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Continuation of Selpercatinib Beyond Progression in *RET* Fusion-Positive NSCLC: Data from LIBRETTO-001 Study

Alexander Drilon[1], Jason Chan[2], Jacob Sands[3], Daniel Tan[4], Jared Weiss[5], Ben Solomon[6], Yu Jung Kim[7], Melissa Johnson[8], Tarun Puri[9], Maria Anna Sarno[9], Suhyun Kang[9], Victoria Soldatenkova[9], Chi-Wei Duann[9], Sylwia Szymczak[9], Vivek Subbiah[10], Benjamin Besse[11]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]University of California San Francisco, San Francisco, CA, USA; [3]Dana-Faber Cancer Institute, Boston, MA, USA; [4]National Cancer Centre Singapore, Singapore; [5]Lineberger Comprehensive Cancer Center at the University of North Carolina, Chapel Hill, NC, USA; [6]Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; [7]Seoul National University Bundang Hospital, Seongnam, Republic of Korea; [8]Sarah Cannon Research Institute, Nashville, TN, USA; [9]Eli Lilly and Company, Indianapolis, IN, USA, [10]MD Anderson Cancer Center, Houston, TX, USA; [11]Gustave Roussy, Villejuif, France

Background

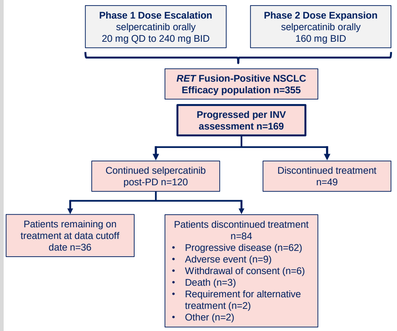
- **Selpercatinib, a first-in-class highly selective RET kinase inhibitor[1] with central nervous system (CNS) activity[2], is approved in various regions for patients with *RET* fusion-positive NSCLC**
- ***RET* fusions are a driver alteration in 1~2% of NSCLC patients[3]**
- **Selpercatinib has demonstrated clinically meaningful and durable antitumor activity with a favorable safety profile in patients with advanced or metastatic *RET* fusion-positive NSCLC in the ongoing phase 1/2 LIBRETTO-001 trial[4]**
- **Patients treated in the phase 1/2 LIBRETTO-001 trial were permitted to continue selpercatinib beyond progressive disease (PD) if the patient derived ongoing benefit**

Objective

- **Here we present an exploratory posthoc analysis of safety and efficacy outcomes in a subset of NSCLC patients (n=120) continuing selpercatinib beyond PD per investigator assessment**

STUDY DESIGN

The Phase 1/2 LIBRETTO-001 Trial: Selpercatinib in Patients with *RET*-altered Cancers



Study Design
- Patients were permitted to continue selpercatinib beyond PD if the patient was deriving ongoing benefit according to the investigator (INV)
- Outcomes were retrospectively analyzed using a data cut of 15-Jun-21

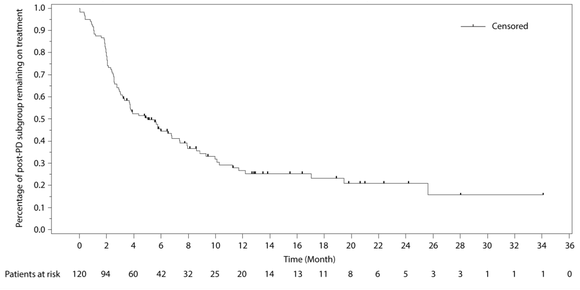
Primary Endpoint
- Time on treatment post-progression

Secondary Endpoints Included
- Safety
- Frequency of local therapy

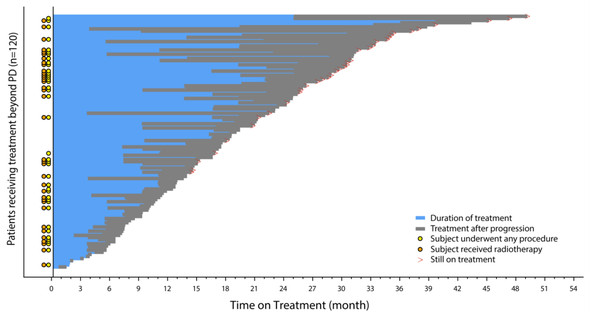
Efficacy population includes all patients enrolled 6 months prior to data cutoff date.

Duration of Treatment in the Post-PD Subgroup

- The median duration of treatment (DOT) prior to PD was 10.9 months (range 0.6-39.5)
- The median DOT post-PD was 5.0 months (range 0.0-34.1+)
- 45% of patients remained on treatment at 6 months post-PD



Swimmer Plot of Duration of Treatment, Including Treatment Post-Progression



Swimmer plot of treatment based on investigator assessments

Baseline Disease Characteristics

- Baseline characteristics were similar between the NSCLC efficacy population (n=355) and the subset of post-PD patients (n=120)
- Post-PD subgroup had a higher rate of baseline CNS metastases

Analysis sets	NSCLC efficacy population (n=355)	Post-PD subgroup (n=120)
Age – Median (range) in years	61.0 (23-92)	62.0 (23-87)
Sex, n (%)		
Male	152 (42.8)	47 (39.2)
Female	203 (57.2)	73 (60.8)
ECOG performance-status score, n (%)		
0	131 (36.9)	38 (31.7)
1	212 (59.7)	76 (63.3)
2	12 (3.4)	6 (5.0)
Smoking history, n (%)		
Never smoker	241 (67.9)	82 (68.3)
Former smoker	108 (30.4)	35 (29.2)
Current smoker	6 (1.7)	3 (2.5)
RET fusion partner, n (%)		
KIF5B	227 (63.9)	87 (72.5)
CCDC6	71 (20.0)	16 (13.3)
Other	19 (5.4)	8 (6.7)
Prior platinum chemotherapy	247 (69.6)	86 (71.7)
Treatment-naïve	69 (19.4)	22 (18.3)
Baseline CNS metastases, n (%)		
Yes	106 (29.9)	51 (42.5)
No	249 (70.1)	69 (57.5)

Baseline disease characteristics in the *RET* fusion-positive NSCLC efficacy population and post-PD subgroup.

Adverse Events

- No unique safety signals were observed with treatment beyond progression

	NSCLC safety population (n=356)		Post-PD subgroup before PD date (n=120)		Post-PD subgroup after PD date (n=120)	
Preferred or Composite Term	**Any Grade**	**Grade ≥3**	**Any Grade**	**Grade ≥3**	**Any Grade**	**Grade ≥3**
Diarrhea	184 (51.7)	15 (4.2)	48 (40.0)	4 (3.3)	19 (15.8)	2 (1.7)
Edema	178 (50.0)	2 (0.6)	53 (44.2)	0 (0.0)	28 (23.3)	0 (0.0)
Dry mouth	163 (45.8)	0 (0.0)	52 (43.3)	0 (0.0)	6 (5.0)	0 (0.0)
Fatigue	153 (43.0)	8 (2.2)	51 (42.5)	1 (0.8)	30 (25.0)	1 (0.8)
Aspartate aminotransferase increased	149 (41.9)	37 (10.4)	41 (34.2)	12 (10.0)	16 (3.3)	4 (3.3)
Alanine aminotransferase increased	147 (41.3)	53 (14.9)	40 (33.3)	17 (14.2)	12 (10.0)	2 (1.7)
Hypertension (AESI)	141 (39.6)	68 (19.1)	41 (34.2)	20 (16.7)	7 (5.8)	4 (3.3)
Rash	130 (36.5)	4 (1.1)	36 (30.0)	2 (1.7)	9 (7.5)	0 (0.0)
Nausea	112 (31.5)	4 (1.1)	22 (18.3)	0 (0.0)	22 (18.3)	0 (0.0)
Abdominal pain	101 (28.4)	5 (1.4)	24 (20.0)	0 (0.0)	13 (10.8)	2 (1.7)
Constipation	96 (27.0)	5 (1.4)	28 (23.3)	0 (0.0)	15 (12.5)	1 (0.8)
Headache	94 (26.4)	3 (0.8)	30 (25.0)	1 (0.8)	9 (7.5)	0 (0.0)
Blood creatinine increased	92 (25.8)	10 (2.8)	16 (13.3)	0 (0.0)	6 (5.0)	2 (1.7)
Cough	87 (24.4)	0 (0.0)	29 (24.2)	0 (0.0)	11 (9.2)	0 (0.0)
Dyspnea	84 (23.6)	16 (4.5)	28 (23.3)	1 (0.8)	17 (14.2)	1 (0.8)
Pyrexia	79 (22.2)	1 (0.3)	18 (15.0)	1 (0.8)	7 (5.8)	0 (0.0)
Vomitting	78 (21.9)	4 (1.1)	16 (13.3)	0 (0.0)	10 (8.3)	0 (0.0)
ECG QT prolongation (AESI)	74 (20.8)	21 (5.9)	19 (15.8)	3 (2.5)	11 (9.2)	2 (1.7)
Thrombocytopenia	74 (20.8)	20 (5.6)	21 (17.5)	5 (4.2)	7 (5.8)	3 (2.5)
Decrease appetite	73 (20.5)	1 (0.3)	20 (16.7)	0 (0.0)	16 (13.3)	0 (0.0)

Treatment-Emergent Adverse Events of any Grade occurring in ≥ 20% of patients. The component preferred terms comprising each composite term are shown in italics. NSCLC safety population (n=356) includes all patients with *RET*-fusion positive NSCLC who received at least one or more doses of selpercatinib. The table presents adverse events in the 120 patients before and after PD.

Patients Receiving Localized Treatment

- Of the 120 patients who continued selpercatinib beyond progression, 40 patients received localized treatment for progressing lesions
  - Median time on treatment post-PD for the 40 patients was 5.4 months (0.0-25.6)
  - Includes 36 patients who received radiotherapy (RT), of whom 12 patients received brain RT
- Median time on treatment post-PD for the 84 patients who did not receive RT was 3.56 months (0.0-34.1)

Conclusions

- A subset of patients with *RET* fusion-positive NSCLC appear to have derived ongoing clinical benefit from continuing selpercatinib treatment beyond PD
- The exact magnitude could not be determined in this exploratory posthoc analysis
- Duration of post-progression therapy appeared longer in patients who received localized therapy to progressive lesion. A formal analysis of outcomes in patients who had widespread progression versus oligometastatic or solitary site progression is ongoing
- There were no new safety signals associated with treatment beyond progression

Acknowledgments: We would like to thank the Clinical Trial participants and their caregivers, without whom this work would not be possible. Medical writing support was provided by James Hegarty, an employee of Eli Lilly and Company.

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2. **Subbiah V., et .al., *Clin Cancer Res* 2021**
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4. **Drilon A., et. al., *NEJM* 2020**

Disclosures: served on honoraria/advisory boards for Ignyta/Genentech/Roche, Loxo/Bayer/Lilly, Takeda/Ariad/Millenium, TP Therapeutics, AstraZeneca, Pfizer, Blueprint Medicines, Helsinn, Beigene, BergenBio, Hengrui Therapeutics, Exelixis, Tyra Biosciences, Verastem, MORE Health, Abbvie, 14ner/Elevation Oncology, ArcherDX, Monopteros, Novartis, EMD Serono, Medendi, Repare RX, Nuvalent, Merus, Chugai Pharmaceutical, Remedica Ltd , mBrace, AXIS, EPG Health, Harborside Nexus, Liberum, RV More, Ology, Amgen, TouchIME, Janssen, Entos, Treeline Bio, Prelude, Applied Pharmaceutical Science, Inc, AiCME, i3 Health, and MonteRosa; associated research paid to institution from Pfizer, Exelixis, GlaxoSmithKlein, Teva, Taiho, and PharmaMar; received royalties from Wolters Kluwer; CME honoraria included the following Medscape, OncLive, PeerVoice, Physicians Education Resources, Targeted Oncology, Research to Practice, Axis, Peerview Institute, Paradigm Medical Communications, WebMD, MJH Life Sciences, Med Learning, Imedex, Answers in CME, Clinical Care Options, EPG Health, JNCC/Harborside, Liberum, and Remedica Ltd; Equity in Treeline Bio; Copyright: Selpercatinib-Osimertinib (filed/pending).
Other: Merck, Puma, Merus, and Boehringer Ingelheim.

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drilona@mskcc.org

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