IASLC 2020 World Conference on Lung Cancer Singapore: Highlights

February 22, 2021

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INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER
Conquering Thoracic Cancers Worldwide

CME ACCREDITED

Simultaneous WCLC 2020 publication by Baohui Han:

https://www.jto.org/article/S1556-0864(20)31101-1/fulltext

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Disclosures

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- Advisory role and consultant: Novartis, Bayer, Boehringer Ingelheim, Celgene, Astra Zeneca, Eli-lily, Loxo
- Travel and honorarium: Merck, Pfizer, Novartis, Boehringer Ingelheim, Roche, Takeda
- Research funding: Novartis, Astra Zeneca, GlaxoSmithKline, Bayer, Pfizer

Yi-long Wu, MD

- Honoraria: AstraZeneca, Boehringer Ingelheim, BMS, Eli Lilly, Hengrui, MSD, Pfizer, Roche and Sanofi;
- Consulting or advisory role: AstraZeneca, Boehringer Ingelheim, Novartis, Merck, MSD, Roche and Takeda
- Research funding to the institution: AstraZeneca, Boehringer Ingelheim, BMS, Hengrui, Pfizer and Roche

Ross Soo, MBBS, PhD, FRACP

- Advisory Board: Amgen, Astra-Zeneca, Bayer, BMS, Boehringer Ingelheim, Lilly, Merck, Novartis, Pfizer, Roche, Taiho, Takeda, Yuhan
- Research grant: Astra-Zeneca, Boehringer Ingelheim

All other planners, reviewers and staff reported no relevant financial relationships.

All relevant financial relationships have been mitigated

Selected Abstracts from Day 2

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Overview of abstracts

- Biomarkers for checkpoint inhibitors
- Improving on outcomes for stage III NSCLC
- Antibody drug conjugates and novel targeted therapies
- Adjuvant therapy post surgery for EGFR mutated 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.

Response to cemiplimab by PDL1 status tiers

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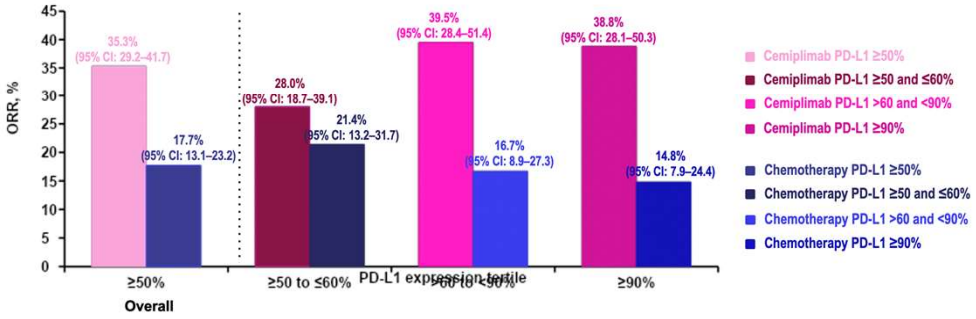
PD-L1 Expression Levels Correlate with Objective Response Rate (N=475)



CI, confidence interval; ORR, objective response rate; PD-L1, programmed cell death-ligand 1.

Data cut-off date: March 1, 2020

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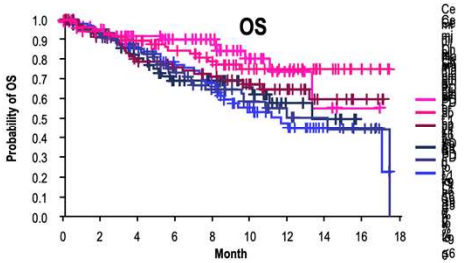
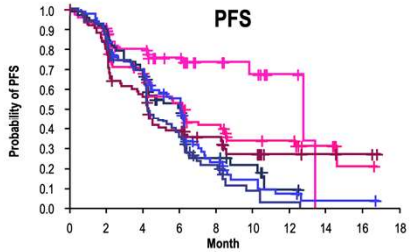
PD-L1 Expression Levels Correlate with OS and PFS (N=475)



	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)

CI, confidence interval; HR, hazard ratio; NE, not evaluable; NR, not reached; OS, overall survival; PD-L1, programmed cell death-ligand 1; PFS, progression-free survival.

Data cut-off date: March 1, 2020

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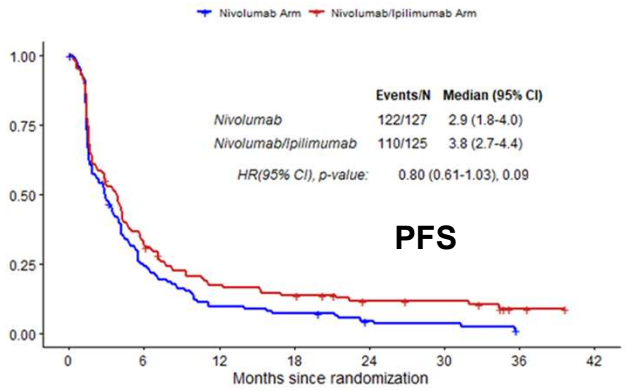
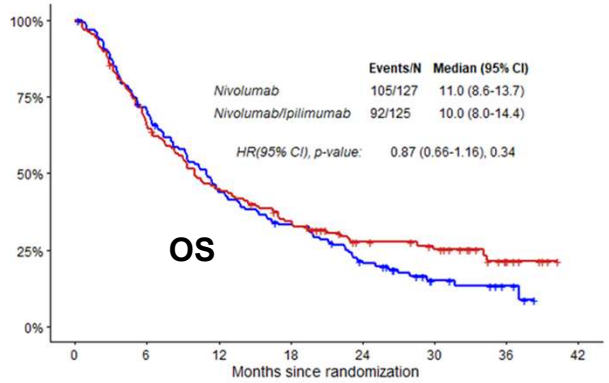
Lung MAP Studies: Previously treated, IO-naïve, stage IV Sq NSCLC

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

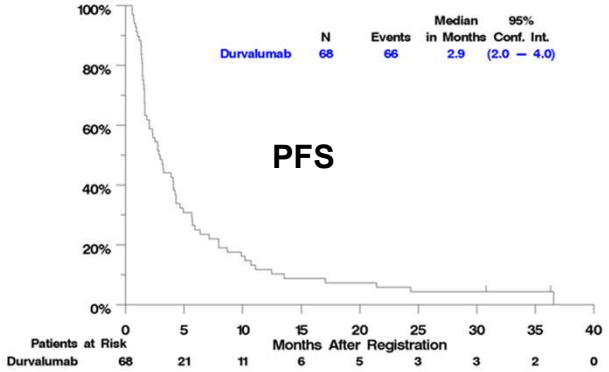
Gettinger S. et al (ASCO 2019, WCLC 2019)

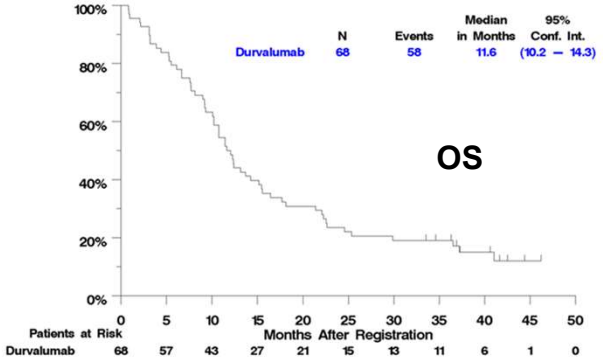




S1400A: Single-arm phase II study: Durvalumab

Borghaei H et al. Clin Lung Cancer, in press





Tumor Mutational Burden as a Continuous Variable

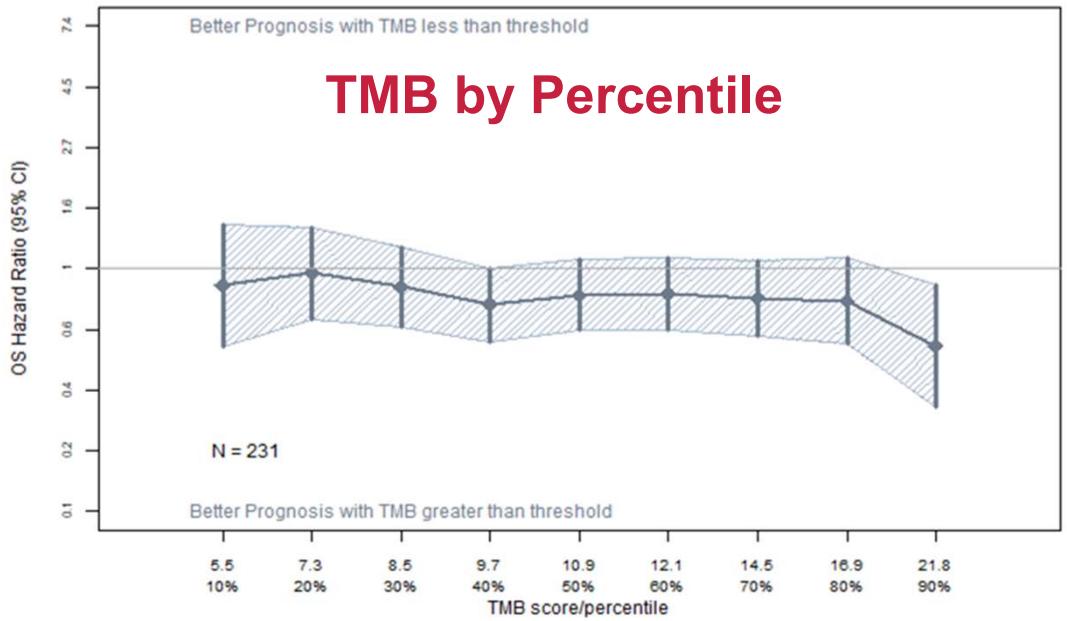
TMB by Value (per 10-unit difference)

Total pts: 252 on S1400I
68 on S1400A

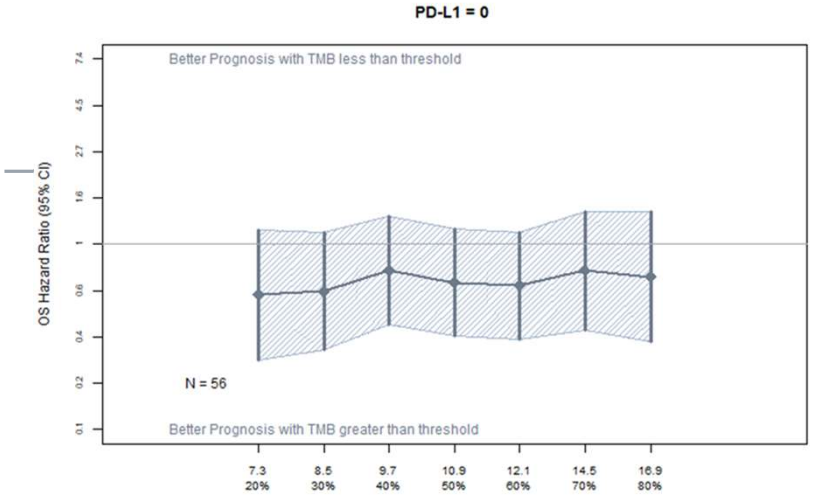
Overall Survival: higher TMB; HR; 0.80 (95% CI: 0.67;0.94), p=0.008

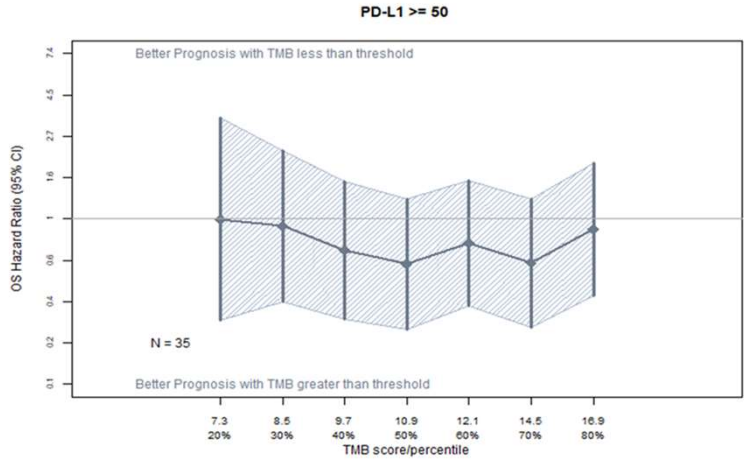
Progression Free Survival: HR: 0.80 (95% CI; 0.69;0.93), p=0.004

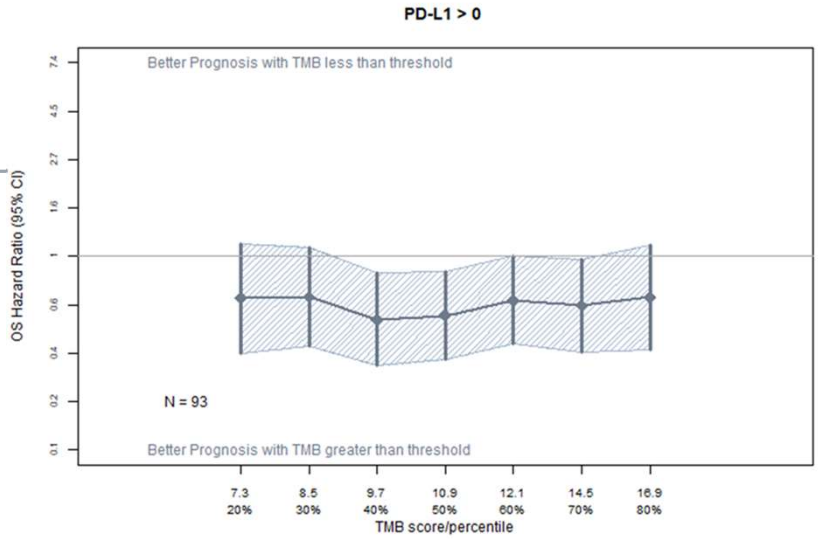
HIGHER TMB WAS SIGNIFICANTLY ASSOCIATED WITH IMPROVED OS AND PFS.



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



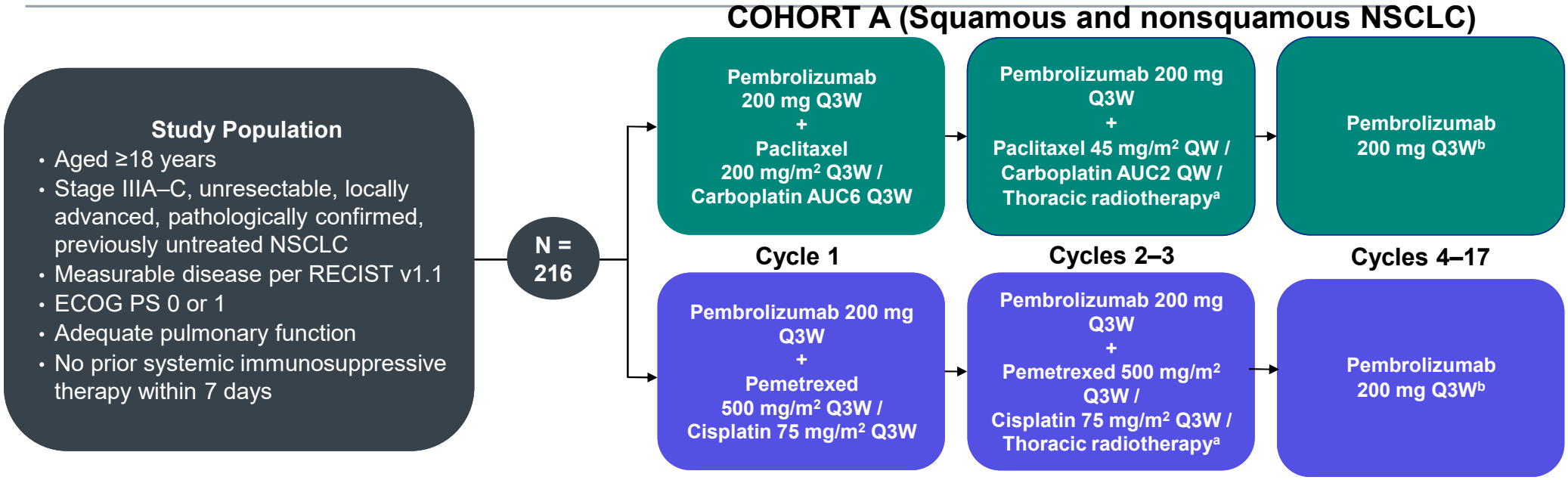




Association between TMB (continuous) and different PD-L1 expression groups : S1400I

HRs ≤ 1.0 in all subgroups of PD-L1 expression.

KEYNOTE-799 (NCT03631784)



Primary Objectives

- ORR per RECIST version 1.1 by BICR
- Percentage of patients who develop grade ≥3 pneumonitis

Secondary Objectives

- PFS, OS, safety

Statistical Analysis Details

- Efficacy assessed in all patients with first study dose before or on October 31, 2019 (PE population)
- Safety assessed in all patients in the as-treated population

BICR, blinded, independent central review; PE, primary efficacy.

[a]60 Gy in 30 daily 2-Gy fractions. [b]Treatment will continue until cycle 17 is completed or until documented disease progression, unacceptable AEs, intercurrent illness that prevents further administration of treatment, or study withdrawal. Pembrolizumab therapy will be discontinued permanently in patients who develop grade ≥3 or recurrent grade 2 pneumonitis.

ORR and Duration of Response

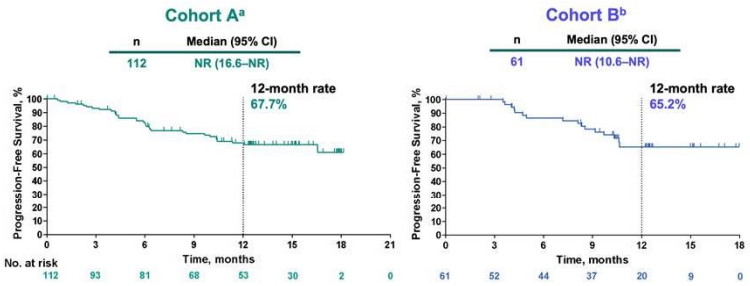
By BICR per RECIST v1.1 (Primary Efficacy Population)

	Cohort A[a] n = 112		Cohort B[b] n = 61	
PE Population	n = 112		n = 61	
ORR, n (%) [95% CI]	78 (69.6) [60.2–78.0]		43 (70.5) [57.4–81.5]	
CR	4 (3.6)		3 (4.9)	
PR	74 (66.1)		40 (65.6)	
SD, n (%)	21 (18.8)		12 (19.7)	
PD, n (%)	1 (0.9)		0	
Not evaluable, n (%)	2 (1.8)		0	
No assessment, n (%)	10 (8.9)		6 (9.8)	
DOR, median (range),[c] mo	NR (1.4+ to 16.1+)		NR (2.0+ to 15.9+)	
DOR ≥12 mo,[c] n (%)	31 (82.2)		5 (72.1)	
PD-L1 Status	**TPS <1% (n = 21)**	**TPS ≥1% (n = 66)**	**TPS <1% (n = 17)**	**TPS ≥1% (n = 26)**
ORR, n (%)	14 (66.7)	49 (74.2)	11 (64.7)	18 (69.2)
Histology	**Nonsquamous (n = 39)**	**Squamous (n = 73)**	**Nonsquamous (n = 61)**	**Squamous (n = 0)**
ORR, n (%)	27 (69.2)	51 (69.9)	43 (70.5)	NA

CI, confidence interval; DOR, duration of response; NR, not reached.
[a]Squamous and nonsquamous. [b]Nonsquamous only. [c]Kaplan-Meier estimate. "+" indicates there is no progressive disease by the time of last disease assessment.
Data cutoff date: July 30, 2020.

Progression-Free Survival

By BICR per RECIST v1.1 (Primary Efficacy Population)



[a]Squamous and nonsquamous. [b]Nonsquamous only.
Data cutoff date: July 30, 2020.

Incidence of Grade ≥3 Pneumonitis/Safety

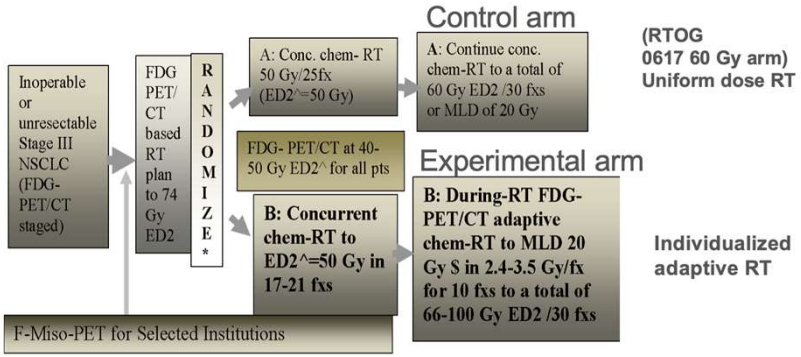
Per NCI-CTCAE Version 4.0 (All-Treated Patients)

	Cohort A[a] (n = 112)	Cohort B[b] (n = 101)
Grade ≥3 pneumonitis (all cause),[c,d] n (%) [95% CI]	**9 (8.0) [3.7–14.7]**	**8 (7.9) [3.5–15.0]**
Treatment-related AEs, n (%)	105 (93.8)	96 (95.0)
Grades 3–5	72 (64.3)	47 (46.5)
Led to death	4[c] (3.6)	1 (1.0)
Led to discontinuation of any treatment component	38 (33.9)	16 (15.8)
Discontinued pembrolizumab	27 (24.1)	15 (14.9)
Discontinued radiotherapy	2 (1.8)	0
Discontinued any chemotherapy	18 (16.1)	3 (3.0)
Immune-mediated AEs and infusion reactions, n (%)	59 (52.7)	36 (35.6)
Grades 3–5	18 (16.1)	10 (9.9)
Led to death[d]	4 (3.6)	1 (1.0)

[a]Squamous and nonsquamous. [b]Nonsquamous only. [c]Includes immune-mediated AE of "pneumonitis" and the MedDRA preferred term of "radiation pneumonitis". [d]Includes 4 patients (3.6%) with grade 5 pneumonitis in cohort A and 1 patient (1.0%) with grade 5 interstitial lung disease in cohort B. These events were classified as both treatment-related events and under immune-mediated AEs and infusion reactions.
Data cutoff date: July 30, 2020.

Role of PET-directed adaptation of RT

RTOG1106 Study Schema



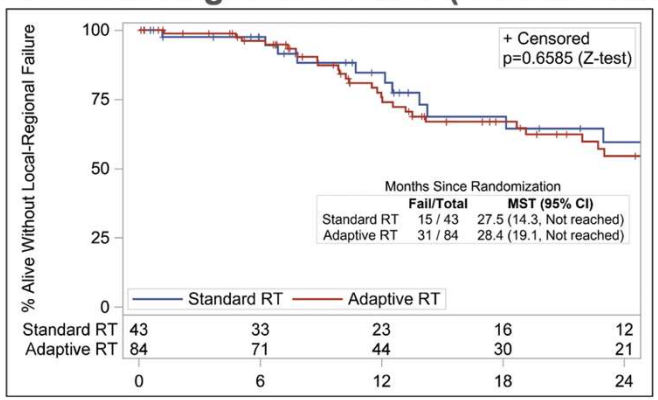
*Randomization: 1:2 for control and experimental arms, stratified by GTV (200 cc) and MLD (14 Gy)

Results-5: Thoracic Adverse Events

	Standard RT (n=42)	Adaptive RT (n=80)
Any Grade 2+ Adverse Event	37 (88.1%)	78 (97.5%)
Grade 2+ Esophagitis	13 (31.0%)	34 (42.5%)
Grade 2+ Respiratory, Thoracic, and Mediastinal Disorders	19 (45.2%)	35 (43.8%)
Grade 2+ Cardiac Disorders	2 (4.8%)	4 (5.0%)

*Adverse events graded per CTCAE v4.0 criteria and reported as possibly, probably, or definitely related to treatment

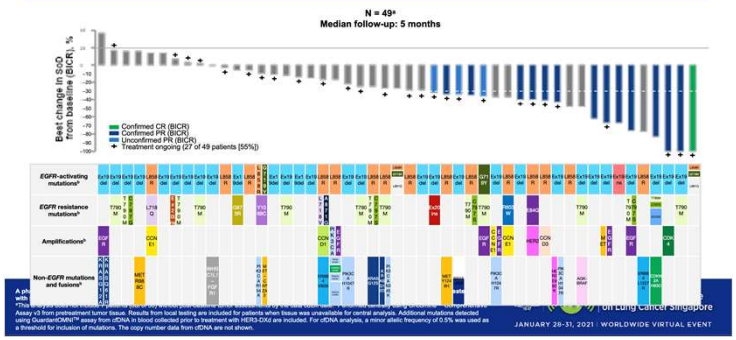
Results-6: Local-Regional Control (Central Review)

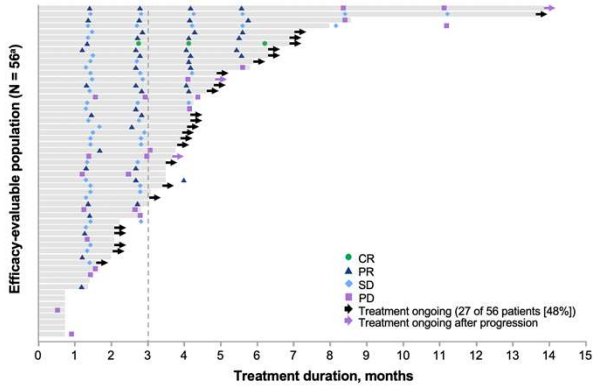


NRG ONCOLOGY™

HER3 and Trop2 Antibody drug conjugates

HER3-DXd 5.6 mg/kg Demonstrated Antitumor Activity in *EGFR*-Mutated NSCLC With Diverse TKI Resistance Mechanisms

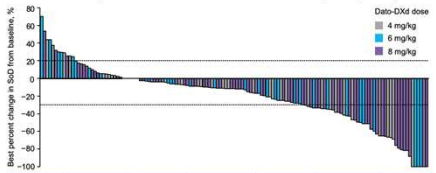




Activity according to BICR evaluation (efficacy-evaluable population) N = 56ª	
Confirmed BOR, n/N (%)	
CR	1/56 (2%)
PR	13/56 (23%)
SD	25/56 (45%)
PD	9/56 (16%)
NE	8/56 (14%)
Confirmed ORR, % (n/N; 95% CI)	25% (14/56; 14.4-38.4)
DCR, % (n/N; 95% CI)	70% (39/56; 55.9-81.2)
Median TTR, months (range)	2.0 (1.2-2.8)
Median DOR, months (range)	6.9 (3.0-7.0)

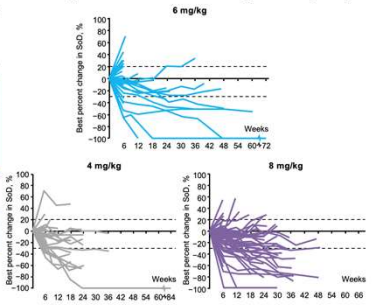
Antitumor Activity of Dato-DXd

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)

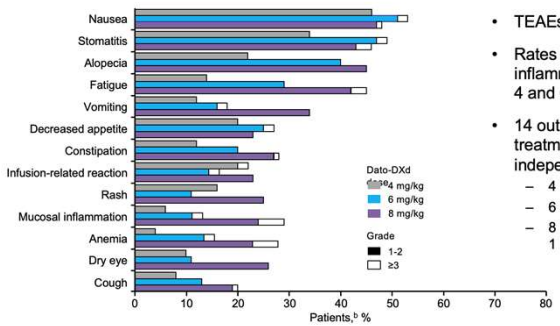
Change in Sum of Diameters for Target Lesions (BICR)



Preliminary Progression-free Survival (BICR)ᶜ

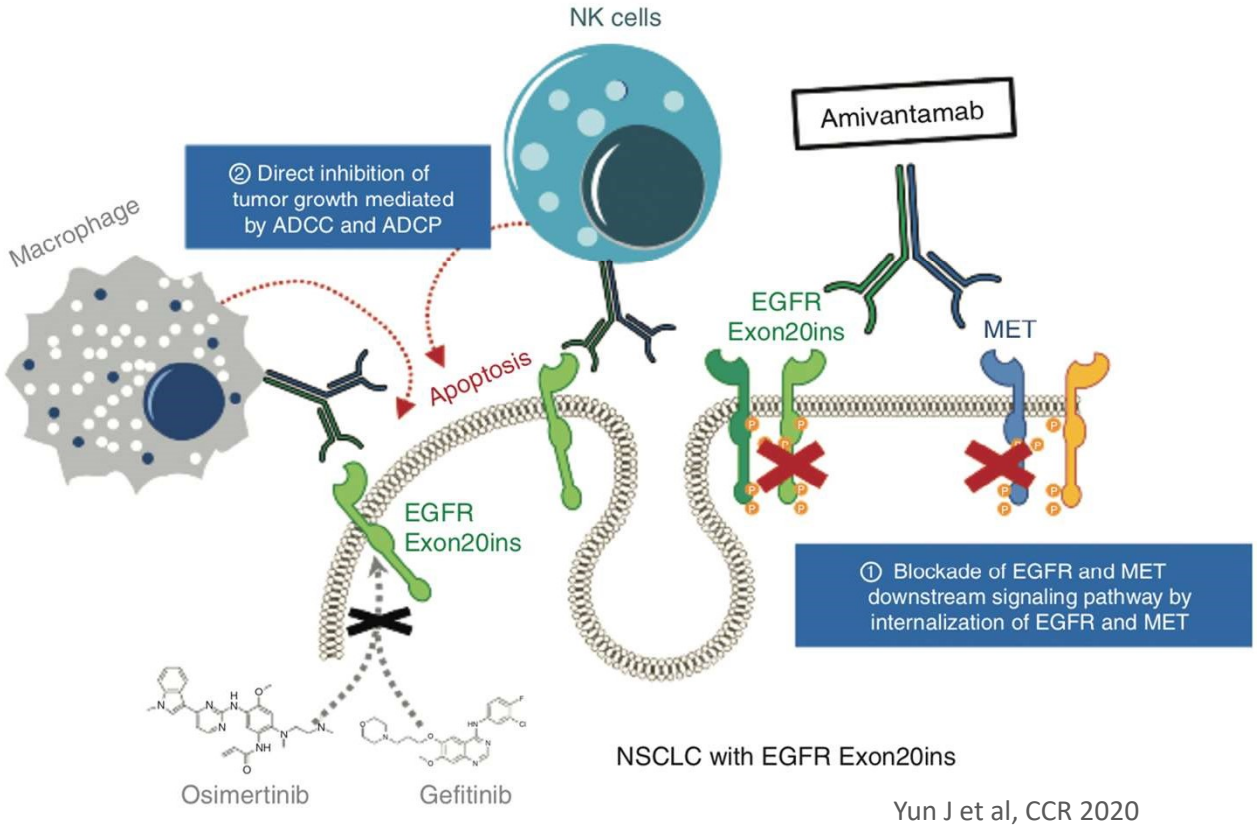
- Median PFS (95% CI)
  - 4 mg/kg: 4.3 months (2.0-NE), 6 mg/kg: 8.2 months (1.5-11.8), 8 mg/kg: 5.4 months (4.1-7.1)

TEAEs in ≥15% of Patientsª



- TEAEs were predominantly nonhematologic
- Rates of grade ≥3 stomatitis and mucosal inflammation were higher with 8 mg/kg vs 4 and 6 mg/kgᶜ
- 14 out of 175 patients (8%) had treatment-related ILD as adjudicated by an independent committeeᵈ
  - 4 mg/kg: 1 patient (grade 3)
  - 6 mg/kg: 1 patient (grade 2)
  - 8 mg/kg: 12 patients (8 patients grade 1-2; 1 patient grade 3; 3 patients grade 5)

Amivantamab: EGFR-MET bispecific antibody



Yun J et al, CCR 2020

CHRYSALIS

EGFR Ex20ins NSCLC (n=81)

Phase I

Dose Escalation Cohorts 140–1750 mg ***Advanced NSCLC***

RP2D

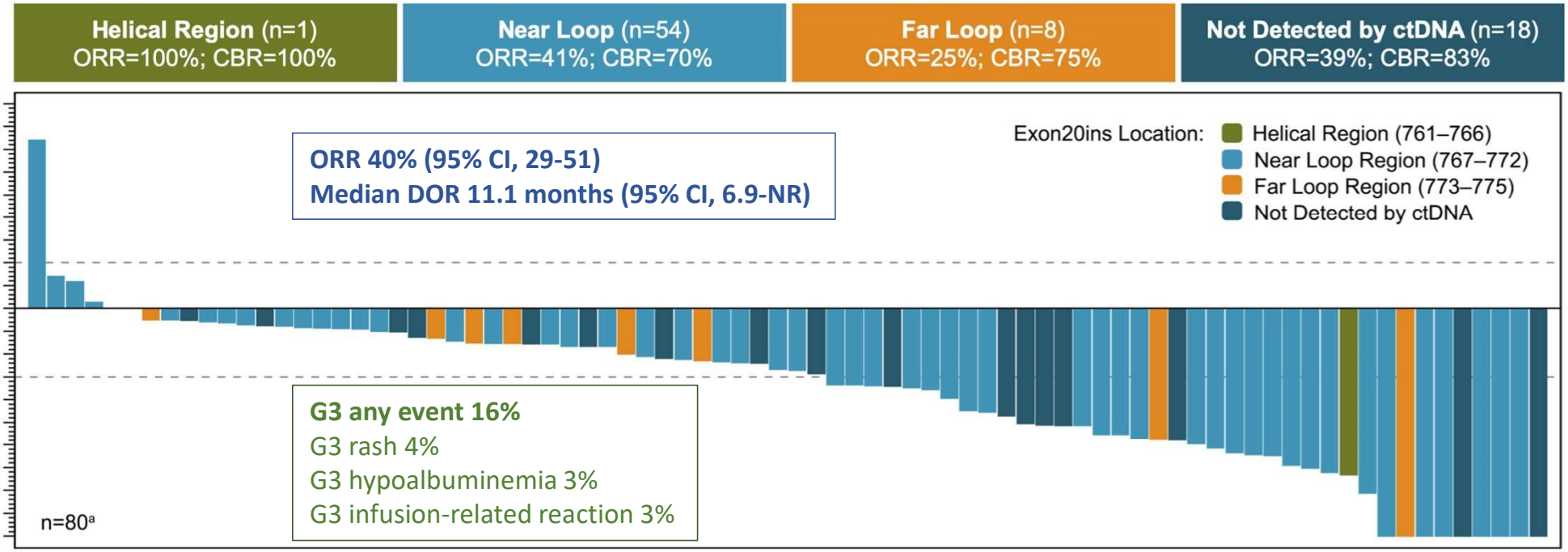
1050 mg (<80 kg)
1400 mg (≥80 kg)
C1 QW, C2+ Q2W

Dose Expansion Cohort D ***EGFR Exon20ins***

Post-platinum Exon20ins Treated at RP2D (N=114; *Safety Population*)

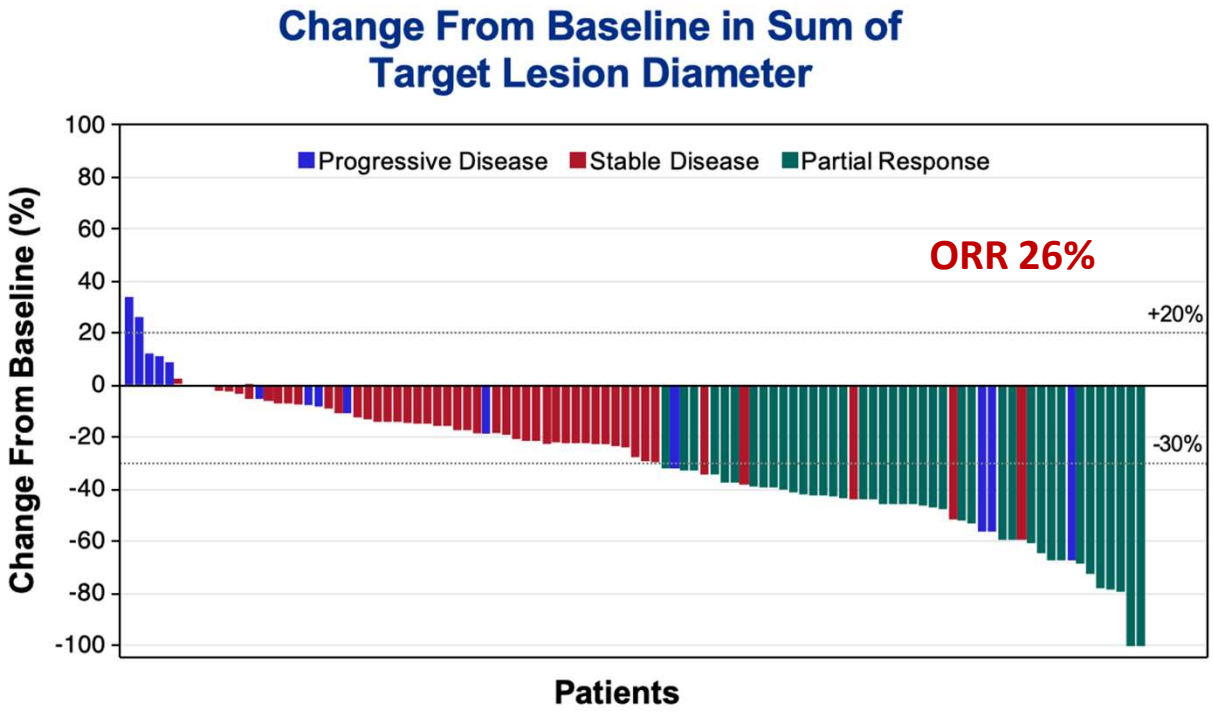
Post-platinum Exon20ins with ≥3 Disease Assessments at Clinical Cut-off[a] (n=81; *Efficacy Population*)

Amivantamab in post-platinum Ex20ins NSCLC



25 distinct Exon20ins variants identified by NGS of ctDNA (Guardant360®) from 63 evaluable patient samples

Mobocertinib results in a reduction in target lesion volume in post-platinum treated *EGFR* Ex20ins patients



94/114 (82%) had a reduction from baseline in sum of target lesion diameter

Post-platinum treated cohort
N = 114

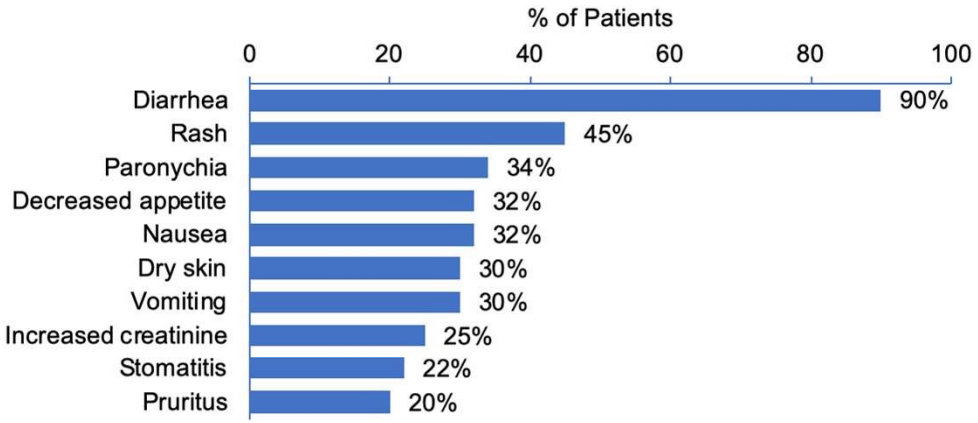
Study	N
Phase 1	6
Phase 2 Expansion	22
EXCLAIM	86

***ORR in EXCLAIM cohort: 23%**

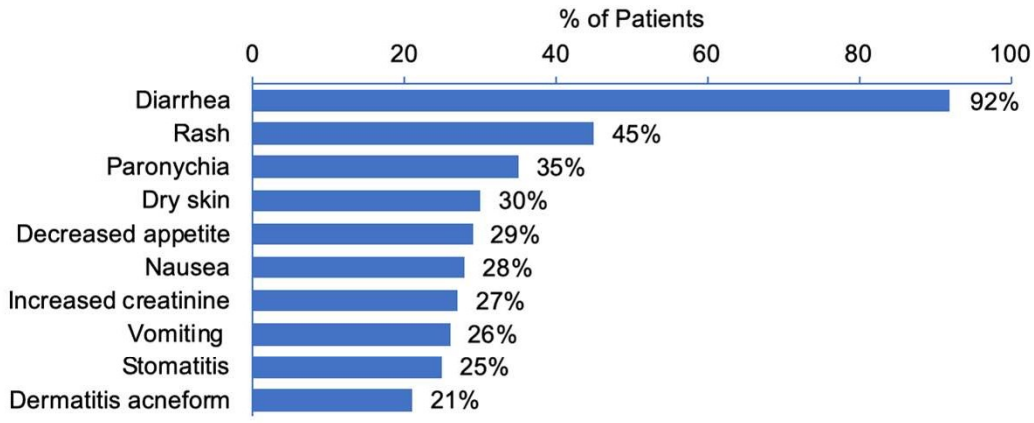
Side effect profile of Mobocertinib

All-Grade TRAEs Observed in ≥20% of Patients

PPP Cohort (N=114)



EXCLAIM Cohort (N=96)

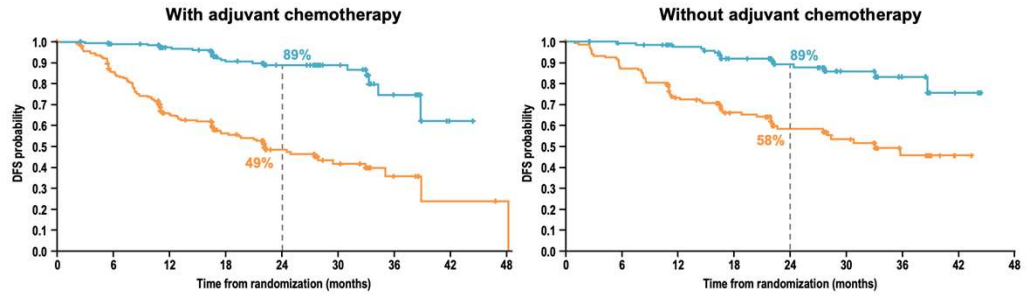


Grades 3/4 TRAEs in ≥5% of Patients, n (%)	PPP Cohort (N=114)
Diarrhea	25 (22)
Anemia	6 (5)
Dyspnea	6 (5)

Grades 3/4 TRAEs in ≥5% of Patients, n (%)	EXCLAIM Cohort (N=96)
Diarrhea	15 (16)

ADAURA: Impact of adjuvant chemotherapy and QOL

DFS in patients with and without adjuvant chemotherapy (overall population)

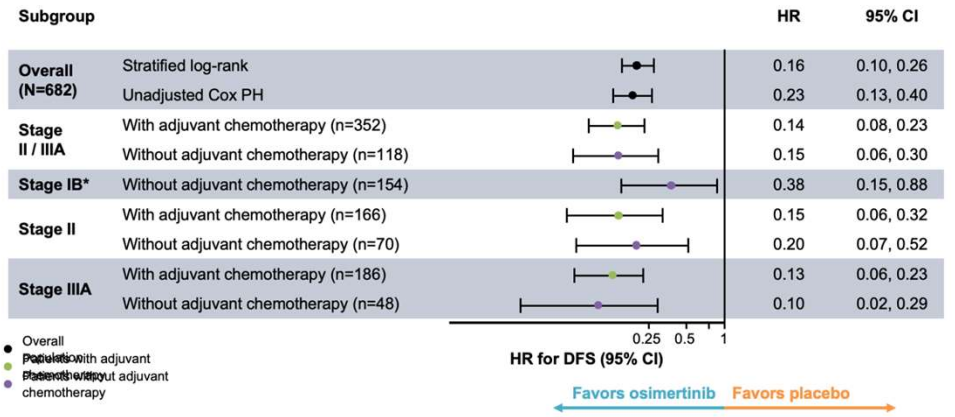


	DFS events, patients (%)	Median DFS, months (95% CI)	HR (95% CI)
Osimertinib (n=203)	22 (11)	NR (38.8, NC)	**0.16**
Placebo (n=207)	103 (50)	22.1 (17.4, 32.9)	**(0.10, 0.26)**
Maturity 30%: osimertinib 11%, placebo 50%			

	DFS events, patients (%)	Median DFS, months (95% CI)	HR (95% CI)
Osimertinib (n=136)	15 (11)	NR (NC, NC)	**0.23**
Placebo (n=136)	56 (41)	33.1 (22.6, NC)	**(0.13, 0.40)**
Maturity 26%: osimertinib 11%, placebo 41%			

Wu, Tsuboi et al. N Engl J Med 2020;383:1711–23. ADAURA data cut-off: January 17, 2020.
Tick marks indicate censored data. NC, not calculable, NR, not reached.

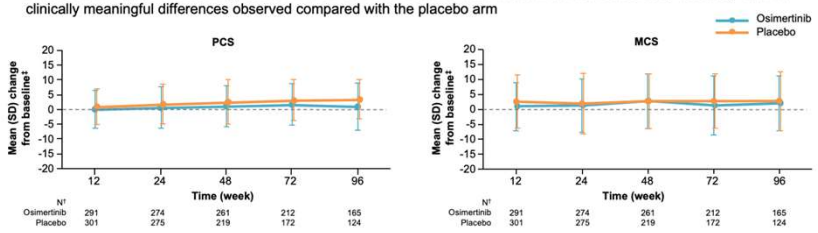
DFS in patients with and without adjuvant chemotherapy, by disease stage



ADAURA data cut-off: January 17, 2020.
Performed using a Cox proportional hazards model including treatment, subgroup and a treatment-by-subgroup interaction term.
*Subgroup categories with less than 20 events, such as patients with stage IB disease with adjuvant chemotherapy, were excluded from the analysis. A HR of less than 1 favors osimertinib.

Adjusted mean change in SF-36 physical (PCS) and mental (MCS) component summary T-scores

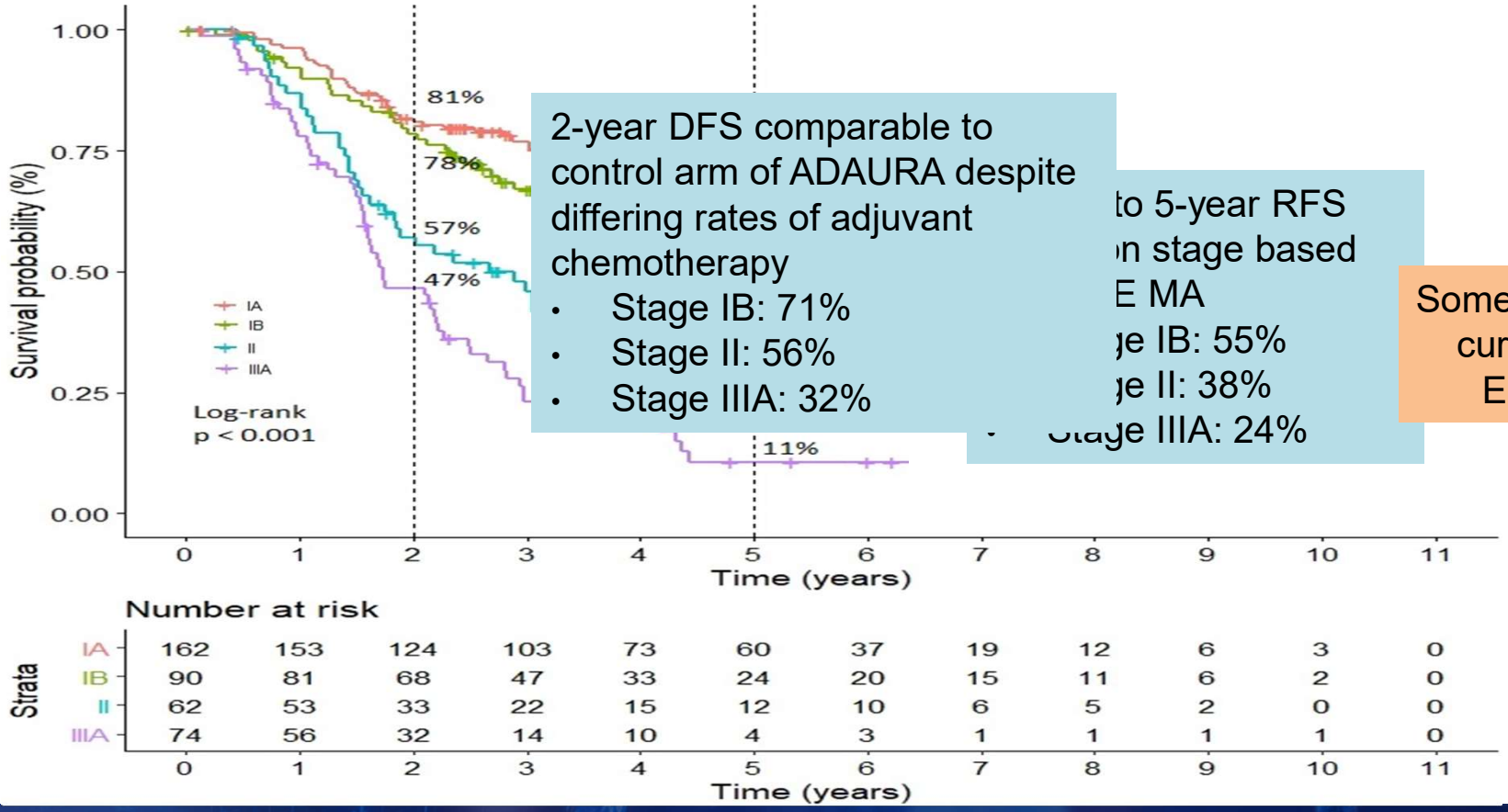
- In disease-free patients receiving osimertinib, SF-36 PCS and MCS were maintained from baseline to week 96,* with no clinically meaningful differences observed compared with the placebo arm



	Mixed model of repeated measures – adjusted mean change from baseline (95% CI)			Definition of clinically meaningful change based on the 3rd edition of the SF-36 scoring manual
SF-36 component	Osimertinib	Placebo	Osimertinib - placebo	
PCS	1.13 (0.54, 1.72)	2.31 (1.70, 2.91)	-1.18 (-2.02, -0.34)	±2
MCS	1.34 (0.60, 2.08)	2.68 (1.92, 3.44)	-1.34 (-2.40, -0.28)	±3

*Change from baseline was examined until Week 96, to ensure balanced comparison between arms, given the earlier discontinuation in completing the SF-36 health survey in the placebo arm, due to earlier events of disease recurrence. †Number of patients with data available at each visit. ‡Error bars represent SD. Data cutoff: 17 Jan 2020

EGFR M+DFS knowledge bank (n=389)



2-year DFS comparable to control arm of ADAURA despite differing rates of adjuvant chemotherapy

- Stage IB: 71%
- Stage II: 56%
- Stage IIIA: 32%

to 5-year RFS
n stage based
E MA
ge IB: 55%
ge II: 38%
Stage IIIA: 24%

Some patients are cured without EGFR TKI

IASLC 2020 World Conference on Lung Cancer Singapore: Highlights from Day 3

Yi-Long Wu
Tenured Professor of Guangdong Lung Cancer Institute,
Guangdong Provincial People's Hospital
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IASLC
INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER
Conquering Thoracic Cancers Worldwide

Topics

Lung Cancer Screen

Perioperative adjuvant treatment

Target KRAS

Immunotherapy combo for advanced NASCLC

Immunotherapy for mesothelioma

PLATFORM trial

National Lung Cancer Screening Program in Taiwan: The TALENT Study

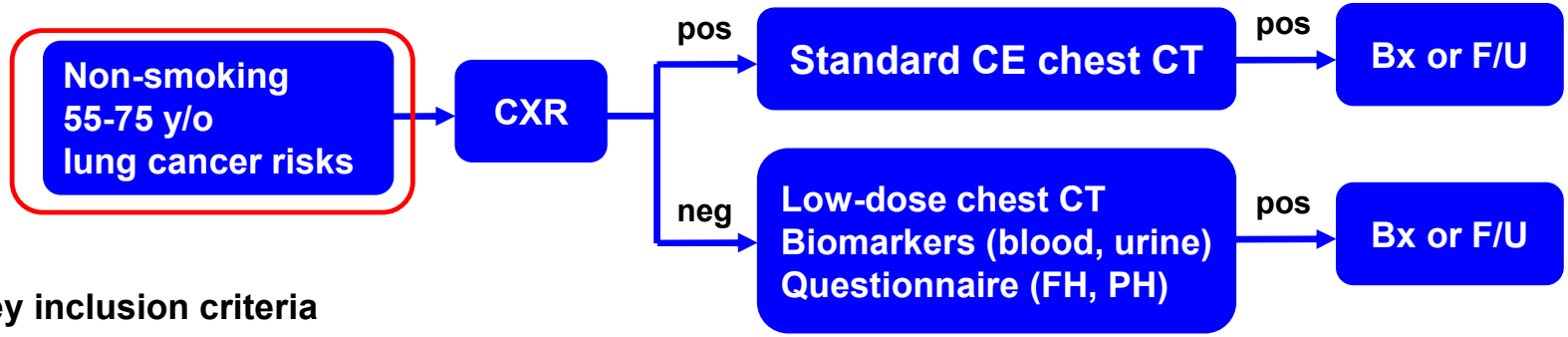
Pan-Chyr Yang MD, PhD

On Behalf of TALENT Study Group

National Taiwan University
Institute of Biomedical Sciences
Center of Genomics, Academia Sinica

Taiwan Lung Cancer Screening in Never Smoker Trial (TALENT)

From Feb 2015 to July 2019, 17 medical centres participated



- **Key inclusion criteria**
  - **55-75 y/o[a]**
  - **Never smoking or SI < 10 PY and had quit > 15 yrs**
  - **Having one of the following risks**
    - **family history of lung cancer (≤ 3-degree)**
    - **environmental tobacco smoking history**
    - **chronic lung disease (TB, COPD)**
    - **cooking index[b] ≥ 110**
    - **cooking without using ventilation**
  - **Negative CXR**

- **Data cutoff: September 30, 2020**
- **13,207 subjects screened, 12,011 enrolled**
- **6009 (50%) with family history**

[a] **Subjects with lung cancer FH: >50 yrs or > the age at diagnosis of the youngest lung cancer case in the family**
[b] **2/7 x days with cooking by pan-frying, stir-frying, or deep-frying in 1 week (maximum=21) x Yrs with cooking**

What are the discovery from TALENT study?

More early cases with lung cancer were discovered

- T0 lung cancer detection rate: 313/12,011= **2.6%,** NLST: 1.1%, NELSON: 0.9%
- Invasive lung cancer: 255/12,011= **2.1%**. Multiple primary lung cancer: **17.9%**
- LDCT positive: 17.4% (GGO > 5mm, S/PS > 6mm) #. Invasive procedures: 3.4%
- Lung cancer confirmed: **96.5% stage 0-1**. LDCT features: GGO 47%, S 19%, PS 34%
- Prevalence of lung cancer w/ or w/o family history: **3.2% vs 2.0%** (p< 0.001)

Histologic Diagnosis	(n)
Adenocarcinoma in situ (AIS)	58
Minimally invasive adenocarcinoma (MIA)	71
Invasive adenocarcinoma (INAD)	183
Adenosquamous carcinoma	1
Total	313

Stage 0	58
Stage IA	218
Stage IB	26
Stage IIA	0
Stage IIB	3
Stage IIIA	2
Stage IIIB	1
Stage IV	5

What are the discovery from TALENT study?

High risk factor for non-smoker lung cancer: Family history

	Absence		Presence		R.R. (95% CI)	p
	n	%	n	%		
Lung cancer family history						< 0.001
First-degree family						< 0.001
Father						0.077
Mother						0.010
Brother						< 0.001
Sister						< 0.001
Second degree family						0.238
Third degree family						1.000
Environmental tobacco exposure						0.813
Chronic lung disease history						0.038
Cooking index ≥110						0.201
Cooking without ventilation						0.513

Risk of cancer for male and female relatives.

		Case relatives N (%) with cancer	Control relatives N (%) with cancer	Adjusted OR[a] (95% CI)	p
First-degree male relatives					
Any cancer	No	241 (75.79)	423 (83.1)	1.54 (1.08–2.20)	0.017
	Yes	77 (24.21)	86 (16.9)		
Lung cancer	No	291 (91.51)	490 (96.27)	2.25 (1.21–4.18)	0.011
	Yes	27 (8.49)	19 (3.73)		
First-degree female relatives					
Any cancer	No	264 (83.02)	469 (92.14)	2.37 (1.51–3.71)	<0.001
	Yes	54 (16.98)	40 (7.86)		
Lung cancer	No	298 (93.71)	504 (99.02)	7.31 (2.68–19.93)	<0.001
	Yes	20 (6.29)	5 (0.98)		

[a] Adjusted for sex, lung disease history, living environment, and occupational exposure.

Association between family history and risk of lung cancer in various population-based studies.

Type of relationship	Lung cancer [OR (95% CI)]					Any cancer [OR (95% CI)]				
	Wu et al. [5]	Mayne et al. [7]	Gorlova et al. [12]	Gao et al. [13]	Brenner et al. [14]	Wu et al. [5]	Mayne et al. [7]	Gorlova et al. [12]	Gao et al. [13]	Brenner et al. [14]
Sample size	216	437	316	101	622	216	437	316	122	622
Overall	3.7 (1.6–8.5)[a]	–	1.39 (0.91–2.13)[c]	1.69 (0.96–2.98)[f]	0.9 (0.4–2.1)[g]	2.6 (1.6–4.1)[b]	–	1.25 (1.05–1.50)[c]	1.25 (0.81–1.92)[f]	–
Father	2.3 (0.6–9.4)[a]	1.87 (0.79–4.42)[e]	2.09 (0.93–4.64)[c]	–	–	2.3 (0.9–5.6)[b]	1.67 (1.12–2.48)[e]	1.20 (0.84–1.71)[c]	–	–
Mother	7.5 (1.7–34.2)[a]	0.67 (0.11–3.99)[e]	0.37 (0.14–0.96)[d]	–	–	4.0 (1.5–10.4)[b]	1.24 (0.85–1.80)[e]	0.94 (0.65–1.35)[c]	–	–
Brother	0.5 (0.1–6.2)[a]	1.77 (0.85–3.68)[e]	1.75 (0.74–3.63)[c]	–	–	3.5 (1.1–11.0)[b]	1.58 (1.04–2.40)[e]	1.34 (0.91–1.97)[c]	–	–
Sister	–	4.14 (0.88–19.46)[e]	2.18 (0.59–7.22)[c]	–	–	1.5 (0.6–3.7)[b]	1.66 (1.11–2.47)[e]	1.17 (0.77–1.75)[c]	–	–

[a] OR adjusted for pack-years of smoking, age, and years of cooking.
[b] OR adjusted for gender, age, pack-years of smoking, years of cooking, and education.
[c] Adjusted for ethnicity, gender and age of the proband, gender, age, smoking status, birth cohort of the relative, and type of relationship to the proband, where appropriate.
[d] Adjusted for spousal smoking and for the covariates above, as appropriate.
[e] ORs shown are crude ORs from conditional logistic regression analyses; therefore, they are based upon those pairs for which both the case and the control had informative data.
[f] Adjusted for age (5-year interval), sex, residence (5 areas), education (5 categories), passive smoking (childhood at home, adulthood at home, at work).
[g] Adjusted for age, sex, education, and ethnicity.

Lin & Wu, Lung Cancer 2015

What is clinical significance of the TALENT study?

Lung Cancer Screen:

Not only for tobacco exposure also for family lung cancer history

Topics

Lung Cancer Screen

Perioperative adjuvant treatment

Target KRAS

Immunotherapy combo for advanced NASCLC

Immunotherapy for mesothelioma

PLATFORM trial

International Tailored Chemotherapy Adjuvant (ITACA) Phase III study of Pharmacogenomic-Driven versus Standard Adjuvant Chemotherapy in completely Resected Stage II-IIIA Non-Small Cell Lung Cancer

Silvia Novello

(**on behalf of the ITACA investigators**)

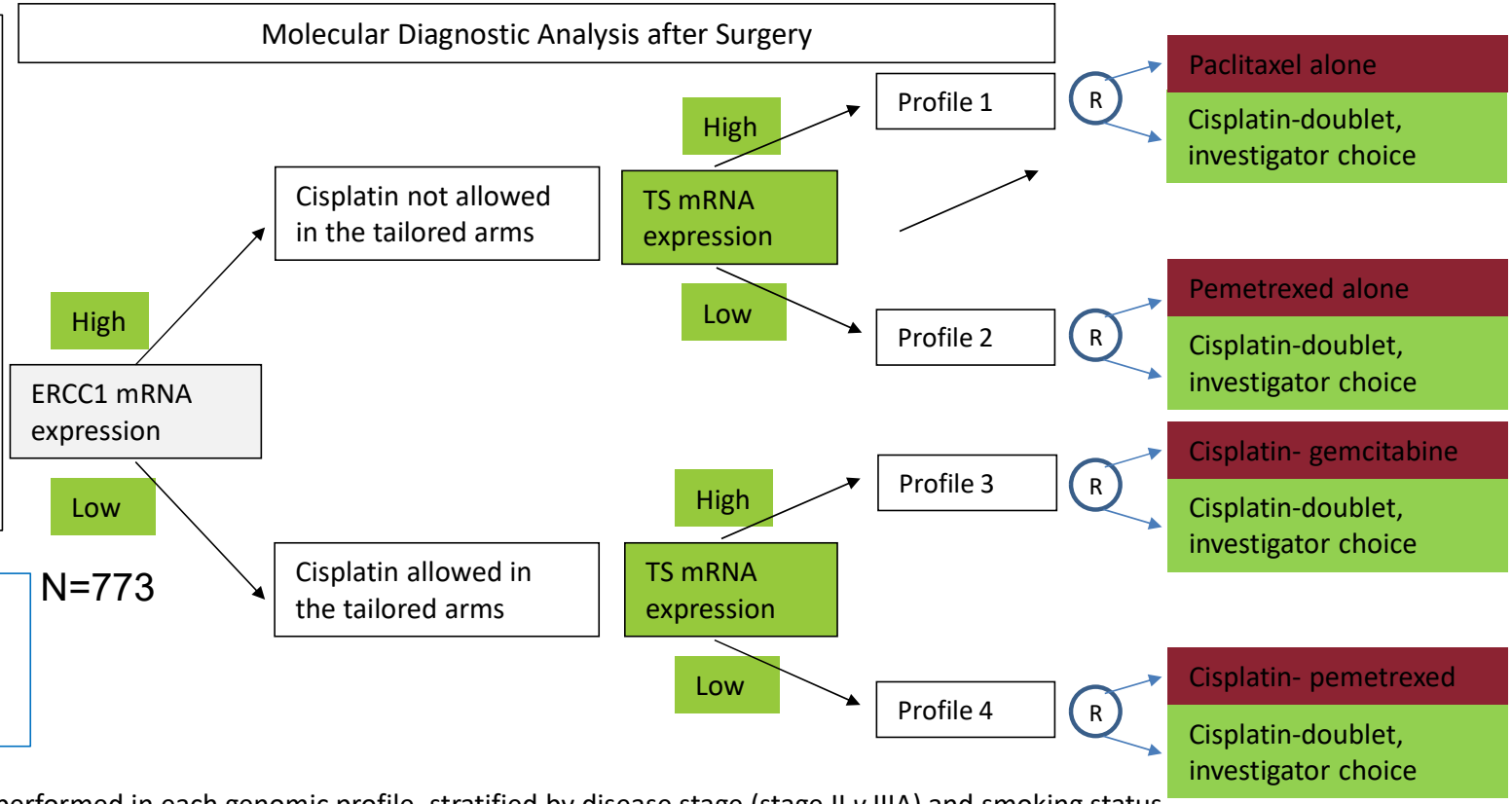
University of Turin,

Department of Oncology

silvia.novello@unito.it

ITACA trial : Design of the study

- Completely resected NSCLC R0 stage II-IIIA, Complete mediastinal LN resection or sampling
- ECOG PS 0-1
- Interval of 45-60 days between surgery and start of chemotherapy
- Adequate organ functions
- No prior malignancies except for treated basal cell or squamous cell skin cancer, in situ cervical cancer, or other cancers from which the patient has been disease-free for at least five years prior to enrolment



N=773

- 8Aug 2008: first pt randomized; 29Aug 2014 last pt randomized
- Dec 2010: Study Amendment for Staging (21% pts randomized)

- Randomization (allocation ratio of 1:1) performed in each genomic profile, stratified by disease stage (stage II *v* IIIA) and smoking status (never/former versus current)
- For the primary statistical analysis all control arms were grouped together (standard arm) as well as all tailored arms (tailored arm)

Surgical and Clinical Outcomes With Neoadjuvant Atezolizumab in Resectable Stage IB-IIIB NSCLC: LCMC3 Trial Primary Analysis

Jay M. Lee,[1] Jamie Chaft,[2] Alan Nicholas,[3] G. Alexander Patterson,[4] Saiama N. Waqar,[4] Eric M. Toloza,[5] Eric Haura,[5] Dan J. Raz,[6] Karen L. Reckamp,[7] Robert E. Merritt,[8] Dwight Owen,[8] David J. Finley,[9] Ciaran J. McNamee,[10] Justin D. Blasberg,[11] Edward B. Garon,[1] John D. Mitchell,[12] Robert C. Doebele,[12] Frank Baciewicz,[13] Misako Nagasaka,[14] Harvey I. Pass,[15] Katja Schulze,[3] See Phan,[3] Ann Johnson,[3] Paul A. Bunn,[12] Bruce E. Johnson,[16] Mark G. Kris,[2] David J. Kwiatkowski,[10] Ignacio I. Wistuba,[17] David P. Carbone,[8] Valerie W. Rusch[2]

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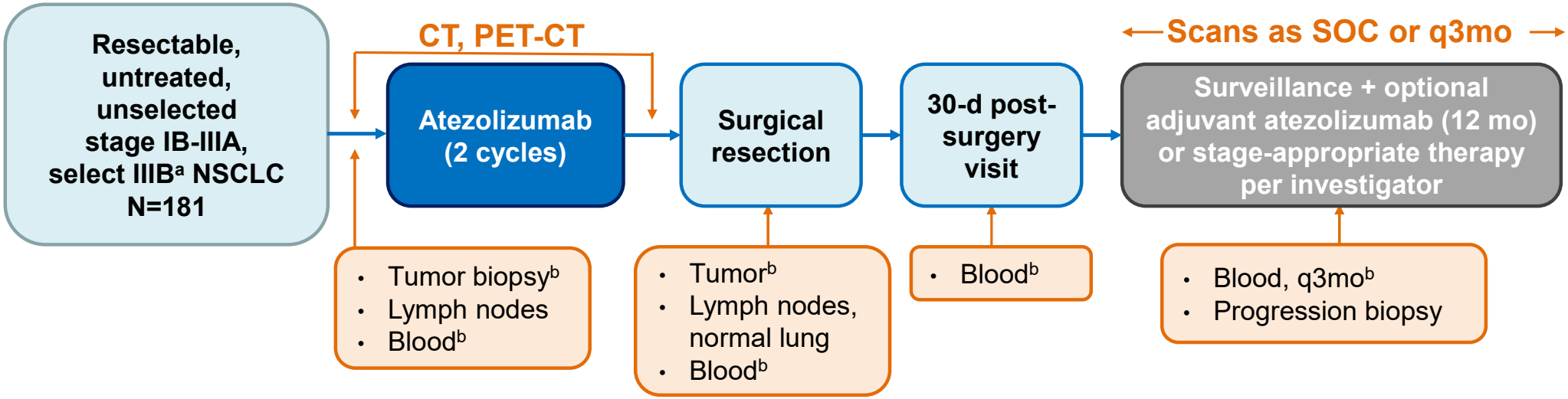
LCMC3 study design



Primary endpoint:

- Major pathologic response (≤10% viable tumor cells)

Secondary endpoints:

- Pathologic response by PD-L1
- Radiographic response by
  - PD-L1, TMB, neoantigen, gene expression profiling

Exploratory endpoints:

- DFS, OS
- Biomarkers
  - ctDNA, TCRseq, flow cytometry, IF, IHC, NGS

Safety:

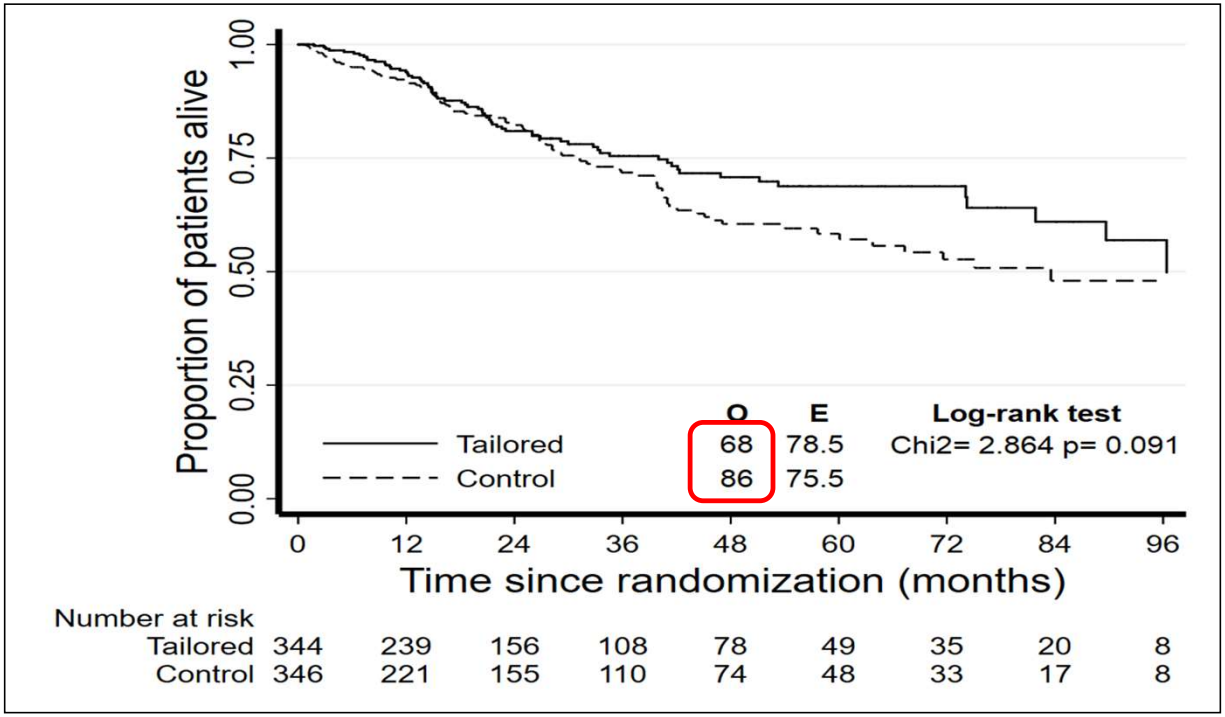
- Adverse events

NCT02927301

ctDNA, circulating tumor DNA; DFS, disease-free survival; IF, immunofluorescence; NGS, next-generation sequencing; PET-CT, positron emission tomography–computed tomography; q3mo, every 3 months. SOC, standard of care; TCRseq, T-cell receptor sequencing; TMB, tumor mutational burden.

[a] T4 due to mediastinal organ invasion were excluded. [b] Mandatory

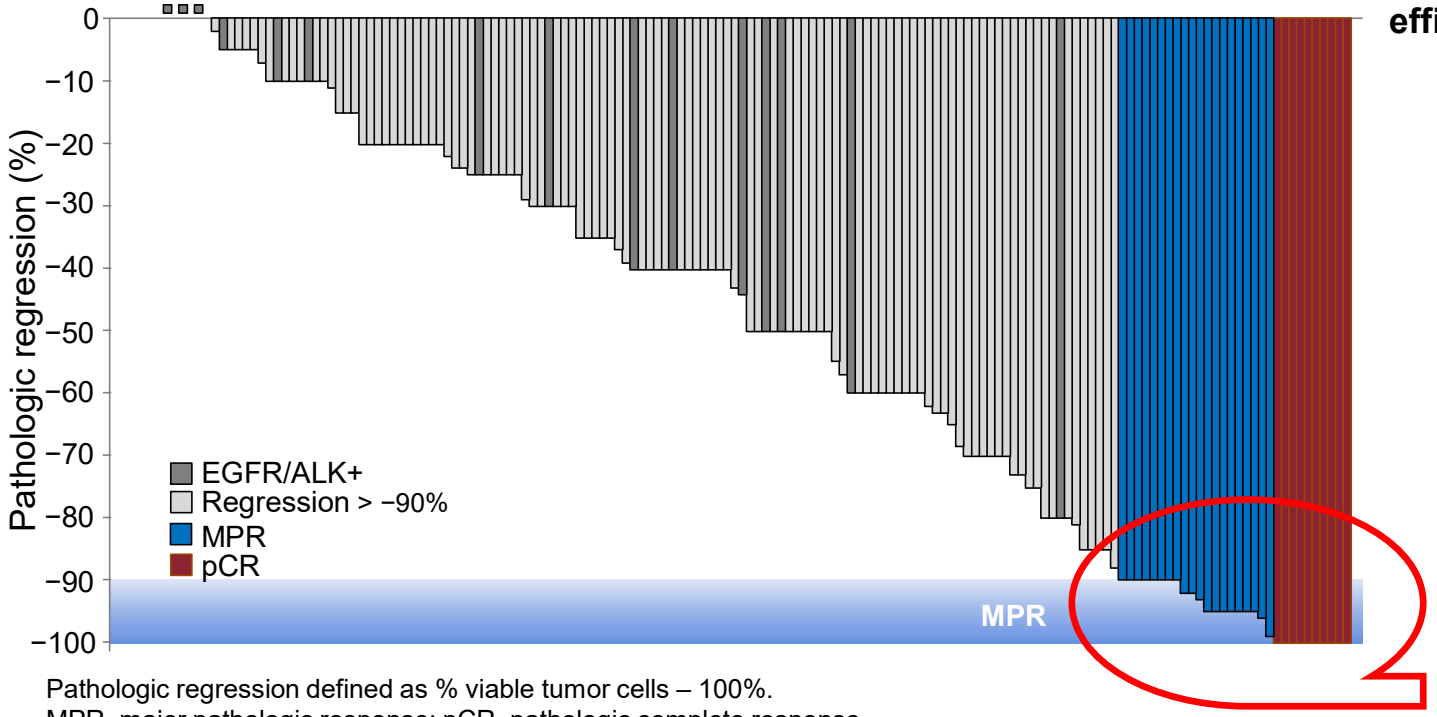
What are the discovery from ITACA study?



- **Median follow up** of 28.2 months (IQR: 9.9-55.8 months)
- **N. of deaths:** 154 (46% of expected events; 22% of ITT population)
- **HR (95%CI):** 0.76 (0.55-1.04)
- **Median OS, Tailored:** 96.4 (81.8- NR)
- **Median OS, Control:** 83.5 (60.1- NR)

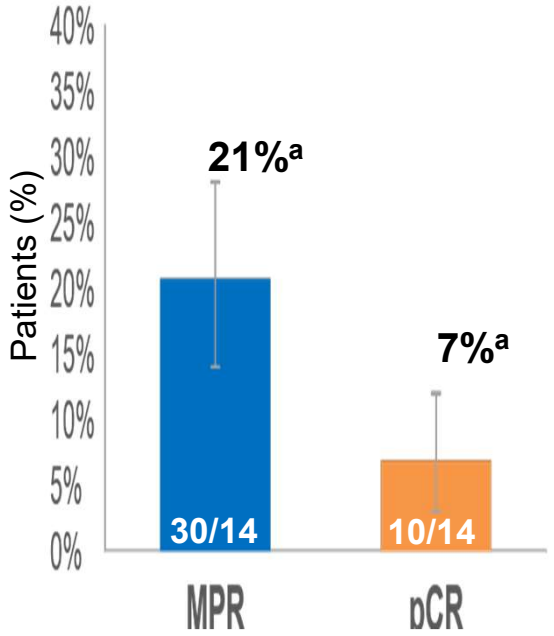
What are the discovery from LCMC3 study?

Pathologic response in surgery population (n=159)



Pathologic regression defined as % viable tumor cells – 100%.
MPR, major pathologic response; pCR, pathologic complete response.
[a] Error bars indicate 95% CI.

Major pathologic response in primary efficacy population (n=144)



What is clinical significance of the ITACA & LCMC3 study?

- It is impossible to tailor adjuvant chemotherapy for complete resected lung cancer patients selected by precision genomic aberration

- Monotherapy with PD-L1 inhibitor atezolizumab as neoadjuvnt treatment achieved a promising results with MPR of 21% and pCR of 7%

Topics

Lung Cancer Screen

Perioperative adjuvant treatment

Target KRAS

Immunotherapy combo for advanced NASCLC

Immunotherapy for mesothelioma

PLATFORM trial

CodeBreaK 100: Registrational Phase 2 Trial of Sotorasib in *KRAS* p.G12C Mutated Non-small Cell Lung Cancer

Bob T. Li,[1] Ferdinandos Skoulidis,[2] Gerald Falchook,[3] Adrian Sacher,[4] Vamsidhar Velcheti,[5] Grace K. Dy,[6] Timothy J. Price,[7] Hossein Borghaei,[8] Martin Schuler,[9] Terufumi Kato,[10] Toshiaki Takahashi,[11] Alexander Spira,[12] Suresh Ramalingam,[13] Benjamin Besse,[14] Fabrice Barlesi,[15] Qui Tran,[16] Agnes Ang,[16] Abraham Anderson,[16] Haby Henary,[16] Gataree Ngarmchamnanrith,[16] Ramaswamy Govindan,[17] Jürgen Wolf[18]

[1]Memorial Sloan Kettering Cancer Center, New York, New York, USA; [2]The University of Texas MD Anderson Cancer Center, Houston, Texas, USA; [3]Sarah Cannon Research Institute at HealthONE, Denver, Colorado, USA; [4]Princess Margaret Cancer Centre, University Health Network, Toronto, Ontario, Canada; [5]Thoracic Medical Oncology, Perlmutter Cancer Center, New York University, New York, New York, USA; [6]Roswell Park Cancer Institute, Buffalo, New York, USA; [7]The Queen Elizabeth Hospital and University of Adelaide, Woodville South, Australia; [8]Fox Chase Cancer Center, Philadelphia, PA, USA; [9]Department of Medical Oncology, West German Cancer Center, University Hospital Essen, Essen, German Cancer Consortium (DKTK), Germany; [10]Kanagawa Cancer Center, Yokohama, Japan; [11]Division of Thoracic Oncology, Shizuoka Cancer Center, Shizuoka, Japan; [12]Virginia Cancer Specialists Research Institute, Fairfax, VA, The US Oncology Network, TX; Johns Hopkins Medicine, Baltimore, MD, USA [13]Division of Medical Oncology, Emory University School of Medicine, Winship Cancer Institute, Atlanta, GA, USA; [14]Department of Cancer Medicine, Gustave Roussy, Villejuif, France; [15]Gustave Roussy, Villejuif, France; [16]Amgen Inc. Thousand Oaks, California, USA; [17]Alvin J Siteman Cancer Center at Washington University School of Medicine, St Louis, Missouri, USA. [18]Department of Internal Medicine, Center for Integrated Oncology, University Hospital Cologne, Cologne, Germany

CodeBreaK 100 Trial Design

clinicaltrials.gov identifier: NCT03600883

Screening / Enrollment

Key Eligibility:

- Locally advanced or metastatic NSCLC
- *KRAS* p.G12C mutation as assessed by central testing of tumor biopsies
- Progressed on prior standard therapies[a]
- No active brain metastases

Sotorasib was orally administered at 960 mg once daily until disease progression[b]

Radiographic scan every 6 weeks up to week 48 and once every 12 weeks thereafter

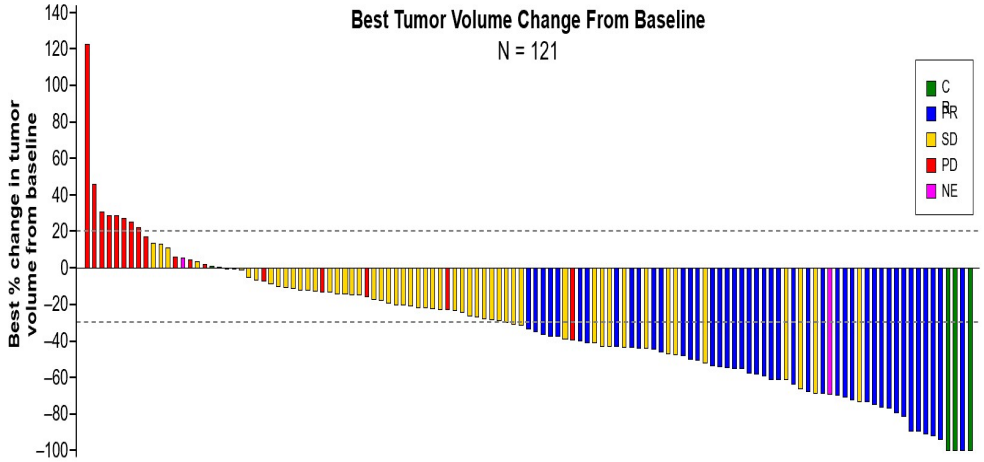
Primary endpoint: ORR (RECIST 1.1) by blinded independent central review
Key secondary endpoints: DoR; disease control rate; TTR; PFS; OS; safety
Exploratory endpoints: Evaluation of biomarkers (PD-L1, co-occurring mutations)

Safety and Long-term Follow-up[c]

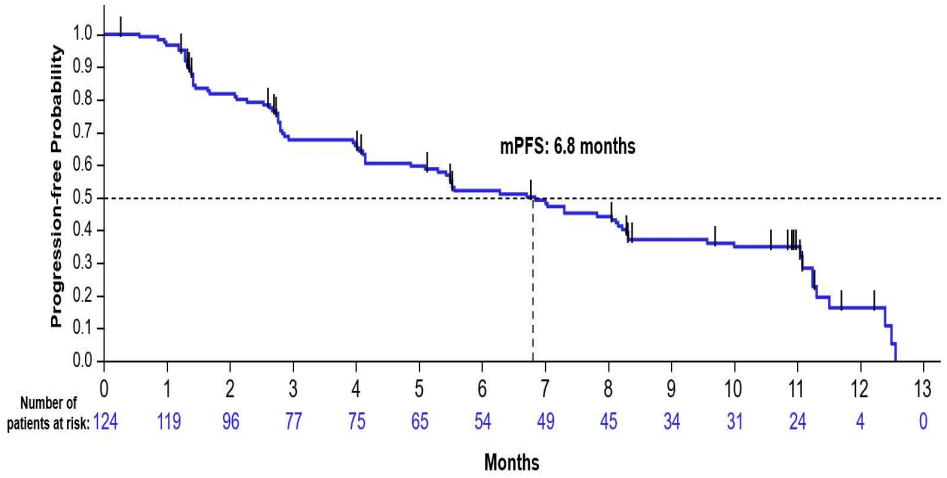
a: no more than 3 prior lines of therapies were allowed; b: treatment beyond disease progression was allowed if certain criteria were met; c: safety follow-up occurs 30 (+7) days after the last dose of sotorasib; long-term follow-up occurs every 12 (±2) weeks for up to 3 years.
NSCLC: non-small cell lung cancer; ORR: objective response rate; DoR: duration of response; TTR: time to response; PFS: progression-free survival; OS: overall survival; PD-L1: programmed death-ligand 1; RECIST: Response Evaluation Criteria in Solid Tumors.

Depth of Tumor Response & Progression free Survival

Tumor shrinkage of any magnitude was observed in 81% of patients (101/124) Median percentage of best tumor shrinkage among all responders was 60%



Median progression-free survival was 6.8 months (95% CI: 5.1, 8.2)



What are the discovery from CodeBreaK 100 study?

Drug	Trial	N	RR	DOR	PFS
Sotorasib	Phase I	59	32.2%	10.9 months	6.3 months
Adagrasib	Phase I/II	51	Results of Phase 2 trial repeated that of Phase 1 trial		
Sotorasib	Phase II	126	37.1%	10.0 months	6.8 months

- Most common TRAEs are GI toxicities (nausea, vomiting, diarrhea, ALT/AST increases)
- Most TRAEs are grade 1 and 2
- TRAEs leading to discontinuations < 10%

Hong et al., NEJM 2020; Jänne et al. ENA 2020; Li et al. WCLC 2020

What is clinical significance of the CodeBreaK100 study?

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$KRAS^{G12C}$ Inhibition with Sotorasib in Advanced Solid Tumors

D.S. Hong, M.G. Fakih, J.H. Strickler, J. Desai, G.A. Durm, G.I. Shapiro, G.S. Falchook, T.J. Price, A. Sacher, C.S. Denlinger, Y.-J. Bang, G.K. Dy, J.C. Krauss, Y. Kuboki, J.C. Kuo, A.L. Coveler, K. Park, T.W. Kim, F. Barlesi, P.N. Munster, S.S. Ramalingam, T.F. Burns, F. Meric-Bernstam, H. Henary, J. Ngang, G. Ngarmchamnanrith, J. Kim, B.E. Houk, J. Canon, J.R. Lipford, G. Friberg, P. Lito, R. Govindan, and B.T. Li

FDA Approval Sought for Sotorasib for KRAS G12C–Mutated Advanced or Metastatic NSCLC on Dec 17, 2020

Topics

Lung Cancer Screen

Perioperative adjuvant treatment

Target KRAS

Immunotherapy combo for advanced NSCLC

Immunotherapy for mesothelioma

PLATFORM trial

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

Michael Boyer,[1] Mehmet A.N. Şendur,[2] Delvys Rodríguez-Abreu,[3] Keunchil Park,[4] Dae Ho Lee,[5] Irfan Çiçin,[6] Perran Fulden Yumuk,[7] Francisco J. Orlandi,[8] Ticiana A. Leal,[9] Olivier Molinier,[10] Nopadol Soparattanapaisam,[11] Adrian Langleben,[12] Raffaele Califano,[13] Balazs Medgyasszay,[14] Te-Chun Hsia,[15] Gregory A. Otterson,[16] Lu Xu,[17] Bilal Piperdi,[17] Ayman Samkari,[17] Martin Reck[18]

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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

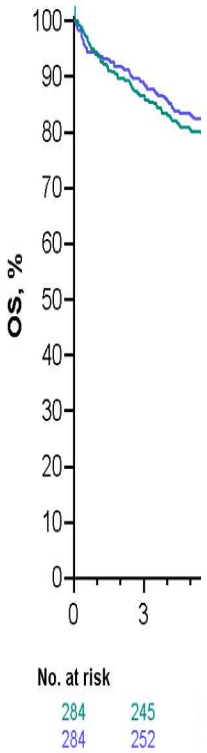
End Points

- **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.

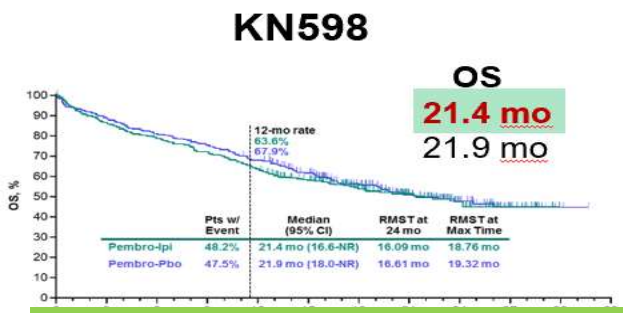
[a]Alpha controlled using the graphical method of Maurer and Bretz. [b]Randomization stratification factors applied to all stratified analyses. [c]RMST is an alternative means of assessing a treatment effect; it is defined as the average survival from time 0 to a specified time point and is equivalent to the area under the KM curve from time 0 to the specified time point.

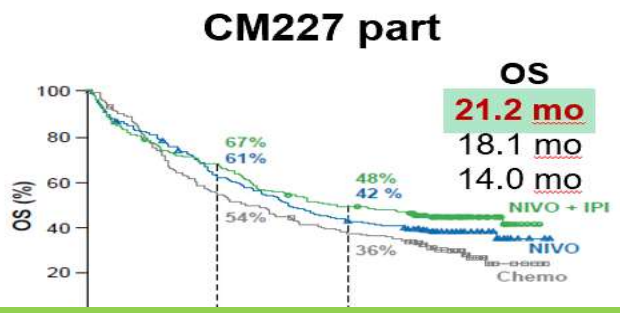
What are the discovery from KeyNote 598 study?



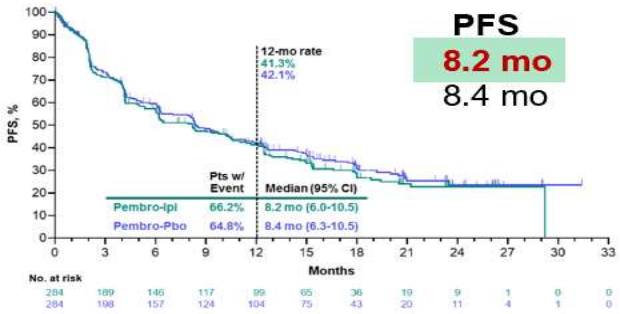
OS

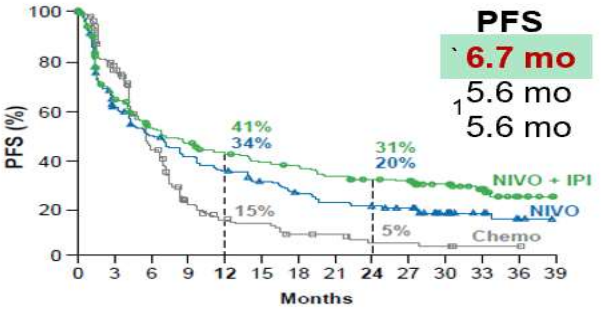
PFS





Combo immunotherapy group in KN598 and CM227 demonstrate comparable efficacy data but one negative & one positive results





What are the discovery from KeyNote 598 study?

No suggestion of further OS advantage with immunochemotherapy over immuotherapy in PD-L1≥50% population

	KN024[1]	KN042[2]	IMPOWER 110[3]	IMPOWER-Lung1[4]	**KN189[5]**	KN407[6]
N[a]	154	299	107	365	132	73
Design	Pembro vs Chemo	Pembro vs Chemo	Atezo vs Chemo	Cemipli vs Chemo	Pem+Chemo vs Chemo	Pem+Chemo vs Chemo
PDL1 Stratum	≥50%	≥50%	TC3 or IC3	≥50%	≥50%	≥50%
mPFS, mo HR	7.7 vs 5.5 HR 0.5	7.1 vs 6.4 HR 0.81	8.1 vs 5.0 HR 0.63	6.2 vs 5.6 HR 0.59	11.1 vs 4.8 HR 0.36	8.0 vs 4.2 HR 0.37
mOS, mo HR	26.3 vs 13.4 HR 0.62	20.0 vs 12.2 HR 0.7	20.2 vs 13.1 HR 0.59	22.1 vs 14.3 HR 0.68	27.7 vs 10.1 HR 0.59	NR HR 0.64
2-y OS, %	51.7 vs 34.5	44.7vs 31.1	NR	48.6 vs 29.7	51.9 vs 39.4	NR
5-y OS, %	31.9 vs 16.3	NR	NR	NR	NR	NR

Single-agent Immunotherapy has become the new standard care for PD-L1≥50% advanced NSCLC

Topics

Lung Cancer Screen

Perioperative adjuvant treatment

Target KRAS

Immunotherapy combo for advanced NASCLC

Immunotherapy for mesothelioma

PLATFORM trial

Nivolumab Versus Placebo in Relapsed Malignant Mesothelioma: Preliminary results from the CONFIRM Phase 3 Trial

Dean Fennell[1], Christian Ottensmeier[2], Raffaele Califano[3], Gerard G Hanna[4], Sean Ewings[5], Kayleigh Hill[5], Sam Wilding[5], Sarah Danson[6], Mavis Nye[5], Nicola Steele[7], Lucy Johnson[5], Joanne Lord[8], Calley Middleton[5], Ellice Marwood[5], Peter Szlosarek[9], Sam Chan[10], Aarti Gaba[1], Liz Darlison[11], Peter Wells-Jordan[1], Cathy Richards[1], Charlotte Poile[1], Jason F Lester[12], Gareth Griffiths[5]

[1]University of Leicester, UK; [2] University of Liverpool, UK; [3]The University of Manchester, UK; [4]Peter MacCallum Cancer Centre, University Melbourne, Australia; [5]CRUK Southampton Clinical Trials Unit, University of Southampton, UK; [6]University of Sheffield, UK; [7]Beatson West of Scotland Cancer Centre, UK; [8]Southampton Health Technology Assessments Centre, University of Southampton, UK; [9]Barts Cancer Institute, UK; [10]York Teaching Hospital NHS Foundation Trust, UK; [11]Mesothelioma UK; [12]South West Wales Cancer Centre, UK.

CONFIRM Trial Design

Key eligibility criteria:
Mesothelioma
> 1 prior line of therapy
ECOG status 0 or 1

Randomised 2:1
Stratified by histology
(epithelioid or non-epithelioid)

Recruited
April 2017 – March 2020

Nivolumab (n=221)
240mg in 30-min IV infusion on day 1 of 14-day cycle

Placebo (n=111)
240mg sterile solution in 30-min IV infusion on day 1 of 14-day cycle

Administered until progression, unacceptable toxicity, withdrawal or 12m

Target sample size: 336
Study halted recruitment at n=332 due to COVID-19 pandemic but sufficient event/follow-up

Co-primary outcomes:
- Overall survival
- Investigator-reported progression-free survival

Secondary outcomes:
- RECIST-determined progression-free survival
- Response rate
- EQ-5D
- Safety

Funders:
- Cancer Research UK/SU2C (C16728/A21400)
- BMS (investigator initiated)

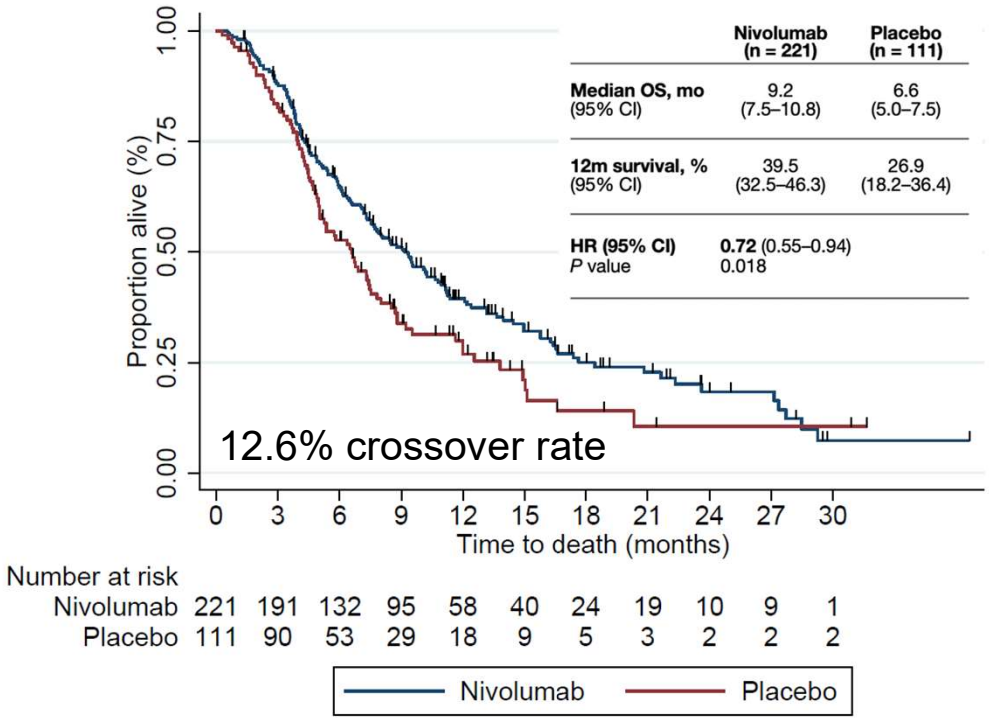
COORDINATING GROUP:
Southampton Clinical Trials Unit

SPONSOR:
University of Southampton

What are the discovery from CONFIRM study?

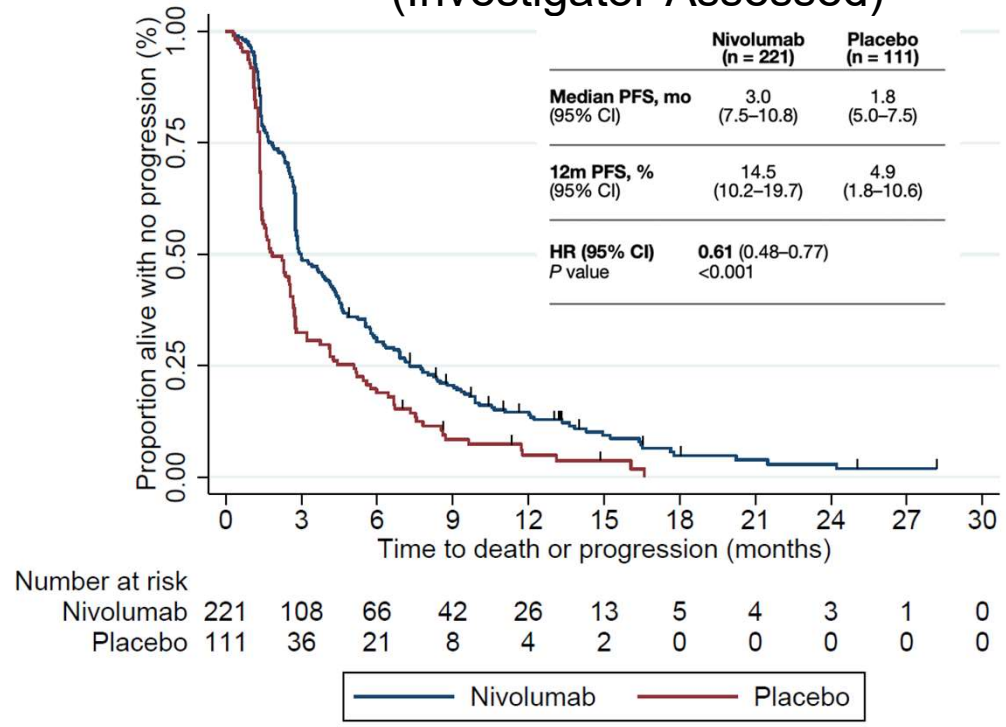
CONFIRM: Met Co-Primary Endpoints

OS



PFS

(Investigator-Assessed)



Immunotherapy Studies in Relapsed Mesothelioma

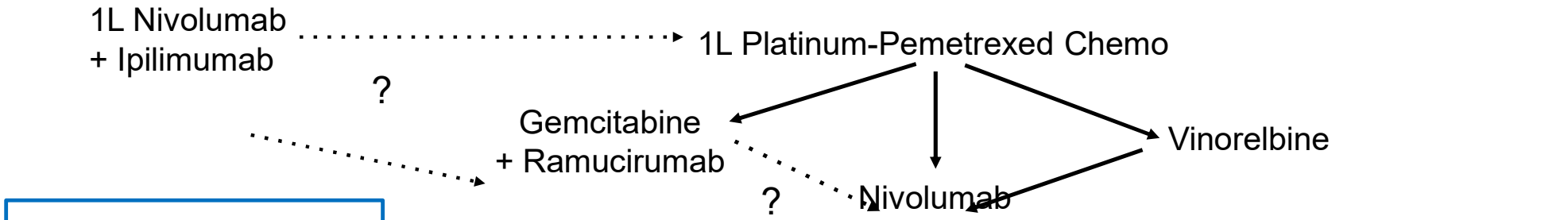
IASLC

Study	Phase	Agent (s)	n	ORR	mPFS (m)	mOS (m)
KN 028	Ib	Pembrolizumab	25 (PD-L1 pos)	20%	5.4m	18m
JAVELIN	Ib	Avelumab	53	9%	4.1m	10.7m
Treme (Italy)	II	Tremelimumab	29	14%	6.2m	11.3m
MERIT	II	Nivolumab	34	29%	6.1m	17.3m
Pembro (Chicago)	II	Pembrolizumab	64	22%	4.1m	11.5m
NIBIT-meso1	II	Treme / Durva	40 (30% 1L)	28%	5.7m	16.6m
INITIATE	II	Nivo / Ipi	34	29%	NR: >6.2m	NR: >12.7m
MAPS2	II	Nivo or Nivo/Ipi	63 & 62	19% & 28%	4.0m & 5.6m	11.9m & 15.9m
DETERMINE	IIb	Treme vs placebo	571 (2:1)	4.5%	2.8m	7.7m
PROMISE-meso	III	Pembro vs Chemo	144	22%	2.5m	10.7m
CONFIRM	III	Nivo vs placebo	332	10.4%	3.0m	9.2m

Alley et. al., *Lancet Oncol,* 2017; Hassan et. al., *JAMA Oncol*, 2019; Calabro et. al., *Lancet Respir Med*, 2015; Okada et. al., *Clin Cancer Res,* 2019; Desai et. al., *WCLC*, 2018; Calabro et. al., *Lancet Respir Med*, 2018; Disselhorst et. al., *Lancet Respir Med*, 2019; Scherpereel et. al., *Lancet Oncol*, 2019; Maio et. al., *Lancet Oncol*, 2017; Popat et.al., *Ann Oncol,* 2019; Fennell et.al., *WCLC,* 2020

What is clinical significance of the CONFIRM study?

- The phase III CONFIRM placebo-controlled study met both PFS and OS endpoints, with 12.6% improvement in 12-month survival rate.



Awaiting results from 1L IO combination stuides

? Nivo + Ipi

? Other CPI(s)

Need Biomarkers

Much still needs to be learned

Topics

Lung Cancer Screen

Perioperative adjuvant treatment

Target KRAS

Immunotherapy combo for advanced NASCLC

Immunotherapy for mesothelioma

PLATFORM trial

HUDSON

An Open-Label, Multi-Drug, Biomarker-Directed, Phase II Platform Study in Patients with Non-Small Cell Lung Cancer, who Progressed on an anti-PD(L)-1 Therapy

Benjamin Besse

Institut Gustave Roussy, Villejuif and Paris-Sud University, Paris, France

On behalf of the HUDSON study group

B. Besse, M. Awad, P. Forde, M. Thomas, K. Park, G. Goss, N. Rizvi, F. Huemer, M. Hochmair, J. Bennouna, J. Cosaert, Z. Szucs, P. Mortimer, R. Hobson, K. Sachsenmeier, E. Dean, H. Ambrose, C. Hayward, M. Dressman, S. Barry, J. Heymach

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

Group A: biomarker matched (n=85)

Central molecular screen† (n=617)

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

HRRm STK11	olaparib and durvalumab (PARPi) 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)

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)

Primary endpoint:

- Overall response rate

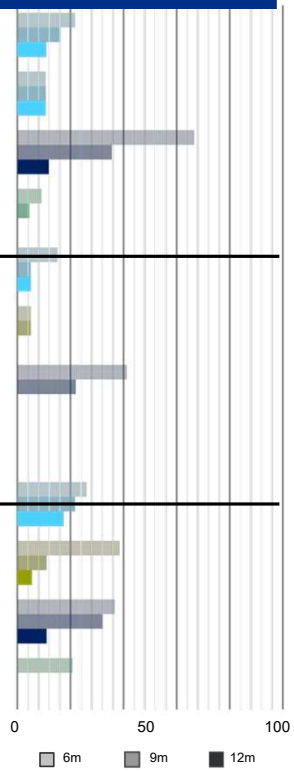
Secondary endpoints:

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

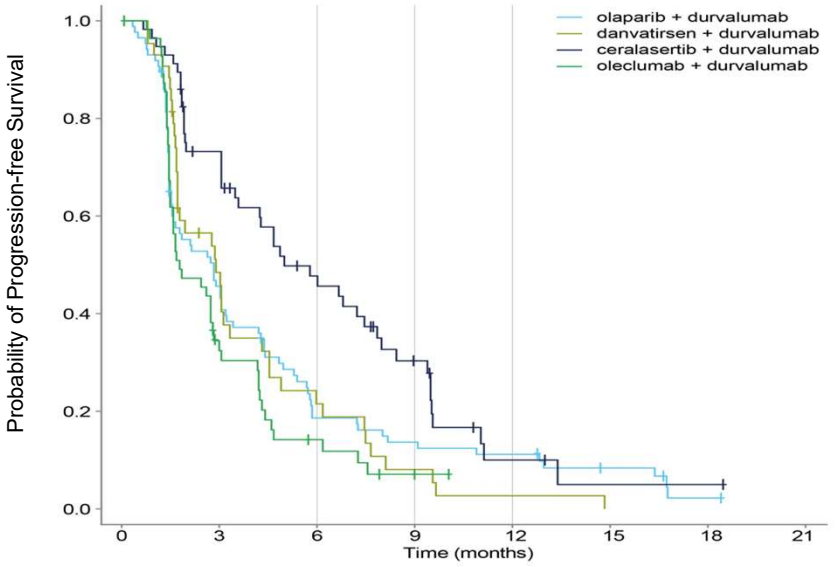
†Immunohistochemistry was also performed. ‡PD on ICI within 24 weeks (fresh biopsy or archived tissue); §PD on ICI > 24 weeks (fresh biopsy or archived tissue). ATM, ataxia-telangiectasia mutated; ATRi, ataxia-telangiectasia receptor inhibitor; CD73, cluster of differentiation 73; HER2, human epidermal 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)

HUDSON – ORR and median PFS

	N	mF/U m	ORR n (%)	Median PFS m (80% CI)	PFS rate (%) 6, 9 and 12 m
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)	
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)	
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)



Olaparib	87	36	15	11	9	5	1	0
Danvatirsen	45	17	8	3	1	0		
Ceralasertib	62	39	22	12	3	1	1	0
Oleclumab	57	16	6	1	0			

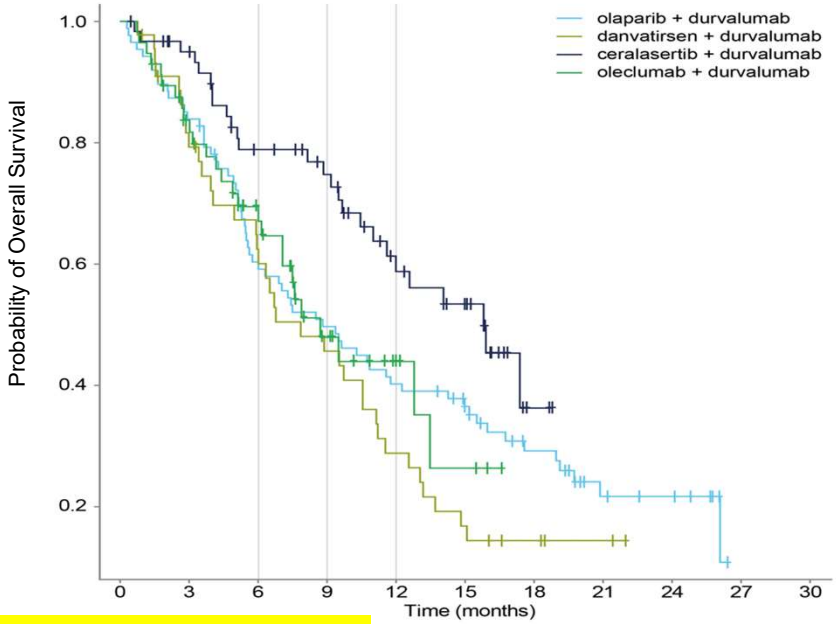
Data in italics are not yet mature; treatment modules include the biomarker selected, primary resistance and acquired resistance cohorts for each drug combination
73H, signal transducer and activator of transcription 3-73H; ATM, ataxia-telangiectasia mutated; CI, confidence interval; HRR, homologous 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

	N	mF/U m	Median OS m (80% CI)	OS rate (%) 6, 9 and 12 m
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)*	
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)	
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			

Data in italics are not yet mature; treatment modules incl
73H, signal transducer and activator of transcription 3-73
mF/U, median follow-up; NC, not calculated; OS, overall s

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



	34	27	18	9	7	0	
	12	7	4	2	0		
	23	17	2	0			
	6	3	0				

Significance:
HUDSON demonstrates that molecularly stratified enrolment in the immune therapy failed setting is feasible

Thank you for your attention

Selected Day 4 Abstracts

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IASLC
INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

Disclosures

Ross Soo, MBBS, PhD, FRACP

- **Advisory Board:** Amgen**,** Astra-Zeneca, Bayer, BMS, Boehringer Ingelheim, Lilly, Merck, Novartis, Pfizer, Roche, Taiho, Takeda, Yuhan
- **Research grant:** Astra-Zeneca, Boehringer Ingelheim

IASLC 2020 World Conference on Lung Cancer Singapore

A phase 1 study of AMG 757, a half-life extended bispecific T-cell engager (BiTE®) immuno-oncology therapy against DLL3, in SCLC

Taofeek K. Owonikoko,[1] Michael Boyer,[2] Melissa Johnson,[3] Ramaswamy Govindan,[4] Luis Paz-Ares Rodrigues, [5] Fiona H. Blackhall,[6] Rene J. Boosman,[7] Stéphane Champiat,[8] Horst-Dieter Hummel,[9] W. Victoria Lai,[10] Hibiki Udagawa, [11] Anne C. Chiang,[12] Afshin Dowlati,[13] Christine L. Hann,[14] Ravi Salgia,[15] Everett E. Vokes,[16] Mukul Minocha,[17] Nooshin Hashemi Sadraei,[17] Aditya Shetty,[17] Marie-Anne Damiette Smit,[17] Yiran Zhang,[17] Amrita Pati,[17] Sumi Roy,[17] Beate Sable,[17] Hossein Borghaei[18]

[1]Emory University School of Medicine, Atlanta, GA, USA; [2]Chris O'Brien Lifehouse, Camperdown, NSW, Australia; [3]Sarah Cannon Research Institute, Tennessee Oncology, Nashville, TN, USA; [4]Washington University Medical School, St. Louis, MO, USA; [5]Hospital Universitario 12 de Octubre, Universidad Complutense & Ciberonc, Madrid, Spain; [6]The Christie NHS Foundation Trust, University of Manchester, Manchester, UK; [7]The Netherlands Cancer Institute, Amsterdam, Netherlands; [8]Gustave Roussy, Paris-Saclay University, Villejuif, France; [9]Comprehensive Cancer Center Mainfranken, University Hospital Wuerzburg, Wuerzburg, Germany; [10]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [11]National Cancer Center Hospital East, Kashiwa, Chiba, Japan; [12]Yale School of Medicine, New Haven, CT, USA; [13]University Hospitals Seidman Cancer Center and Case Western Reserve University, Cleveland, OH, USA; [14]Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD, USA; [15]City of Hope Hospital, Duarte, CA, USA; [16]University of Chicago Medicine and Biological Sciences, Chicago, IL, USA; [17]Amgen Inc., Thousand Oaks, CA, USA; [18]Fox Chase Cancer Center, Philadelphia, PA, USA

Key Eligibility Criteria & Baseline Demographics

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

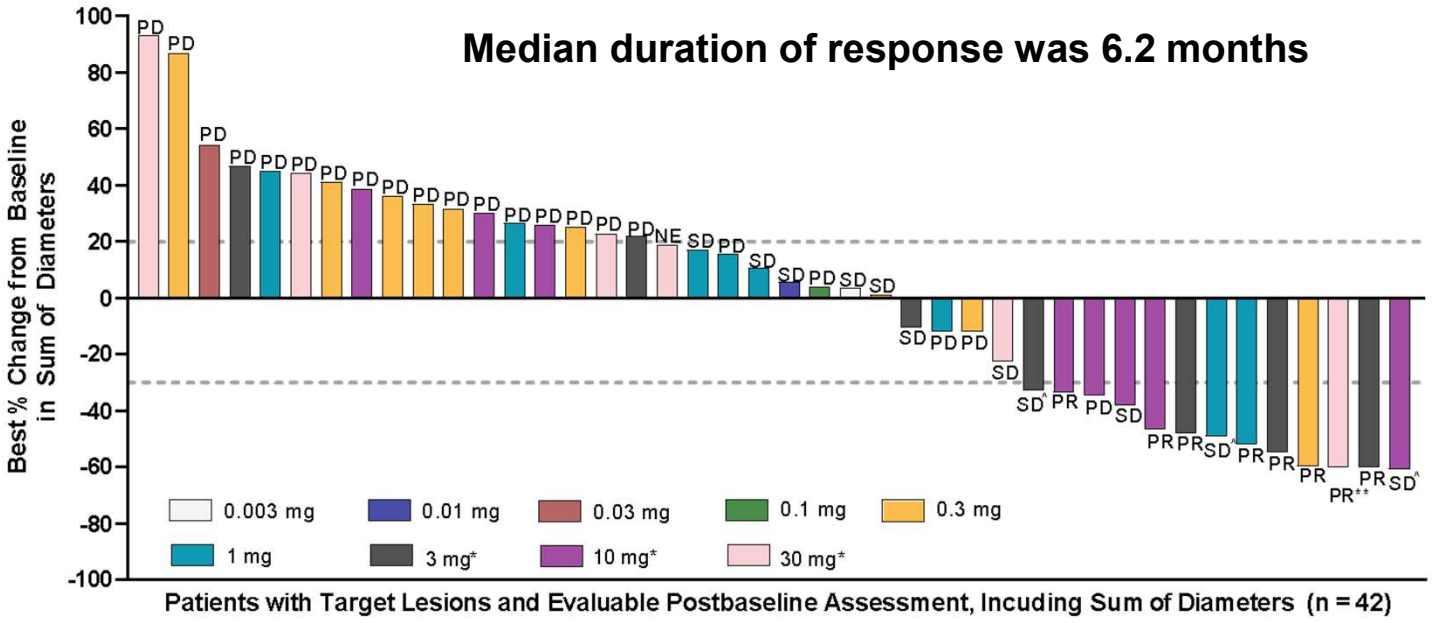
Exclusion Criteria

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

Baseline Characteristic	All Patients (N = 52)
Median age, years (range)	64 (32–80)
Current/former smoker, n (%)	8 (15) / 36 (69)
ECOG performance status: 0–1, n (%)	51 (98)
Prior lines of therapy	
1–2, n (%)	39 (75)
≥ 3, n (%)	13 (25)
Median (range)	2 (1–6)
Prior PD-1 or PD-L1 treatment, n (%)	23 (44)
Extensive stage disease at initial diagnosis, n (%)	50 (96)
Brain / liver metastases, n (%)	13 (25) / 25 (48)

ECOG, Eastern Cooperative Oncology Group; PD-1, programmed death-1; PD-L1, programmed death-ligand 1; SCLC, small cell lung cancer.

AMG 757 Demonstrates Anti-Tumor Activity in Patients with SCLC



Modified RECIST 1.1 Response, n (%)	Patients† (N = 51)
PR, confirmed	7 (14)
0.3 mg target dose	1/12 (8)
1 mg target dose	1/8 (13)
3 mg target dose	3/9 (33)
10 mg target dose	2/10 (20)
PR, unconfirmed	1 (2)
30 mg target dose	1 (2)
SD	11 (22)
Disease control rate, %	37

PR** indicates the PR is unconfirmed. SD^ indicates patients who had an initial PR, but did not have confirmation of PR on the subsequent scan. NE indicates PD in the post-baseline scan and came off study without further confirmation scan.
*Step dosing. †Includes patients who received ≥ 1 dose of AMG 757 and had at least 8 weeks follow-up. NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.

Adverse Events (AEs) Summary

Treatment-related AEs	Patients (N = 52)	
	All Grades, n (%)	Grade ≥ 3, n (%)*
Any treatment-related AE	41 (79)	12 (23)
Treatment-related AEs in ≥ 10% of patients		
CRS	**23 (44)**	**1 (2)†**
Pyrexia	10 (19)	0
Fatigue	7 (14)	0
Anemia	5 (10)	1 (2)
Nausea	5 (10)	0

*Includes one patient with grade 5 pneumonitis; † Grade 3 CRS, more detail presented on next slide.
AE, adverse event; CRS, cytokine release syndrome; DLT, dose limiting toxicity.

- Treatment-emergent AEs occurred in 51/52 (98%) patients
  - Grade ≥ 3 occurred in 27 (52%) patients
- Treatment-related AEs occurred in 41 (79%) patients, resulting in discontinuation in 1 (2%) patient
  - The one DLT was grade 5 pneumonitis and occurred in 1 (2%) patient

AMG 757 monotherapy demonstrated a favorable safety profile

Conclusions

- The results presented herein support AMG 757 as the first half-life extended BiTE® immuno-oncology therapy with a favorable safety profile and a durable response profile
  - Grade 3 treatment-related AEs occurred in 12 (23%) patients
  - CRS events were primarily grade 1 or 2 with only 1 case (2%) of grade 3 CRS
  - Only 1 discontinuation of treatment due to treatment-related AEs
  - Encouraging efficacy was observed during dose exploration, with confirmed PR in 14% of patients; response was durable, with a median duration of 6.2 months
- Dose optimization for monotherapy is ongoing

IASLC 2020 World Conference on Lung Cancer Singapore

EFFICACY AND SAFETY PROFILE OF LURBINECTEDIN-IRINOTECAN IN PATIENTS WITH RELAPSED SCLC

Results from a phase Ib-II trial

Santiago Ponce[1], Gregory M. Coté[2], Alejandro Falcón[3], Elizabeth Jimenez-Aguilar[1], Jessica J Lin[2], Inmaculada Sánchez Simón[3], María José Flor[3], Rafael Núñez[4], Ana M Jiménez[4], Eva Jiménez[4], Sonia Extremera[4], Carmen Kahatt[4], Ali Zeaiter[4], Luis Paz-Ares[1]

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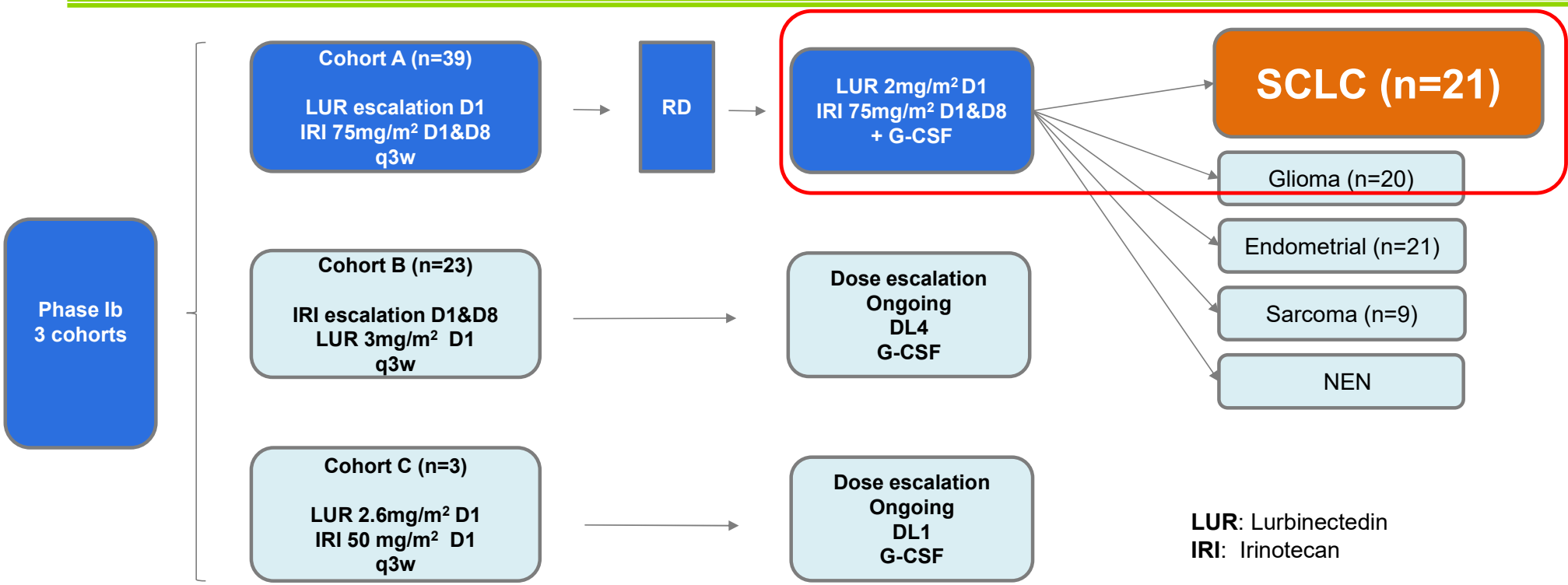
Study Design



LUR: Lurbinectedin
IRI: Irinotecan

SCLC cohort, Baseline characteristics (n=21)

Baseline Characteristics		n= 21
Median age	Years	61 (52-74)
Sex	Male Female	48% 52%
ECOG	0 1	24% 76%
LDH	>ULN	76%
Stage at diagnosis	Limited Extensive	19% **81%**
Most common sites (no lung)	Lymph nodes Liver Adrenal Bone	90% **48%** 38% 38%
Bulky disease	1 lesion > 50mm	29%

Baseline Characteristics		n= 21
Sum longest diameters mm.	Median (range)	86 (19-180)
CNS metastases PCI		**24%** 48%
Prior lines for advanced disease	Median (range) 1 line 2 lines	1 (1-2) 62% **38%**
Best response to prior platinum	CR-PR SD PD UNK	71% 5% **19%** 5%
CTFI	Median (months) <90 days ≥90 days	**3.2 months** 38% 62%

SCLC cohort, Safety (n=21)

Adverse Events and Laboratory abnormalities		Grade 1-2, %	Grade 3-4, %
Treatment-related adverse events	Fatigue	66.7	23.8*
	Nausea	57.1	-
	Vomiting	38.1	4.8
	Diarrhea	33.3	28.6**
	Constipation	19	-
	Abdominal pain	4.8	-
	Anorexia	52.4	-
	Febrile neutropenia	-	9.5
Laboratory abnormalities	Anemia	81	19
	Neutropenia	33.3	61.9***
	Thrombocytopenia	66.7	9.5
	ALT increase	57.1	4.8
	AST increase	61.9	4.8

ALT, alanine aminotransferase; AST, aspartate aminotransferase; IRI, irinotecan; LUR, lurbinectedin.

*1 episode per patient (n=5 pts) **All were grade 3. 1 episode per patient, except in 1 patient (2 episodes of 1 day of duration each)
*** 6/21 pts (28.6 %) neutropenia grade 4

Related AEs summary / dose modifications / supportive treatment	n (%)
Any AE	21 (100)
AE ≥ grade 3	16 (76.2)
SAEs	6 (28.5)
Related AEs leading to death	**0 (0.0)**
Related AEs leading to treatment discontinuation	**0 (0.0)**
Dose delays treatment related	6 (28.6)
Dose reductions	11 (52.4)
Transfusions (red blood)	7 (33.3)

SCLC cohort, efficacy table (n=21)

	All patients (n=21)	CTFI		Setting	
		≥90 days (n=13)	<90 days (n=8)	2nd line (n=13)	3rd line (n=8)
Median number of cycles (range)	8+ (1-20)	10+ (6-20)	6+ (1-8)	8+ (3-21)	8+ (1-18)
Objective Response Rate (PR)	**62%**	**69%**	**50%**	**77%**	**38%**
Clinical Benefit Rate (PR+SD>4m)	81%	92.3%	62.5%	92.3%	62.5%
Disease Control Rate (PR+SD)	90%	100%	75%	100%	75%
Median DOR (m) (95% CI)	6.7+ (3.0-N.R)	7.5+ (3.0-N.R)	3.7+ (2.8-3.7)	6.7+ (3.0-N.R)	3.0+ (3.0-N.R)
Median PFS (m) (95% CI)	**6.2+ (4.3-8.5)**	**8.1+ (4.3-N.R)**	**4.8+ (0.7-5.0)**	**8.5+ (4.8-N.R)**	**4.2+ (0.7-7.2)**

N.R not reached

CONCLUSIONS

- The combination of lurbinectedin and irinotecan after failure of first-line therapy, demonstrates remarkable antitumor activity in SCLC
- Noticeable activity is being observed in pts with poor prognosis such as those with resistant disease (CTFI <90 days), in the 3rd line setting and those with brain metastases.
- Toxicity is transient and manageable, being mainly hematological abnormalities, fatigue and diarrhea, with no discontinuations due to AE and no toxic deaths
- This cohort of patients with SCLC is being expanded up to 47 patients
- Further development of this combination is warranted in pts with SCLC

IASLC 2020 World Conference on Lung Cancer Singapore

Whole Exome Sequencing Reveals the Potential Role of Hereditary Predisposition in Small Cell Lung Cancer, a Tobacco-Related Cancer

Nobuyuki Takahashi[1], Camille Tlemsani[1], Lorinc Pongor[1], Vinodh N. Rajapakse[1], Manoj Tyagi[1], Xinyu Wen[1], Grace-Ann Fasaye[1], Keith T. Schmidt[1], Chul Kim[2], Arun Rajan[1], Shannon Swift[1], Linda Sciuto[1], Rasa Vilimas[1], Santhana Webb[1], Samantha Nichols[1], William Douglas Figg[1], Yves Pommier[1], Kathleen Calzone[1], Seth M. Steinberg[1], Jun S. Wei[1], Udayan Guha[1], Clesson E. Turner[3], Javed Khan[1], Anish Thomas[1]

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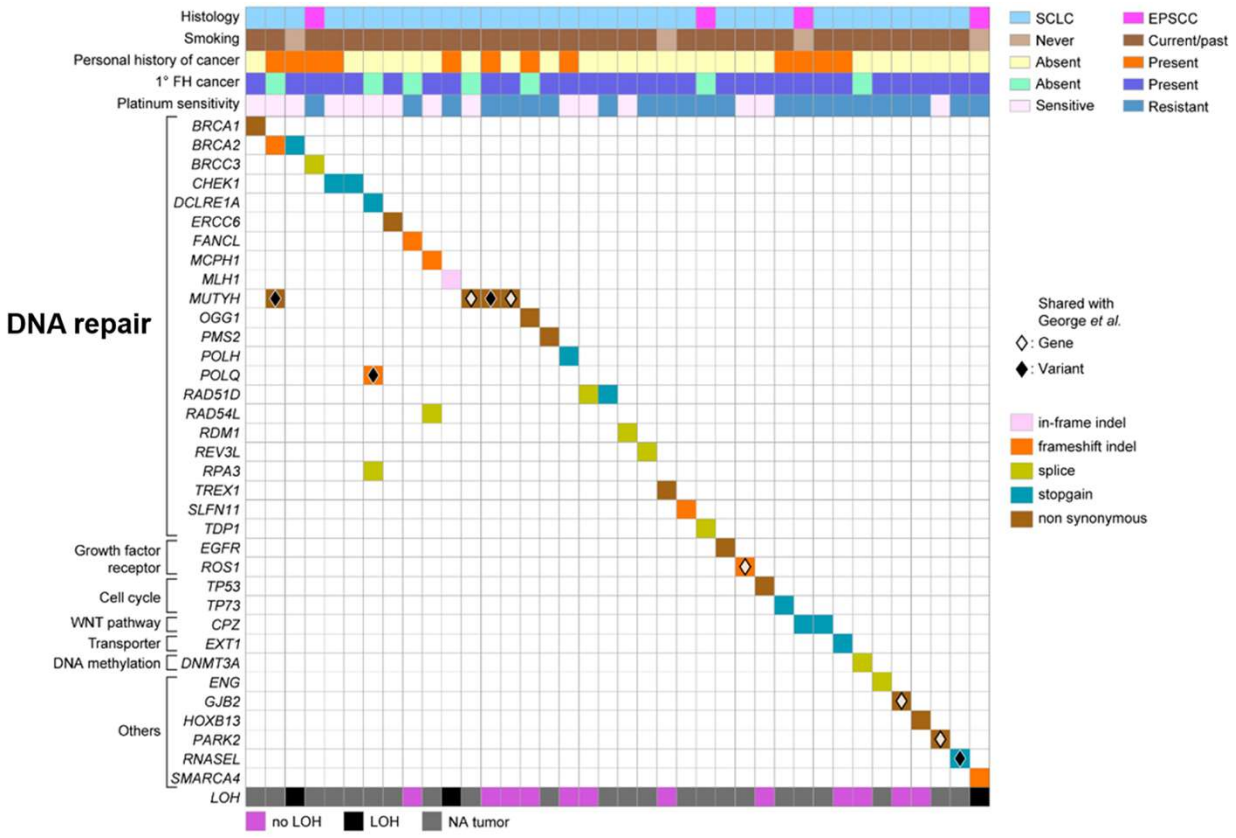
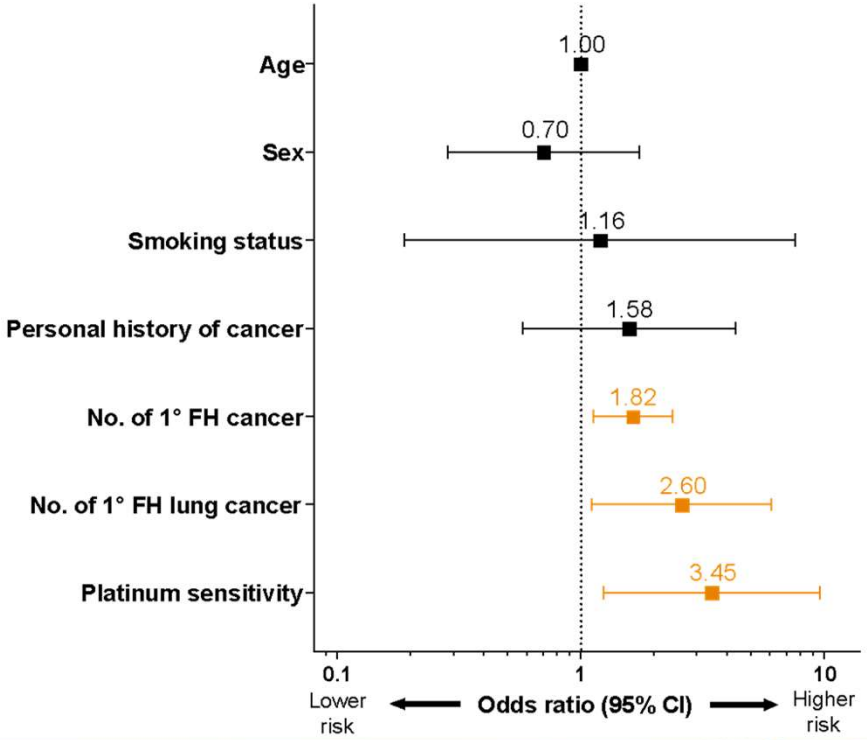
NIH NATIONAL CANCER INSTITUTE Center for Cancer Research



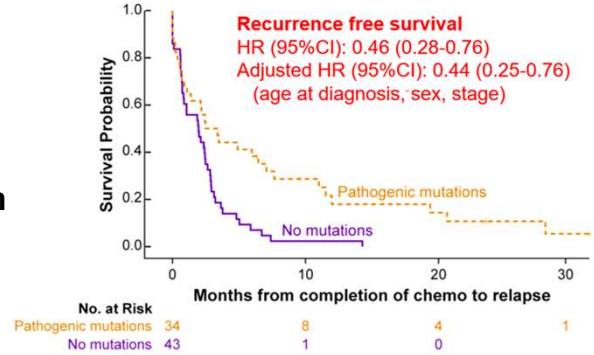
Germline mutations are highly prevalent in patients with SCLC

- 34/77 (44.2%) of SCLC patients had a P/LP germline mutation
- 9/77 (11.7%) of SCLC patients had a P/LP germline mutation in ACMG genes
- Most genes were involved in DNA repair (66.7%)
- 3/31 cases with available tumor had loss of heterozygosity (*BRCA2*, *MLH1*, *SMARCA4*)

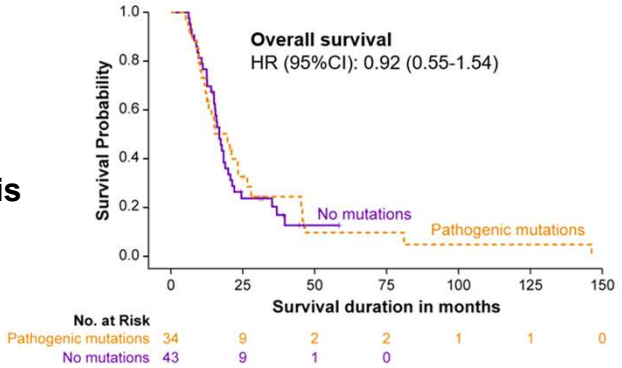
Germline genotype is associated with family history of cancer and platinum sensitivity



Recurrence free survival with platinum



Overall survival since diagnosis



Updated efficacy, safety, and dosing management of poziotinib in previously treated EGFR and HER2 exon 20 NSCLC patients

R Cornelissen[1], MC Garassino[2], X Le[3], J Clarke[4], N Tchekmedyian[5], J Goldman[6], F Lebel[7], G Bhat[7], MA Socinski[8]

[1]Erasmus Medical Center, Netherlands; [2]Fondazione IRCCS Istituto Nazionale dei Tumori, Italy; [3]The Univ Texas MD Anderson Cancer Center, TX; [4]Duke Cancer Institute, NC; [5]Pacific Shores Medical Group, CA; [6]Univ California Los Angeles, CA; [7]Spectrum Pharmaceuticals, CA; [8]AdventHealth Cancer Institute, FL

Efficacy in patient subgroups

EGFR

- Responses observed regardless of lines of therapy in EGFR cohorts

HER2

- Higher responses (38.7%) observed in patients with ≥3 prior lines of therapy than overall
- Clinical activity seen in all 14 patients with baseline CNS metastasis; Responses seen in 4 (28.6%); none had progression in brain lesion resulting in CNS specific DCR of 100%

Exon 20 mutations Type

- No clear differences between types of Exon 20 mutations in EGFR or HER2 cohorts

	2L EGFR Exon 20 (N=115) ORR % (n/N)	2L HER2 Exon 20 (N=90) ORR % (n/N)
Lines of Therapy		
1 Line	14.3 (7/49)	23.3 (7/30)
2 Lines	13.8 (4/29)	20.7 (6/29)
3+ Lines	16.2 (6/37)	**38.7 (12/31)**
Chemotherapy only	10.3 (3/29)	31.8 (7/22)
TKI	6.9 (2/29)	NA
HER2 therapy	NA	24.0 (6/25)
Immune checkpoint inhibitors	21.1 (12/57)	**27.9 (12/43)**
Stable brain metastasis at baseline	8.3 (1/12)	**28.6 (4/14)**

Conclusions

- **Successfully met primary endpoint for 2L HER2 exon 20 insertion mutations**
  - ORR was 27.8% in 2L HER2 cohort
  - Higher response rates (38.7%) seen in heavily pre-treated HER2 cohort (≥3 lines of therapy)
- Clinical activity seen in previously-treated NSCLC patients with EGFR and HER2 exon 20 insertions across common mutational profile
  - DCR of 68.7% and 70% respectively
- Clinically meaningful responses (28.6%) observed in 14 HER2 patients with brain metastases at entry with no progression in brain lesion (CNS specific DCR of 100%)
  - Activity in CNS metastatic disease for both EGFR and HER2 cohorts
- Safety profile similar to second generation TKI's

VISION: Cohort A baseline characteristics

VISION comprises a large population of elderly patients with *MET* exon 14 skipping NSCLC

- VISION is a single-arm, Phase II trial of tepotinib in patients with *MET*-altered NSCLC (NCT02864992)[1]
  - Cohort A enrolled patients with *MET* exon 14 skipping NSCLC
- Patients were mostly elderly, half were male, half had smoking history, and most had adenocarcinoma
- Baseline characteristics were similar in the safety population, comprising all patients with *MET* exon 14 skipping NSCLC who received at least one dose of tepotinib across Cohorts A and C (N=255)

Baseline characteristics		Treatment-naïve (n=69)	Previously treated (n=83)	Overall (N=152)
Median age, years (range)		74.0 (56–94)	72.6 (41–88)	73.1 (41–94)
Sex, %	Male/Female	52.2/47.8	51.8/48.2	52.0/48.0
Race,† %	White/Asian	81.2/17.4	62.7/31.3	71.1/25.0
ECOG PS, %	0/1	36.2/63.8	19.3/80.7	27.0/73.0
Smoking history,‡ %	Yes/No	62.3/37.7	43.4/47.0	52.0/42.8
Histology,§ %	Adenocarcinoma/ Squamous	84.1/8.7	88.0/10.8	86.2/9.9
Brain metastases at baseline,¶ %		14.5	15.7	15.1

Best responses to prior therapies

- Any (n=83)
  - 2 CRs (2.4%)
  - 24 PRs (28.9%)
- Platinum-based CT* (n=74)
  - 2 CRs (2.7%)
  - 19 PRs (25.7%)
- IO + platinum-based CT (n=10)
  - 3 PRs (30.0%)

Additional information on tepotinib. *Prior platinum-based CT for metastatic disease. †Race was unknown or missing in four patients, one patient was Black/African American, and one patient was 'other'. ‡Smoking history was missing in eight patients. §Two patients had adenosquamous histology (one treatment-naïve and one previously treated), three patients had sarcomatoid (all treatment naïve), and one patient had NSCLC-NOS (treatment naïve). ¶Baseline brain metastases identified by IRC or investigator.

CR, complete response; CT, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; IO, immunotherapy; MET, mesenchymal-epithelial transition factor; NOS, not otherwise specified; NSCLC, non-small cell lung cancer; PR, partial response.

1. Paik PK et al. N Engl J Med. 2020;383(10):931-943.

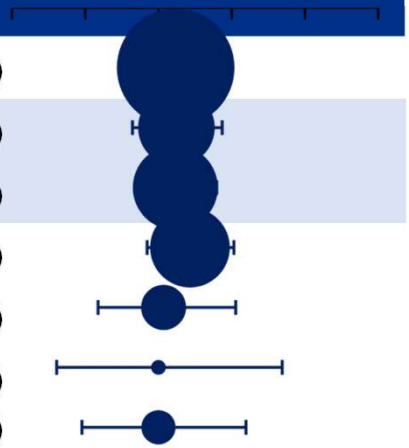
VISION: Cohort A overall efficacy

Tepotinib demonstrated clinical activity irrespective of therapy line in this elderly patient population

Efficacy according to IRC	Treatment-naïve (n=69)	Previously treated (n=83)	Overall (N=152)
ORR, % (95% CI)	**44.9** (32.9, 57.4)	**44.6** (33.7, 55.9)	**44.7** (36.7, 53.0)
BOR, n (%)			
CR	0	0	0
PR	31 (44.9)	37 (44.6)	68 (44.7)
SD	16 (23.2)	23 (27.7)	39 (25.7)
PD	13 (18.8)	13 (15.7)	26 (17.1)
NE	9 (13.0)	10 (12.0)	19 (12.5)
Median DOR, months (95% CI)	10.8 (6.9, ne)	11.1 (9.5, 18.5)	11.1 (8.4, 18.5)
Median PFS, months (95% CI)	8.5 (6.8, 11.3)	10.9 (8.2, 12.7)	8.9 (8.2, 11.2)

Data cut-off: July 1, 2020.

	N	ORR (95% CI) by IRC
Overall	152	44.7 (36.7, 53.0)
Treatment-naïve	69	44.9 (32.9, 57.4)
Previously treated	83	44.6 (33.7, 55.9)
Platinum-based CT*	74	48.6 (36.9, 60.6)
Also received IO	29	41.4 (23.5, 61.1)
As combination†	10	40.0 (12.2, 73.8)
As single-agent in a separate line†‡	20	40.0 (19.1, 63.9)



ORR (%) and 95% CI

*Platinum-based CT for metastatic disease; three patients had stage III NSCLC at study entry and are, therefore, not included in this categorization. †One patient received IO as monotherapy and in combination with platinum-based CT and, as such, is included in both subgroups. ‡Patients could have received first-line platinum-based CT followed by second-line single-agent IO, or vice versa.
BOR, best overall response; CI, confidence interval; CR, complete response; CT, chemotherapy; DOR, duration of response; IRC, independent review committee; NE, not evaluable; ne, not estimable; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease.

Methods and Demographics

Adult phase I trial (NCT02122913)
- Age ≥18 years
- Advanced solid tumors

n=1

Adult/adolescent phase II basket trial (NAVIGATE, NCT02576431)
- Age ≥12 years
- Advanced solid tumors
- TRK fusion cancer

n=13

14 patients with TRK fusion lung cancer

Patient characteristics	
Median age, range	52 (25–76)
Sex, n (%)	
Male	8 (57)
Female	6 (43)
***NTRK* fusion, n (%)**	
NTRK1	11 (79)
NTRK2	0
NTRK3	3 (21)
CNS metastases at baseline, n (%)	
Yes	7 (50)
No	7 (50)
Number of prior systemic therapies, median (range)†	3 (0–5)
Number of prior systemic therapies, n (%)	
0	1 (7)
1	4 (29)
2	2 (14)
≥3	7 (50)

Dosing
- Larotrectinib, 100 mg BID continuously
- 28-day cycles

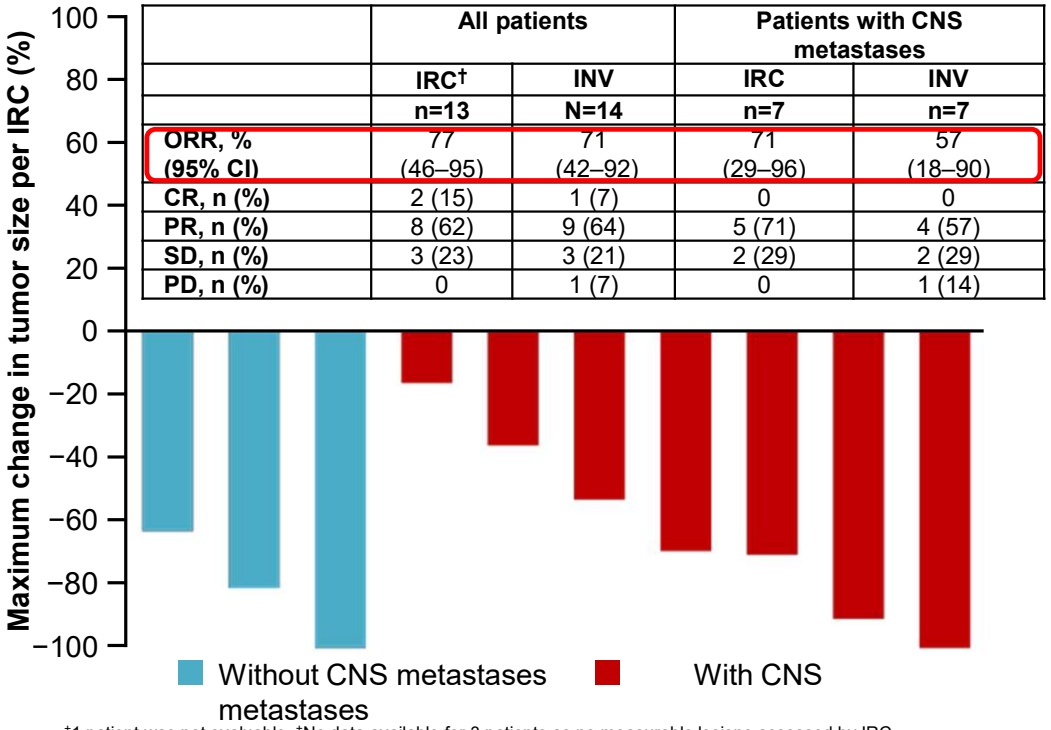
Endpoints
- **Primary**
  - Best ORR per IRC and INV (RECIST v1.1)
- **Secondary**
  - DoR
  - PFS
  - OS
  - Safety

Data cut-off: July 15, 2019

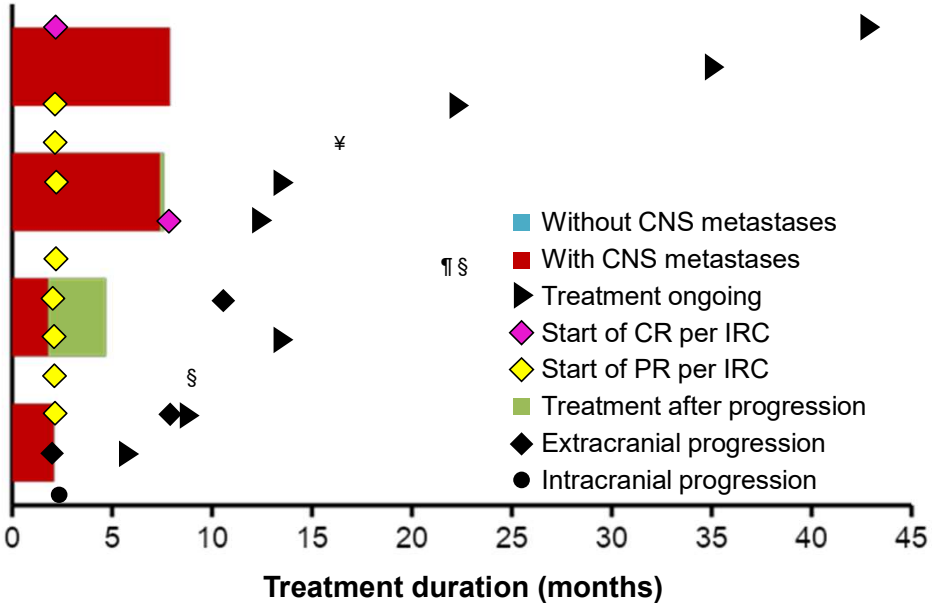
†Median prior systemic therapies for CNS metastases patients = 1 (range 0–4). The best overall response to prior therapy was PR in two patients, SD in two patients and PD in one patient. Responses were unavailable for two patients.
BID, twice daily; CNS, central nervous system; DoR, duration of response; INV, investigator; IRC, independent review committee; *NTRK*, neurotrophic tyrosine receptor kinase; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; RECIST, response evaluation criteria in solid tumors; SD, stable disease; TRK, tropomyosin receptor kinase.

Best Response to Larotrectinib per IRC‡

	All patients		Patients with CNS metastases	
	IRC†	INV	IRC	INV
	n=13	N=14	n=7	n=7
ORR, % (95% CI)	77 (46–95)	71 (42–92)	71 (29–96)	57 (18–90)
CR, n (%)	2 (15)	1 (7)	0	0
PR, n (%)	8 (62)	9 (64)	5 (71)	4 (57)
SD, n (%)	3 (23)	3 (21)	2 (29)	2 (29)
PD, n (%)	0	1 (7)	0	1 (14)



Treatment Duration



- Duration of treatment: 2.1 to 39.6+ months
- Treatment ongoing in 9 (64%) patients at data cut-off, including 3 of 7 patients with CNS metastases
- Median time to response was 1.8 months (range: 1.7–7.3)

†1 patient was not evaluable. ‡No data available for 3 patients as no measurable lesions assessed by IRC.
¶Patient had 100% reduction in CNS lesions. §Patient discontinued at the physician's decision. ¥Patient discontinued due to protocol deviation.
CI, confidence interval; CNS, central nervous system; CR, complete response; INV, investigator; IRC, independent review committee; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

TRIDENT-1 Study Design and Early Interim Phase 2 Data as of August 2020

ROS1+ Advanced NSCLC				*NTRK*+ Advanced Solid Tumors	
EXP-1 ROS1 TKI naïve (n=55)	**EXP-2** 1 prior ROS1 TKI AND 1 platinum-based chemotherapy (n=60)	**EXP-3** 2 prior ROS1 TKIs AND No prior chemotherapy (n=40)	**EXP-4** 1 prior ROS1 TKI AND No prior chemotherapy (n=60)	**EXP-5** TRK TKI naïve (n=55)	**EXP-6** TRK TKI pretreated (n=40)
ORR **86% (6/7)** 95% CI, 42–100	**ORR** **40% (2/5)** 95% CI, 5–85	**ORR** **40% (2/5)** 95% CI, 5–85	**ORR** **67% (4/6)** 95% CI, 22–96	**Not Reported**	**ORR** **50% (3/6)** 95% CI, 12–88

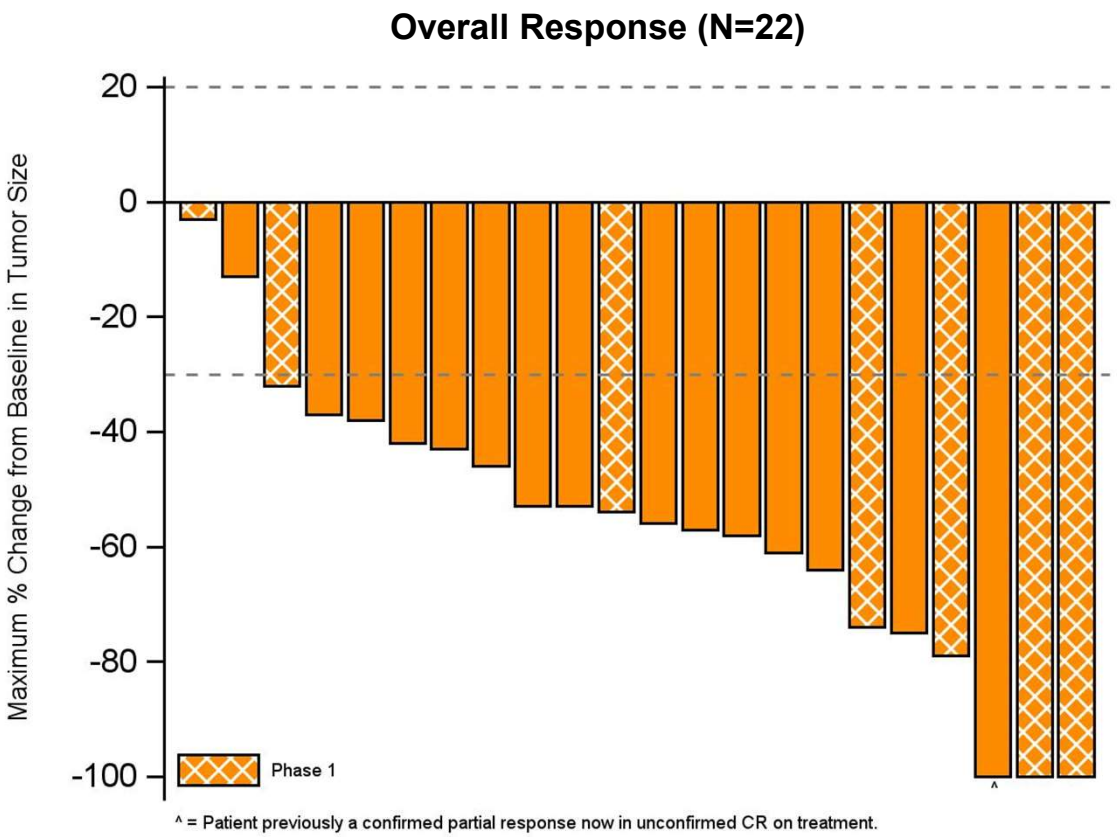
Today's presentation will focus on UPDATED Phase 2 EXP-1 data (N=15) utilizing a data cutoff of 31 December 2020:
- Median age 58 (range 30-76); ECOG PS 1 = 60%; Prior Chemotherapy Use = 20%

Previously reported Phase 1 *ROS1*+ TKI-Naïve results (N=11) based on data cutoff by BICR of 22 July 2019:

- ORR: 91% (10/11) (95% CI: 59 – 100)
  - ORR 86% (6/7) at or above the Phase 2 recommended dose
- Median DOR (95% CI): 23.1 months (5.6 - NR)
- Median PFS (95% CI): 24.6 months (7.2 - NR)

Phase 2 data cut-off date December 31, 2020, responses confirmed by investigator assessment. Phase 1 data cut-off date July 22, 2019 responses confirmed by BICR, and December 31, 2020 for duration of treatment. Phase 1 data includes only patients treated at or above repotrectinib RP2D.
BICR, blinded independent central review; CI, confidence interval; DOR, duration of response; EXP, expansion; NR, not reached; NSCLC, non-small cell lung cancer; ORR, overall response rate; PFS, progression-free survival; RP2D, recommended Phase 2 dose; TKI, tyrosine kinase inhibitor

Clinical Activity in *ROS1*+ TKI Naïve Advanced NSCLC Patients



	Phase 2 N=15	Phase 1+2 N=22
Confirmed ORR, % (95% CI)	93% (68–100)	91% (71–99)

N=22 patients with baseline and at least two post baseline scans
- *N=15 Phase 2 patients*
- *N=7 Phase 1 patients treated at or above the Phase 2 recommended dose*

As of 31 December 2020, the 16th patient in Phase 2 has an unconfirmed PR and is on treatment awaiting a second post-baseline confirmatory scan.

cORR, confirmed overall response rate; ORR, overall response rate.