Lung Cancer UPDATES
IASLC HIGHLIGTHS
28-31 ENERO 2021
VIRTUAL

Iniciativa científica de:
GECP lung cancer research

Inmunoterapia en CPNCP avanzado

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Inmunoterapia en CPNCP avanzado

Abstracts más destacados

Clinical trials:

- ***PS01.09*** *- Pembrolizumab Plus Ipilimumab vs Pembrolizumab Plus Placebo as 1L Therapy for Metastatic NSCLC of PD-L1 TPS ≥50%: KEYNOTE-598*
- ***FP13.02****- Pembrolizumab + Pemetrexed-Platinum vs Pemetrexed-Platinum for Metastatic NSCLC: 4-Year Follow-up From KEYNOTE-189*
- ***FP13.01****- 5-Year Survival Update From KEYNOTE-010:Pembrolizumab Versus Docetaxel in Previously Treated, PD-L1-Positive Advanced NSCLC*
- ***OA01.07*** *- A Phase II Study of the Oral Selective AXL Inhibitor Bemcentinib with Pembrolizumab in Patients with Advanced NSCLC*
- ***OA07.08*** *- HUDSON: An Open-Label, Multi-Drug, Biomarker-Directed, Phase II Platform Study in Patients with NSCLC, who Progressed on Anti-PD(L)1 Therapy*
- ***OA07.09*** *- Sintilimab in Combination with Anlotinib as First-Line Therapy for Advanced NSCLC: Final Analysis of Primary Endpoints*

Biomarkers studies:

- ***OA01.03*** *- Clinical Benefits of First-Line (1L) Cemiplimab Monotherapy by PD-L1 Expression Levels in Patients With Advanced NSCLC*
- ***OA01.04*** *- Tumor Mutation Burden (TMB) by Next Generation Sequencing (NGS) Associates with Survival (OS) in Lung-MAP Immunotherapy Trials S1400I and S1400A*

PS01.09 - Pembrolizumab Plus Ipilimumab vs Pembrolizumab Plus Placebo as 1L Therapy for Metastatic NSCLC of PD-L1 TPS ≥50%: KEYNOTE-598

Phase III, randomized, doble-blind, placebo controlled, multicentre trial

KEYNOTE-598 Study Design

Key Eligibility Criteria

- Stage IV NSCLC
- No prior systemic therapy
- ECOG PS 0 or 1
- PD-L1 TPS ≥50%[a]
- No targetable *EGFR* mutations or *ALK* translocations[b]
- No known untreated CNS metastases
- ≥1 lesion measurable per RECIST v1.1

Stratification Factors

- ECOG PS (0 vs 1)
- Region (East Asia vs not East Asia)
- Histology (squamous vs nonsquamous)

R (1:1)

- Pembrolizumab 200 mg Q3W for up to 35 doses + Ipilimumab 1 mg/kg Q6W for up to 18 doses
- Pembrolizumab 200 mg Q3W for up to 35 doses + Saline Placebo Q6W for up to 18 doses

End Points

- **Dual primary:** OS and PFS per RECIST v1.1 by BICR
- **Key secondary:** ORR and DOR per RECIST v1.1 by BICR and safety

[a]Assessed centrally using the PD-L1 IHC 22C3 pharmDx assay (Agilent).
[b]Patients with *ROS1* rearrangement were also excluded if *ROS1* testing and treatment were locally approved and accessible.
KEYNOTE-598 ClinicalTrials.gov identifier, NCT03302234. BICR, blinded independent central review.

Baseline Characteristics

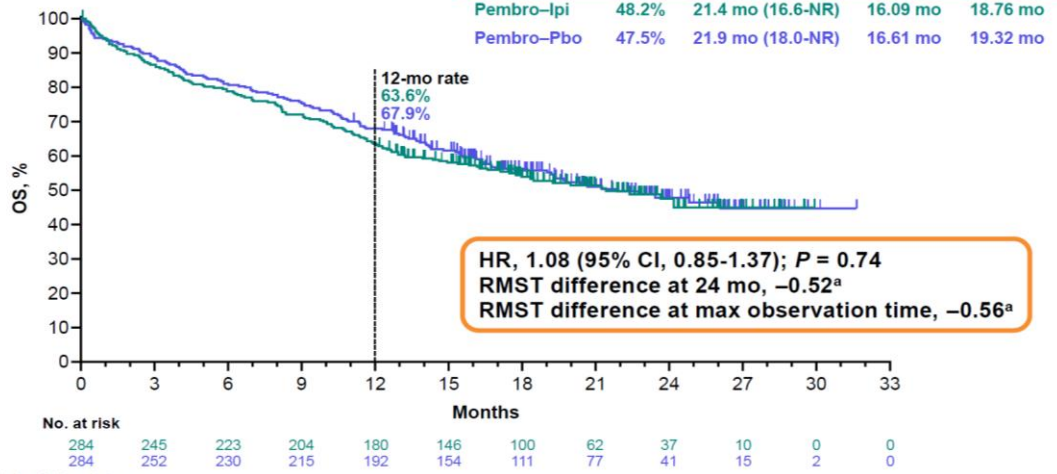
	Pembrolizumab–Ipilimumab (N = 284)	Pembrolizumab–Placebo (N = 284)
Age, median (range), years	64 (35-85)	65 (35-85)
Men	202 (71.1%)	191 (67.3%)
Enrolled in East Asia	32 (11.3%)	31 (10.9%)
ECOG PS 1	183 (64.4%)	180 (63.4%)
Former/current smoker	255 (89.8%)	259 (91.2%)
Histology		
Squamous	77 (27.1%)	81 (28.5%)
Nonsquamous	207 (72.9%)	203 (71.5%)
Brain metastases	31 (10.9%)	29 (10.2%)

Boyer M, WCLC 2020

PS01.09 - Pembrolizumab Plus Ipilimumab vs Pembrolizumab Plus Placebo as 1L Therapy for Metastatic NSCLC of PD-L1 TPS ≥50%: KEYNOTE-598

Overall Survival

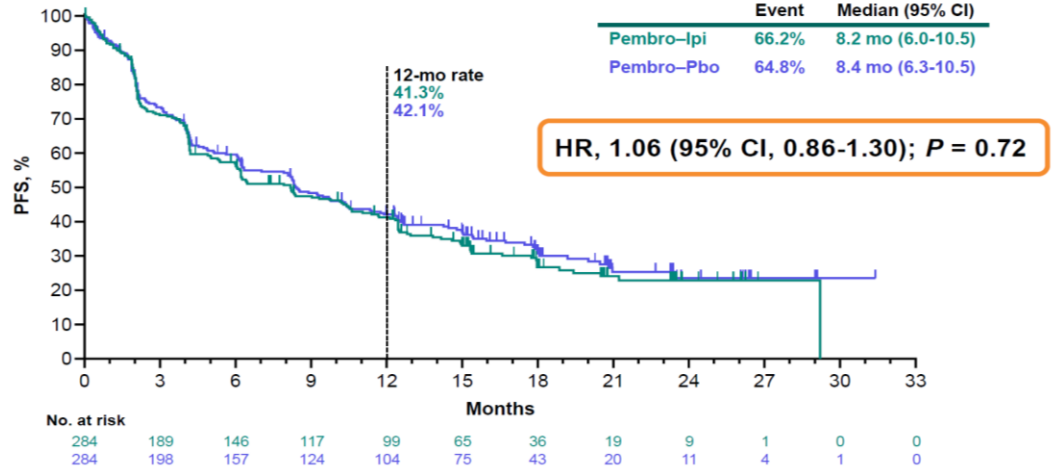
	Pts w/ Event	Median (95% CI)	RMST at 24 mo	RMST at Max Time
Pembro–Ipi	48.2%	21.4 mo (16.6-NR)	16.09 mo	18.76 mo
Pembro–Pbo	47.5%	21.9 mo (18.0-NR)	16.61 mo	19.32 mo



[a]Nonbinding futility criteria met.
Data cutoff date: Sep 1, 2020.

Progression-Free Survival

	Pts w/ Event	Median (95% CI)
Pembro–Ipi	66.2%	8.2 mo (6.0-10.5)
Pembro–Pbo	64.8%	8.4 mo (6.3-10.5)

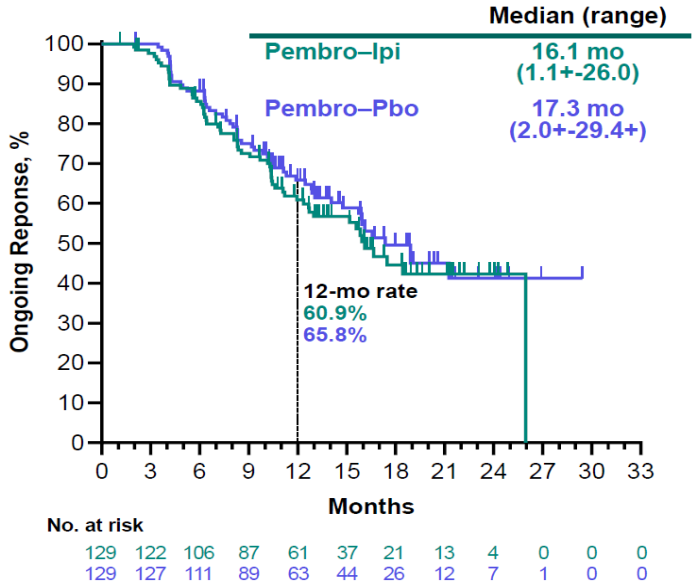


Data cutoff date: Sep 1, 2020.

Summary of Response

	Pembro–Ipi N = 284	Pembro–Pbo N = 284
ORR, % (95% CI)	45.4% (39.5-51.4)	45.4% (39.5-51.4)
Best response, n (%)		
CR	13 (4.6%)	8 (2.8%)
PR	116 (40.8%)	121 (42.6%)
SD	70 (24.6%)	73 (25.7%)
PD	51 (18.0%)	44 (15.5%)
NE[a]	6 (2.1%)	6 (2.1%)
NA[b]	28 (9.9%)	32 (11.3%)

Duration of Response



Boyer M, WCLC 2020

PS01.09 - Pembrolizumab Plus Ipilimumab vs Pembrolizumab Plus Placebo as 1L Therapy for Metastatic NSCLC of PD-L1 TPS ≥50%: KEYNOTE-598

Adverse Events and Exposure

No. of Patients (%)	Treatment-Related AEs		Immune-Mediated AEs and Infusion Reactions[a]	
	Pembro–Ipi (N = 282)	Pembro–Pbo (N = 281)	Pembro–Ipi (N = 282)	Pembro–Pbo (N = 281)
Any grade	215 (76.2%)	192 (68.3%)	126 (44.7%)	91 (32.4%)
Grade 3-5	99 (35.1%)	55 (19.6%)	57 (20.2%)	22 (7.8%)
Serious	78 (27.7%)	39 (13.9%)	54 (19.1%)	20 (7.1%)
Led to death	7 (2.5%)	0	6 (2.1%)	0
Led to discontinuation[b]				
Ipi or placebo only	17 (6.0%)	9 (3.2%)	5 (1.8%)	3 (1.1%)
Both drugs	54 (19.1%)	21 (7.5%)	34 (12.1%)	12 (4.3%)

Median Treatment Exposure, Pembrolizumab–Ipilimumab vs Pembrolizumab–Placebo

- No. of cycles[c]: 10 vs 15
- Months on ipilimumab or placebo: 5.6 vs 8.8
- Months on pembrolizumab: 6.3 vs 9.7

[a]Events were considered regardless of attribution to treatment by the investigator. [b]Patients could discontinue ipilimumab/placebo and continue pembrolizumab; pembrolizumab discontinuation required ipilimumab/placebo discontinuation. [c]One cycle = 3 weeks. Data cutoff date: Sep 1, 2020.

Conclusions:

- Adding Ipi to Pembro did not improve efficacy as 1L therapy for NSCLC PD-L1 ≥ 50%
- Pembro + Ipi was associated with greater toxicitiy than Pembro + Placebo
- Pembrolizumab monotherapy remains standard-of-care 1L treatment for this population of patiens

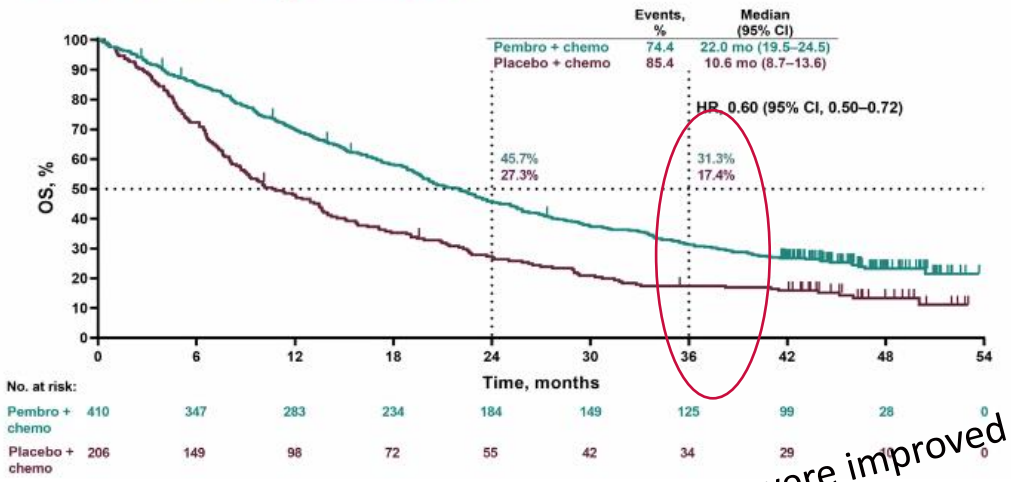
Questions:

- PD-L1 ≥50% NSCLC patients: Pembro vs. Pembro + Ipi → Pembro but Pembro vs. Pembro + ChT → ¿?
- Are PD-L1 ≥ 50% patients may not be the benefit population for combo… Information regarding TMB?

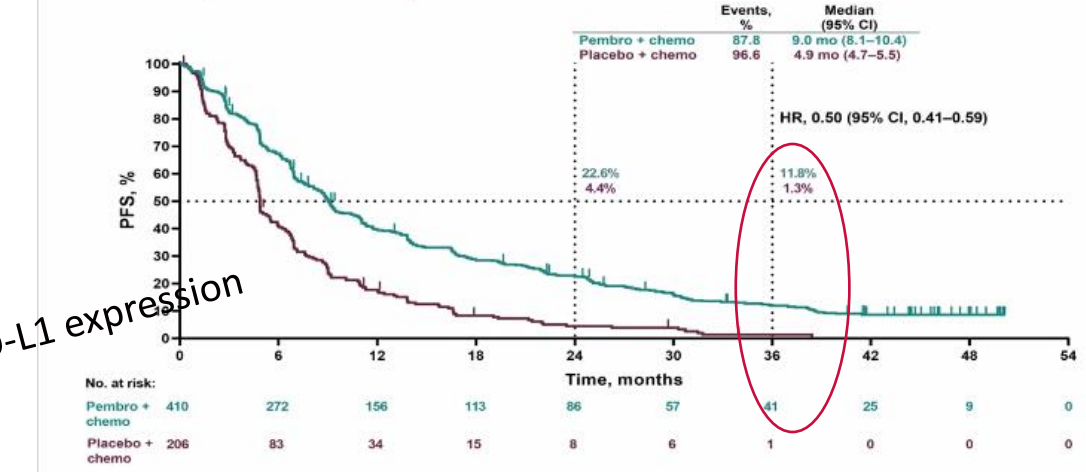
Boyer M, WCLC 2020

FP13.02- Pembrolizumab + Pemetrexed-Platinum vs Pemetrexed-Platinum for Metastatic NSCLC: 4-Year Follow-up From KEYNOTE-189

OS, ITT Population

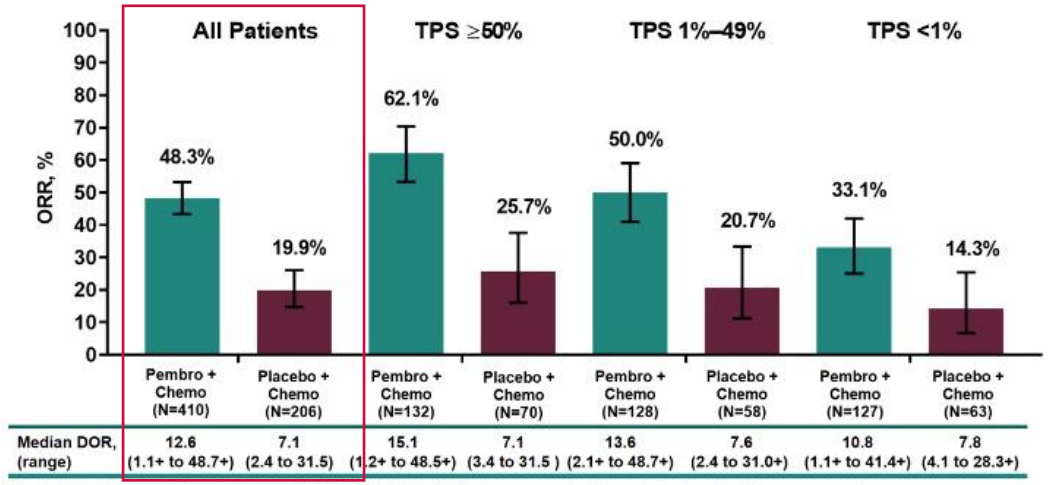


PFS,[a] ITT Population



OS and PFS were improved irrespectively of PD-L1 expression

ORR and DOR[a]

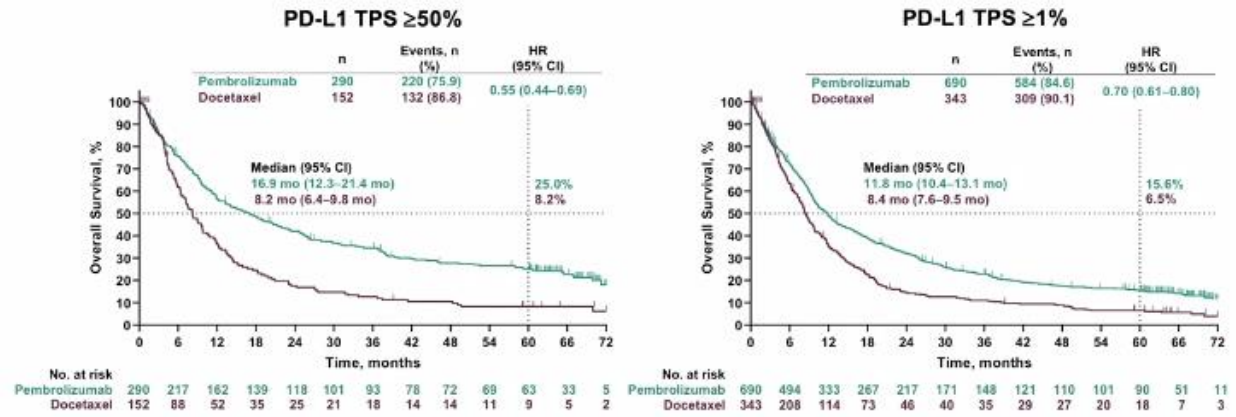


[a]Based on blinded independent central review per RECIST v1.1. "+" indicates there is no progressive disease by the time of last disease assessment.
Data cutoff: August 28, 2020.

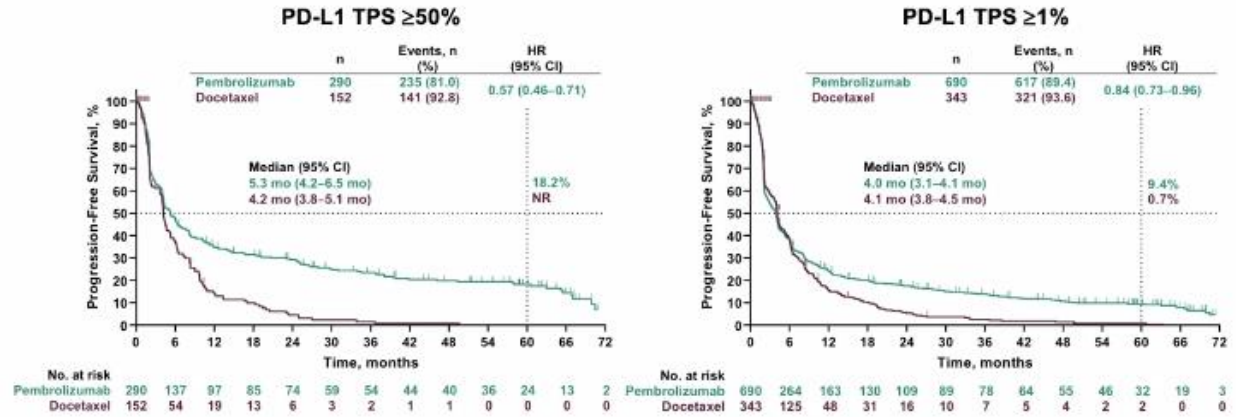
Gray J, WCLC 2020

FP13.01- 5-Year Survival Update From KEYNOTE-010:Pembrolizumab Versus Docetaxel in Previously Treated, PD-L1-Positive Advanced NSCLC

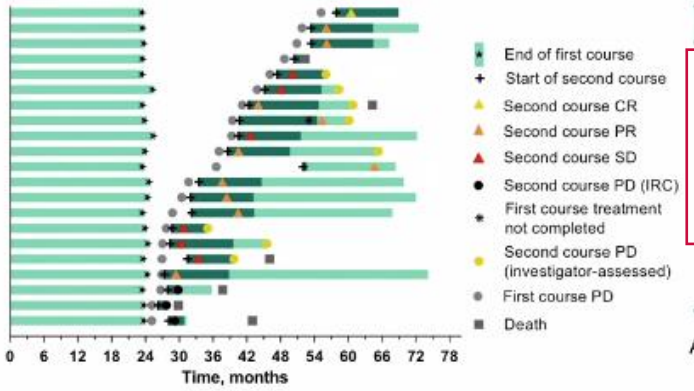
Overall Survival



Progression-Free Survival[a]



Treatment Duration and Time to Response
Second-Course Pembrolizumab[a]



Second-Course Response	N = 21
Objective response[b], n (%)	11 (52.4)
Best objective response[b], n (%)	
Complete response	1 (4.8)
Partial response	10 (47.6)
Stable disease	6 (28.6)
Progressive disease[c]	3 (14.3)
No assessment	1 (4.8)

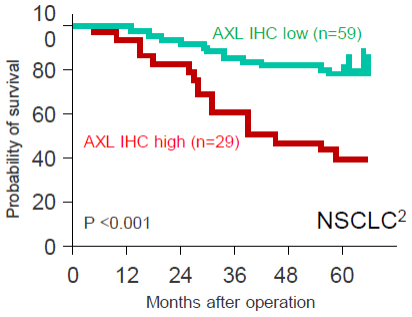
At data cutoff, 15/21 patients (71.4%) were alive

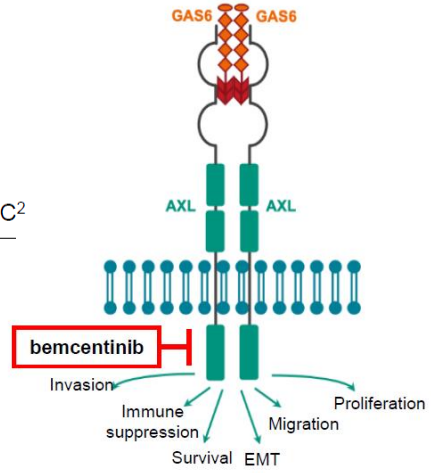
Herbst R, WCLC 2020

OA01.07 - A Phase II Study of the Oral Selective AXL Inhibitor Bemcentinib with Pembrolizumab in Patients with Advanced NSCLC

Study Rationale

- AXL drives tumor **EMT and resistance to CTL-mediated tumor cell killing**[1]
- AXL receptor tyrosine kinase is **negatively prognostic** in many cancers including NSCLC[2]
- AXL expression is associated with **anti-PD-1 therapy failure** in melanoma patients[3]
- AXL is expressed by immuno-suppressive **tumor-associated M2 macrophages and dendritic cells**[4]
- Bemcentinib is a first-in-class highly **selective, potent, oral small molecule AXL kinase inhibitor**
- Bemcentinib **reverses EMT, repolarizes TAMs and potentiates immunotherapy** in mouse models[4]





Study Design

Cohort A
- Previously treated with a platinum-containing chemotherapy
- CPI-naïve
- Demonstrable PD

Interim Analysis
Cohort A
Stage 1
N=22 patients
(each patient has the potential for at least 24 weeks follow-up)

Final Analysis
Cohort A
Stage 2
N=48 patients
(each patient has the potential for at least 24 weeks follow-up)

Cohort B
- Previously treated with PD-L1 or PD-1 inhibitor mono- therapy
- ≥12 weeks clinical benefit followed by PD

Interim Analysis
Cohorts B
Stage 1
N=16 patients
(each patient has the potential for at least 24 weeks follow-up)

Final Analysis
Cohorts B
Stage 2
N=29 patients
(each patient has the potential for at least 24 weeks follow-up)

Cohort C
- Previous 1st line combination checkpoint inhibitor + platinum doublet
- ≥12 weeks clinical benefit on 1st line therapy followed by PD

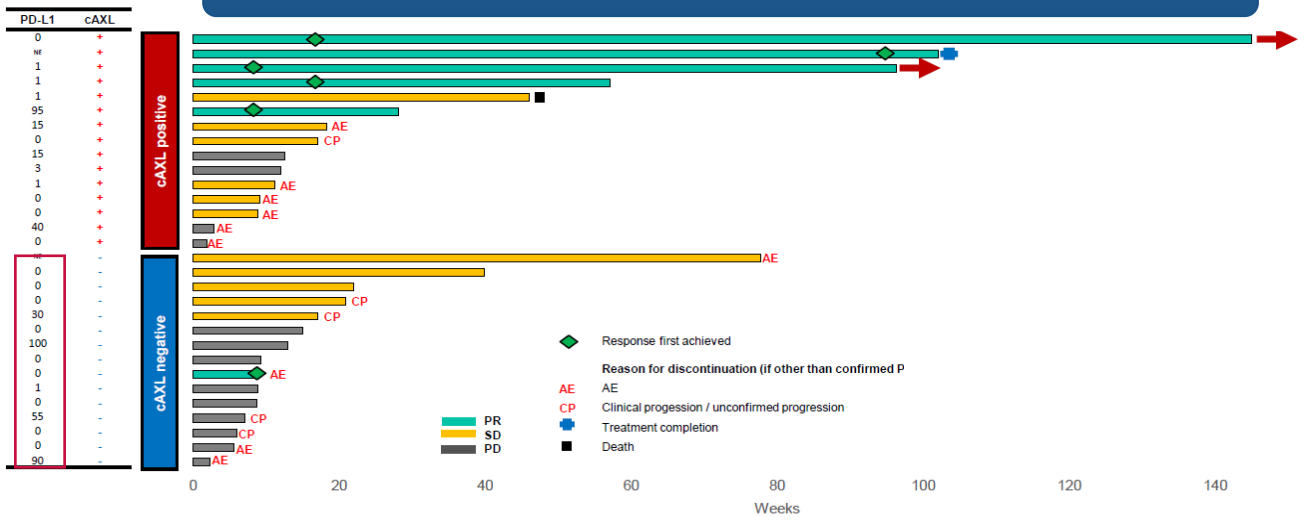
Interim Analysis
Cohorts C
Stage 1
N=13 patients
(each patient has the potential for at least 24 weeks follow-up)

Final Analysis
Cohorts C
Stage 2
N=29 patients
(each patient has the potential for at least 24 weeks follow-up)

Matthew G. Krebs, WCLC 2020

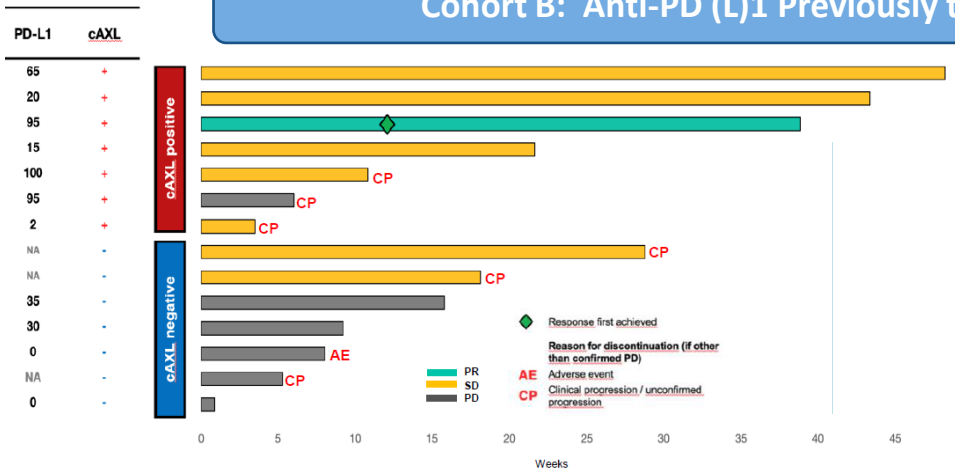
OA01.07 - A Phase II Study of the Oral Selective AXL Inhibitor Bemcentinib with Pembrolizumab in Patients with Advanced NSCLC

Cohort A: Platinum based-Cht Previously treated, IO naive



Cut-off: 27 Nov 2020

Cohort B: Anti-PD (L)1 Previously treated



Efficacy of Bemeciclib + Pembrolizumab

	ORR	CBR
cAXL positive (n=15)	5 (33%)	11 (73%)
cAXL negative (n=15)	1 (7%)	6 (40%)

Ongoing – rates at cut-off	ORR	CBR
cAXL positive (n=7)	1 (14%)	6 (86%)
cAXL negative (n=7)	0 (0%)	2 (29%)

Matthew G. Krebs, WCLC 2020

OA01.07 - A Phase II Study of the Oral Selective AXL Inhibitor Bemcentinib with Pembrolizumab in Patients with Advanced NSCLC

Most frequently occurring treatment-related* AEs (≥10% dosed patients), n=75

Preferred term	Any grade n (%)	Grades ≥3 n (%)
Alanine aminotransferase increased	25 (33)	9 (12)
Aspartate aminotransferase increased	24 (32)	6 (8)
Diarrhoea	24 (32)	1 (1)
Asthenia	14 (19)	4(5)
Pruritus	12 (16)	0
Nausea	11 (15)	0
Blood creatinine increased	10 (13)	0
Electrocardiogram QT prolonged	10 (13)	1 (1)
Fatigue	10 (13)	1 (1)
Anaemia	9 (12)	2 (3)
Decreased appetite	8 (11)	0

n=3 (4%) pts reported G4 and no pts. reported G5 AEs

Conclusions:

- ORR 33% in patients Cht-previously treated AXL+ population. Limitation: low level of PD-L1 expression (64% of PD-L1 neg) in AXL- subgroup
- Limited signs of clinical benefit in the cohort of patients CPI-previously treated

Questions:

- AXL evaluation criteria?
- Are the combination better than pembro monotherapy?
- More data are required

Recruitment ongoing in CPI-refractory (Cohort B) and chemo-CPI refractory (Cohort C) patient populations

Matthew G. Krebs WCLC 2020

OA07.08 - HUDSON: Phase II Platform Study in Patients with NSCLC, who Progressed on Anti-PD(L)1 Therapy

HUDSON study design

- Locally advanced or metastatic NSCLC
- Previous platinum-based chemotherapy
- Failed Anti-PD(L)1 treatment
- Biopsiable disease
- Targetable EGFR, ALK, ROS1, BRAF, MET or RET alterations were excluded

Central molecular screen† (n=617)

Group A: biomarker matched (n=85)

HRRm	olaparib and durvalumab (PARPi)
STK11	olaparib and durvalumab (PARPi)
ATM	ceralasertib and durvalumab (ATRi)
CD73	oleclumab and durvalumab (CD73i)
HER2e	trastuzumab deruxtecan and durvalumab (HER2i)
HER2m	trastuzumab deruxtecan and durvalumab (HER2i)

Group B: biomarker non-matched (n=177)

Primary resistance‡ (n=74)

- olaparib and durvalumab (PARPi)
- danvatirsen and durvalumab (STAT3i)
- ceralasertib and durvalumab (ATRi)
- oleclumab and durvalumab (CD73i)

Acquired resistance§ (n=103)

- olaparib and durvalumab (PARPi)
- danvatirsen and durvalumab (STAT3i)
- ceralasertib and durvalumab (ATRi)
- oleclumab and durvalumab (CD73i)
- cediranib and durvalumab (VEGFi)

617 screened → 262 enrolled (42%)

85 patients, biomarker-matched (13%)

HRRm	3%	olaparib and durvalumab (PARPi)
STK11	3%	olaparib and durvalumab (PARPi)
ATM	3%	ceralasertib and durvalumab (ATRi)
CD73	4%	oleclumab and durvalumab (CD73i)
HER2e		trastuzumab deruxtecan and durvalumab (HER2i)
HER2m		trastuzumab deruxtecan and durvalumab (HER2i)

Primary endpoint:

- Overall response rate

Secondary endpoints:

- Progression-free survival
- Overall survival
- Disease control rate
- Safety and tolerability

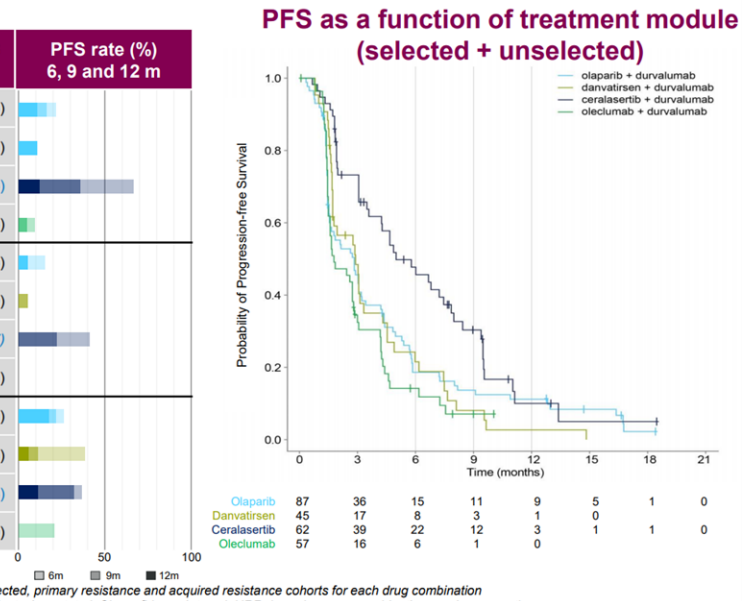
†Immunohistochemistry was also performed. ‡PD on ICI within 24 weeks (fresh biopsy or archived tissue); §PD on ICI > 24 weeks (fresh biopsy or archived tissue). ATM, ataxia-telangiectasia mutated; ATRi, ataxia-telangiectasia receptor inhibitor; CD73, cluster of differentiation 73; HER2, human epidermal growth factor receptor 2; HRR, homologous recombination repair; NSCLC, non-small-cell lung cancer; PARPi, poly ADP ribose polymerase inhibitor; PD, progression of disease; STAT3i, Signal transducer and activator of transcription 3 inhibitor; STK11, Serine/threonine kinase 11 (also known as LKB1)

Besse B, WCLC 2020

OA07.08 - HUDSON: Phase II Platform Study in Patients with NSCLC, who Progressed on Anti-PD(L)1 Therapy

HUDSON – ORR and median PFS

	Durvalumab combination	N	mF/U m	ORR n (%)	Median PFS m (80% CI)
Biomarker selected	Olaparib HRR	21	2.8	2 (9.5)	2.79 (1.48 – 5.26)
	Olaparib STK11	21	1.4	1 (4.8)	1.41 (1.38 – 1.81)
	Ceralasertib ATM	18	*5.0*	*2 (11.1)*	*7.43 (3.45 – 9.46)*
	Oleclumab 73H	23	1.5	0 (0)	1.58 (1.41 – 2.76)
Primary resistance	Olaparib	22	2.8	0 (0)	3.38 (2.10 – 4.93)
	Danvatirsen	23	1.7	0 (0)	1.68 (1.64 – 2.99)
	Ceralasertib	20	2.6	2 (10.5)	*4.24 (1.94 – 6.77)*
	Oleclumab	9	1.4	0 (0)	1.41 (1.35 – 1.81)
Acquired resistance	Olaparib	23	4.2	1 (4.3)	4.17 (2.69 – 4.37)
	Danvatirsen	22	2.8	0 (0)	3.09 (2.83 – 6.14)
	Ceralasertib	24	4.6	2 (8.3)	4.96 (3.55 – 5.98)
	Oleclumab	25	2.6	1 (4.2)	2.63 (1.64 – 2.79)

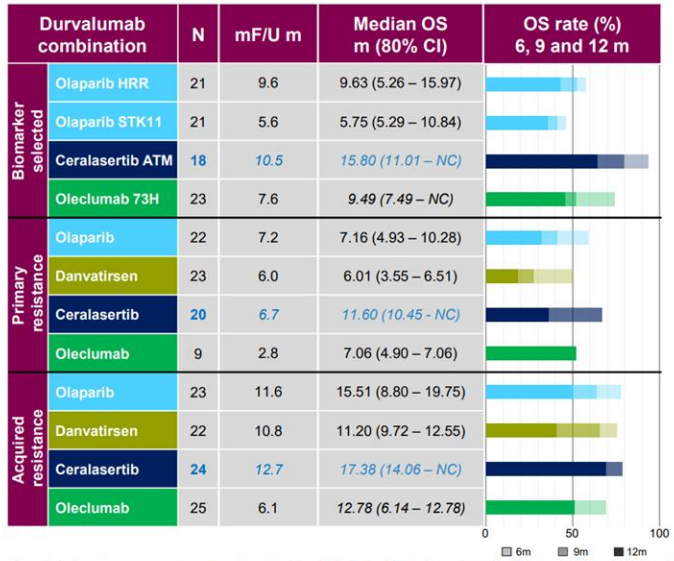


PFS as a function of treatment module (selected + unselected)

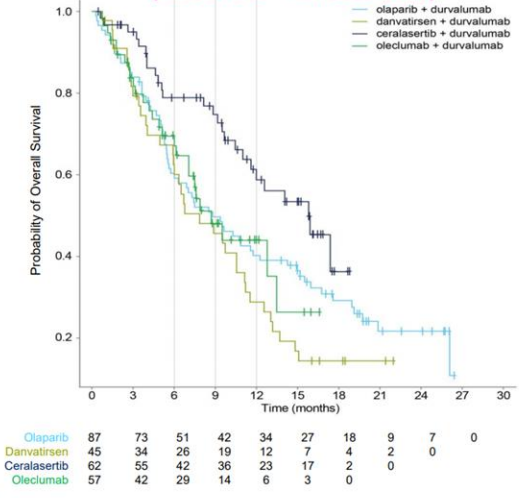
Data in italics are not yet mature; treatment modules include the biomarker selected, primary resistance and acquired resistance cohorts for each drug combination
73H, signal transducer and activator of transcription 3-73H; ATM, ataxia-telangiectasia mutated; CI, confidence interval; HRR, homologous recombination repair; m, months; mF/U, median follow-up; NC, not calculated; ORR, objective response rate; PFS, progression-free survival; STK11, Serine/threonine kinase 11 (also known as LKB1)

HUDSON – median OS

	Durvalumab combination	N	mF/U m	Median OS m (80% CI)
Biomarker selected	Olaparib HRR	21	9.6	9.63 (5.26 – 15.97)
	Olaparib STK11	21	5.6	5.75 (5.29 – 10.84)
	Ceralasertib ATM	18	*10.5*	*15.80 (11.01 – NC)*
	Oleclumab 73H	23	7.6	*9.49 (7.49 – NC)*
Primary resistance	Olaparib	22	7.2	7.16 (4.93 – 10.28)
	Danvatirsen	23	6.0	6.01 (3.55 – 6.51)
	Ceralasertib	20	*6.7*	*11.60 (10.45 - NC)*
	Oleclumab	9	2.8	7.06 (4.90 – 7.06)
Acquired resistance	Olaparib	23	11.6	15.51 (8.80 – 19.75)
	Danvatirsen	22	10.8	11.20 (9.72 – 12.55)
	Ceralasertib	24	*12.7*	*17.38 (14.06 – NC)*
	Oleclumab	25	6.1	*12.78 (6.14 – 12.78)*



OS as a function of treatment module (selected + unselected)



Data in italics are not yet mature; treatment modules include the biomarker selected, primary resistance and acquired resistance cohorts for each drug combination
73H, signal transducer and activator of transcription 3-73H; ATM, ataxia-telangiectasia mutated; CI, confidence interval; HRR, homologous recombination repair; m, months; mF/U, median follow-up; NC, not calculated; OS, overall survival; STK11, Serine/threonine kinase 11 (also known as LKB1)

Conclusions:

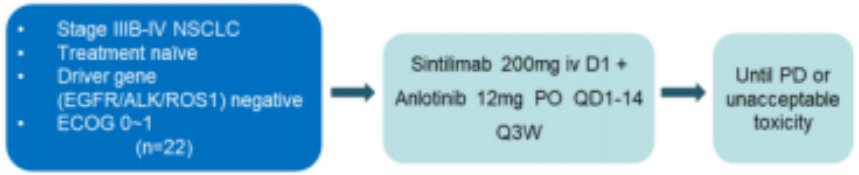
- Preliminary efficacy data for ceralasertib (ATMi) + Pembrolizumab in biomarker selected (ATM low or mutated population) and unselected population
- Patients with *STK11* mut have de poorest outcomes

Questions:

- More data about these drugs efficacy and potential biomarkers are required

Besse B, WCLC 2020

OA07.09 - Sintilimab in Combination with Anlotinib as First-Line Therapy for Advanced NSCLC: Final Analysis of Primary Endpoints.



This is one arm from a multi-cohort phase I trial (NCT03628521).

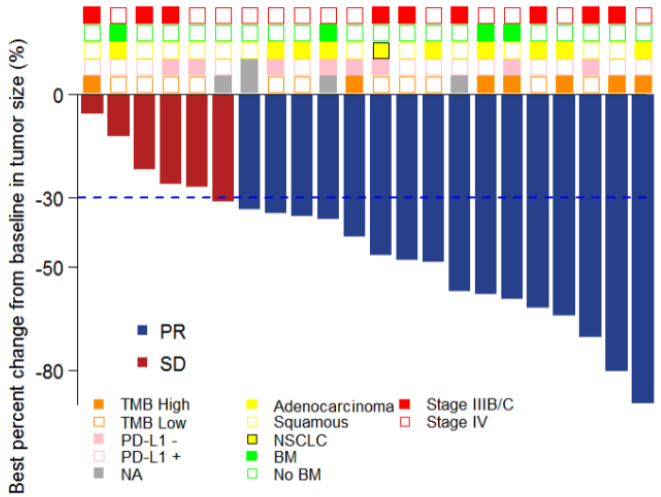
Primary Endpoint:
- Overall response rate (ORR)
- Safety

Secondary Endpoint:
- Disease control rate (DCR)
- Progression free survival (PFS)
- Overall Survival (OS)

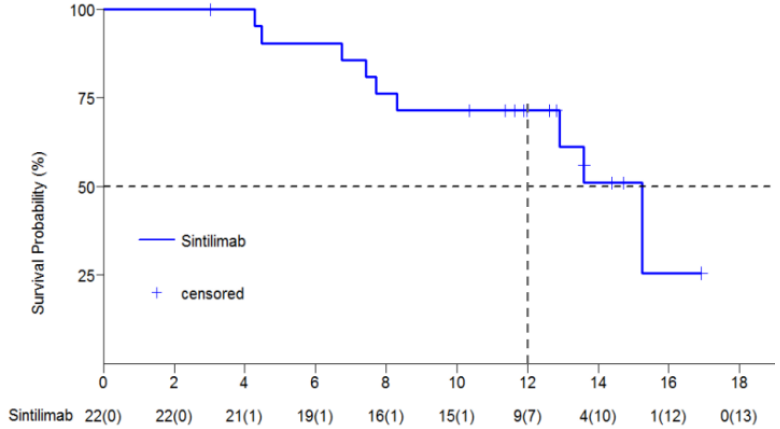
RESPONSE RATE

Response Rate and Duration (N=22)	
CR , n (%)	-
PR , n (%)	16 (72.7)
SD , n (%)	6 (27.3)
ORR , % (95%CI)	72.7 (49.8, 89.3)
DCR , % (95%CI)	100 (84.6, 100)
Median TTR, month (95% CI)	1.6 (1.4, 2.9)
Median DOR, month (95% CI)	NR (3.2, NC)

CR/PR were confirmed in subsequent assessments at least four weeks later.
Data cut-off: Apr. 30th, 2020



PFS



Median follow-up: 15.8 months (range, 8.3-19.3)
Data cut-off: Apr. 30th , 2020

SAFETY

TreAdverse Events ≥ 20%, No.(%)	Any Grade	Grade 3
Hemorrhage*	13 (59.1)	0(0.0)
Hypothyroidism	11(50.0)	0(0.0)
Uric acid increased	9(40.9)	0(0.0)
Hand-foot skin reaction	8(36.4)	1(4.5)
Hypoalbuminemia	8(36.4)	0(0.0)
Hypertension	7(31.8)	2(9.1)
ALT increased	7(31.8)	0(0.0)
Direct bilirubin increased	7(31.8)	0(0.0)
Rash	5(22.7)	1(4.5)
Pneumonitis	5(22.7)	0(0.0)
Immune-related pneumonitis	3(13.6)	0(0.0)

84.6% (11/13) hemorrhage events were Grade 1. 3 patients experienced transient Grade 1 hemoptysis. Only one patient with Grade 2 urinary occult blood required medication

Treatment related AEs (TRAE), n (%)	22 (100)
≥ Grade 3 TRAEs *	12 (54.4)
≥ Grade 3 irAEs	1 (4.5)

Conclusions:

- Preliminary efficacy data for this Cht free combination in first line patients without selection by PD-L1 expression

Questions:

- A phase II randomized trial (NCT04124731) is currently ongoing to further investigate this new ChT free strategy

Baohi Han, WCLC 2020

OA01.03 - Clinical Benefits of First-Line (1L) Cemiplimab Monotherapy by PD-L1 Expression Levels in Patients With Advanced NSCLC

EMPOWER-Lung 1 Study Design

Key Eligibility Criteria
- Treatment-naïve advanced NSCLC
- PD-L1 ≥50%
- No *EGFR*, *ALK*, or *ROS1* mutations
- ECOG PS 0 or 1
- Treated, clinically stable CNS metastases and controlled hepatitis B or C or HIV were allowed

Stratification Factors:
- Histology (squamous vs non-squamous)
- Region (Europe, Asia, or ROW)

R 1:1

Arm A
Cemiplimab monotherapy IV
350 mg Q3W
Treat until PD or 108 weeks

PD → Optional continuation of cemiplimab + 4 cycles of chemotherapy

Arm B
4–6 cycles of investigator's choice chemotherapy

PD → Optional crossover to cemiplimab monotherapy

Follow-up

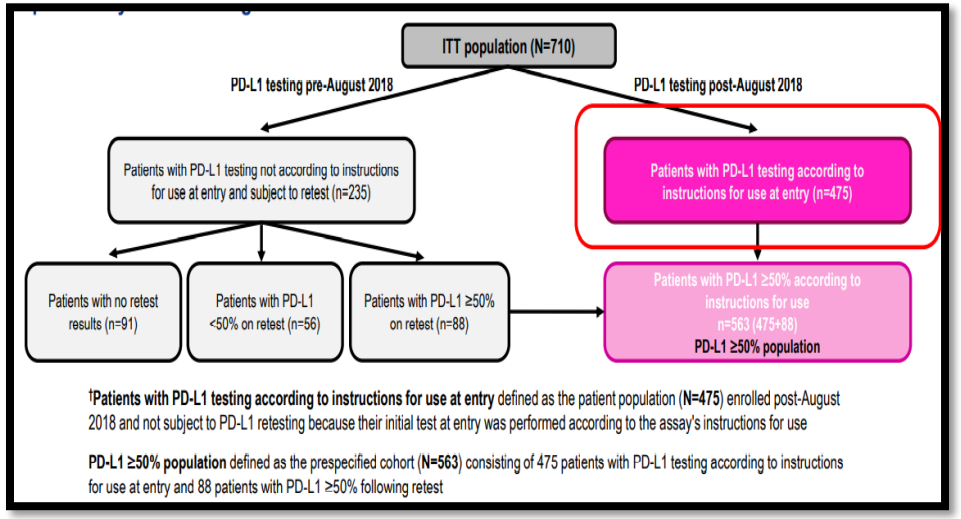
N=710

Endpoints:
- Primary: OS and PFS
- Secondary: ORR (key), DOR, HRQoL, and safety

ALK, anaplastic lymphoma kinase; CNS, central nervous system; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HIV, human immunodeficiency virus; HRQoL, health-related quality of life; IV, intravenous; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-L1, programmed cell death-ligand 1; PFS, progression-free survival; Q3W, every 3 weeks; R, randomized; ROS1, c-ros oncogene 1; ROW, rest of the world.

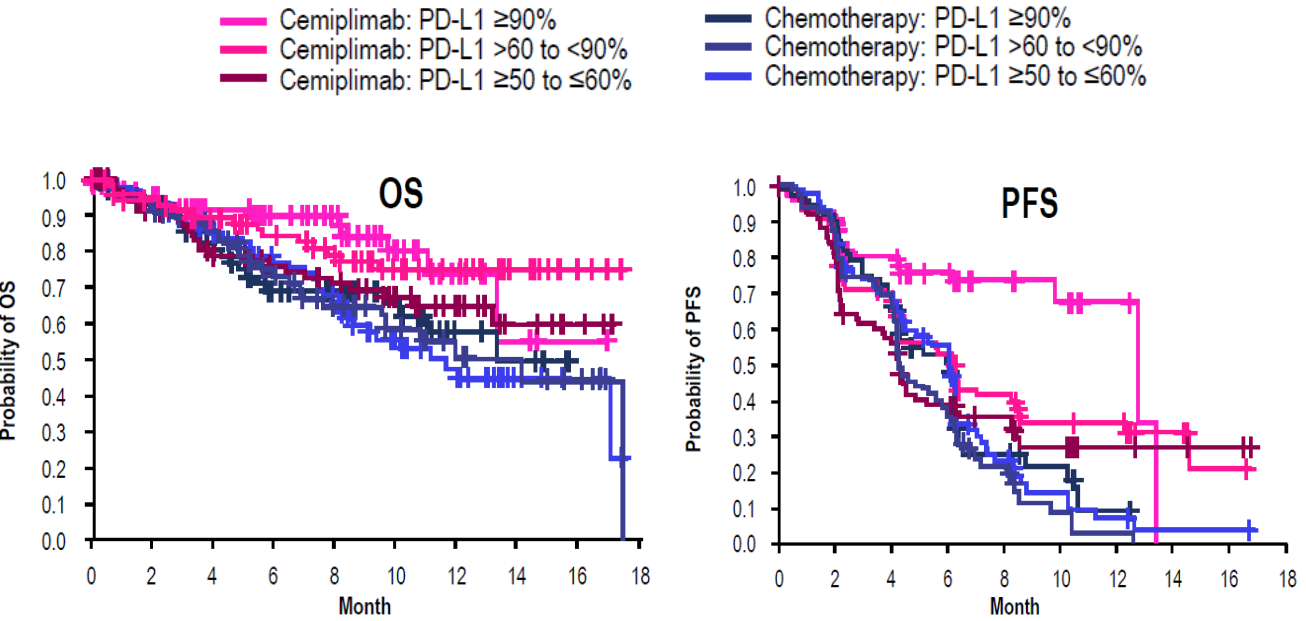
- EMPOWER-Lung 1 (NCT03088540) is a Phase 3 study which compared first-line cemiplimab monotherapy with investigator's choice chemotherapy. In the ITT and prespecified PD-L1 ≥50% populations:
  - Cemiplimab showed superior median OS and PFS versus chemotherapy[6]
  - Cemiplimab produced higher ORR and longer DOR versus chemotherapy[6]
  - Incremental improvements in survival outcomes were observed with increasing PD-L1 levels for cemiplimab, but not chemotherapy[6]

Exploratory analysis on pts with PD-L1 testing according to instructions for use at entry (N=475)



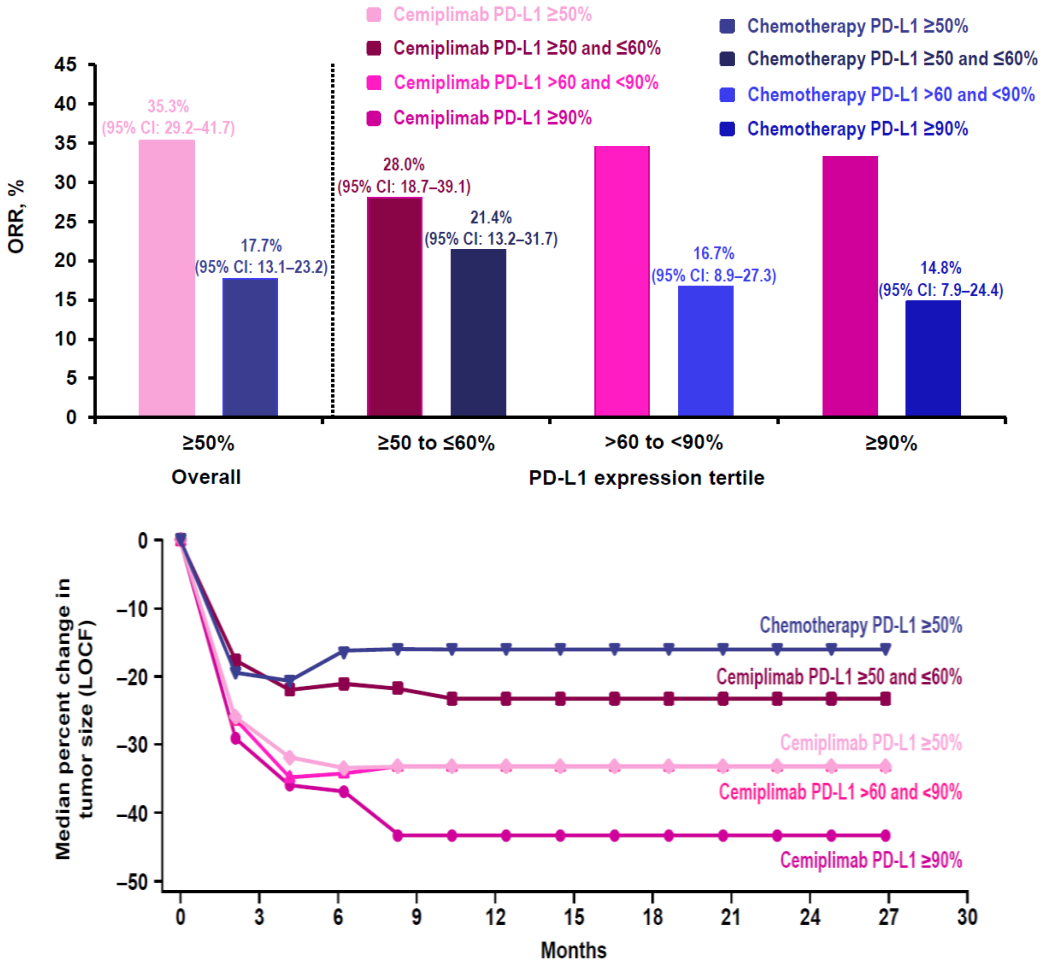
Saadettin Kilickap, WCLC 2020

OA01.03 - Clinical Benefits of First-Line (1L) Cemiplimab Monotherapy by PD-L1 Expression Levels in Patients With Advanced NSCLC



	Median, months (95% CI)			HR (95% CI)
	Cemiplimab (N=238)		Chemotherapy (N=237)	
≥90%	NR (13.4–NE)	vs	13.3 (10.2–NE)	0.54 (0.27–1.10)
>60 to <90%	NR (NE–NE)	vs	14.2 (9.6–17.5)	0.49 (0.26–0.92)
≥50 to ≤60%	NR (13.2–NE)	vs	11.7 (8.3–NE)	0.74 (0.44–1.24)

	Median, months (95% CI)			HR (95% CI)
	Cemiplimab (N=238)		Chemotherapy (N=237)	
≥90%	12.7 (9.8–13.4)	vs	6.1 (4.2–6.2)	0.33 (0.19–0.58)
>60 to <90%	6.2 (4.2–8.4)	vs	4.3 (4.1–5.9)	0.57 (0.38–0.85)
≥50 to ≤60%	4.3 (2.8–5.2)	vs	6.0 (4.4–6.2)	0.89 (0.61–1.29)



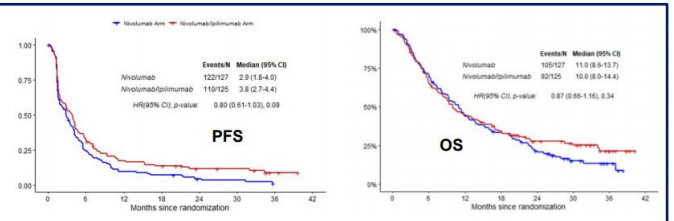
PD-L1 expression correlates with OS, PFS, RR and Tumor size reduction

Saadettin Kilickap, WCLC 2020

OA01.04 - Tumor Mutation Burden (TMB) by Next Generation Sequencing (NGS) Associates with Survival (OS) in Lung-MAP Immunotherapy Trials S1400I and S1400A

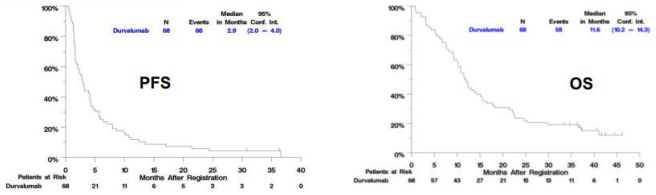
S1400I: Randomized Phase III study: Nivolumab + Ipilumumab vs Nivolumab

Gettinger S. et al (ASCO 2019, WCLC 2019)



S1400A: Single-arm phase II study: Durvalumab

Borghaei H et al. Clin Lung Cancer. in press



Tumor Mutational Burden as a Continuous Variable

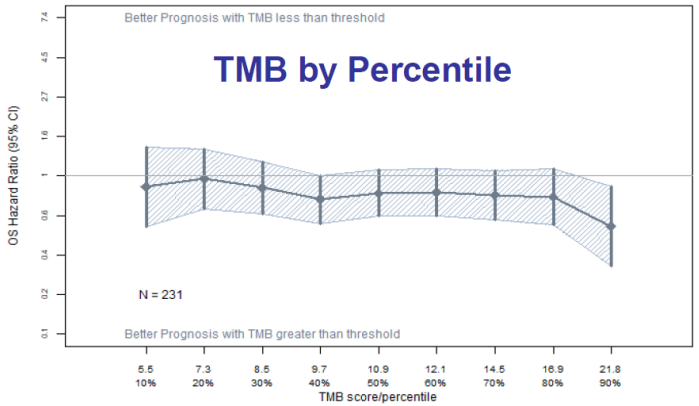
TMB by Value (per 10-unit difference)

Total pts: 252 on S1400I
68 on S1400A

Overall Survival: higher TMB; HR; 0.80 (95% CI: 0.67;0.94), p=0.008

Progression Free Survival: HR: 0.80 (95% CI; 0.69;0.93), p=0.004

HIGHER TMB WAS SIGNIFICANTLY ASSOCIATED WITH IMPROVED OS AND PFS.

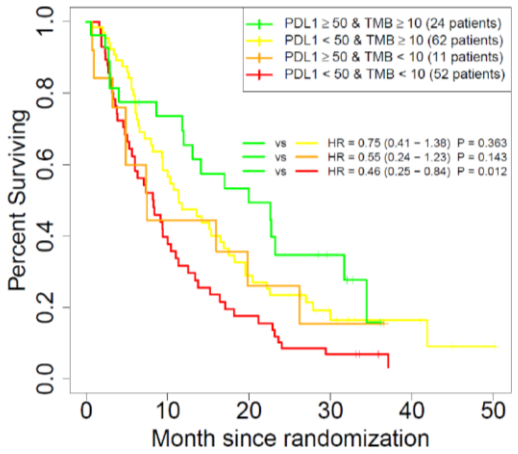


The relative risk of death comparing OS between patients with TMB levels above versus below the thresholds

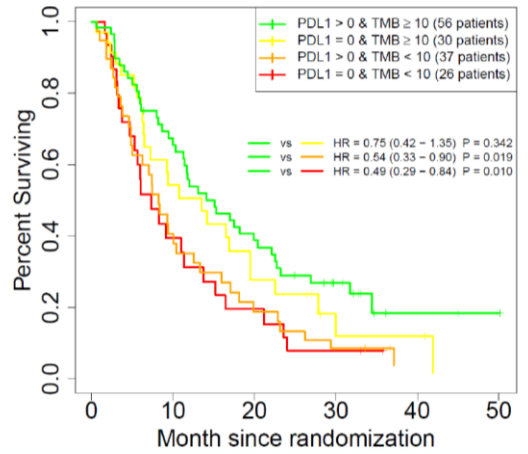
Combining PDL-1 and TMB Analysis:

- Patients high in both outperformed all other groups

OS KM by TMB at 10 and PDL1 at 50%



OS KM by TMB at 10 and PDL1 pos/neg



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MUCHAS GRACIAS

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