase II trial met its primary endpoint of DCR at 12 weeks, showing promising efficacy with manageable toxicity. Further investigation of CDK4/6 inhibition in relapsed MM is warranted.

Patient Demographics		Abemaciclib (n = 26)
Age, years, median (IQR)		67.4 (47 - 82)
Gender	Male	23 (88%)
	Female	3(11.5%)
Smoking status	Smoker	2 (8%)
	Non-smoker	14 (54%)
	Ex-smoker	10 (38%)
Mesothelioma subtype	Epithelioid	21 (81%)
	Biphasic/NOS	5 (19%)
Asbestos exposure	No	2 (8%)
	Yes	20 (77%)
	Unknown	4 (15.4%)
ECOG status	0	4 (15%)
	1	22 (85%)
Primary tumour site	Thoracic	26 (100%)
	Abdominal	0(0%)

Data are n (%), unless otherwise stated.
Abbreviations: ECOG= Eastern Cooperative Oncology Group

12 week DCR was 54%. 24 week DCR was 23.1% with ORR: partial response rate was 15.4% (figures 1 and 2).

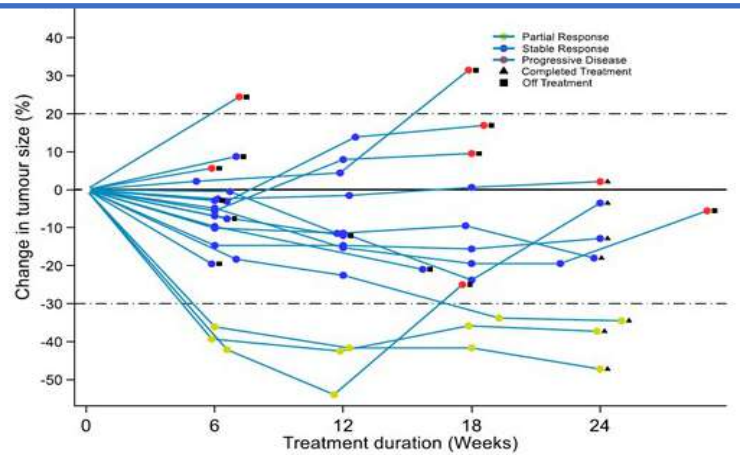


Figure 2. Spider plot showing change in tumour volume over time

A phase II study of palbociclib for recurrent or refractory advanced thymic epithelial tumor (KCSG LU17-21). (Myung-Ju Ahn et al.)

Phase II Opel label

Recurrent TET

Primary endpoint: Progression-free survival (PFS)

Secondary endpoints: Overall response rate (ORR), Duration of response (DR) and Overall survival (OS), per RECIST v1.1, as assessed by investigator. Sefety (Type, incidence, severity (as graded by National Cancer Institute Common Terminology Criteria for Adverse Events [NCI CTCAE] version 4.03)

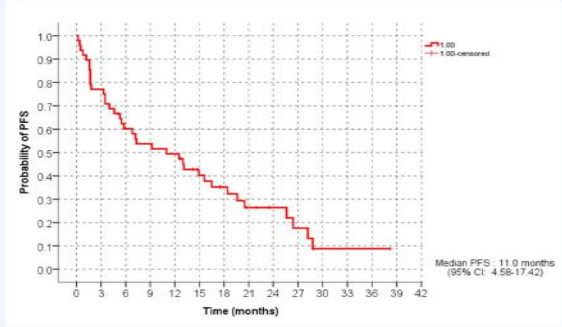
- Palbociclib monotherapy is well tolerated with encouraging efficacy in patients with TETs after platinum-based chemotherapy
- **PFS 11.0m [4.6-17.4]** (median follow-up 14.5m)

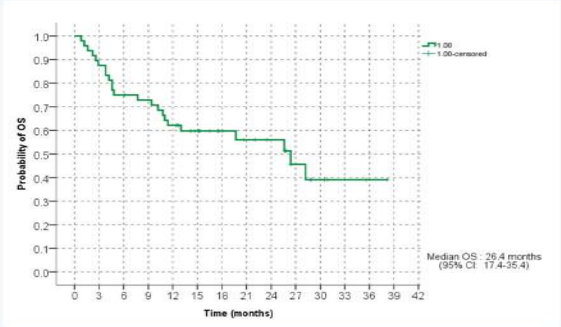
Table 1. Baseline characteristics

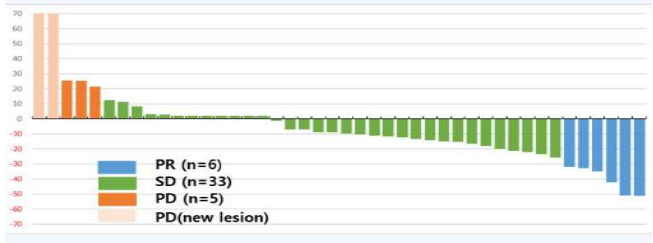
Patient Characteristics	No of patients	%
Age (median: 54 years,32-92)		
<60 years	33	68.8%
≥60 years	15	31.2%
Sex		
Male	26	54.2%
Female	22	45.8%
ECOG PS		
0	2	4.2%
1	46	95.8%
Histology		
A	1	2.1%
B1	2	4.2%
B2	8	16.7%
B3	13	27.1%
C	23	47.9%
Unknown	1	2.1%
Masaoka stage		
IV-A	13	27.1%
IV-B	33	68.8%
Unknown	2	4.2%
History of thymectomy		
Yes	21	43.8%
No	27	56.2%
Line of previous chemotherapy		
1	31	64.6%
2	11	22.9%
3	5	10.4%
4	1	2.1%

Table 2. Summary of adverse events

Adverse Event	Any grade	Grade=>3
Neutropenia	30 (62.5%)	20 (41.7%)
Anemia	18 (37.5%)	7 (14.6%)
Thrombocytopenia	13(27.1%)	5 (10.4%)
Fever	9(18.8%)	0 (0%)
Fatigue	8 (16.7%)	0 (0%)
Anorexia	5 (10.4%)	0 (0%)
Diarrhea	5 (10.4%)	0 (0%)
Nausea	4 (8.4%)	0 (0%)
Constipation	4 (8.4%)	0 (0%)
Alopecia	4 (8.4%)	0 (0%)
Pneumonitis	4 (8.4%)	2 (4.2%)
Herpes zoster	3 (6.25%)	0 (0%)
Increased blood creatinine	2 (4.2%)	0 (0%)
Increased AST	1 (2.1%)	0 (0%)
Increased ALT	1(2.1%)	1(2.1%)
Increased bilirubin	1(2.1%)	0 (0%)







- **SG 26.4 m [17.4-35.4]**
- **ORR 13.6%**

Lung Cancer UPDATES
ASCO HIGHLIGTHS
04-08 JUNIO 2021

Iniciativa científica de:
GECP
lung cancer research

GRACIAS POR LA ATENCIÓN

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