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Intracranial efficacy of selpercatinib in *RET* fusion-positive non-small cell lung cancers on the LIBRETTO-001 trial

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CONFLICT OF INTEREST STATEMENT

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TRANSLATIONAL RELEVANCE

Brain metastases frequently occur in *RET* fusion-positive non-small cell lung cancers (NSCLCs), with an approximate 50% lifetime prevalence reported. Intracranial metastases are a major cause of morbidity and mortality in this patient population. Thus, there is a need for novel RET-directed, targeted therapy strategies with high efficacy. Selpercatinib, a selective and potent RET inhibitor, shows compelling preliminary evidence of activity in patients with brain metastases. This phase 1/2 trial (LIBRETTO-001) evaluated the efficacy and safety of selpercatinib in patients with *RET* fusion-positive NSCLCs with intracranial metastases. In this study, selpercatinib was well tolerated, achieving high intracranial response rate, and prolonged intracranial duration of response and intracranial progression-free survival. Combined, these results support selpercatinib as a new standard of care therapy for the primary treatment of brain metastases for patients with *RET* fusion-positive NSCLC.

ABSTRACT

Purpose: We report the intracranial efficacy of selpercatinib, a highly potent and selective RET inhibitor, approved in the US for *RET* fusion-positive non-small cell lung cancers (NSCLCs).

Methods: In the global phase 1/2 LIBRETTO-001 trial (NCT03157128) in advanced *RET*-altered solid tumors, selpercatinib was dosed orally (160mg twice/day) in 28-day cycles. Patients with baseline intracranial metastases had MRI/CT scans every 8-weeks for 1 year (12-weeks thereafter). In this pre-planned analysis of *RET* fusion-positive NSCLC patients with baseline intracranial metastases, the primary endpoint was independently-assessed intracranial objective response rate (ORR) per RECIST 1.1. Secondary endpoints included intracranial disease control rate, intracranial duration of response, and intracranial progression-free survival (PFS) independently reviewed.

Results: Eighty NSCLC patients had brain metastases at baseline. Patients were heavily pretreated (median=2 systemic therapies, range=0–10); 56% of patients received ≥1 course of intracranial radiation (14% whole brain radiotherapy, 45% stereotactic radiosurgery). Among 22 patients with measurable intracranial disease at baseline, intracranial ORR was 82% (95%CI=60–95), including 23% with complete responses. Among all intracranial responders (measurable and non-measurable, n=38), median duration of intracranial response was not reached (95%CI=9.3–NE) at a median duration of follow-up of 9.5 months (IQR=5.7,12.0). At 12 months, 55% of intracranial responses were ongoing. In all 80 patients, median intracranial PFS was 13.7 months (95%CI=10.9-NE) at a median duration of follow-up of 11.0 months (IQR=7.4,16.5). No new safety signals were revealed in patients with brain metastases compared to the full NSCLC trial population.

Conclusion: Selpercatinib has robust and durable intracranial efficacy in *RET* fusion-positive NSCLC patients.

INTRODUCTION

The *RET* (rearranged during transfection) proto-oncogene encodes the RET receptor tyrosine kinase, a transmembrane glycoprotein that is involved in the development and maintenance of several tissue types.[1] Activating *RET* alterations, such as recurrent gene fusions, lead to ligand-independent, constitutively active RET tyrosine kinase signaling that drives oncogenesis and tumor progression.[2-4] Oncogenic *RET* fusions are found in 1-2% of non-small cell lung cancers (NSCLCs).[5,6] A global multi-institutional registry of patients with *RET* fusion-positive NSCLC found that approximately half of these patients develop brain metastases during their lifetime;[7] leptomeningeal disease has also been observed.[8]

Intracranial sanctuary site metastasis is a liability shared by many other oncogene-addicted cancers, including *EGFR*-mutant or *ALK* fusion-positive NSCLCs. A major advance in the management of these tumors has been the development of brain-penetrant tyrosine-kinase inhibitors.[9,10] These agents not only prevent or delay intracranial treatment failure, but are also increasingly utilized as primary therapy for patients with brain metastases instead of localized interventions such as radiotherapy, an intervention potentially associated with long-term quality of life impairment.[11]

Selpercatinib (LOXO-292), a highly potent and selective RET inhibitor, has marked and durable efficacy in patients with treatment-naïve or platinum chemotherapy-treated *RET* fusion-positive NSCLCs.[12] Based on these data, selpercatinib has received approval in the US for any line of therapy of *RET* fusion-positive metastatic NSCLCs, and is the first RET-selective inhibitor granted EU approval.[13,14] Given that several *RET* fusion-positive cancers harbor a proclivity for intracranial metastasis, selpercatinib was specifically designed to achieve levels in the central nervous system (CNS) necessary to inhibit RET. Consistently,

selpercatinib demonstrated robust intracranial efficacy in orthotopically implanted *RET* fusion-positive tumors in mice.[15]

Preclinical observations, anecdotal case reports [8,15] and preliminary experience from a prospective clinical trial [7] suggest that selpercatinib is active in patients with brain metastases. To date, however, the true intracranial efficacy of selpercatinib in a large prospective series of *RET* fusion-positive NSCLCs remains unknown. To address this key evidence gap, we conducted a pre-planned analysis of selpercatinib in patents with *RET* fusion-positive NSCLC and brain metastases enrolled to the global phase 1/2 LIBRETTO-001 trial (NCT03157128).

METHODS

Study design and treatment

LIBRETTO-001 is an ongoing, global, first-in-human, open label, phase 1/2 clinical trial (ClinicalTrials.gov NCT03157128) open at 89 investigative sites in 16 countries. A total of 31 sites from 11 countries enrolled at least one patient with a *RET* fusion-positive NSCLC and investigator-assessed brain metastases at baseline in the analysis dataset used here. Full details of the trial design have been published.[12] Briefly, patients eligible for this pre-planned analysis were required to meet the following inclusion criteria: age ≥12 years; presence of a prospectively-identified *RET* fusion as determined by locally-obtained testing performed in a certified laboratory; ECOG performance status 0–2; adequate organ function; and a QTc interval of ≤470 msec. Any number of prior therapies were permitted. Brain imaging was a requirement at baseline for all *RET* fusion-positive solid tumor NSCLC patients. Magnetic resonance imaging (MRI) was preferred; computerized tomography (CT) with contrast was acceptable if MRI was contraindicated. Patients with known brain metastases were eligible

for the trial if neurological symptoms and CNS imaging were stable and their steroid dose was stable for 14 days prior to the first dose of selpercatinib, and no CNS surgery or radiation had been performed for 28 days (14 days for stereotactic radiosurgery/SRS) prior to dosing. All prior local treatments for CNS disease (e.g., surgery, whole brain radiation, SRS), the start and stop dates for each prior local therapy, and the specific lesions treated (if SRS and/or surgery) were recorded. For patients who had received CNS radiation prior to the trial, intracranial lesions needed to show post-radiation progression to be selected as a target lesion at baseline.

This protocol adhered to the principles of the Declaration of Helsinki and the Good Clinical Practice Guidelines of the International Conference on Harmonization. The institutional review board of each investigative site approved the trial, and all patients provided written informed consent.

Selpercatinib doses ranged from 20 mg once daily to 240 mg twice daily for patients enrolled in the phase 1 dose escalation portion of the study. Dose escalation to dose levels determined to be safe was allowed for phase 1 patients after a minimum of 1 cycle of treatment. In the phase 2 portion of the study, selpercatinib was dosed orally at 160 mg twice daily (BID) in 28-day continuous cycles. Treatment continued until death, progressive disease, unacceptable toxicity, or withdrawal of consent. Patients could continue selpercatinib treatment after documented progression if they were continuing to derive clinical benefit in the opinion of the investigator.

The main efficacy endpoint for the current analysis was intracranial objective response rate (ORR) by RECIST 1.1 [16] determined by an independent review committee (IRC), a pre-

planned secondary endpoint for the overall LIBRETTO-001 program. The IRC was composed of expert radiologists who were blinded to investigator-determined systemic response. IRC radiologists were provided with prior or on-study radiation information and a history of all prior treatments for CNS disease. Intracranial ORR (%) was defined as the proportion of patients with a best overall intracranial response of complete response (CR) or partial response (PR) relative to the total number of patients with baseline intracranial disease. All responses were required to be confirmed by a repeat assessment performed no sooner than 28 days later. Intracranial disease control rate (DCR) was defined as the percentage of patients who had a best overall intracranial response of CR, PR, or stable disease (SD) lasting 16 weeks or more after selpercatinib initiation. Consistent with RECIST 1.1, patients with exclusively non-measurable intracranial disease at baseline could be classified for best overall response as CR (in the case where all non-measurable lesions resolved), progressive disease (PD), or non-CR/non-PD. Another pre-specified secondary endpoint was intracranial duration of response (DoR) as determined by IRC, defined as the time from start of an intracranial response until intracranial progression or death, regardless of cause. Intracranial progression-free survival (PFS) was an exploratory endpoint defined as the time from treatment start to intracranial disease progression as assessed by IRC or death from any cause. Extracranial progression was not included in the intracranial PFS assessment. Safety was another exploratory endpoint for the population with NSCLC and intracranial metastases.

Trial Assessments

Radiological tumor assessments (MRI, preferentially; computerized tomography CT, with and without intravenous contrast when MRI was clinically contraindicated) were conducted at baseline for all phase 2 *RET* fusion-positive solid tumor NSCLC patients. Repeat brain

imaging using the same modality as at baseline was conducted for all patients with brain metastases identified by baseline imaging every 8 weeks for 1 year, and every 12 weeks thereafter. Safety was assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events (version 4.03). [17]

Statistical Analysis

All analyses were pre-specified in the Statistical Analysis Plan. The Clopper-Pearson method was used to construct 95% CIs for response rates. Kaplan-Meier method was used to estimate median for intracranial DoR and PFS. Median follow up was calculated using the reverse Kaplan Meier method, i.e. median follow up is calculated like the Kaplan-Meier estimate of the survival function, but with the meaning of the status indicator reversed so that the event of interest becomes the censor. SAS statistical software, version 9.2 (SAS Institute, Cary, NC) was used to perform all analyses.

Data Sharing

Eli Lilly and Company provides access to all individual participant data collected during the trial, after anonymization, with the exception of pharmacokinetic or genetic data. Data are available to request 6 months after the indication studied has been approved in the USA and EU and after primary publication acceptance, whichever is later. No expiration date of data requests is currently set once they are made available. Access is provided after a proposal has been approved by an independent review committee identified for this purpose and after receipt of a signed data sharing agreement. Data and documents, including the study protocol, statistical analysis plan, clinical study report, and blank or annotated case report forms will be provided in a secure data sharing environment for up to 2 years per proposal. For details on submitting a request, see the Vivli website: www.vivli.org.

RESULTS

Baseline patient characteristics and treatment

A total of 531 patients with *RET* fusion-positive cancers were enrolled to phase 1 or phase 2 of the trial between May 2017 and June 17, 2019, including 80 patients with *RET* fusion-positive NSCLC and investigator-determined baseline brain metastases (92.5% by MRI, 5% by CT, 2.5% missing) that met criteria for inclusion in the current analysis (online appendix, Figure S1). Among these 80 patients, 22 patients had at least one baseline measurable intracranial lesion and 58 had exclusively non-measurable baseline intracranial lesions.

The demographic and disease characteristics of patients with baseline brain metastases are summarized in Table 1. The median age was 62 years (range 36–86 years), and most patients had an ECOG performance status of zero or one. Consistent with previous analyses, the most common *RET* fusion partner was *KIF5B* (70% of patients). Most patients had received prior systemic therapy (91%), with a median of two prior treatments (range 0–10), including 79% of patients who were treated with platinum-based chemotherapy and 41% of patients who were treated with one or more multi-kinase inhibitors. Prior therapy for brain metastases included surgery in 9%, stereotactic radiosurgery in 45%, and whole brain radiotherapy (WBRT) in 14% of patients. Of the 45 patients who received prior cranial radiotherapy, 73% had completed this therapy at least 2 months prior to beginning selpercatinib treatment.

At the time of data cut-off, 46 of the 80 NSCLC patients with brain metastases (58%) remained on therapy with selpercatinib; 23 of the 80 patients (29%) had discontinued treatment due to progressive disease (any progressive disease, not limited to intracranial metastases progression) (online appendix, Table S1). After accounting for intra-patient dose

escalation permitted during the phase 1 portion of the trial, 95% of patients received at least one dose of selpercatinib at the recommended phase 2 dose of 160 mg twice daily.

Selpercatinib intracranial efficacy

At the time of the data cutoff, the median duration of follow-up was 9.5 months (interquartile range, IQR 5.7, 12.0 months). Among the 22 patients with measurable intracranial disease at baseline, the intracranial ORR was 82% (95% CI = 60–95), including 23% with a complete response and 59% with a partial response (Table 2, Figure 1). In addition, 18% of patients exhibited stable disease as the best response to selpercatinib. Because all the patients achieved a tumor response or disease stabilization, the intracranial disease control rate was 100%. Among the subset of eight patients with measurable disease and prior cranial radiotherapy, the intracranial ORR was 75% (six of eight patients responding, 95% CI = 35–97) (online appendix, Table S2). The intracranial ORR for patients without prior cranial radiotherapy was 86% (12 of 14 patients responding, 95% CI = 57–98).

Among the remaining 58 patients with exclusively non-measurable intracranial disease at baseline, 34% (20 of 58 patients) achieved a complete intracranial response on the basis of complete resolution of all non-measurable lesions and 29 patients had non-CR/non-PD (CR and non-CR/non-PD corresponds to the clinical benefit rate for non-measurable intracranial disease). Only five patients (9%) had progressive disease as best intracranial response (online appendix, Table S3).

Thirty-eight patients from the 80-patient population (48%) with baseline brain metastases had an intracranial response to selpercatinib. Among this group of responders, the median intracranial DoR was not reached (95% CI = 9.3, NE) (Table 3, Figure 2A) at a median

duration of follow-up of 9.5 months (IQR 5.7,12.0). Overall, 71% were censored at the time of the analysis. At 1-year, 55% (95% CI = 32–73) of intracranial responses were ongoing. Of note, the longest intracranial response was ongoing at 21.2 months. Among all 80 patients, the median intracranial PFS was 13.7 months (Table 3, Figure 2B), although this median estimate is unstable as only 30 patients (38%) had experienced an event at a median duration of follow-up of 11.0 months (IQR 7.4,16.5). Time to response and response duration are displayed in Figure 3 for all responders (n=38).

Selpercatinib safety

Among patients with NSCLC and baseline brain metastases, selpercatinib treatment was associated with a low rate of treatment discontinuation due to adverse events judged by the investigator as possibly related to selpercatinib treatment (TRAEs) (3%, two of 80 patients). Table S4 summarizes total (all grade) treatment-emergent adverse events (TEAEs) and TRAEs. TEAEs and TRAEs were reported at similar levels in patients with baseline intracranial disease as in all *RET* fusion-positive NSCLCs with and without intracranial disease (n=253).

Among patients with intracranial disease, most TEAEs and TRAEs were low grade (Table S5). The only TEAEs reported as grade 3/4 in >10% of patients with NSCLC and baseline brain metastases were alanine aminotransferase (ALT) increase (18%), aspartate aminotransferase (AST) increase (11%), hypertension (21%, all grade 3), and hyponatraemia (11%). Grade 3/4 elevated ALT and AST and hypertension were reported at similar levels as TRAEs. No Grade 5 TRAEs were reported among the patients with NSCLC and baseline brain metastases.

DISCUSSION

Intracranial metastases are a major cause of morbidity and mortality for patients with oncogene-addicted cancers. The results of this global, multicenter study demonstrate that selpercatinib has robust intracranial efficacy by blinded independent review of patients with *RET* fusion-positive NSCLCs and brain metastases. The drug achieved a high intracranial response rate and the intracranial duration of response and intracranial progression-free survival were prolonged. Moreover, selpercatinib treatment was well tolerated in this patient population, with no new safety signals identified. Taken together, these data support selpercatinib as a new standard of care for primary treatment of brain metastases for patients with *RET* fusion-positive NSCLC. Comprehensive molecular profiling analysis is warranted in the future to further analyze the biomarkers of intracranial response and resistance to selpercatinib.

The intracranial activity of selpercatinib in this phase 1/2 trial is broadly consistent with the intracranial activity observed with other contemporary targeted therapies for genomically-driven NSCLCs. In *ALK* fusion-positive lung cancers, alectinib achieved an intracranial ORR of 64%, an intracranial disease control rate of 90%, and durable disease control (median intracranial duration of response of 10.8 months) among patients with measurable disease in a comparable analysis of two single arm phase 2 trials.[10] At 6 months, 58% of patients were progression/death-free. In *EGFR*-mutant lung cancers, osimertinib achieved an intracranial ORR of 54% and an intracranial disease control rate of 92% in a pooled analysis of two phase 2 trials. [18] At 6 months, 72% of patients were intracranial progression/death-free. By comparison, selpercatinib treatment resulted in an intracranial ORR of 82% and an intracranial disease control rate of 100%, and at 6 months, 79% of patients were intracranial progression/death-free. Median intracranial duration of response was not reached (95% CI =

9.3, NE). Both alectinib and osimertinib are recognized as standards of care for tyrosine kinase inhibitor-naïve patients with *ALK* fusion-positive and *EGFR*-mutant lung cancers, respectively, similar to the role of selpercatinib in *RET* fusion-positive lung cancers.

Selpercatinib's activity in the CNS has important implications beyond *RET* fusion-positive NSCLCs with brain metastases. A complete response to selpercatinib in leptomeningeal disease has already been described in a patient with *RET* fusion-positive NSCLC,[8] demonstrating the activity of the drug beyond parenchymal disease. Selpercatinib has been shown to be active against intracranial metastases in a patient with *RET* fusion-positive thyroid cancer,[19] a patient with *RET*-mutant medullary thyroid cancer,[20] and a pediatric patient with *RET* fusion-positive congenital mesoblastic nephroma.[21] LIBRETTO-001 continues to enroll patients with non-lung/non-thyroid cancers that harbor *RET* fusions or mutations. Additional confirmation of the drug's activity in this setting will help establish the overall impact of selpercatinib on intracranial disease in patients with RET-dependent cancers of any histology in both adult and pediatric populations.

While this prospective, pre-planned, independently-reviewed analysis has many strengths, it does have some important limitations. Patients in this cohort had received a variety of both systemic and local therapies for management of their *RET* fusion-positive NSCLCs. Despite this, intracranial activity was observed across various treatment subgroups. In addition, at the time of analysis, a majority of patients remained progression-free and a majority of responses were ongoing; thus, stable medians could not be estimated. Ongoing follow-up will reveal more precise estimates of intracranial response durability and progression-free survival. Moreover, this study did not specifically address whether selpercatinib can prevent or delay intracranial progression in patients with NSCLC that begin treatment without intracranial

involvement. As a phase 1/2 trial, LIBRETTO-001 did not require head and neck MRI/CT scans during treatment unless intracranial disease was identified at baseline and the trial could not address this question. Intriguingly, other tyrosine kinase inhibitors with substantial intracranial activity have already been shown to prolong the time to the acquisition of central nervous system metastases in fusion-positive lung cancers compared to earlier-generation kinase inhibitors with less optimal intracranial activity.[22,23] However, there is a lack of prospective data evaluating long-term outcomes of tyrosine kinase inhibitors alone compared to SRS and tyrosine kinase inhibitors in managing brain metastases.

Selpercatinib is currently being evaluated in LIBRETTO-431 (NCT04194944), an ongoing randomized, global, phase 3 study of selpercatinib versus platinum-pemetrexed with or without pembrolizumab in treatment-naïve patients with *RET* fusion-positive NSCLCs. This trial will allow the further characterization of selpercatinib activity in patients with NSCLC and intracranial metastases.

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532

Table 1. Demographic and disease characteristics of patients with *RET* fusion-positive NSCLC and intracranial disease

Characteristics	All patients with *RET* fusion-positive NSCLC and intracranial metastases (N=80)
Age	
Median (range), years	62 (36–86)
Sex, n (%)	
Female	54 (68)
Male	26 (33)
Race, n (%)	
White	44 (55)
Asian	31 (39)
Black or African American	2 (3)
Other	2 (3)
Unknown	1 (1)
Smoking history, n (%)	
Never	63 (79)
Former	16 (20)
Current	1 (1)
ECOG performance status, n (%)	
0	22 (28)
1	54 (68)
2	4 (5)
NSCLC histological subtype, n (%)	
Adenocarcinoma	69 (86)
Large cell neuroendocrine carcinoma	2 (3)
NSCLC-NOS	8 (10)
Other	1 (1)
RET fusion partner, n (%)	
KIF5B	56 (70)
CCDC6	11 (14)
NCOA4	2 (3)
Other	4 (5)
Unknown [a]	7 (9)
Prior therapy, n (%)	
Number of prior systemic regimens	
0	7 (9)
1–2	43 (54)
3 or more	30 (38)
Median prior systemic regimen (range)	2 (0–10)
Type of prior systemic therapy [b]	
Platinum chemotherapy	63 (79)
Anti PD-1/PD-L1 antibody	43 (54)
Multi-kinase inhibitor	33 (41)
Taxane chemotherapy	25 (31)
Other systemic therapy	31 (39)
Intracranial radiotherapy [b]	45 (56)
Whole brain radiation therapy	11 (14)
Stereotactic radiosurgery	36 (45)
Intracranial radiotherapy timing	
Completed >2 months prior to selpercatinib treatment	33 (41)
Intracranial surgery	7 (9)

[a] *RET* fusion identified by molecular analysis with an assay unable to identify the fusion partner (e.g. fluorescence in situ hybridization).
[b] Patients may be counted in more than one row.

Table 2. Intracranial tumor response by independent review committee assessment in patients with *RET* fusion-positive NSCLC and measurable intracranial disease per RECIST 1.1.

	Patients with measurable intracranial disease (N=22)
Intracranial objective response rate, n (%)	18 (82)
95% confidence interval [a]	60 – 95
Intracranial best overall response, n (%)	
Complete response	5 (23)
Partial response	13 (59)
Stable disease	4 (18)
Progressive disease	0
Intracranial disease control rate, n (%) [b]	22 (100)

[a] 95% confidence interval was calculated using Clopper-Pearson method.
[b] Intracranial disease control rate was defined as the percentage of patients who had a best overall intracranial response of complete response, partial response, or stable disease lasting 16 weeks or more after selpercatinib initiation.

Table 3. Duration of intracranial tumor response and intracranial progression-free survival by independent review committee assessment in patients with *RET* fusion-positive NSCLC and measurable and non-measurable intracranial disease

	Total patients (N=80)
Duration of intracranial response	
Responders [a]	38
Censored, n (%) [b]	27 (71)
Intracranial duration of response, median (months) (95% CI) [c,d]	NE (9.3–NE)
Intracranial duration of follow-up, median (months) (IQR) [c]	9.5 (5.7, 12.0)
Intracranial duration of response [c,e]	
% of patients ≥6 months (95% CI)	91 (75– 97)
% of patients ≥12 months (95% CI)	55 (32–73)
Progression-free survival	
Censored, n (%) [b]	50 (62.5)
Median, months (95% CI) [c,d]	13.7 (10.9–NE)
Median follow-up, (months) (IQR) [c]	11.0 (7.4, 16.5)
% progression/death-free [c,e]	
≥6 months (95% CI)	79 (68–87)
≥12 months (95% CI)	55 (41–67)

Abbreviations: CI, confidence interval; IQR, interquartile range; NE, not estimable

[a] Patients with intracranial best response of CR or PR based on independent review committee assessments using RECIST (version 1.1).

[b] Status as of the patient's last disease assessment on or before 16 Dec 2019.

[c] Estimate based on Kaplan-Meier method.

[d] 95% confidence interval was calculated using Brookmeyer and Crowley method.

[e] 95% confidence interval was calculated using Greenwood's formula.

Figure Legend

Figure 1. Intracranial response to selpercatinib. A waterfall plot of the maximum change in intracranial tumor size is shown for the 22 patients with measurable disease at baseline. Vertical bars represent the best percent change from baseline in the sum of diameters for all intracranial target lesions, with the color of the bar representing the corresponding tumor response designation. Symbols represent prior stereotactic radiosurgery (SRS) and prior systemic therapies. Note: because the intracranial best overall response in Table 2 is based on RECIST 1.1 requirements, including the need for a confirmatory scan, the tumor response designation does not exactly correlate with table data.

Abbreviations: MKI, multi-kinase inhibitor

Figure 2. Kaplan-Meier plot of (A) intracranial duration of response and (B) intracranial progression-free survival. (A) The plot depicts the duration of response for all responding patients with measurable or non-measurable intracranial metastases. (B) The plot was constructed with data derived from all patients with measurable or non-measurable intracranial metastases treated with selpercatinib.
Abbreviations: DoR, duration of response; NE, non-estimable; PFS, progression-free survival

Figure 3. Duration of selpercatinib therapy.
Treatment duration, time to intracranial response, and intracranial progression events are shown in this swimmer's plot for patients with measurable and non-measurable intracranial disease (n=38). The complete and partial response symbols indicate the time of the first scan showing an intracranial response (that was then confirmed at a subsequent assessment).

Figure 1

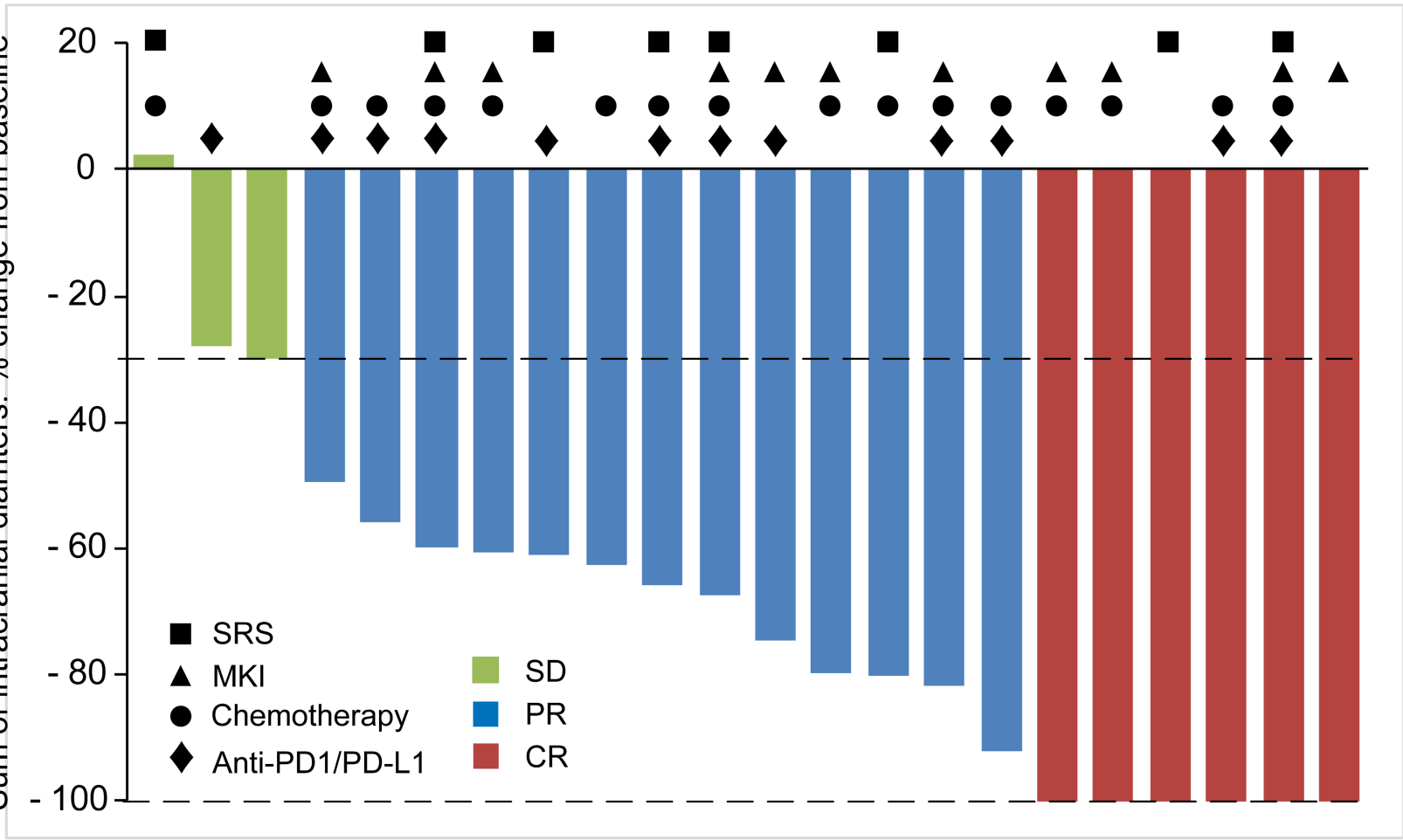
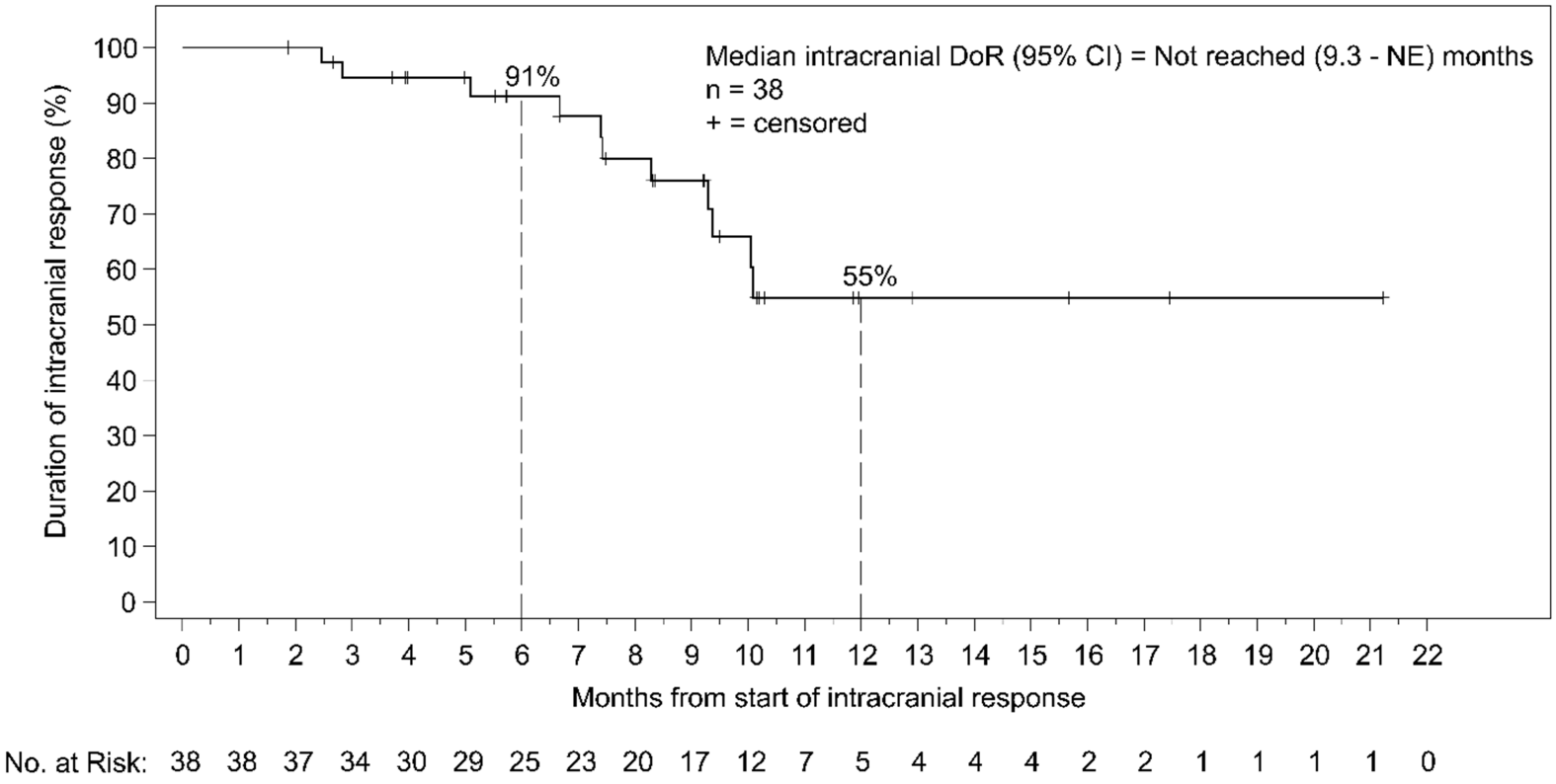


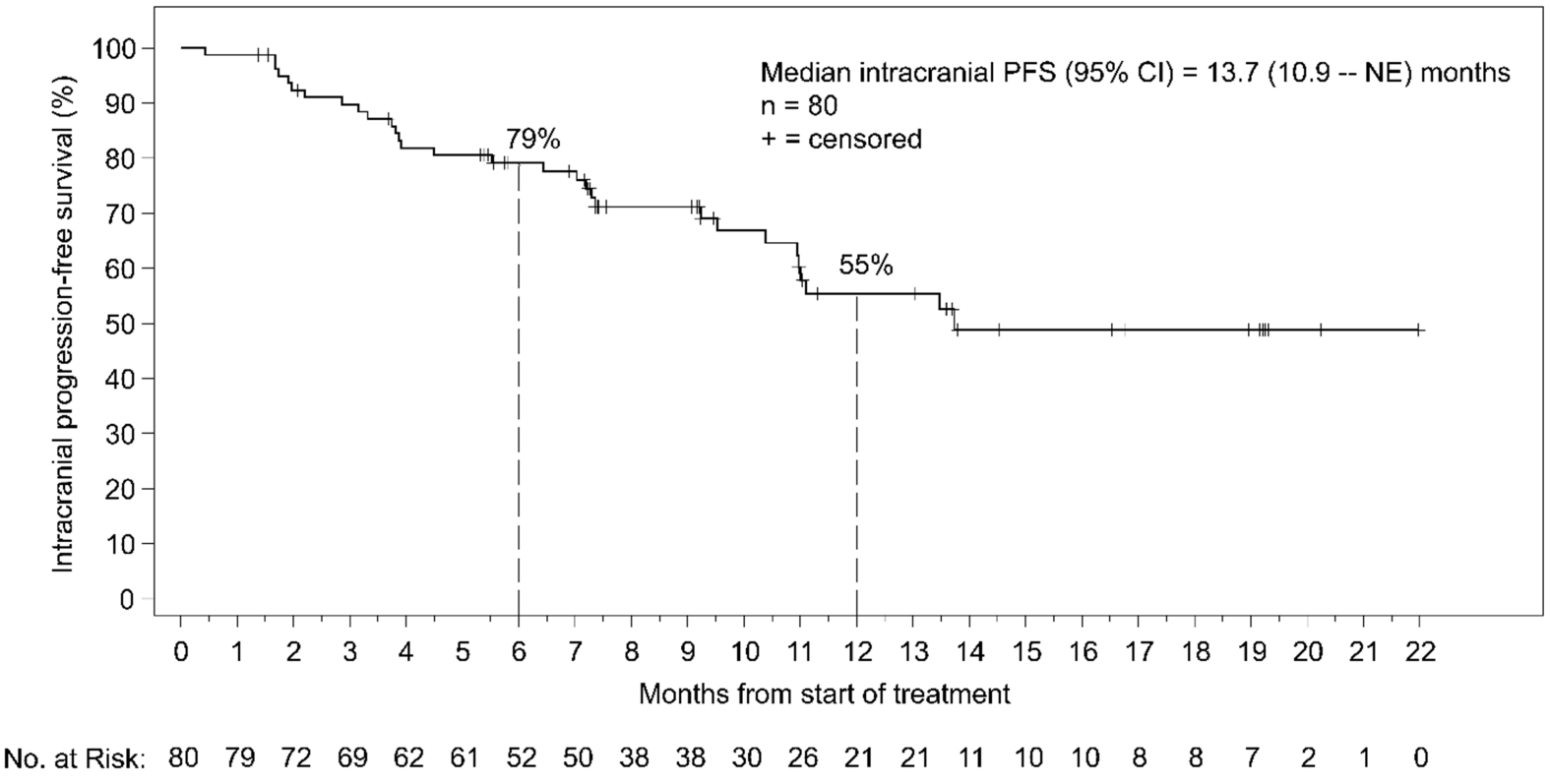
Figure 2

A



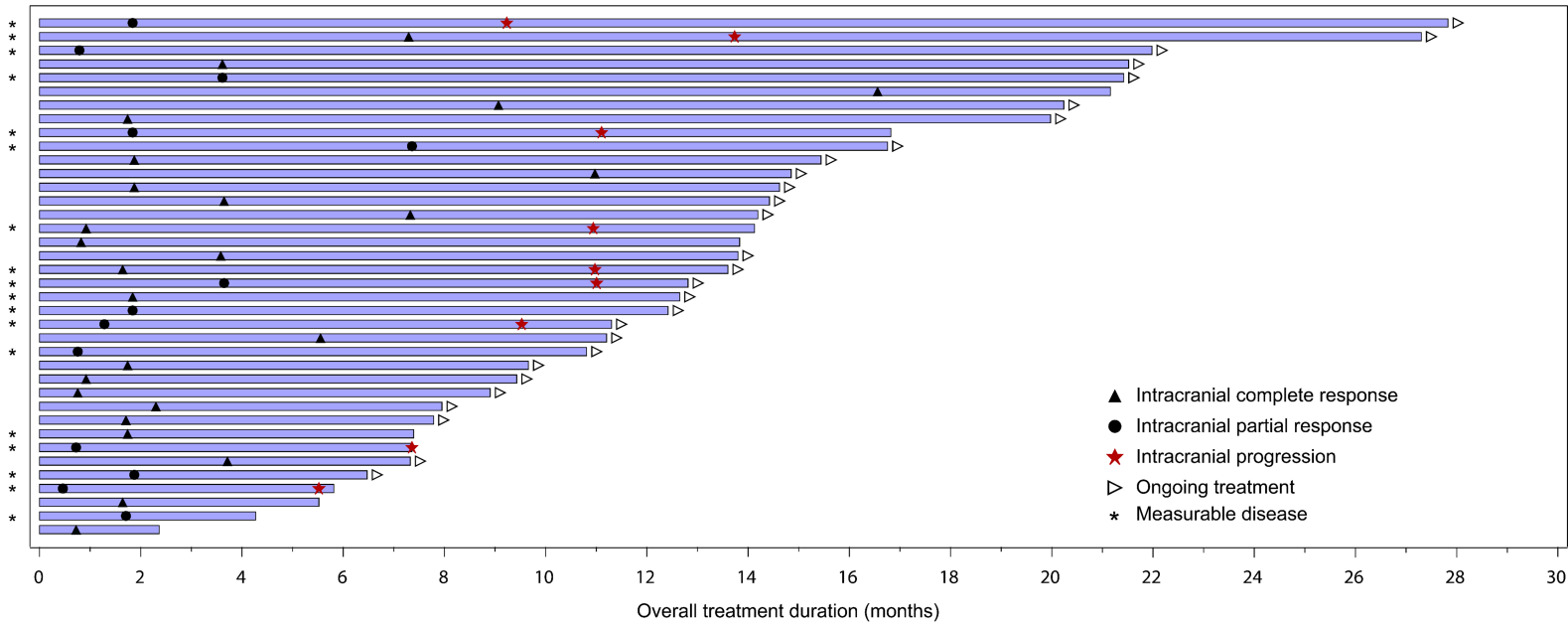
No. at Risk: 38 38 37 34 30 29 25 23 20 17 12 7 5 4 4 4 2 2 1 1 1 1 0

B



No. at Risk: 80 79 72 69 62 61 52 50 38 38 30 26 21 21 11 10 10 8 8 7 2 1 0

Figure 3



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Intracranial efficacy of selpercatinib in RET fusion-positive non-small cell lung cancers on the LIBRETTO-001 trial

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