Lung Cancer UPDATES
IASLC HIGHLIGTHS
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VIRTUAL

Iniciativa científica de:
GECP lung cancer research

Nuevas terapias en CPNCP avanzado

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Nuevas terapias en CPNCP avanzado

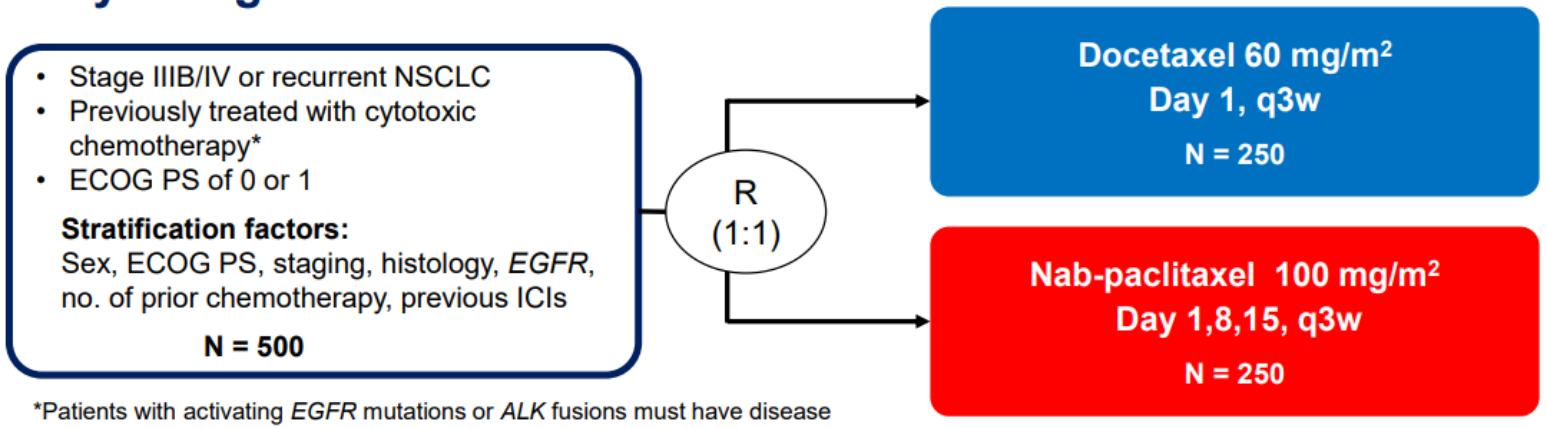
Abstracts más destacados

Clinical trials:

- ***OA03.05*** *- Phase III Study Comparing Nab-Paclitaxel With Docetaxel in Patients With Previously Treated Advanced Non-Small-Cell Lung Cancer*
- ***OA03.03*** *- Datopotamab Deruxtecan (Dato-DXd; DS-1062), a TROP2 ADC, in Patients With Advanced NSCLC: Updated Results of TROPION-PanTumor01 Phase 1 Study*
- ***MA01.06*** *- Phase 2 of Pro-Autophagic Drug ABTL0812 in Combination With First-Line Paclitaxel and Carboplatin in IIIb/IV Squamous NSCLC*

OA03.05 - Phase III Study Comparing Nab-Paclitaxel With Docetaxel in Patients With Previously Treated Advanced Non-Small-Cell Lung Cancer

Study Design



*Patients with activating *EGFR* mutations or *ALK* fusions must have disease progression or intolerance of treatment with one or more EGFR-TKIs.

Primary endpoints: OS

- Non-inferiority margin: hierarchically 1.33 and 1.25 in terms of hazard ratio
- Superiority of nab-PTX will be tested only when non-inferiority is confirmed in overall survival.
- Assumed MST: DTX: 10 months, nab-PTX: 10.5 months, 3 year accrual, 1.5 year follow-up
- α =0.1% (one-sided) for the interim analysis, α = 2.4% (one-sided) for the final analysis, power = 8(

Baseline Characteristics

	DTX (n = 251)	Nab-PTX (n = 252)
Median age (range), y	68 (32–87)	67 (40–83)
< 75 y, n (%)	203 (80.9)	221 (87.4)
Sex*, male, n (%)	173 (68.9)	174 (69.0)
ECOG PS* 0, n (%)	88 (35.1)	85 (33.7)
Histology*, squamous, n (%)	48 (19.1)	50 (19.8)
Smoker, n (%)	175 (69.7)	190 (75.4)
Stage* III/IV, n (%)	209 (83.3)	208 (82.2)
EGFR mutation*, positive, n (%)	58 (23.1)	57 (22.6)
No. of prior chemotherapy*, 1, n (%)	231 (92.0)	229 (90.9)
Previous treatment with ICI*, yes, n (%)	40 (15.9)	41 (16.3)

*Stratification factor

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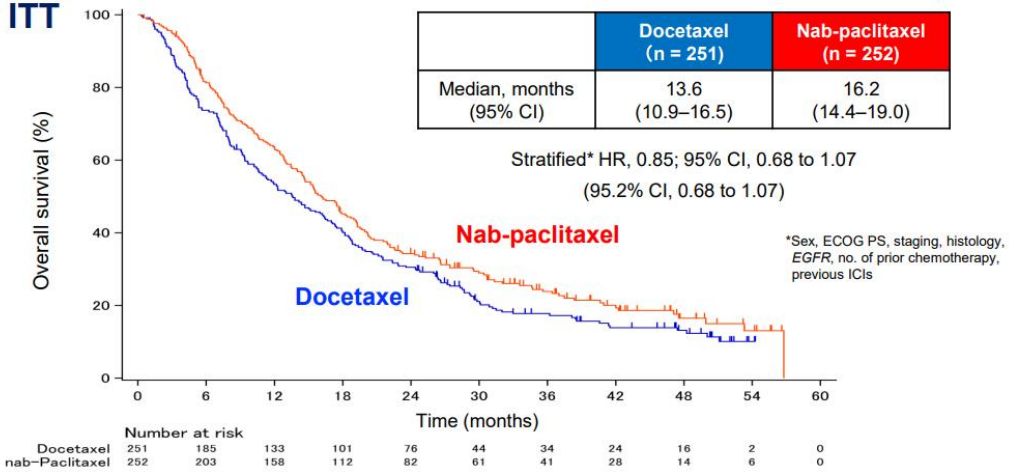
OA03.05 - Phase III Study Comparing Nab-Paclitaxel With Docetaxel in Patients With Previously Treated Advanced Non-Small-Cell Lung Cancer

OS in the ITT



	Docetaxel (n = 251)	Nab-paclitaxel (n = 252)
Median, months (95% CI)	13.6 (10.9–16.5)	16.2 (14.4–19.0)

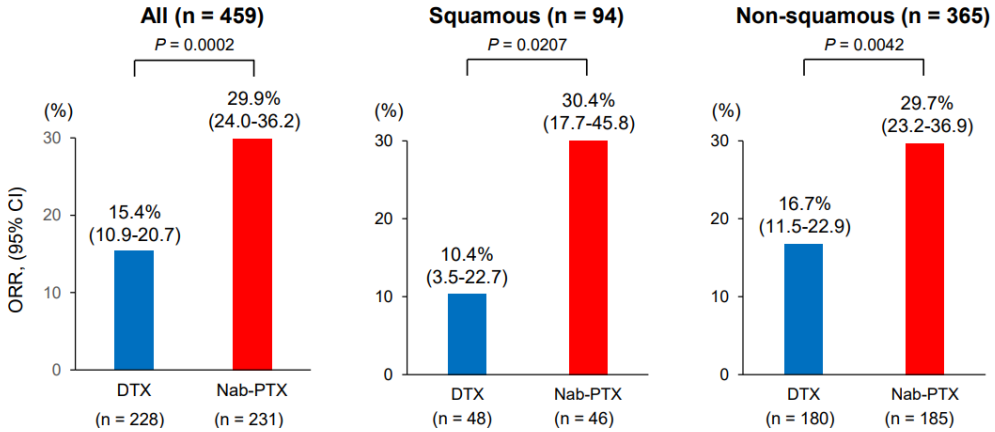
Stratified* HR, 0.85; 95% CI, 0.68 to 1.07
(95.2% CI, 0.68 to 1.07)

*Sex, ECOG PS, staging, histology, *EGFR*, no. of prior chemotherapy, previous ICIs

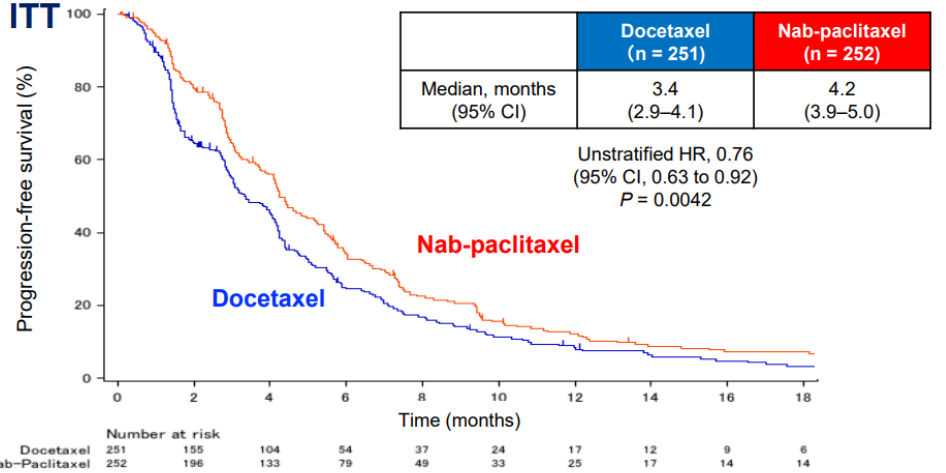
- Non-inferiority of nab-PTX was confirmed (upper limit of 95.2%CI (1.07) < protocol-specified margin of 1.25)
- Superiority was not confirmed by hierarchical test

Objective Response Rate

P: Fisher's exact test



PFS in the ITT

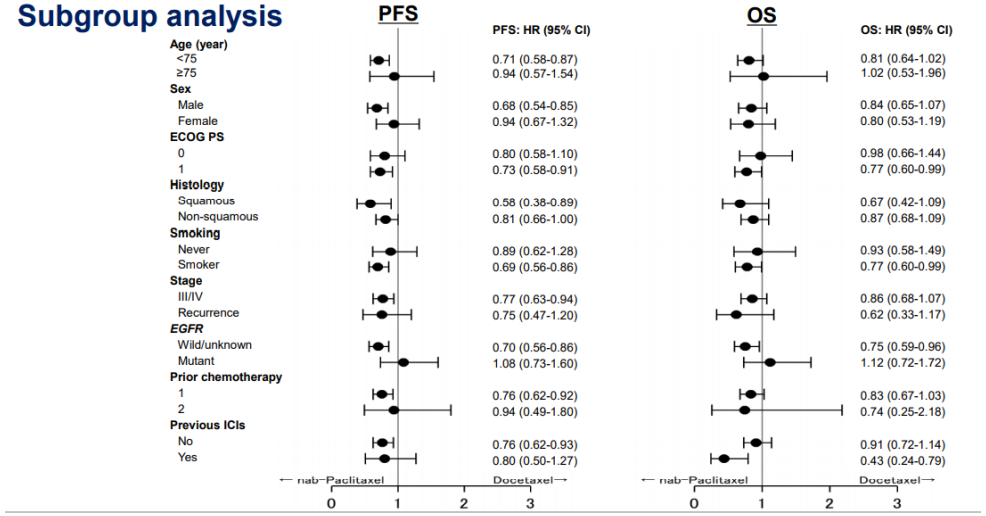


	Docetaxel (n = 251)	Nab-paclitaxel (n = 252)
Median, months (95% CI)	3.4 (2.9–4.1)	4.2 (3.9–5.0)

Unstratified HR, 0.76
(95% CI, 0.63 to 0.92)
P = 0.0042

- PFS benefit was seen with nab-PTX vs DTX

Subgroup analysis



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- *OA03.05 - Phase III Study Comparing Nab-Paclitaxel With Docetaxel in Patients With Previously Treated Advanced Non-Small-Cell Lung Cancer.*

Toxicities

Hematological AEs	Docetaxel (n = 249)		Nab-paclitaxel (n = 245)		*P* value
	Grade 3-4	Grade 4	Grade 3-4	Grade 4	Grade 3-4
Leukopenia	164 (65.9)	29 (11.6)	63 (25.7)	3 (1.2)	<0.0001
Neutropenia	207 (83.1)	144 (57.8)	97 (39.6)	30 (12.2)	<0.0001
Anemia	13 (5.2)	1 (0.4)	12 (4.9)	1 (0.4)	1.0000
Thrombocytopenia	0	0	0	0	NE
Non-hematological AEs	**Docetaxel (n = 249)**		**Nab-paclitaxel (n = 245)**		***P* value**
	All	**Grade 3-4**	**All**	**Grade 3-4**	**All**
Febrile neutropenia	55 (22.1)	55 (22.1)	5 (2.0)	5 (2.0)	<0.0001
Fatigue	143 (57.4)	13 (5.2)	137 (55.9)	16 (6.5)	0.7854
Anorexia	130 (52.2)	13 (5.2)	95 (38.8)	6 (2.4)	0.0029
Interstitial lung disease	21 (8.4)	7 (2.8)	23 (9.4)	10 (4.1)	0.7536
Peripheral sensory neuropathy	50 (20.1)	2 (0.8)	136 (55.5)	24 (9.8)	<0.0001

AE, adverse event; NE, not evaluated

P: chi-square test

Conclusions:

- This study demonsrates the non-inferiority of nab-placlitaxel vs docetaxel 60mg/m2 in terms of OS
- Docetaxel resulted in high incidence of febrile neutropenia but nab-placlitaxel increased the risk for PSN.

In my opinion these results don´t change our standard of care in the second line setting → Docetaxel 75mg/m2

Atsushi Nakamura, WCLC 2020

OA03.03 - Datopotamab Deruxtecan (Dato-DXd; DS-1062), a TROP2 ADC, in Patients With Advanced NSCLC: Updated Results of TROPION-PanTumor01 Phase 1 Study.

TROPION-PanTumor01 (NCT03401385) Study Design

Phase 1 FIH Dose Escalation and Expansion Study

Key inclusion criteria

- Relapsed/refractory advanced/metastatic NSCLC
- Unselected for TROP2 expression[a]
- Aged ≥18 (US) or ≥20 (Japan) years
- ECOG PS 0-1
- Measurable disease per RECIST v1.1
- Stable, treated brain metastases allowed

Dose escalation[1]

Dato-DXd 0.27 mg/kg to 10 mg/kg Q3W[b]

MTD established: 8 mg/kg Q3W

Dose expansion

- 50 patients at 4 mg/kg[c]
- 50 patients at 6 mg/kg[c,d]
- 80 patients at 8 mg/kg[c]

Primary objectives

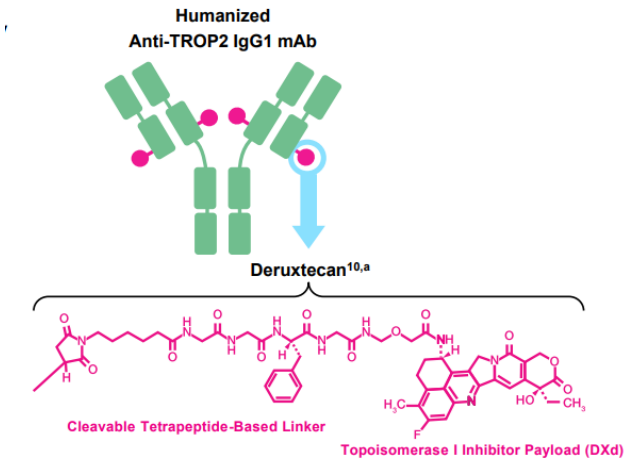
- Establish MTD, Safety, Tolerability

Secondary objectives

- Efficacy, PK

- NSCLC enrollment complete[d]
- TNBC cohort 6 mg/kg Q3W is enrolling; cohorts in other tumor types may be added
- Here we report updated results for the NSCLC dose expansion cohort (175 patients treated at 4, 6, or 8 mg/kg of Dato-DXd)

Dato-DXd molecule



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OA03.03 - Datopotamab Deruxtecan (Dato-DXd; DS-1062), a TROP2 ADC, in Patients With Advanced NSCLC: Updated Results of TROPION-PanTumor01 Phase 1 Study

Patient Demographics and Baseline Characteristics

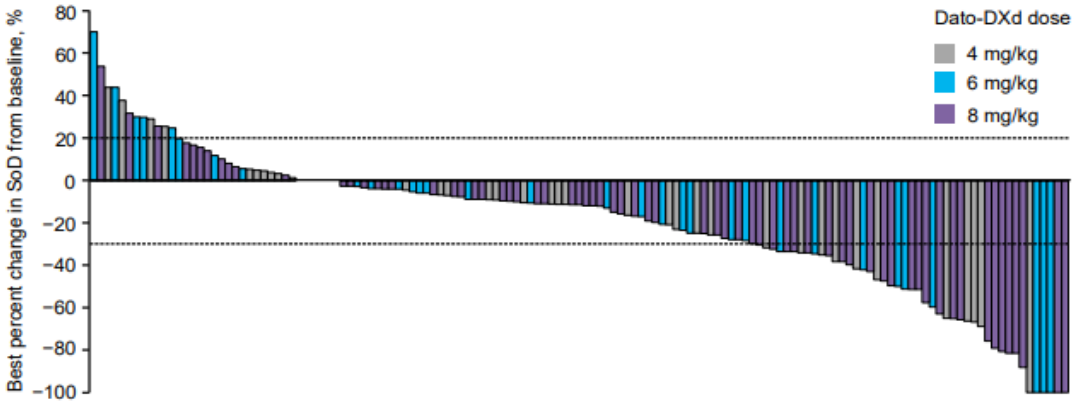
Characteristic	Dato-DXd dose		
	4 mg/kg (n = 50)	6 mg/kg (n = 45)	8 mg/kg (n = 80)
Male, n (%)	27 (54)	26 (58)	41 (51)
Median age (range), y	61 (35-82)	62 (45-76)	64 (31-84)
United States, n (%); Japan, n (%)	29 (58); 21 (42)	36 (80); 9 (20)	63 (79); 17 (21)
ECOG PS 0, n (%)	21 (42)	8 (18)	16 (20)
Nonsquamous histology, n (%)	41 (82)	40 (89)	70 (88)
≥3 prior lines of therapy, n (%)	25 (50)	26 (58)	51 (64)
Previous systemic treatment, n (%)			
Immunotherapy	42 (84)	35 (78)	70 (88)
Platinum-based chemotherapy	44 (88)	43 (96)	78 (98)
Tyrosine kinase inhibitor	10 (20)	6 (13)	14 (18)
History of brain metastases, n (%)	19 (38)	15 (33)	32 (40)
EGFR mutations,[a] n (%)	8 (16)	3 (7)	15 (19)

Overall Safety Summary

	Dato-DXd dose		
	4 mg/kg (n = 50) n (%)	6 mg/kg (n = 45) n (%)	8 mg/kg (n = 80) n (%)
TEAE	48 (96)	41 (91)	79 (99)
Grade ≥3	11 (22)	17 (38)	45 (56)
Treatment-related TEAE	43 (86)	35 (78)	76 (95)
Grade ≥3	5 (10)	7 (16)	27 (34)
Serious TEAE[a]	9 (18)	16 (36)	38 (48)
Treatment related	4 (8)	4 (9)	16 (20)
TEAEs associated with death[b]	4 (8)	1 (2)	7 (9)
Treatment related[c]	1 (2)	0	2 (3)

Patients receiving 8 mg/kg discontinued treatment due to AEs more frequently(76 vs 51 vs 46%) and had a lower median relative dose intensity than patients receiving 4 or 6 mg/kg

Best Change in Sum of Diameters and Overall Response (BICR)



Dato-DXd dose	Response-evaluable patients,[a] n	Confirmed CR/PR,[b] n	CR/PR (too early to be confirmed),[b] n	ORR,[b] % (n)	DCR, % (n)	PD, % (n)
4 mg/kg	40	7	2	23 (9)	73 (29)	15 (6)
6 mg/kg	39	6	2	21 (8)	67 (26)	21 (8)
8 mg/kg	80	19	1	25 (20)	80 (64)	9 (7)

Conclusions:

- Preliminary activity (ORR 21%) in a highly previously treated cohort of patients with refractory advanced NSCLC
- Based on these results , a phase 3 TROPION-Lung01 (NCT04656652) (6 mg/kg of Dato-DXd vs. docetaxel) will carry out in advanced NSCLC previously treated

Questions:

- TROP-2 as a predictive biomarker?

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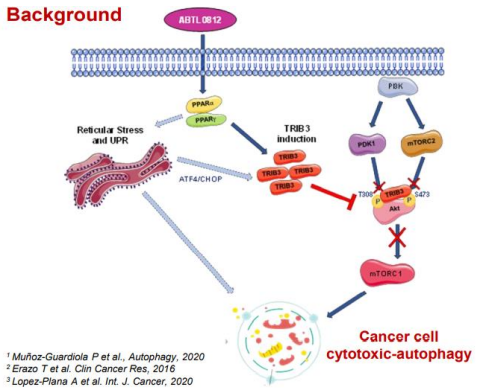
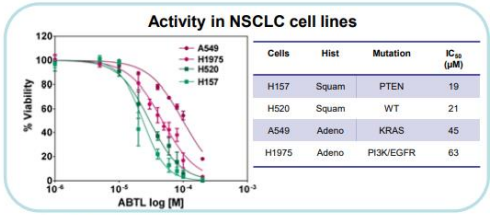
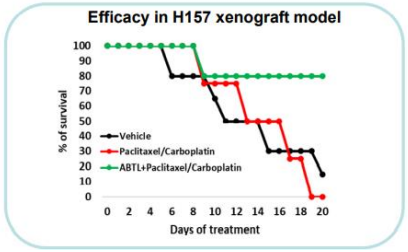
MA01.06 - Phase 2 of Pro-Autophagic Drug ABTL0812 in Combination With First-Line Paclitaxel and Carboplatin in IIIb/IV Squamous NSCLC



[1] Muñoz-Guardiola P et al., Autophagy, 2020
[2] Erazo T et al. Clin Cancer Res, 2016
[3] Lopez-Plana A et al. Int. J. Cancer, 2020



Cells	Hist	Mutation	IC_{50} (µM)
H157	Squam	PTEN	19
H520	Squam	WT	21
A549	Adeno	KRAS	45
H1975	Adeno	PI3K/EGFR	63



Key elegibility criteria:

- Squamous NSCLC
- Patients with mixed tumors, neuroendocrine and adenocarcinoma were excluded
- Non-irradiable stage IIIb or IV
- Patients were excluded if treated with adjuvant or co-adjuvant chemo or radio **less than** 6 months before inclusion.
- Patients with asymptomatic brain metastases were accepted if no grade >2 peripheral neurophathy

Screening
n = 37

Screening failure
n = 2

Included (Safety population)
n = 35

	Safety population
Age, median (range)	66.1 (51.1-76.2)
Gender (male / female %)	88.6 / 11.4
Race (white, %)	100.0
ECOG (0 / 1, %)	31.4 / 68.6
Prior chemotherapy (%)	62.5
Smokers (yes / former / never, %)	34.5 / 62.5 / 3
Stage III / IV (%)	20 / 80

ABTL0812 1300 mg tid oral + 175 mg/m² paclitaxel / 5 AUC carboplatin IV every 3 weeks

Evaluable for efficacy (primary endpoint ORR according to RECIST v1.1)

Full Analysis Set (FAS)
n = 22

Non-evaluable for efficacy

Excluded from FAS
n = 13

ABTL-0812

- Novel oral anti cancer agent
- Induced strong autophagy-mediated death
- Upregulates TRIB3, an endogenous AKT inhibitor
- Elicits reticular stress

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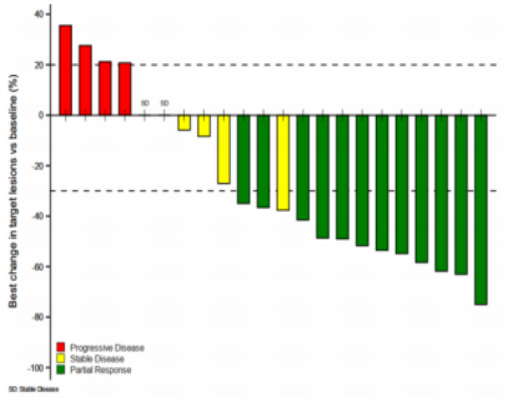
MA01.06 - Phase 2 of Pro-Autophagic Drug ABTL0812 in Combination With First-Line Paclitaxel and Carboplatin in IIIb/IV Squamous NSCLC

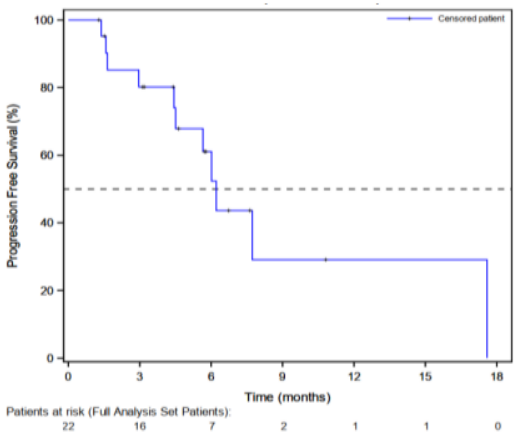
Overall Response Rate



Parameter	ABTL0812+ P/C n=22	Historical data*, n=281
ORR, % (n)	54.5 (12)	31.7 (89)
SD, % (n)	27.3 (6)	44.1 (124)
PD, % (n)	18.2 (4)	13.9 (39)
DOR, median (95% CI)	4.9 (1.4-14.5)	4.9
Chemo cycles, median (95% CI)	4.0 (2.8-4.5)	N.R.

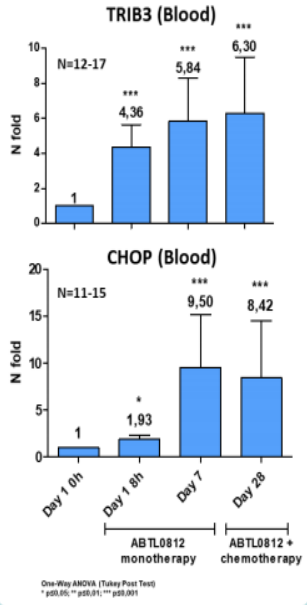
Paz-Ares. NEJM 2018

Progression Free Survival



Parameter	ABTL0812+ P/C n=22	Historical data, n=281*
Median PFS (months), 95% CI	6.2 (4.4-17.6)	4.8* (4.3-5.7)
6-month event free rate (%), 95% CI	61.1 (34.5-79.6)	N.R.
12-month event free rate (%), 95% CI	29.1 (6.2-57.8)	N.R.

PD Biomarkers



Safety Results: AEs observed in >10% patients (n=35)

	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4
ANY ADVERSE EVENT	91.4	11.4	34.3	28.6	17.1
HEMATOLOGICAL					
Neutropenia	28.6	0.0	2.9	11.4	14.3
Anemia	25.7	17.1	5.7	2.9	0.0
Thrombocytopenia	11.4	2.9	5.7	2.9	0.0
Febrile neutropenia	5.7	0.0	0.0	2.9	2.9
NON HEMATOLOGICAL					
Asthenia	57.1	31.4	22.9	2.9	0.0
Diarrhea	40.0	28.6	11.4	0.0	0.0
Alopecia	31.4	22.9	8.6	0.0	0.0
Decreased apetite	28.6	20.0	8.6	0.0	0.0
Nausea	25.7	17.1	8.6	0.0	0.0
Cough	22.9	17.1	5.7	0.0	0.0
Dysgeusia	20.0	14.3	5.7	0.0	0.0
Neurotoxicity	20.0	14.3	2.9	2.9	0.0
Hypomagenesemia	17.1	14.3	2.9	0.0	0.0
Constipation	14.3	14.3	0.0	0.0	0.0
Dyspnea	14.3	11.4	0.0	2.9	0.0
Musculoeskeletal pain	14.3	8.6	5.7	0.0	0.0
Neuropathy, peripheral	14.3	11.4	2.9	0.0	0.0
Pain extremity	14.3	8.6	2.9	0.0	0.0
Abdominal pain, upper	11.4	8.6	2.9	0.0	0.0
Pyrexia	11.4	11.4	0.0	0.0	0.0
Stomatitis	11.4	5.7	5.7	0.0	0.0

Conclusions:

- Preliminary activity (ORR 54.5%) in a small cohort of previously treated patients with refractory advanced SqC

Questions:

- Open label, one arm design…
- More data and controlled trials design are required

Joaquim Bosch, WCLC 2020

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MUCHAS GRACIAS

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