



First-in-human Studies of VRN110755 in NSCLC Patients with EGFR Mutations: Safety, Pharmacokinetics, and Early Efficacy Assessment

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Unmet Medical Needs in EGFR Mutant NSCLC

Indications	Unmet medical needs
Osimertinib (3G TKI) resistance	No approved targeted therapy for post-3 rd gen TKI including C797S resistance
CNS metastasis	Insufficient therapeutic effects and CNS progression by osimertinib
Uncommon mutants	SOC, afatinib has poor tolerability and brain permeability

Reversible, but Long On-Target Residence Time

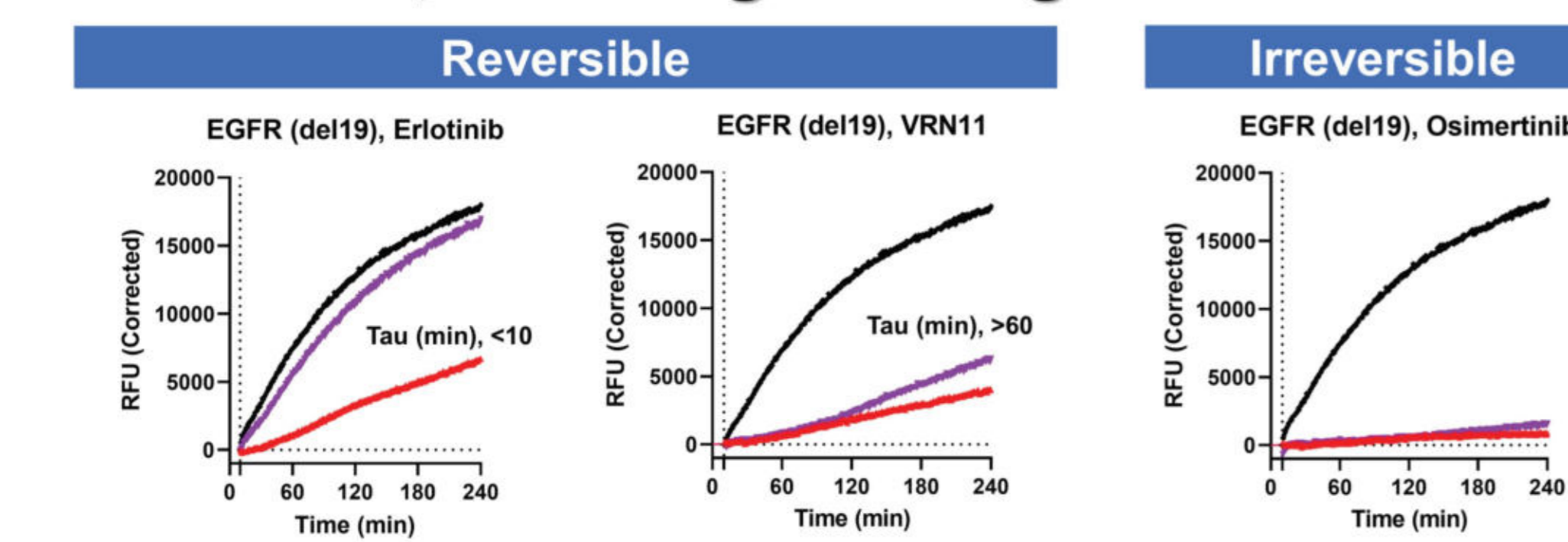
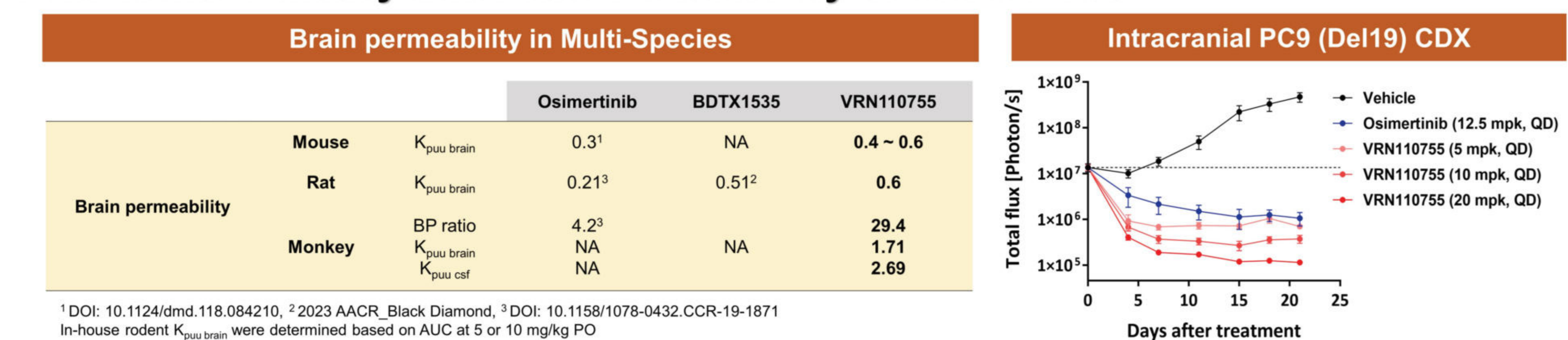


Figure 1. Reversibility and residence time measurement for erlotinib, osimertinib and VRN110755 in EGFR-del19. Catalytic activity EGFR(del19) over time in the presence of 1 mM ATP before and after the drug removal via spin down (AssayQuant, USA). VRN110755 showed reversible binding, but maintains a similarly long residence time for EGFR mutant, like irreversible osimertinib. **Black, no inhibitor control; Red, inhibitor; Purple, inhibitor and spin down**

Anti-Tumor Efficacy and Brain Permeability of VRN110755



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In-house rodent $K_{p,brain}$ were determined based on AUC at 5 or 10 mg/kg PO

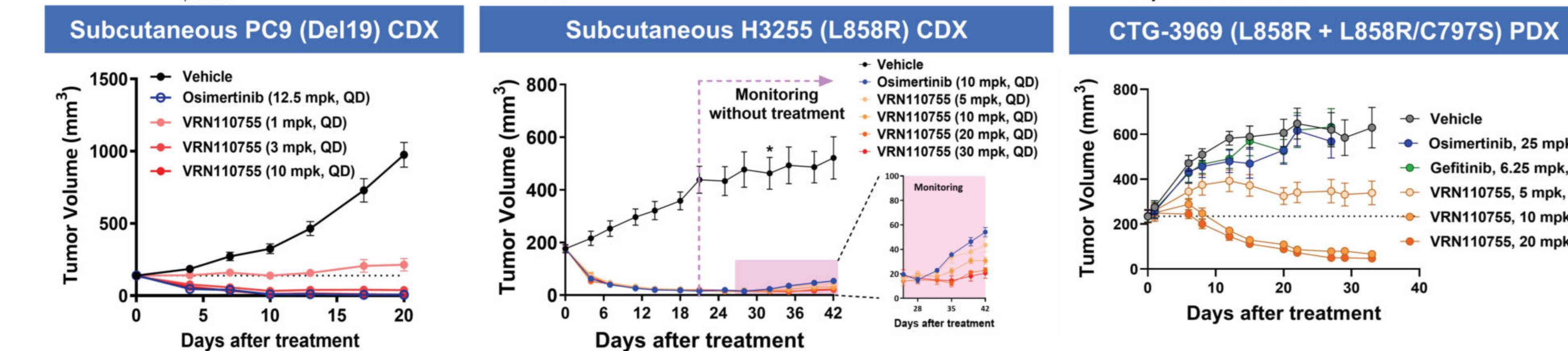


Figure 2. Brain permeability and anti-tumor efficacy of VRN110755. Anti-tumor activities were assessed in subcutaneous and intracranial PC9 (Del19) CDX, H3255 (L858R) CDX, and CTG-3969 PDX (harboring both L858R and L858R/C797S) by daily oral treatment. For comparison in H3255, tumors were further monitored without treatment.

VRN110755 Phase 1a Dose Escalation and Safety Assessment

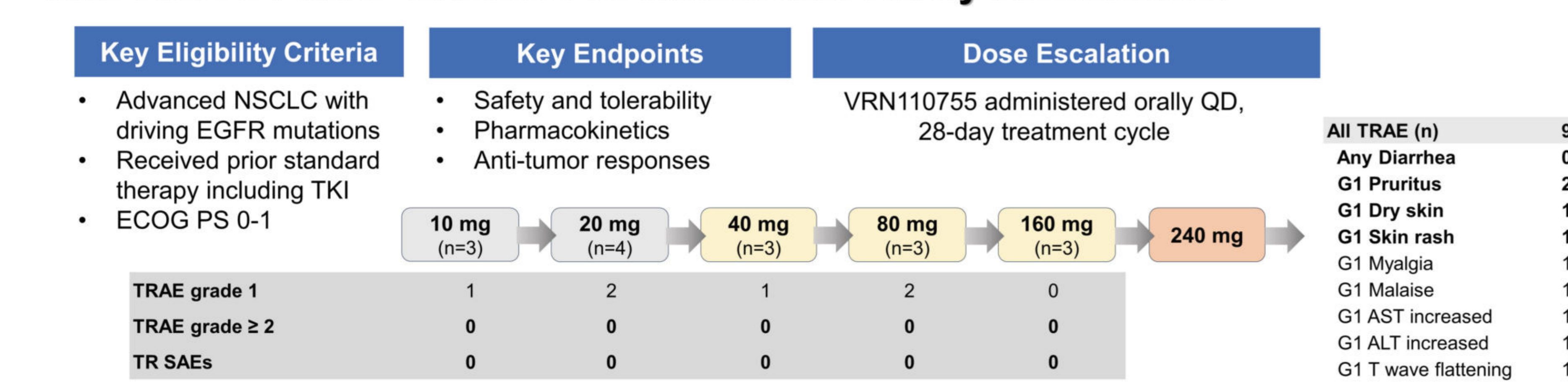
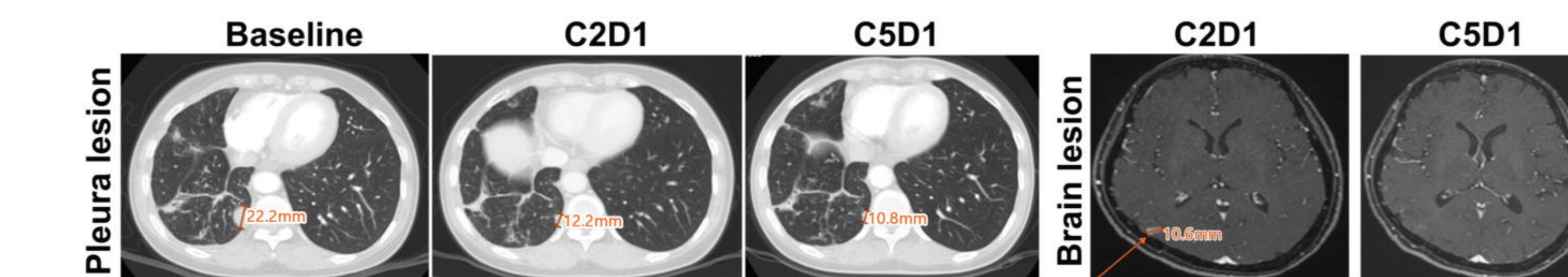


Figure 3. Dose escalation, 3+3 design. Additional eligible patients are enrolled in the backfill cohorts at dose levels that clear DLT evaluation and reach the PK threshold for efficacy. The 80 mg backfill cohort is open and on treatment. **No dose limiting toxicity / No grade 2 or higher TRAE** have been observed. TRAE, treatment-related adverse event. Data cut off, 04 April 2025.

Early Anti-Tumor Responses

10 mg Case Report: Patient with EGFR ^{Del19} NSCLC	VRN110755 Treatment
<ul style="list-style-type: none"> Brain, liver, and lymph node metastasis EGFR^{Del19} at the baseline Five prior systemic treatments including gefitinib and erlotinib 	<ul style="list-style-type: none"> 10 mg QD, 28-week treatment followed by 20 mg QD Liver and lung lesions were stable for 8 months EGFR ctDNA VAF was stable until EOT Best response: SD (including brain lesion) Safety: no TRAE

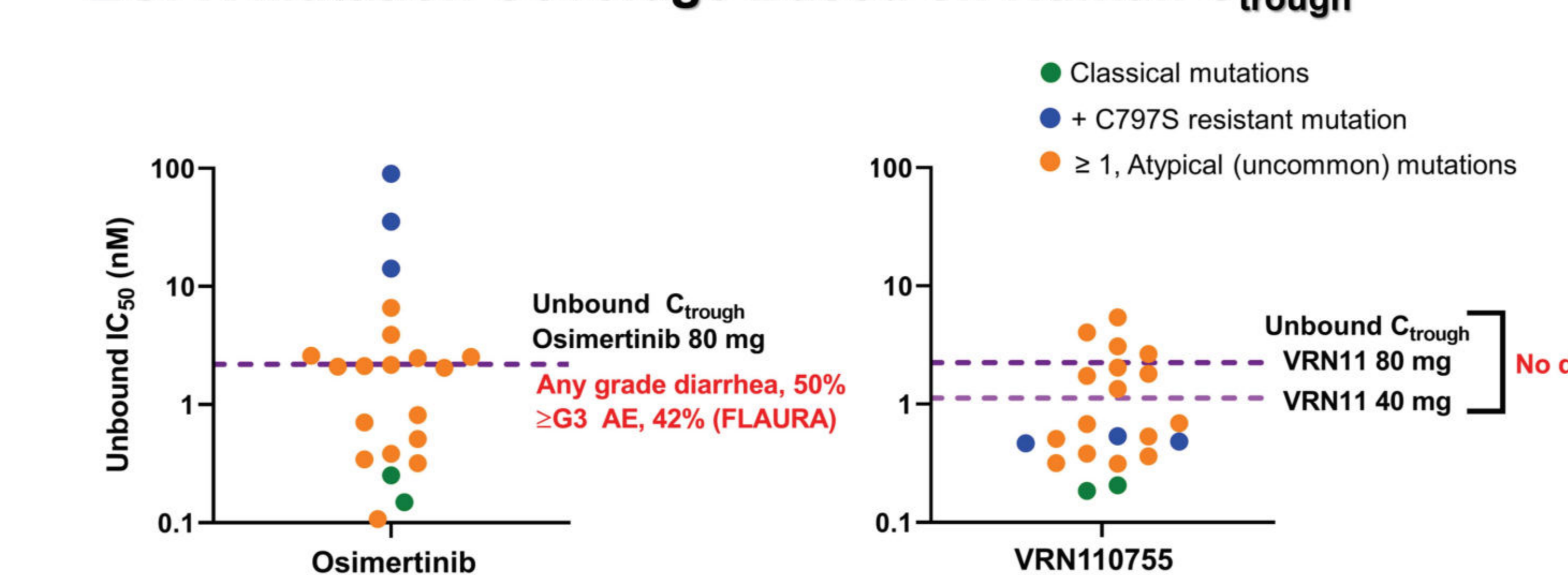
40 mg Case Report: Patient with EGFR ^{L858R/R776H/C797S} NSCLC	VRN110755 Treatment
<ul style="list-style-type: none"> Lung, brain, and pleural metastasis EGFR^{L858R/R776H/C797S} at the baseline Two prior systemic treatments, including dacomitinib and osimertinib 	<ul style="list-style-type: none"> 40 mg QD, 19 weeks Pleura lesion: 51% tumor reduction CNS lesion: tumor disappearance EGFR ctDNA VAF(%): 0.3 to 0 after 2 cycles Best response: unconfirmed PR Safety: grade 1 malaise TRAE



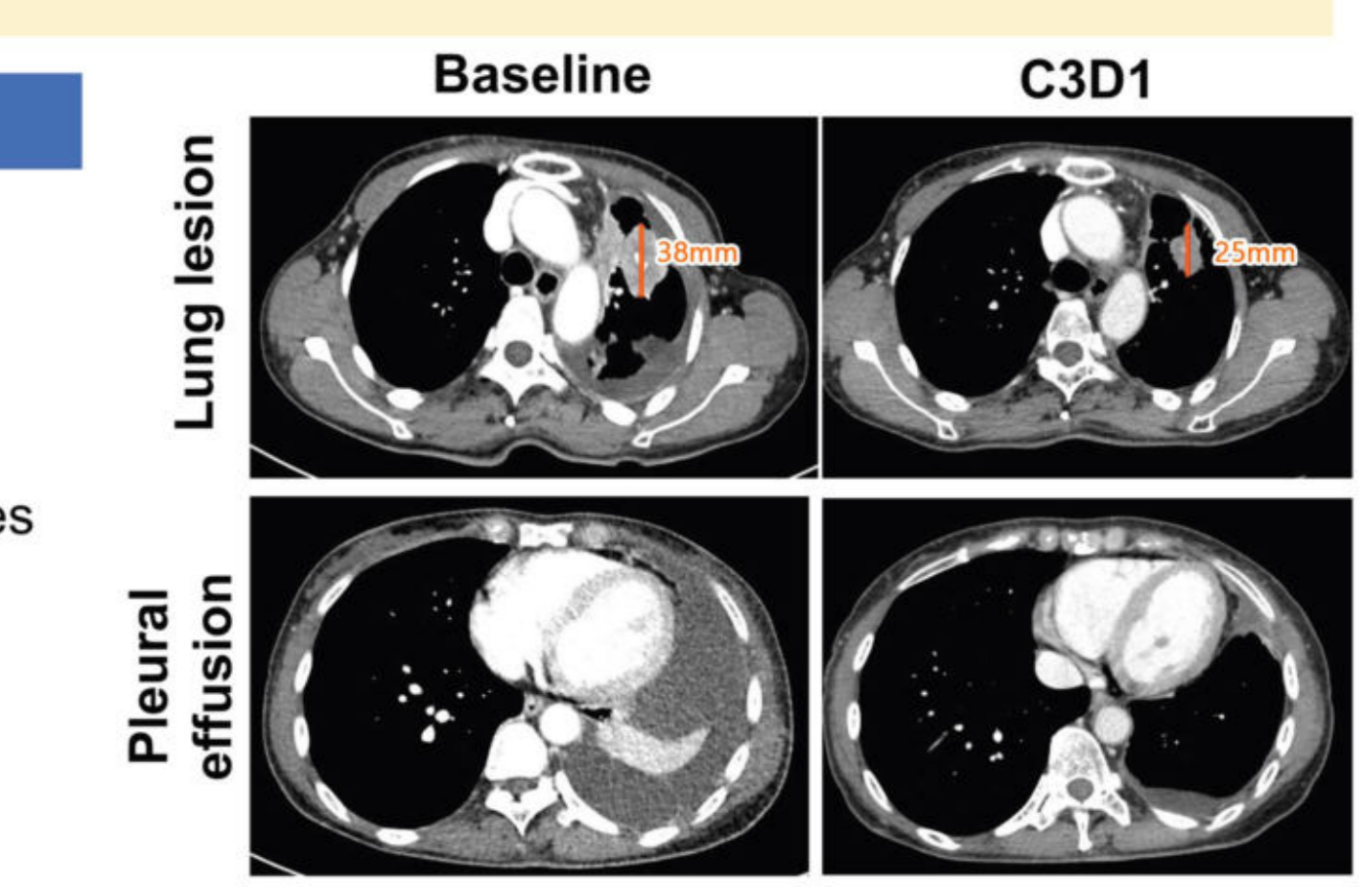
Dose level	10 mg (n=3)			20 mg (n=3)			40 mg (n=3)			80 mg (n=3)			160 mg (n=2)	
Patient's Best Response	Classic	SD ¹	PD	PD	SD	PD	SD	PD	SD	PD	SD	SD	SD	SD
	Acquired C797	Del19	Del19	Del19	L858R	Del19	L858R	L858R	Del19	Del19	Del19			
	Acquired T790						T790M	T790M				T790M		T790M
	Uncommon													
CNS meta		BM		BM	BM		BM	BM			BM		BM	
Prior systemic treatment (n)	5	4	8	4	2	5	2	3	1	2	6	6	6	3
Prior line TKI 1	Gefitinib	Osimertinib	Osimertinib	Erlotinib	Gefitinib	Afatinib	Dacomitinib	Lazertinib	Afatinib	Afatinib	Dacomitinib	Osimertinib	Afatinib	Erlotinib
Prior line TKI 2		Lazertinib	Erlotinib	Lazertinib	Osimertinib	Osimertinib	Osimertinib				Lazertinib		Osimertinib	Osimertinib
Prior line TKI 3			Osimertinib			Lazertinib							JIN-A02	

* case reported. ^{uc}, unconfirmed. N.D., not determined. n, patient number with tumor assessment after more than 1 cycle treatment

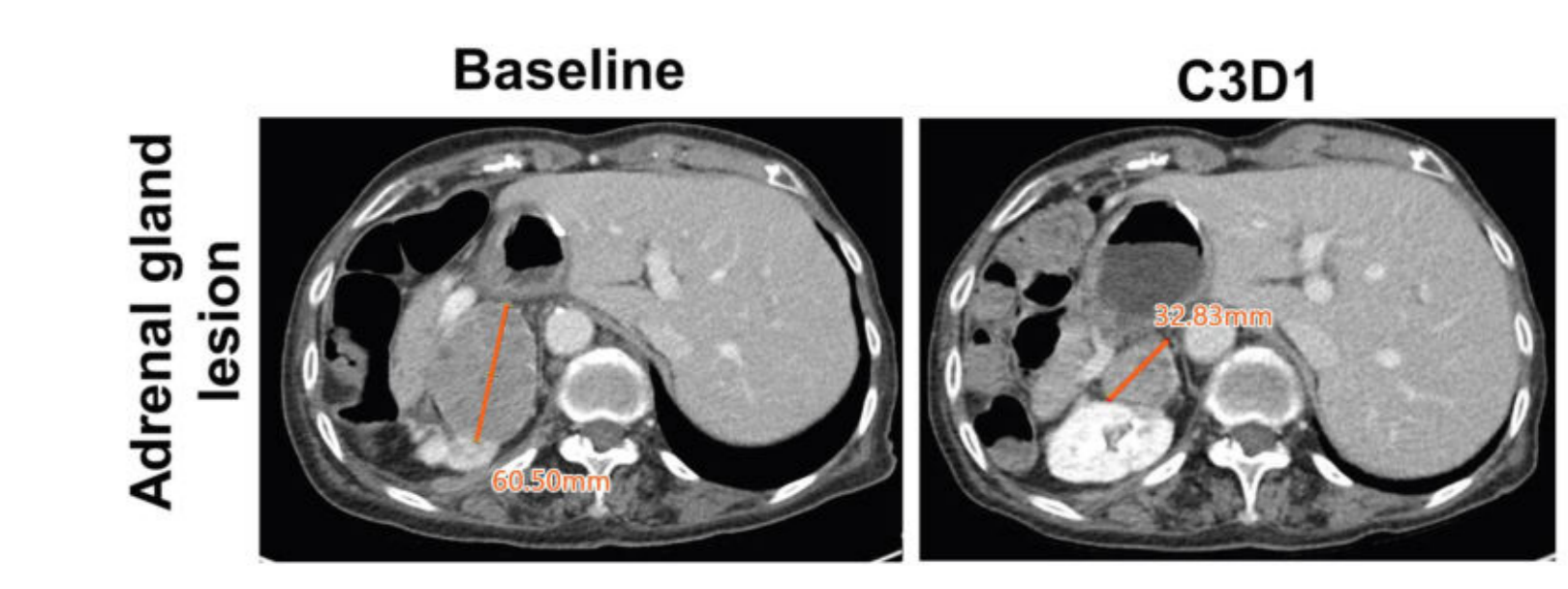
EGFR Mutation Coverage Based on Human C_{trough}



80mg Case Report: Patient with EGFR ^{Del19} NSCLC	VRN110755 Treatment
<ul style="list-style-type: none"> Pleura metastasis EGFR^{Del19} and TP53 mutation at the baseline Two prior systemic treatment including afatinib 	<ul style="list-style-type: none"> 80 mg QD, >15 weeks (on treatment) Lung lesion: 34% tumor reduction Pleural effusion: disappearance EGFR ctDNA VAF(%): 0.1 to 0 after 2 cycles Best response: unconfirmed PR Safety: No TRAE



80 mg Case Report: Patient with EGFR ^{Del19/T790M} NSCLC	VRN110755 Treatment
<ul style="list-style-type: none"> Lung, lymph node, and adrenal gland metastasis EGFR^{Del19/T790M}, TP53 mutation at the baseline Six prior systemic treatments, including dacomitinib and lazertinib 	<ul style="list-style-type: none"> 80 mg QD, > 14 weeks (on-treatment) Adrenal gland lesion: 47% tumor reduction Best response: SD Safety: No TRAE



Summary

- ✓ Dose escalation study VRN110755 with heavily treated (median n=4) EGFR mutation NSCLC patients is undergoing.
- ✓ 20% of enrolled patients have C797S resistance mutant or atypical mutations.
- ✓ Up to 160 mg, VRN110755 showed no Grade ≥2 TRAE, IP-related SAE, or DLT
- ✓ From 40 mg, anti-tumor responses have been observed in the metastatic lesions including the brain.
- ✓ PK analysis showed a linear increase of plasma concentration. 160mg and higher doses are expected to have C_{trough} concentration covering most EGFR mutations.