#IASLCUPDATES

Iniciativa científica de:

GECP lung cancer research

LUNG CANCER UPDATES

IASLC HIGHLIGHTS

7-10 DE SEPTIEMBRE 2019

Con la colaboración de:

Bristol-Myers Squibb

illumina

Lilly

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BARCELONA
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Targeted Therapies

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Hospital Universitario A Coruña, INIBIC

Con la colaboración de:
Bristol-Myers Squibb
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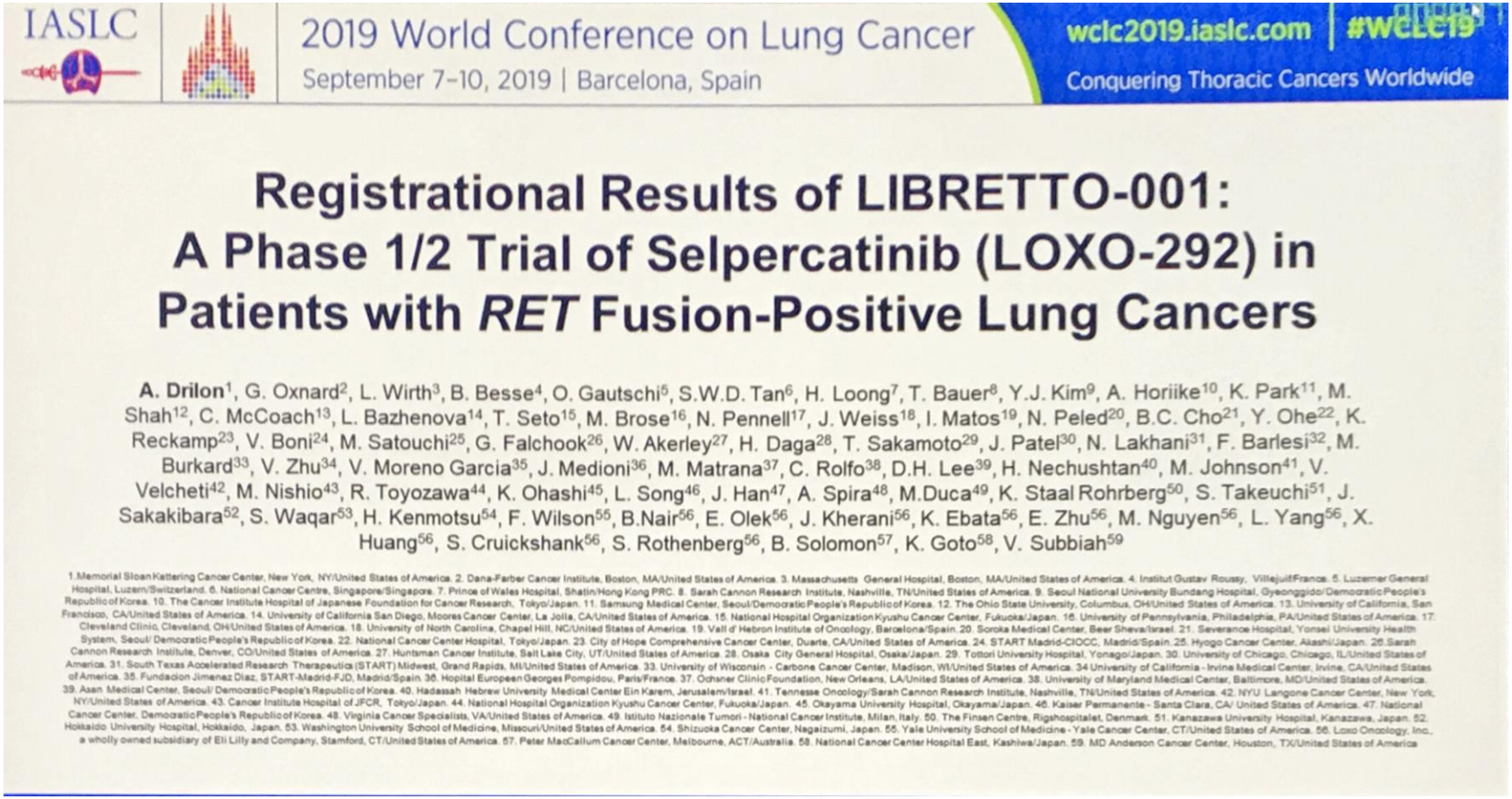
PL02.08 – Registrational Results of LIBRETTO-001: A Phase 1/2 Trial of LOXO-292 in Patients with RET Fusion-Positive Lung Cancers



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2019 World Conference on Lung Cancer
September 7–10, 2019 | Barcelona, Spain

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Conquering Thoracic Cancers Worldwide

Registrational Results of LIBRETTO-001: A Phase 1/2 Trial of Selpercatinib (LOXO-292) in Patients with *RET* Fusion-Positive Lung Cancers

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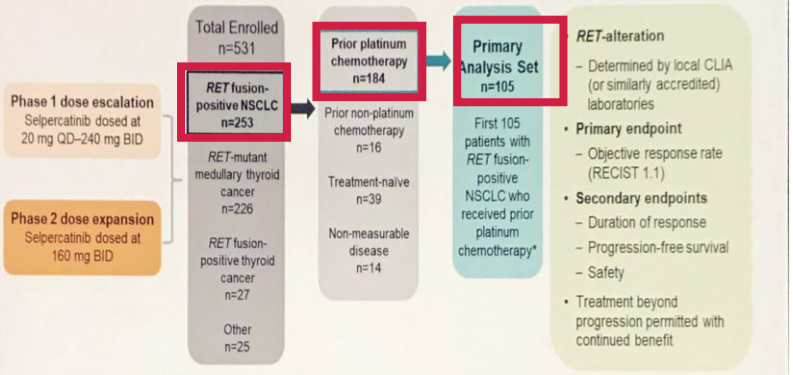
LIBRETTO-001: Selpercatinib in *RET*-altered cancers



NCT03157128; Data cutoff: June 17th, 2019. *Per agreement with FDA, patients with non-measurable disease enrolled during phase 1 dose escalation were eligible for the primary analysis set.

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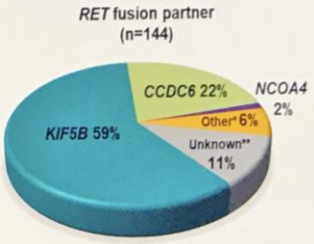
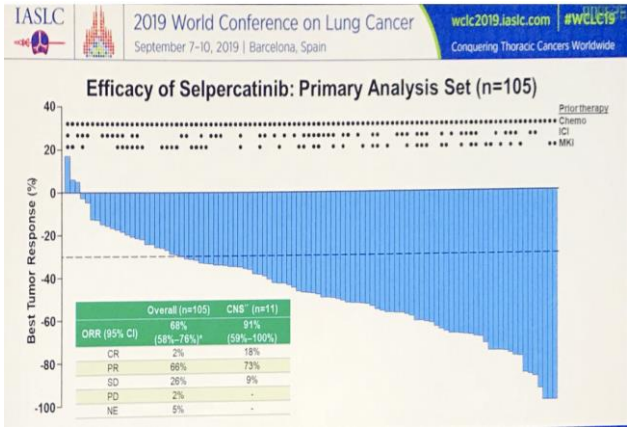
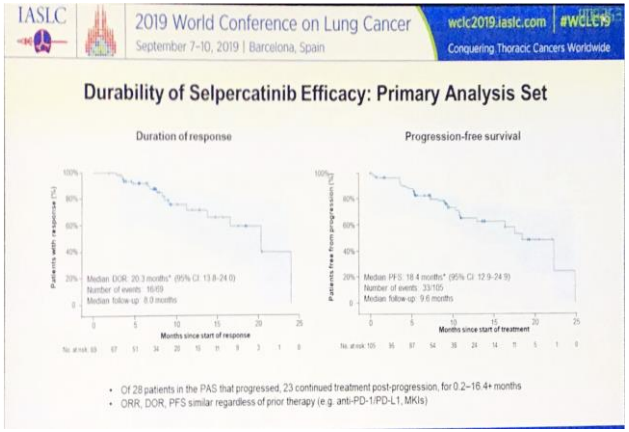
Patient Characteristics	PAS (n=105)	Treatment-naive (n=39)
Female / Male, n (%)	62 (59) / 43 (41)	22 (56) / 17 (44)
Median age (range), years	61 (23–81)	61 (23–86)
ECOG performance status, n (%)		
0	31 (30)	19 (49)
1	72 (69)	20 (51)
2	2 (2)	0
Median prior systemic regimens (range)	3 (1–15)	0
Prior platinum-based chemotherapy, n (%)	105 (100)	-
Prior PD-1/PD-L1 inhibitor, n (%)	58 (55)	-
Concurrent with platinum-based chemotherapy	9 (9)	-
Sequential to platinum-based chemotherapy	49 (47)	-
Prior multikinase inhibitor (MKI), n (%)	50 (48)	-
1	37 (35)	-
≥2	13 (12)	-
Brain metastases, n (%)‡	37 (35)	7 (18)
Measurable disease	104 (99)	39 (100)

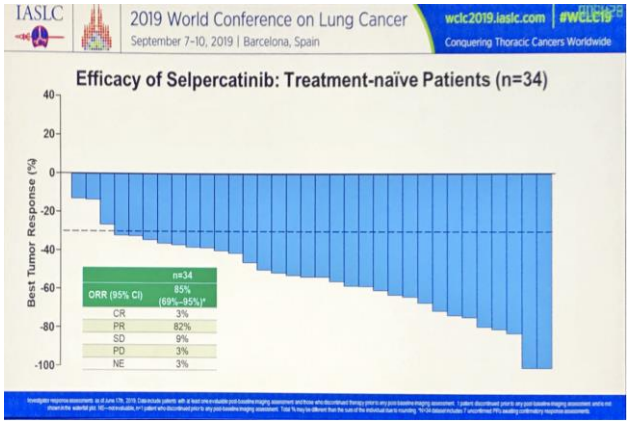


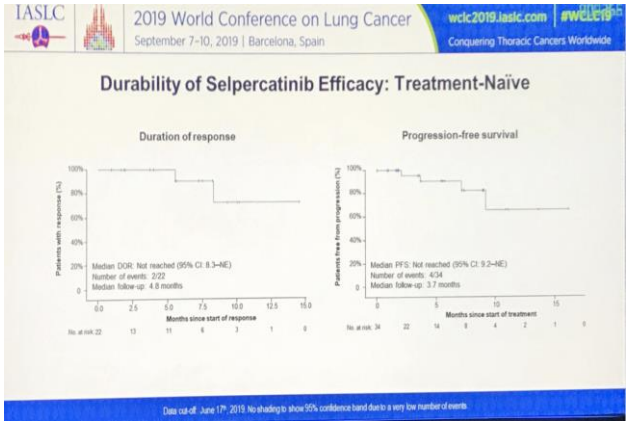
Data cut-off: June 17th, 2019. Total % may be different than the sum of the individual components due to rounding. *Includes KIAA1468 (2), ARHGAP12, CCDC88C, CLIP1, DOCK1 + RBPMS, ERC1, PRKAR1A and TRIM24 (all 1 each). **FISH-positive or PCR-positive; ‡Includes patients with non-target CNS metastases.





Prior Platinum doublet (n=105)
ORR 68%
CNS ORR 91%
mDoR 20.3m
mPFS 18.4m





Treatment Naive (n=34)
ORR 85%
DoR NR
PFS. NR

Drilon A, et al. PL02.08

Is a fase III trial the way to move forward?

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Phase III trials for oncogene targeted therapies – do we need them?

TARGETED THERAPIES

Time to shift the burden of proof for oncogene-positive cancer?

Robert C. Doebele

"...burden of proof for approval should be adjusted for oncogene-targeted therapy..."

→ "ORR 40-50%
PFS 5-6 months"

"Moving forward, do we still need to run randomized phase III trials of oncogene-directed therapies against standard chemotherapy drugs?"[1]

Study	ORR	PFS (mos.)
1L		
LIBRETTO (n=34)[2]	85%	NR
AURA3[3]	31%	4.2
PF1014[4]	45%	7.0
KN189[5]	47.6%	8.8
IMpower150[6]	63.5%	8.3
GLORY (plat-doublet)[7]	51%	7.8
2L (or beyond)		
LIBRETTO (n=105)[2]	68%	18.4
PF1007 (doc or pem)[8]	20%	3.0
REVEL[9] - doc/ram	23%	4.5
- docetaxel	14%	3.0

[1]Doebele Nat Rev Clin Onc 2013 [2]Drilon et al., WCLC 2019; [3]Mok et al., NEJM 2017; [4]Solomon et al., NEJM 201 ; [5]Ghandi et al., NEJM 2018 ; [6]Socinski et al., NEJM 2018; [7]Gautschi et al., JCO 2017 [8]Shaw et al., NEJM 2013; [9]Garon et al., Lancet 2014

MA14.02 – Entrectinib in Patients with ROS1- Positive NSCLC or NTRK Fusion-Positive Solid Tumors with CNS Metastases

BACKGROUND AND INTEGRATED ANALYSIS DESIGN

Efficacy population (data cut-off: May 2018)
Adult patients with metastatic *NTRK* fusion-positive solid tumors or *ROS1* fusion-positive NSCLC
N=54 (*NTRK*) / N=53 (*ROS1*)

ALKA-372-001
Phase I, dose-escalation study
NTRK / *ROS1*
fusion-positive tumors
n=1 / n=9

STARTRK-1
Phase I, dose-escalation study
NTRK / *ROS1*
fusion-positive tumors
n=2 / n=7

STARTRK-2
Phase II, multicenter, global basket study
NTRK / *ROS1*
fusion-positive tumors
n=51 / n=37

Safety population
Patients receiving entrectinib (all tumor types and gene rearrangements)
N=355*

Primary endpoints†
- ORR
- DoR

Secondary endpoints
- PFS† and OS
- **Intracranial ORR† and DoR†**
- **Time to CNS progression†**
- Safety and tolerability

BASELINE CHARACTERISTICS AS REPORTED BY INVESTIGATOR

Baseline characteristics (investigator-assessed)	*NTRK*+ solid tumors (N=54)	*ROS1*+ NSCLC (N=53)
Baseline CNS lesions, n (%)		
Measurable	2 (3.7)	5 (9.4)
Non-measurable	10 (18.5)	18 (34.0)
All	12 (22.2)	23 (43.4)
Time from end of prior RT to first dose, n (%)	N=7 with prior RT	N=15 with prior RT
<2 months	2 (28.6)	9 (60.0)
2 to <6 months	4 (57.1)	2 (13.3)
≥6 months	1 (14.3)	4 (26.7)

Iniciativa científica de: GeCP lung cancer research

Paz-Ares L, et al. MA 14.02

ENTRECTINIB INDUCED CLINICALLY MEANINGFUL DURABLE INTRACRANIAL RESPONSES AS ASSESSED BY BICR

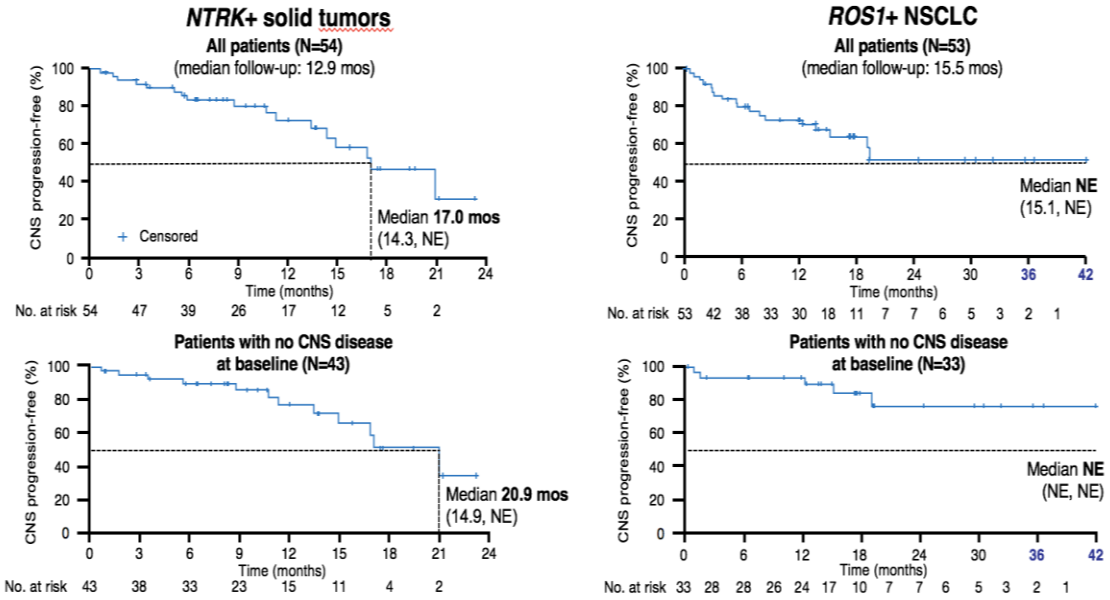
	NTRK+ solid tumors (N=54)			*ROS1*+ NSCLC (N=53)	
	Measurable CNS disease* (n=7)	Measurable and non-measurable CNS disease* (n=11)	*NTRK*+ NSCLC (N=10): Measurable and non-measurable CNS disease* (n=6†)	Measurable CNS disease* (n=12)	Measurable and non-measurable CNS disease* (n=20)
Intracranial ORR, % (95% CI)	57.1 (18.4, 90.1)	54.5 (23.4, 83.3)	66.7	75.0 (42.8, 94.5)	55.0 (31.5, 76.9)
Responders (CR or PR), n	4	6	4	9	11
Median intracranial DoR, months (95% CI)	NE (5.0, NE)	NE (5.0, NE)	NE	12.9 (4.6, NE)	12.9 (5.6, NE)
Responders with progression, n (%)	1 (25.0)	2 (33.3)	—	4 (44.4)	5 (45.5)
Median intracranial PFS, months (95% CI)	NE (2.8, NE)	14.3 (5.1, NE)	—	19.3 (3.8, 19.3)	7.7 (3.8, 19.3)
Patients with progression, n (%)	3 (42.9)	5 (45.5)	—	6 (50.0)	13 (65.0)

*CNS disease at baseline assessed by investigator and confirmed by BICR; †Five patients with measurable disease

Ic ORR 67% in *NTRK*+ NSCLC
ic ORR 55% *ROS1* fusion+ NSCLC

Paz-Ares L, et al. MA 14.02

ENTRECTINIB WAS ASSOCIATED WITH A LONG MEDIAN TIME TO CNS PROGRESSION



- The use of a CNS-penetrant drug such as entrectinib has the potential to provide CNS protection in patients:
  - with existing brain lesions
  - without existing brain lesions