

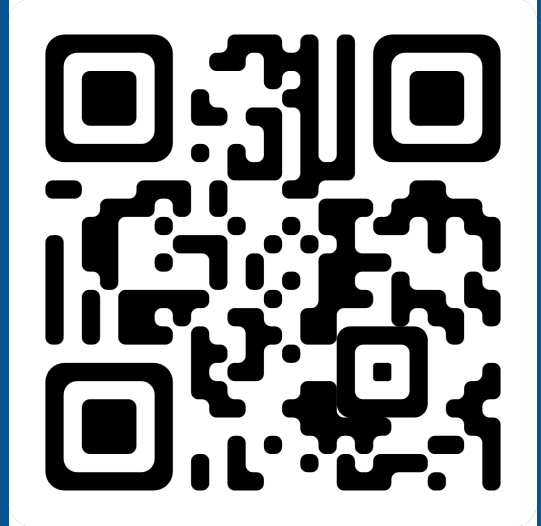
Mobocertinib (TAK-788) in *EGFR* exon 20 insertion–positive metastatic non–small cell lung cancer: treatment beyond progressive disease in platinum-pretreated patients with and without intracranial progressive disease

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Introduction

- EGFR* exon 20 insertion (*EGFR* ex20ins) mutations are present in approximately 5% to 12% of *EGFR*-mutated non–small cell lung cancer (NSCLC) tumors (2% of all NSCLC)^{1,2}
- Therapeutic options for patients with *EGFR* ex20ins+ NSCLC are limited
 - Most patients receive platinum-based chemotherapy as first-line treatment but typically experience disease progression within 6 months^{3–5}
 - First- and second-generation *EGFR* tyrosine kinase inhibitors (TKIs; afatinib, erlotinib, gefitinib) have demonstrated limited efficacy against uncommon *EGFR* mutations, including *EGFR* ex20ins variants, with response rates of approximately 10% and progression-free survival (PFS) of 1–3 months⁹
 - Immune checkpoint inhibitors, alone or in combination with chemotherapy in a mixture of settings, are associated with response rates of 0%–25% and median PFS typically of 2–3 months^{5,7,8}
- There are currently 2 FDA-approved treatment options available to patients with *EGFR* ex20ins mNSCLC refractory to platinum-based chemotherapy, amivantamab and mobocertinib^{9,10}
- Mobocertinib, a potent, irreversible, oral *EGFR* TKI that selectively targets *EGFR* ex20ins mutations,^{11,12} demonstrated clinical activity and a manageable safety profile in the platinum-pretreated patients (PPP) cohort of a phase 1/2 study of patients with *EGFR* ex20ins+ metastatic NSCLC¹³

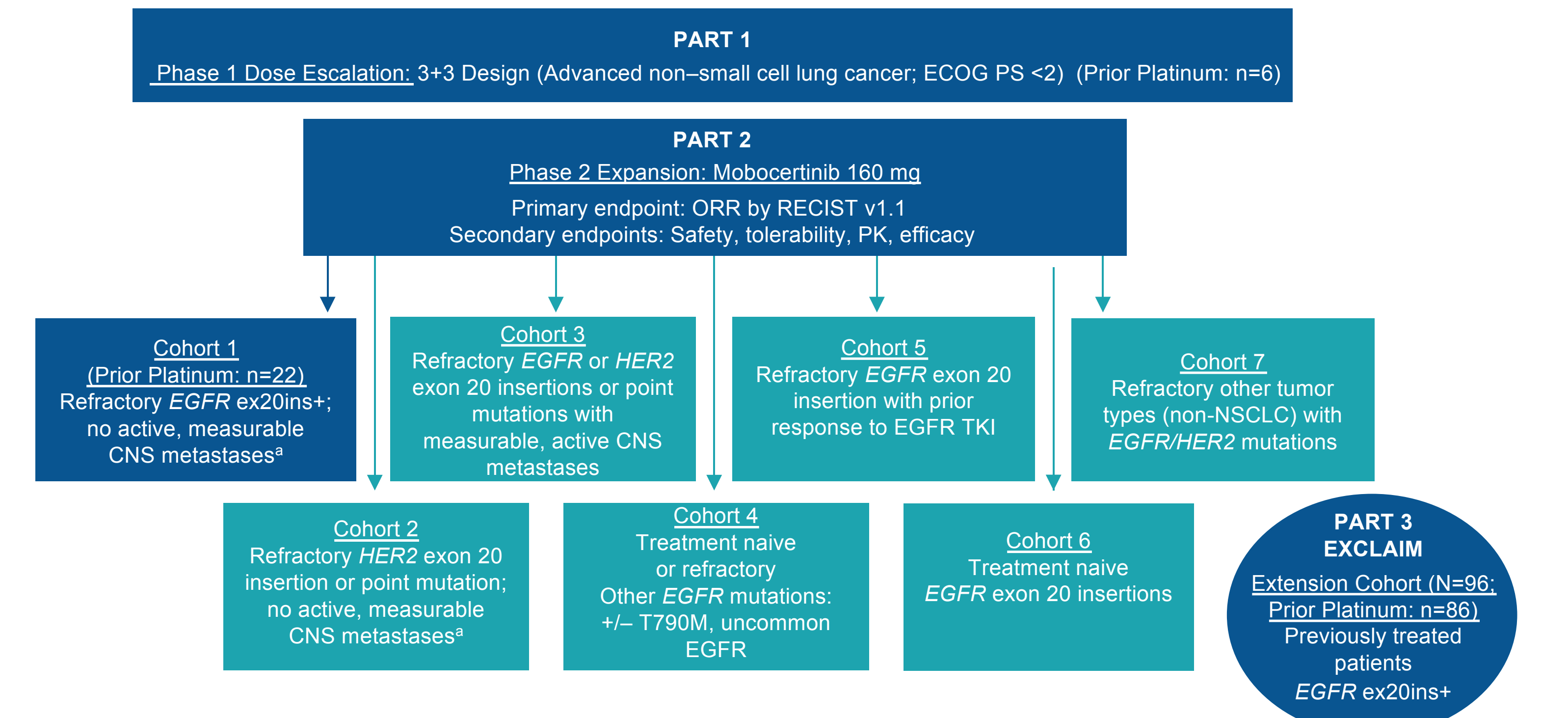
Objective

- We present data from the PPP cohort (n=114) who continued mobocertinib beyond first disease progression with or without brain involvement in the phase 1/2 study

Methods

- This 3-part, open-label, multicenter study (NCT02716116) included dose-escalation and expansion cohorts and the EXCLAIM extension cohort (**Figure 1**)
- Data are presented for the PPP cohort (n=114), which included patients from the dose-escalation/expansion cohorts (n=28) and from EXCLAIM (n=86)¹³
- Eligible patients had ECOG status 0–1, had received ≥1 prior therapy line for locally advanced/metastatic *EGFR* ex20ins+ NSCLC, no response to prior *EGFR* TKI and no active brain metastasis at baseline. Patients with brain metastasis were required to have the brain lesion treated and had no symptoms of brain metastasis before enrollment¹³
- All patients received mobocertinib 160 mg orally QD until progressive disease requiring alternate treatment, intolerable adverse events, or other reasons for discontinuation¹³
- Patients were allowed to continue mobocertinib beyond radiologic disease progression per RECIST, at the discretion of the investigator if evidence of clinical benefit existed¹³

Figure 1. Study Design



Data cutoff date: November 1, 2020
Locations: United States only for phases 1 and 2; United States, Europe, and Asia for phase 2 extension cohort
*Active or measurable (but not both) CNS metastases permitted
Active CNS metastases: Untreated or treated and progressing; measurable CNS metastases: ≥10 mm in longest diameter by contrast-enhanced MRI

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Abbreviations

CI, confidence interval; CNS, central nervous system; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; *EGFR*, epidermal growth factor receptor gene; *EGFR*, epidermal growth factor receptor; ex20ins, exon 20 insertion; *HER2*, human epidermal growth factor receptor 2 gene; IRC, independent review committee; MRI, magnetic resonance imaging; NE, not evaluable; NR, not reached; NSCLC, non-small cell lung cancer; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PPP, platinum-pretreated patients; QD, once daily; PK, pharmacokinetics; RECIST, Response Evaluation Criteria in Solid Tumors, version 1.1; RT, radiation therapy; SD, standard deviation; SRS, stereotactic radiosurgery; TKI, tyrosine kinase inhibitor; WBRT, whole brain radiation therapy

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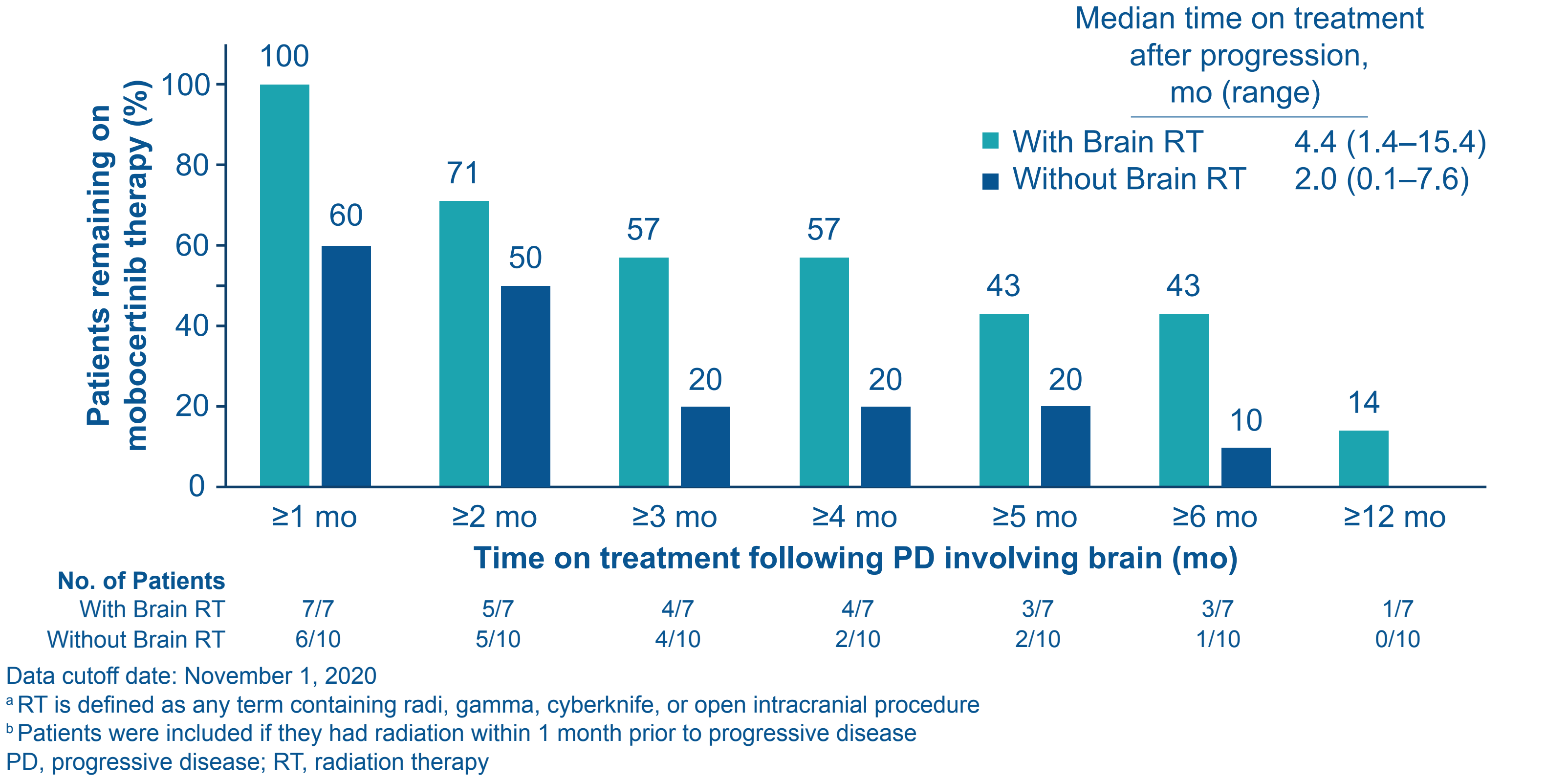
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Disclosures

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Figure 3. Patients Who Remained on Mobocertinib After Disease Progression in the Brain (Per Investigator Assessment) With (n=7) and Without (n=10) Brain RT^{a,b}



Results

- Key patient demographic and baseline characteristics for the PPP cohort are shown in **Table 1**
- Mobocertinib demonstrated deep and durable responses in patients with platinum-pretreated *EGFR* ex20ins+ NSCLC (**Table 2**)¹³
- In the PPP cohort, separate intracranial assessment of brain lesions per modified RECIST criteria was not performed. Response assessment was performed systemically by standard RECIST for all organs with cancer involvement (**Table 3**)
- Brain MRI was required for all patients at baseline and post-baseline assessment, regardless of history or symptom of brain metastasis at baseline
- Tumor assessment after the initial disease progression was managed through regular clinical practice and was not collected as formal tumor assessment the study
- Among patients in the PPP cohort with progressive disease (per investigator assessment; n=64), 21 (33%) had first site of disease progression involving the brain and 11 (17%) had first site of disease progression in the brain only
 - Of the 21 patients, 81% (17/21) continued to receive mobocertinib beyond disease progression and 19% (4/21) continued for ≥6 months (**Figure 2**)
 - Among 43 patients with first site of disease progression that did not involve the brain, 65% continued mobocertinib beyond disease progression; 9% (4/43) of patients continued mobocertinib for ≥6 months (**Figure 2**)
- Of the 17 patients with first site of disease progression in the brain (per investigator) who continued mobocertinib therapy beyond disease progression
 - 7 patients received RT to the brain (including WBRT and stereotactic radiosurgery), 3 of whom remained on mobocertinib for ≥6 months (**Figure 3**)
 - 10 patients remained on mobocertinib therapy but did not receive brain RT, one of whom remained on mobocertinib for ≥6 months (**Figure 3**)

Conclusions

- Mobocertinib may have limited intracranial activity given the numerically lower response rate in patients with baseline brain metastasis
- In patients who progressed on mobocertinib, 33% had first site of disease progression in the brain and 17% had first site of disease progression in the brain only
- Patients with disease progression in the brain may derive overall benefit from ongoing mobocertinib treatment with a combination of RT to treat the brain lesion
- Optimal strategies for treating advanced *EGFR* exon 20–driven NSCLC with brain metastasis warrant continued investigation