Creating Novel Therapeutics
For patients with Excellent Experts
In Drug Design

VORONOI

IR BOOK

October 16, 2026

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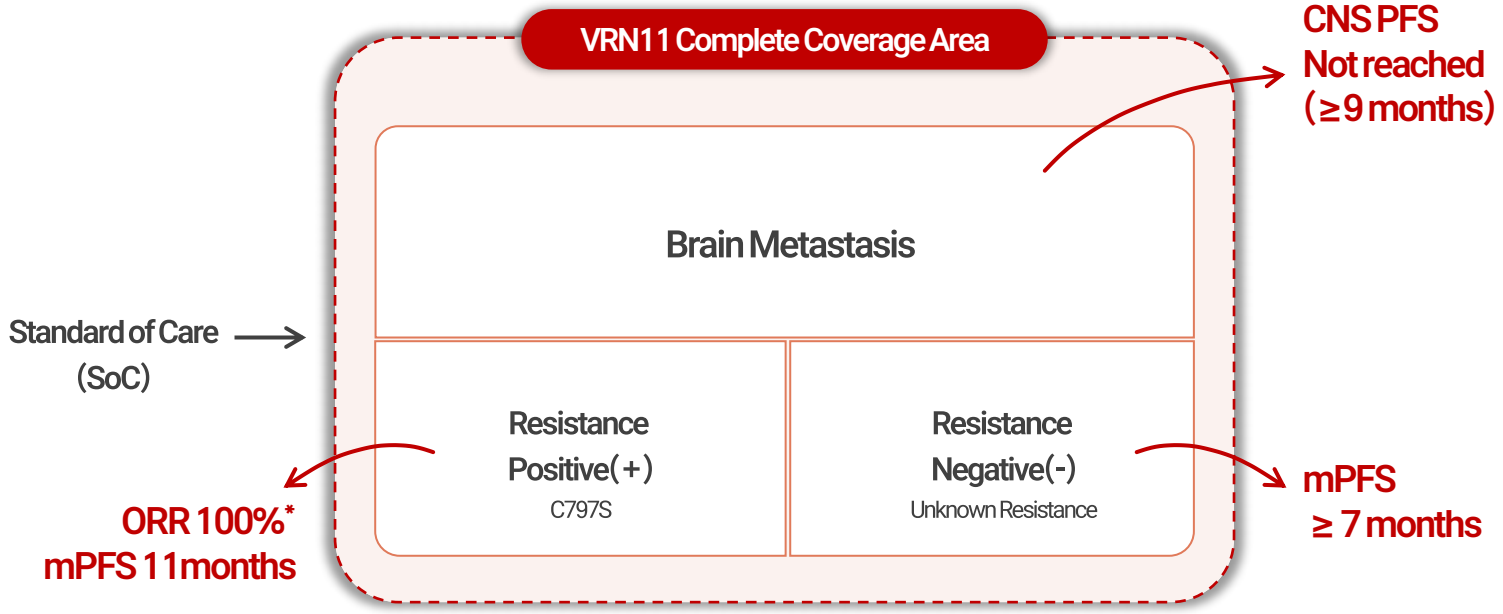
VRN11

EGFR NSCLC Targeted Therapy

1차 치료(1L) 임상 개시의 근거: 2차 치료에서 입증된 광범위한 효능

내성 변이 유무 및 뇌전이 유무를 가리지 않는 커버리지를 통해 표준치료와 경쟁 가능한 임상적 근거 축적 → 1차 표준치료(1L SoC) 패러다임 전환 기대

[EGFR-mutant NSCLC] 1L SoC 이후 VRN11의 커버리지(Broad Coverage)



1차 치료(1L) 임상 개시의 근거

- Osimertinib 포함 이전 치료 이후 환자를 대상으로 한 후속(2L+) 임상에서 우수한 치료 효과 확인
- Osimertinib 승인 용량 대비 높은 표적 억제력(Target engagement) 확인
- 우수한 안전성 프로파일 (≥Grade 3 약물관련 이상반응 3%)

1L 치료 임상 개시

✓ 호주, 홍콩, 싱가포르, 말레이시아, 태국 등에서 1b/2상 진행 중
✓ 다수의 글로벌 병원의 저명한 연구책임자들의 임상 참여

Data cutoff July 2,2026, *유효용량 (≥160mg)을 투약한 EGFR C797S 변이 환자군에서 100%의 객관적 반응률(6/6)
ORR, Objective response rate; PFS, Progression-free survival

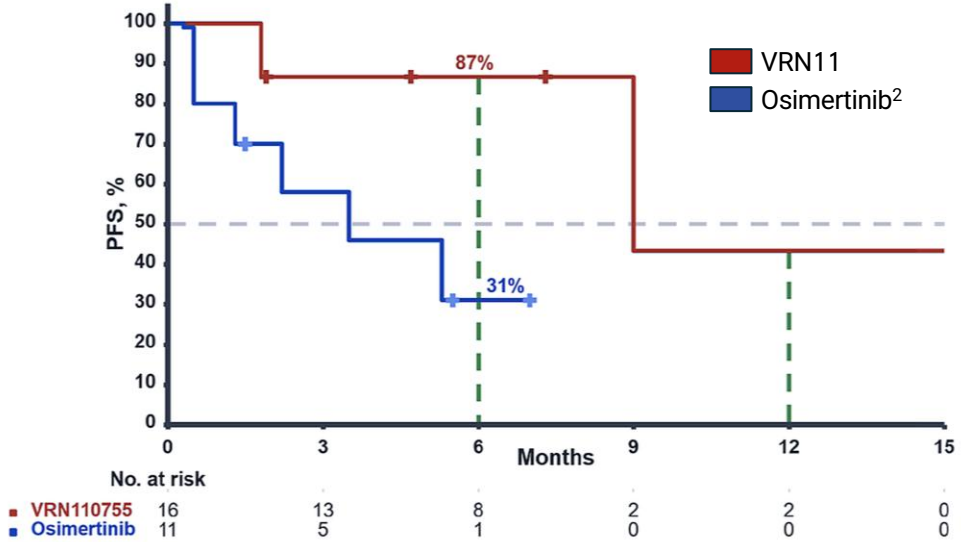
VRN11

Superior brain permeability, Better intracranial PFS

VRN11-Osimertinib 비교: 뇌전이 환자 생존 기간 개선(iPFS)

3세대 EGFR 치료제 이후 뇌 전이된 환자(C797S negative)를 대상으로 9개월의 두개내 무진행생존기간(iPFS) 및 두개내 완전관해(iCR) 25% 확인

[biomarker-negative pts] Comparison of iPFS From Published Studies



✓ 15 patients previously treated with 3rd-gen. EGFR TKIs(15/16)

Efficacy in BM patients

With baseline BM	VRN11 (≥160 mg, C797S negative)	Osimertinib[1,2] (T790M negative)
iPFS	9.0 months (9.0-NR)	3.5 months (1.0-NR)

Intracranial best response by RANO-BM

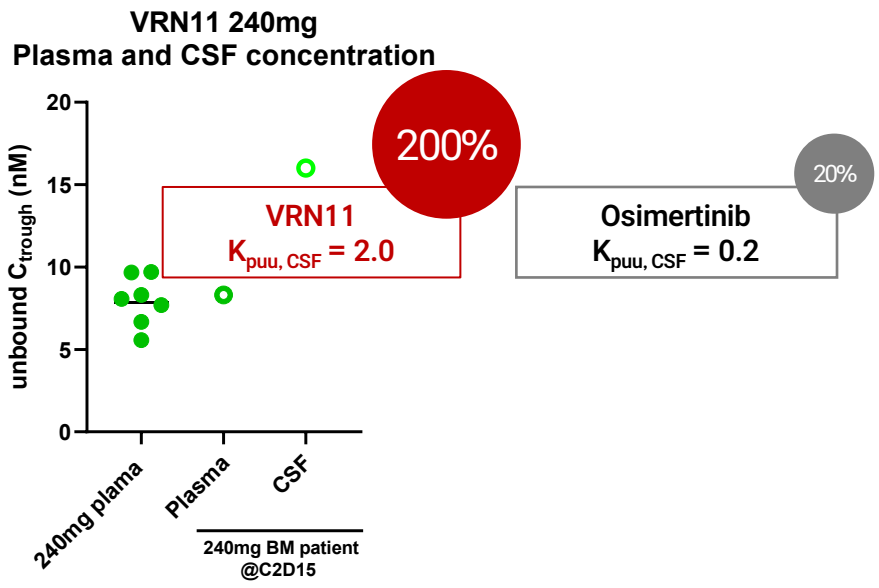
Base CNS lesion	VRN11	Osimertinib
Patients, n	16	11
CR, n	4 (25%)	0 (0%)
PR, n	0 (0%)	1 (9.1%)
SD, n Non-CR/Non-PD, n	12 (75%)	5 (45.5%)
PD, n	0 (0%)	2 (18.2%)
Disease control, n	16 (100%)	6 (54.5%)

Data cutoff July 2,2026
BM, brain metastasis; CNS, central nervous system; CR, complete response; iPFS, intracranial progression-free survival; Non-CR/Non-PD, non-complete response/non-progressive disease; PFS, progression-free survival.
[1]Eide IJZ, et al. Osimertinib in T790M-positive and -negative patients with EGFR-mutated advanced non-small cell lung cancer: the TREM study. Lung Cancer. 2020;143:27–35.
[2]Eide IJZ, et al. Intracranial effect of osimertinib in relapsed EGFR-mutated T790M-positive and -negative non-small cell lung cancer patients: results from a phase II study. Acta Oncol. 2021;60(12):1565–1571.

VRN11-Osimertinib 비교: 뇌 투과율 및 Target Engagement

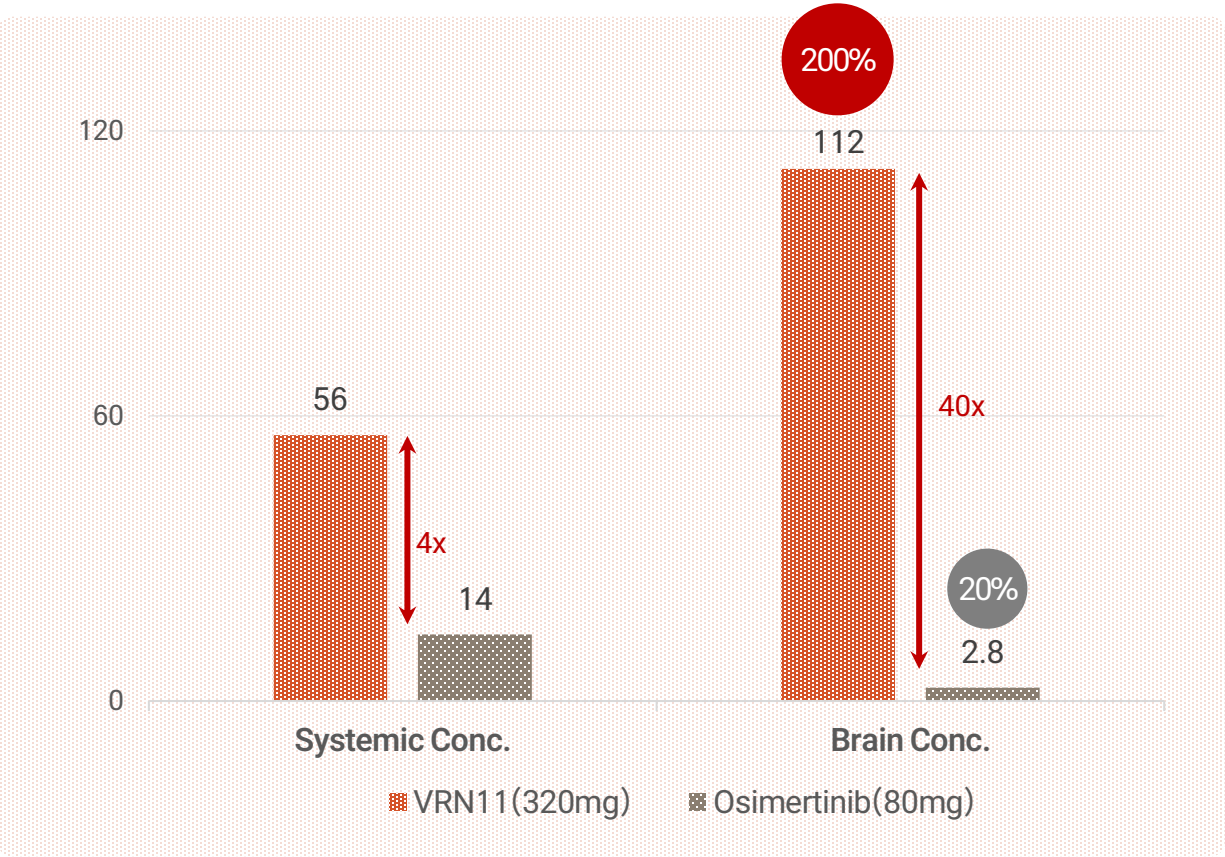
Osimertinib의 뇌 투과율은 20%인 반면, VRN11은 글로벌 최초로 **뇌 투과율 200%**에 대한 **Human PoC Data** 확보
Osimertinib 대비 **폐에서 4배, 뇌에서 40배** 우수한 종양 처치력(Target Engagement) 확인

환자에서의 뇌 투과율(Free Drug Concentration in Brain, $K_{puu,CSF}$)



	Monkey	Human
$K_{p,uu,csf}$	2.6	2.0*
$K_{p,uu,csf}$ of Osimertinib in human has been reported, 0.22[1]		

Target engagement 비교(Systemic - Brain)

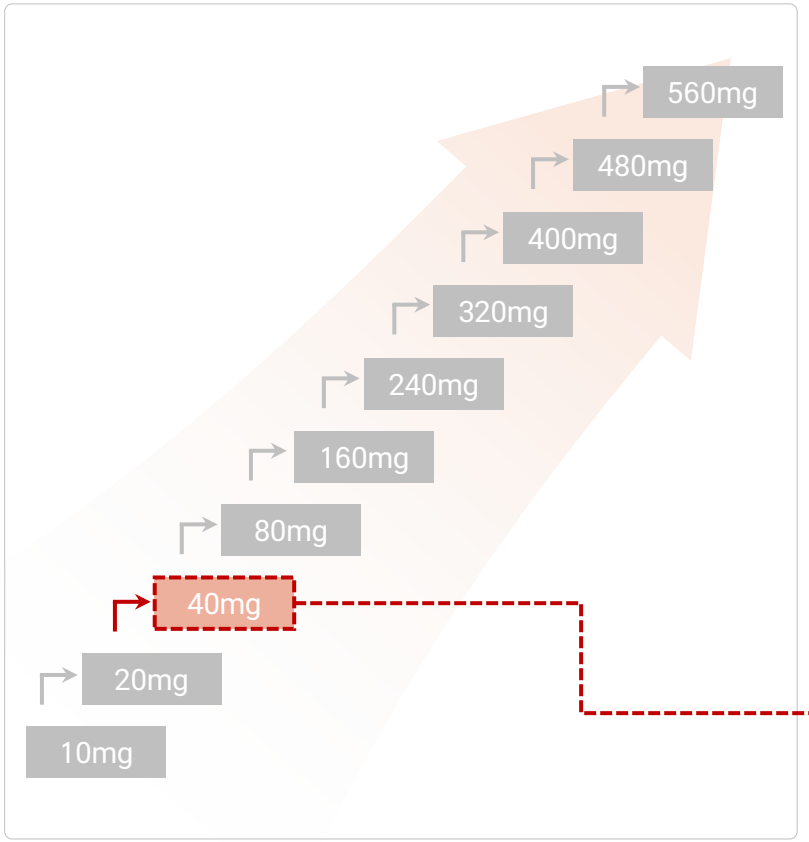


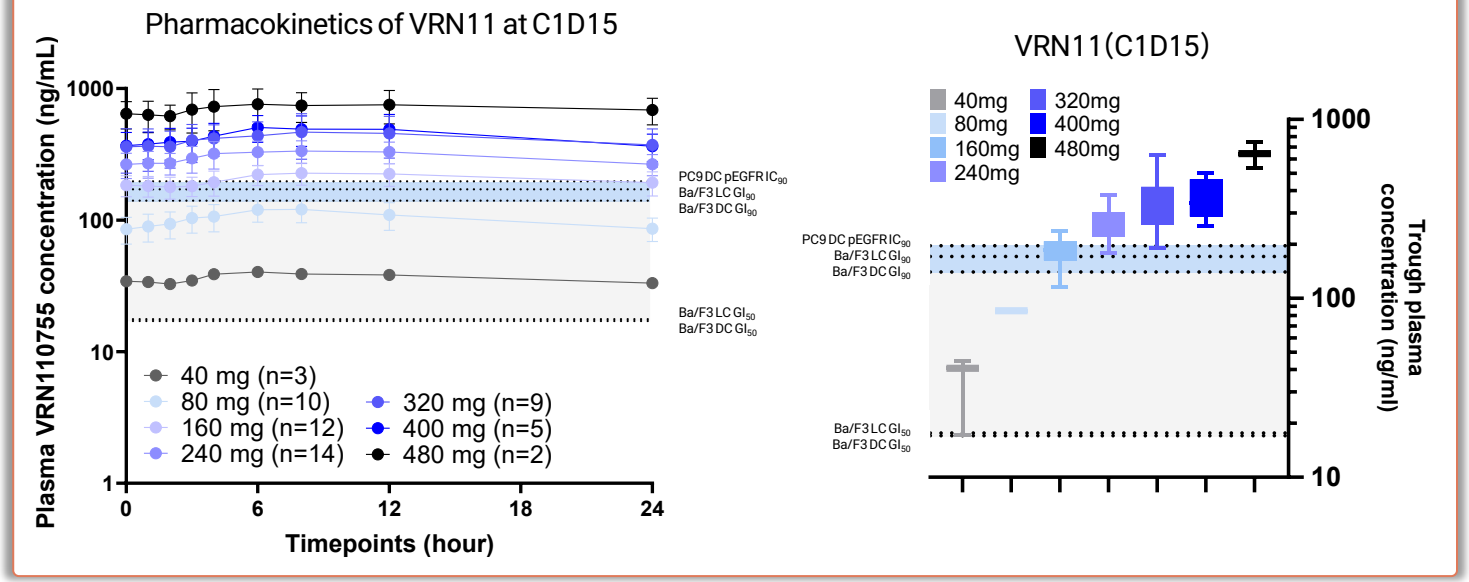
Source: [1]Park S, et al. J Clin Oncol. 2024;42(23):2747–2756
*A representative human PPB, 98.3% was used for calculation, $K_{puu,CSF}$ measured in 1 patient who received 240 mg

Case Report: 뇌전이 환자에서의 치료 효과 (1)

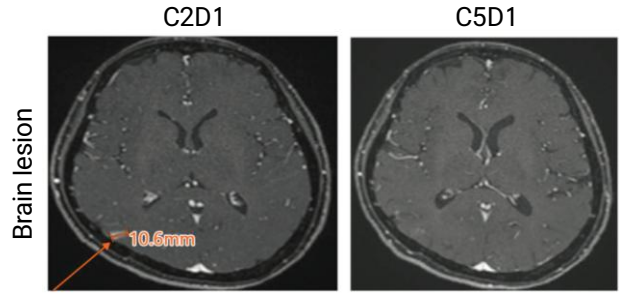
임상 1상 중 40mg부터 뇌 전이 환자에 대한 항암 효과 확인
용량 의존적 혈중 Free drug 농도 증가 확인

Phase 1a. Dose escalation





40mg



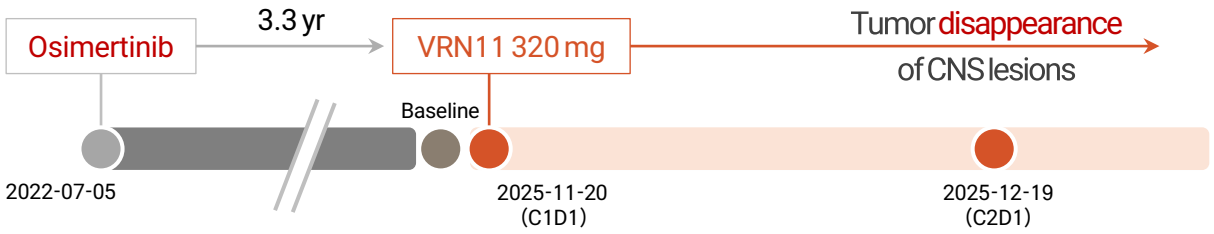
- Lung, brain, and pleural metastasis
- Two prior systemic treatments, including Dacomitinib and Osimertinib
- Tumor disappearance of CNS lesion

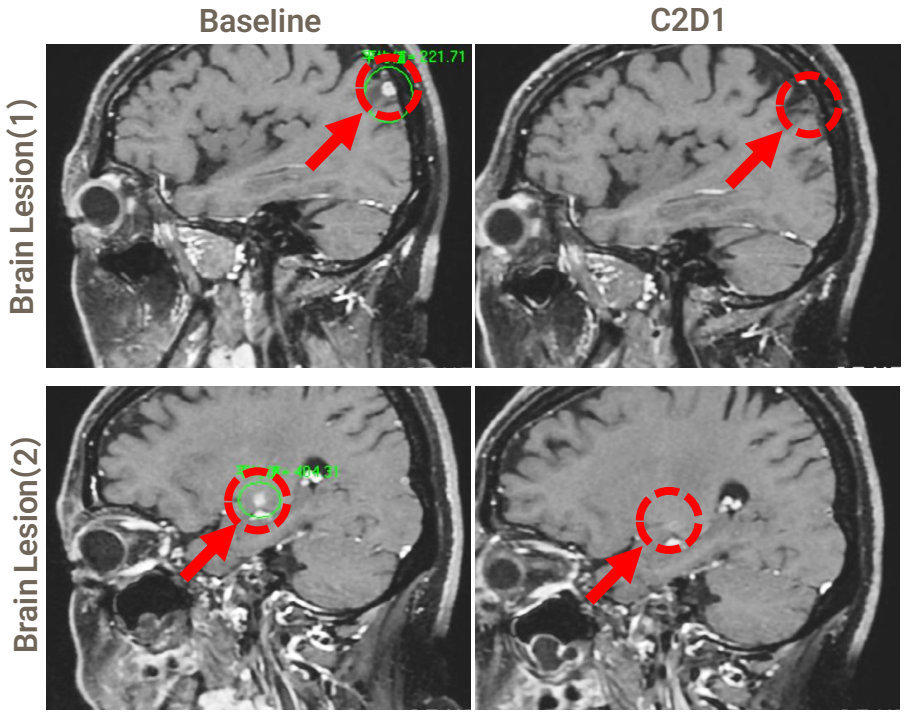
PR, Partial response; SD, Stable disease; PD, Progressive disease; TRAE, treatment-related adverse event; SAE, serious adverse event; DLT, dose limiting toxicity

Case Report: 뇌전이 환자에서의 치료 효과 (2)

3세대 EGFR TKI 치료 후 뇌전이 환자에서 VRN11 투여 후 첫 종양평가 시 뇌 병변 소실 확인
폐 병변 50% 감소로 Overall PR(partial response) 달성

320mg: 47-yr female with EGFR Del19/C797S NSCLC





Baseline and Treatment History

- Lung, Brain, Bone metastasis
- Disease progression **after Osimertinib**

VRN11 Treatment

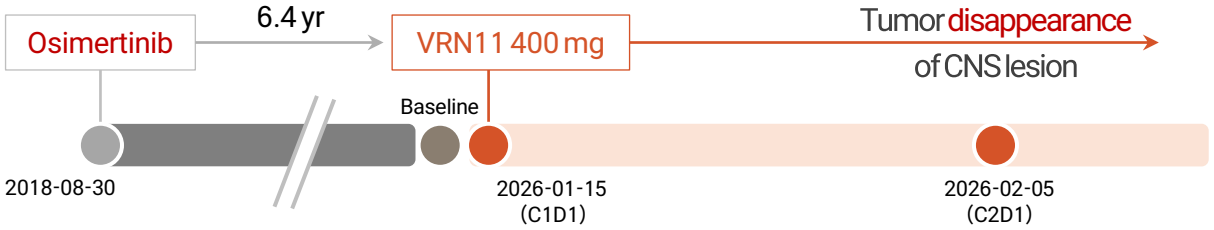
- Lung target lesion: 50% tumor reduction
- **Two brain lesions*** were **absent** at first TA
- Baseline ctDNA of EGFR mutation cleared
- Overall best response: PR

PR, Partial response; SD, Stable disease; PD, Progressive disease; TRAE, treatment-related adverse event; SAE, serious adverse event; DLT, dose limiting toxicity
*Non-target lesion

Case Report: 뇌전이 환자에서의 치료 효과 (3)

3세대 EGFR TKI 치료 후 뇌전이가 발생한 환자에서 VRN11 투여 후 첫 종양평가 시 뇌 병변 소실 확인
폐 병변 38% 감소로 Overall PR(partial response) 달성

400mg: 71-yr male with EGFR L858R NSCLC

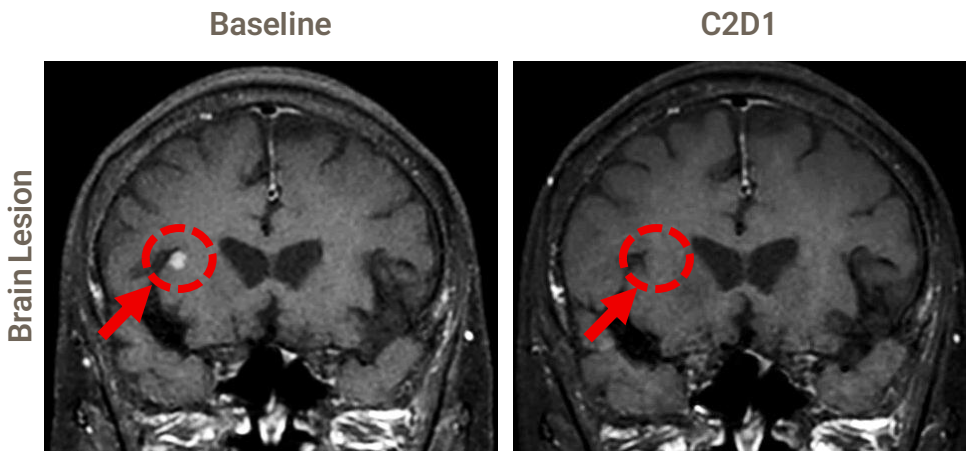


Baseline and Treatment History

- Lung and brain metastasis
- Prior EGFR TKI: **Osimertinib, Lazertinib**

VRN11 Treatment

- Lung target lesion: 38% tumor reduction
- **Brain lesion*: absent**
- Overall best response: PR



PR, Partial response; SD, Stable disease; PD, Progressive disease; TRAE, treatment-related adverse event; SAE, serious adverse event; DLT, dose limiting toxicity
*Non-target lesion

VRN11

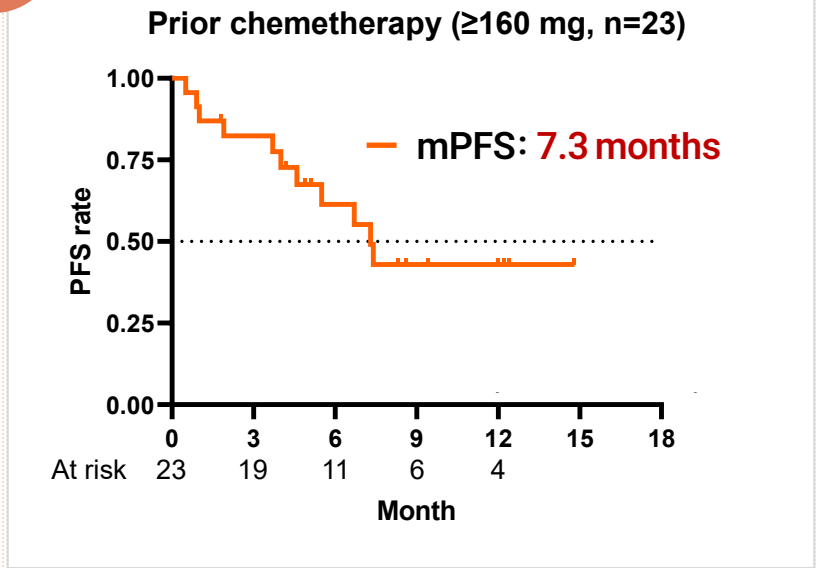
EGFR 2nd Line treatment

VRN11-Osimertinib 비교: Progression-free survival(PFS); 2L treatment

화학요법 치료 이력 환자 대상 VRN11 mPFS 7개월 이상
Heavily pretreated된 환자임에도 불구하고 Osimertinib 4.07개월 대비 현저한 생존기간 연장 효과 입증

C797S -negative

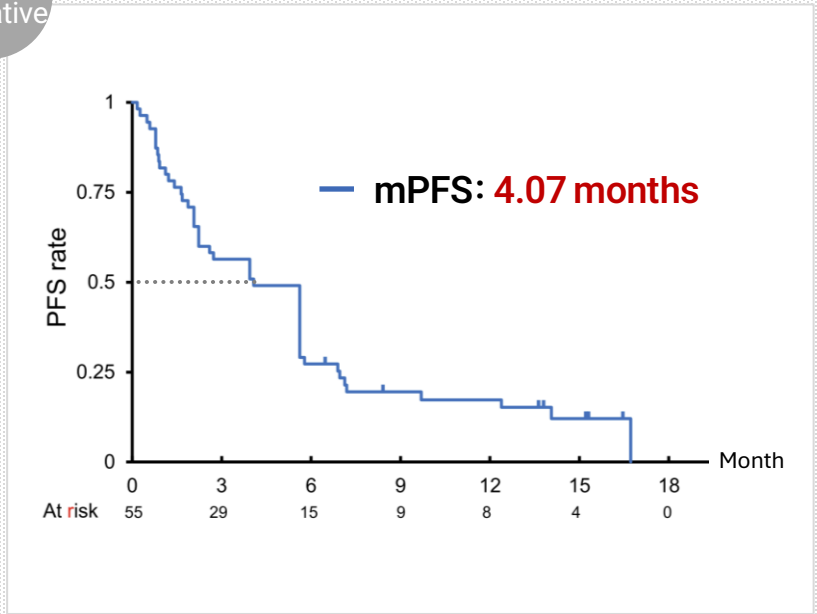
VRN11: Progression-Free Survival (PFS)



Prior EGFR TKI	
Gefitinib	22%
Erlotinib	13%
Afatinib	30%
Dacomitinib	4%
Osimertinib	48%
Lazertinib	35%

T790M -negative

Osimertinib: Progression-Free Survival (PFS)[1]



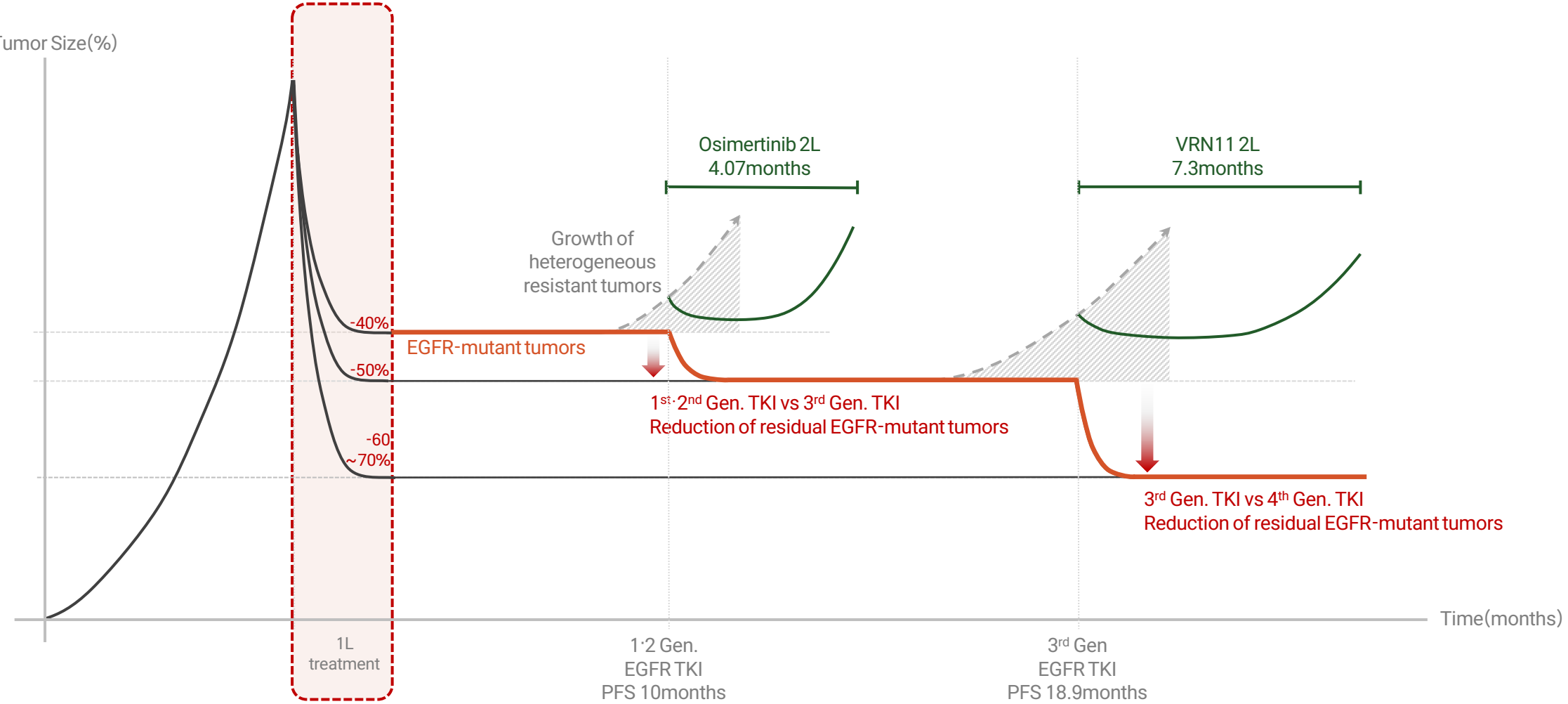
Prior EGFR TKI	
1st- or 2nd-Generation	100%
3rd generation	0%

	VRN11 (C797S negative)	Osimertinib[1] (T790M negative)
mPFS	7.3 months (95% CI, 4.0-NR months)	4.07 months (95% CI 2.1-4.3 months)

PFS, Progression-Free survival;
Source: ASCO2026, [1]Takeda M, et al. Lung Cancer. 2023;177:44–50.

약물의 세대별 종양 억제력과 종양 증식력의 균형

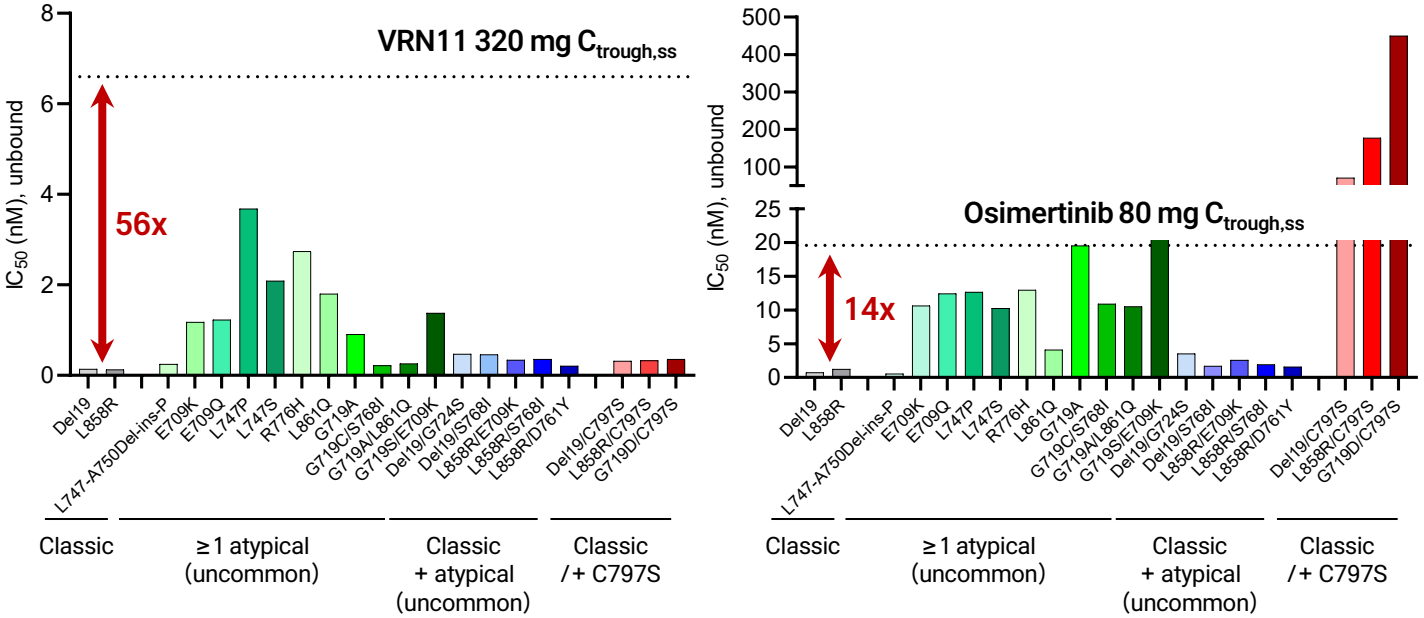
VRN11의 우수한 표적 억제력이 EGFR 의존적인 종양을 3세대 EGFR-TKI보다 더 효과적으로 감소시킴으로써 PFS 연장



EGFR 변이 비소세포폐암에 대한 전임상 및 임상적 효능 근거

VRN11 320mg에서 전반적인 EGFR 변이에 대한 우수한 활성 확인
EGFR del19 및 L858R에서 Osimertinib 80mg 대비 4배 강력한 Target Engagement 확보, 탁월한 뇌 투과율로 CNS 영역서 차별적 우위 확인

In vitro Target Engagement in Ba/F3-engineered Cell Lines



Target engagement ratio

Target engagement ratio (TER)

	VRN11 320mg	Osimertinib 80mg	VRN11 / Osimertinib
Classic	56	14	4x
Classic + C797S	22	< 1	140x
Classic + Atypical	20	9	2x
Atypical	5	2	3x

x 2.0

x 0.2

Target engagement ratio (TER); Brain

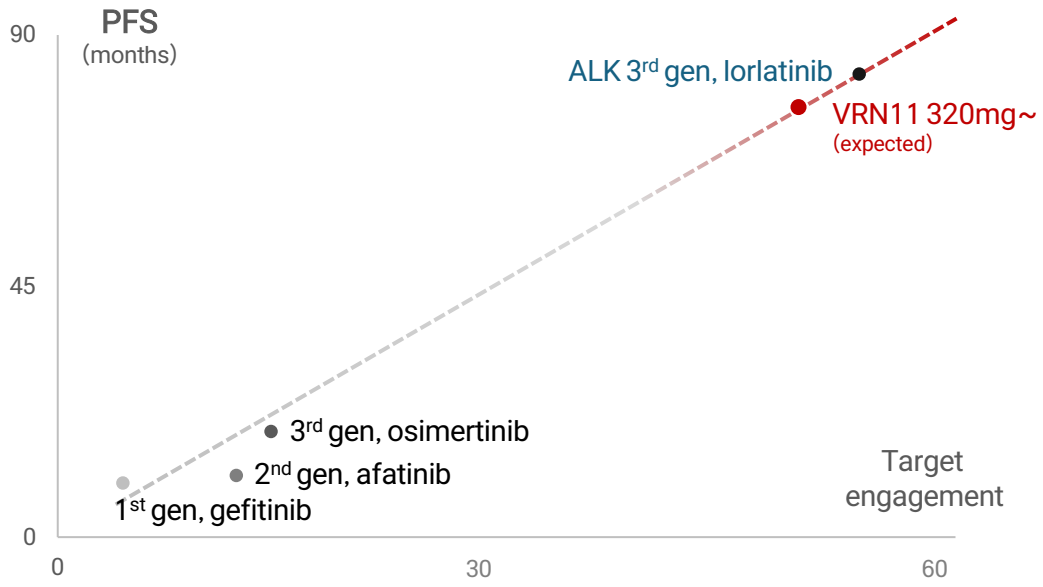
	VRN11 320mg	Osimertinib 80mg	VRN11 / Osimertinib
Classic	112	2.8	40x

Source: ASCO2026

PFS-CNS CR-Target engagement

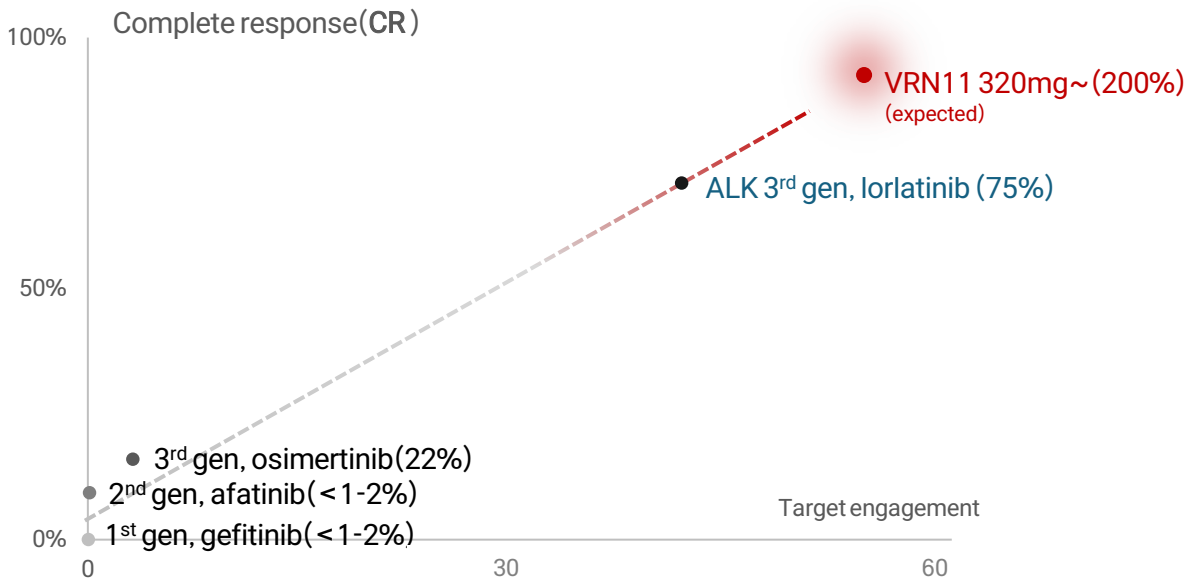
1차 치료 임상에서 기대되는 주요 성과: 두개내 완전관해(iCR)율 70% 이상 및 무진행생존기간(PFS) 7년 이상

Systemic



mPFS	EGFR		ALK
	Osimertinib	VRN11	Lorlatinib
2L+	4.07 m	7.3 m	7.3 m
1L	18.9 m	> 7 y (expected)	> 7 y

CNS

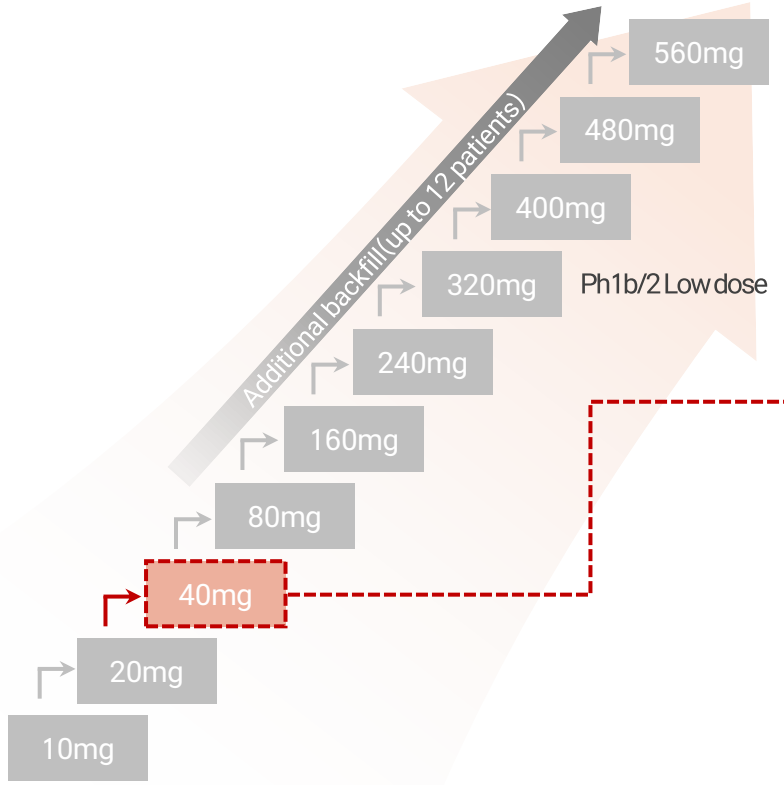


CNS CR	EGFR		ALK
	Osimertinib	VRN11	Lorlatinib
2L+	0%	25%	20%
1L	16%	> 70% (expected)	71%

Source: Douillard JY, et al. Br J Cancer 2014;110:55-62, Sequist LV, et al. J Clin Oncol. 2013 Sep 20;31(27):3327-34, Soria JC, et al. N Engl J Med. 2018 Jan 11;378(2):113-125, Shaw AT, et al. Ann Oncol. 2026 Sep;37(9):1242-1252, Zhao J, et al. Clin Lung Cancer. 2013 Mar;14(2):188-93, Kim M, et al. Drug Metab Dispos. 2019 Apr;47(4):393-404, Park S, et al. J Clin Oncol.2024;42(23):2747–2756, Sun S, et al. J Clin Pharmacol. 2022;62(9):1170-1176, Lu S, et al. Cancer Commun (Lond). 2024 Sep;44(9):1005-1017, Kang L, et al. Front Oncol. 2023 Feb 23;13:1094195, Shaw AT, et al. N Engl J Med. 2020 Nov 19;383(21):2018-2029, Jänne PA, et al. J Clin Oncol. 2024 Mar 1;42(7):808-820, Eide IJZ, et al. Acta Oncol. 2021;60(12):1565–1571, Solomon BJ, et al. Lancet Oncol. 2018;19(12):1654-1667, Takeda M, et al. Lung Cancer. 2023 Mar;177:44-50, in-house

Case Report: 임상 1상 중 40mg부터 뇌 전이 환자에 대한 항암 효과 확인

Phase 1a. Dose escalation

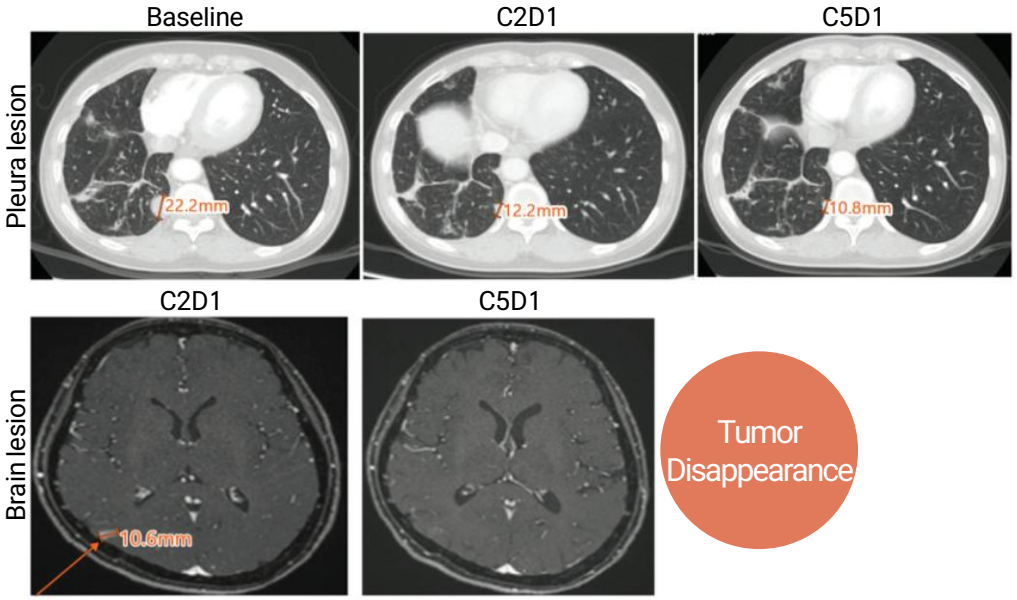


- Up to 12 backfill patients may be enrolled from the 80 mg cohort, subject to SMC safety confirmation.

40mg Case report

40mg

- Lung, brain, and pleural metastasis
- Two prior systemic treatments, including Dacomitinib and **Osimertinib**



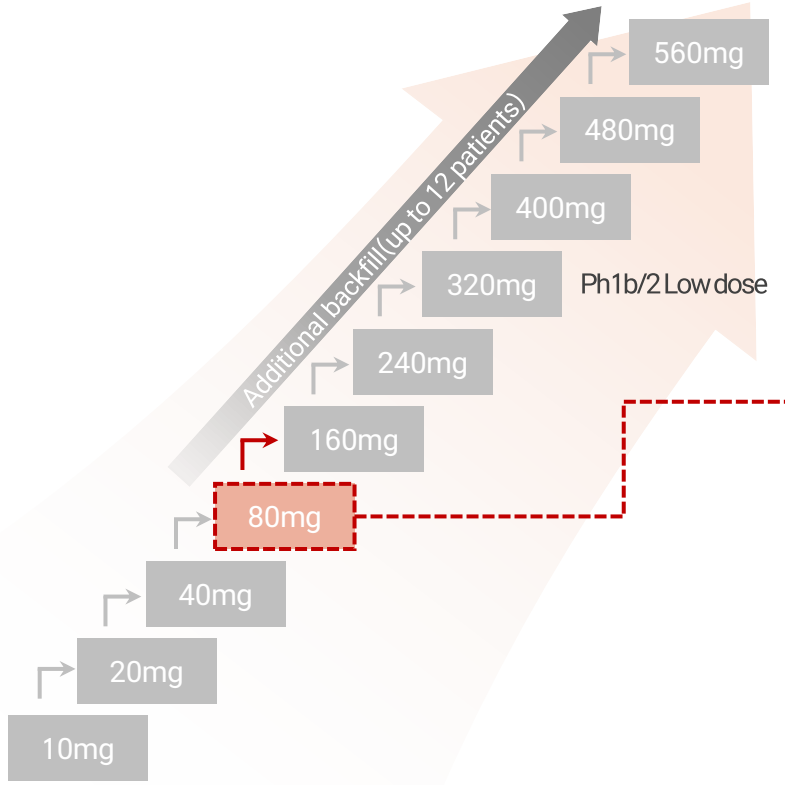
-51% Tumor reduction

Tumor Disappearance

PR, Partial response; SD, Stable disease; PD, Progressive disease; TRAE, treatment-related adverse event; SAE, serious adverse event; DLT, dose limiting toxicity

Case Report: 용량 증량에 따른 치료 효과 개선 (EGFR del19, 80 → 160mg)

Phase 1a. Dose escalation

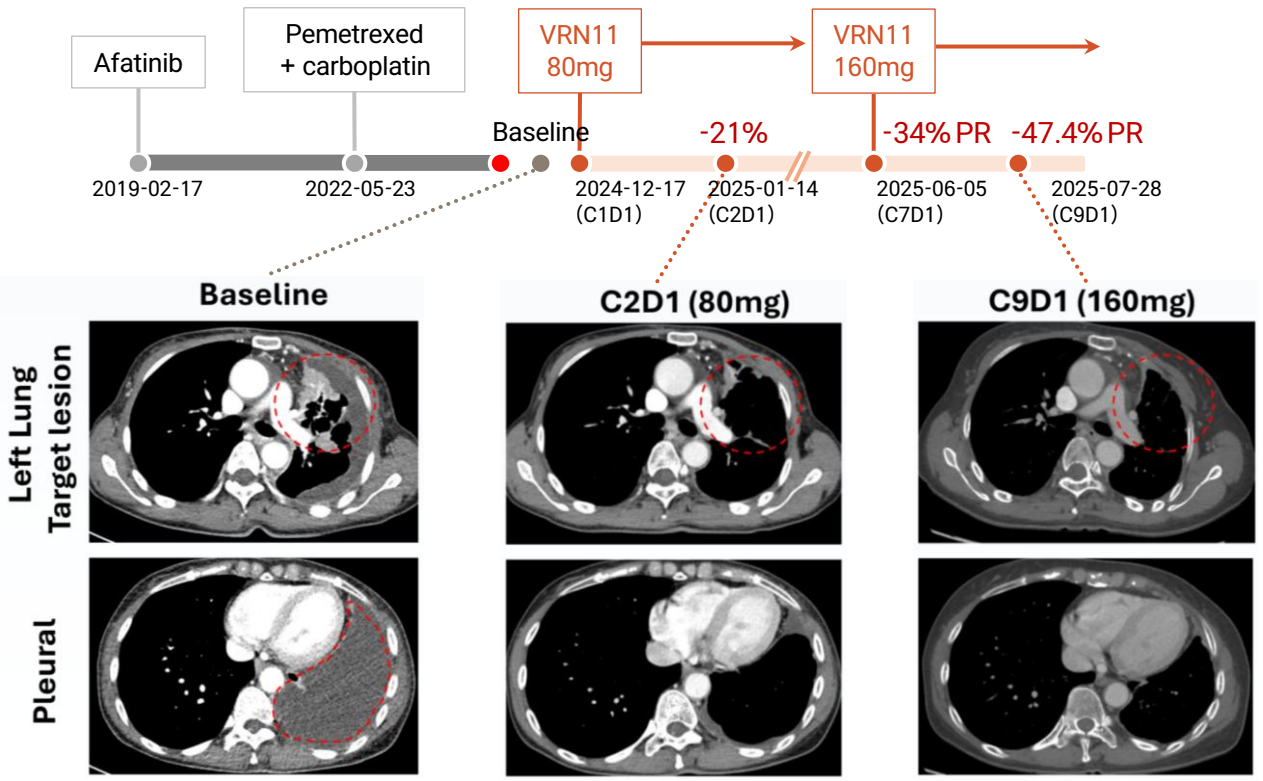


- Up to 12 backfill patients may be enrolled from the 80 mg cohort, subject to SMC safety confirmation.

80mg Case report

80mg → 160mg

- ≥ 19 months, Best response: PR
- Safety: **No TRAE**

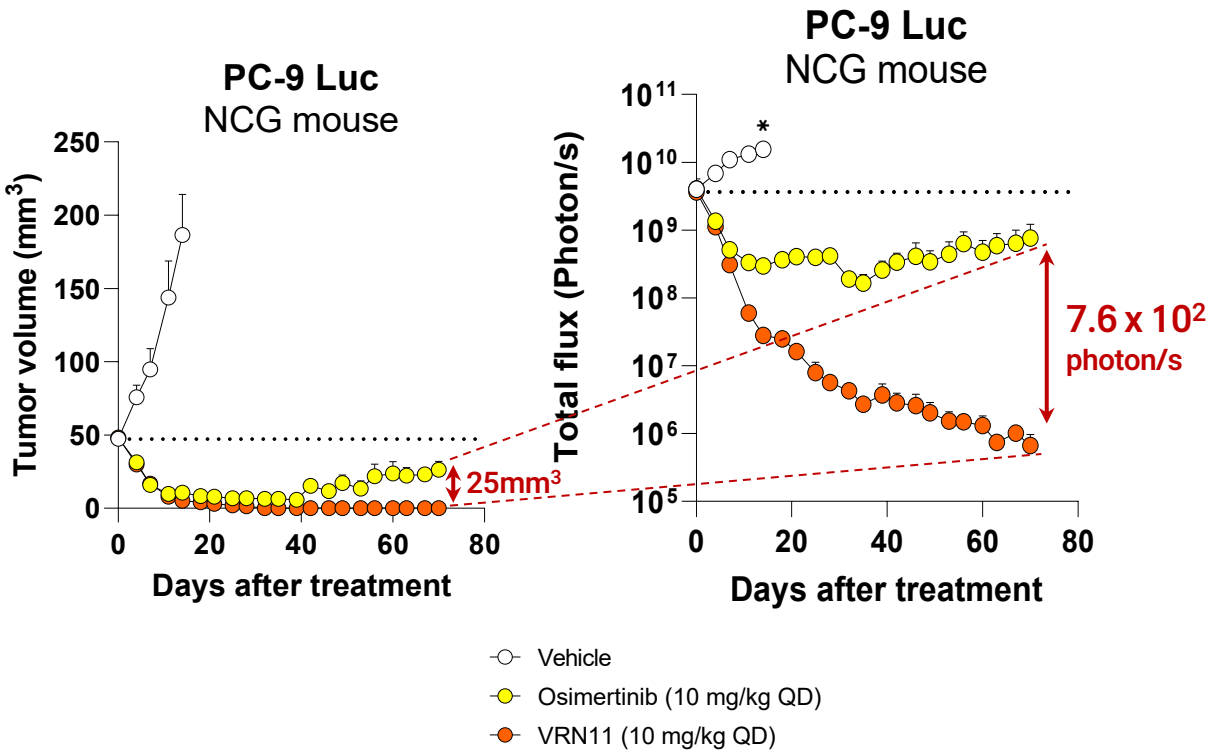


PR, Partial response; SD, Stable disease; PD, Progressive disease; TRAE, treatment-related adverse event; SAE, serious adverse event; DLT, dose limiting toxicity

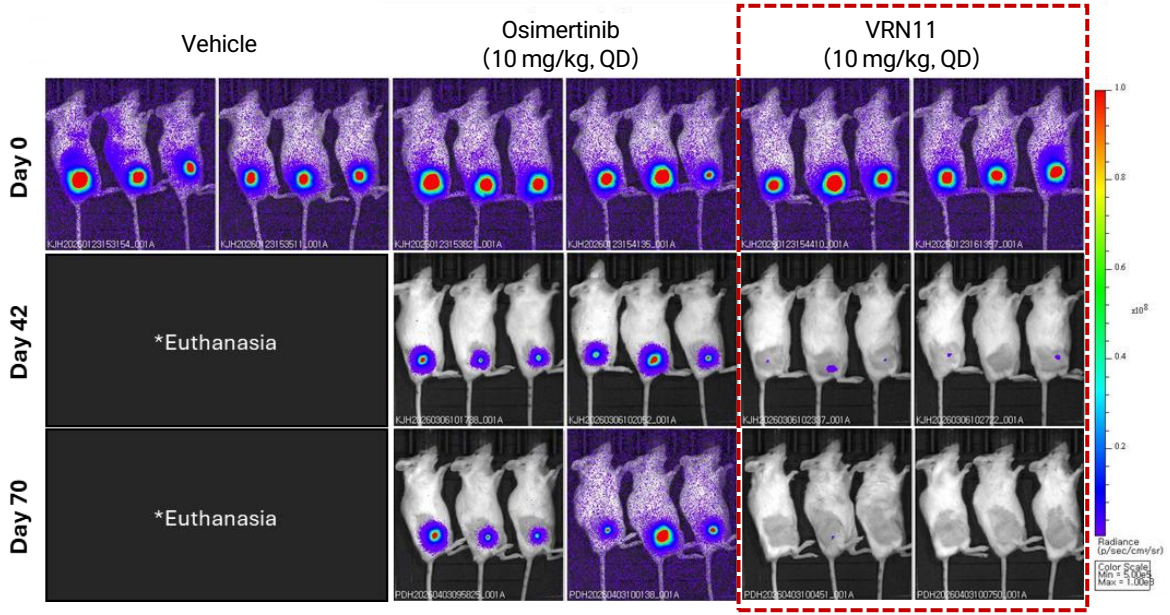
In vivo 모델을 통해 입증된 VRN11의 종양 반응 예측: Deeper Response

CDX 모델에서 Osimertinib 대비 깊은 종양 억제(Depth of Response) 효과 확인

Subcutaneous CDX model(PC9 _ Del19)

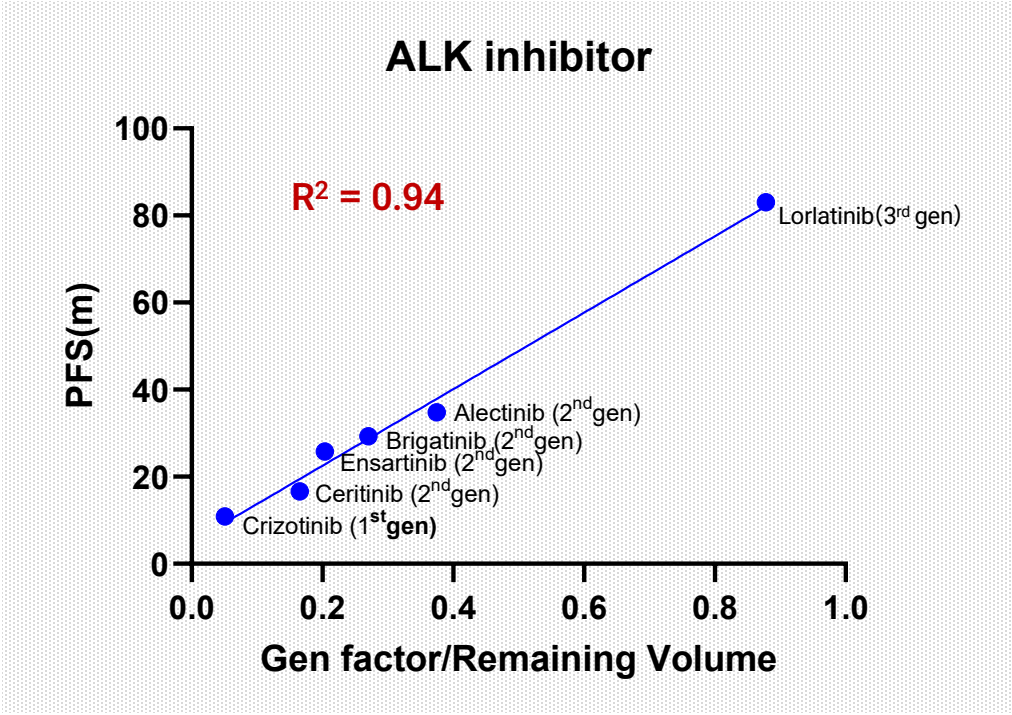


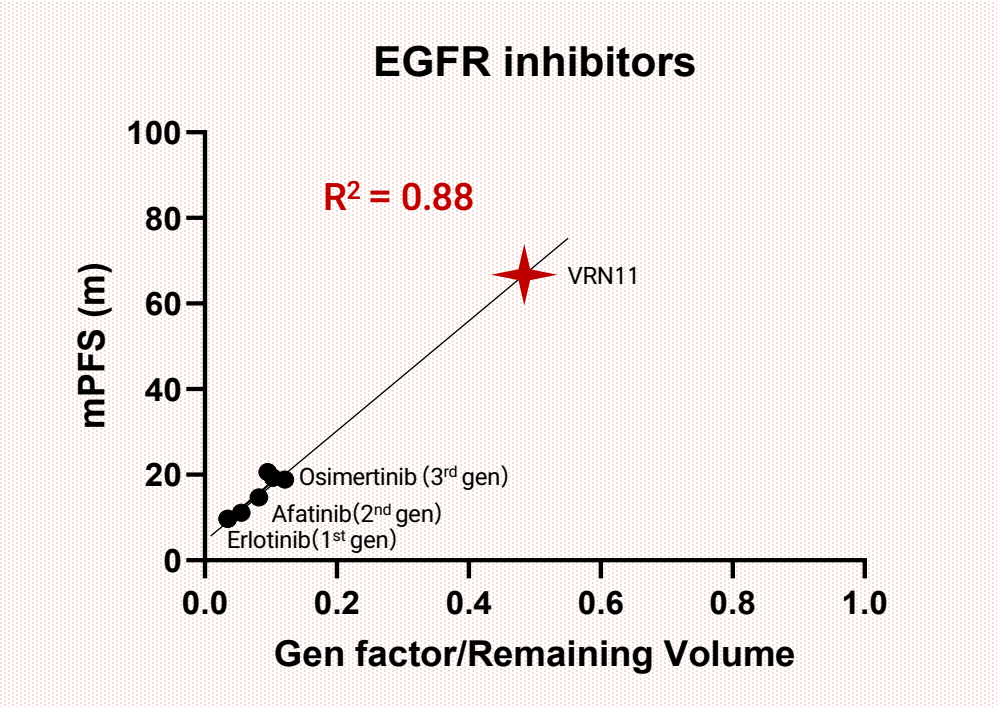
Luciferase signal in SC model

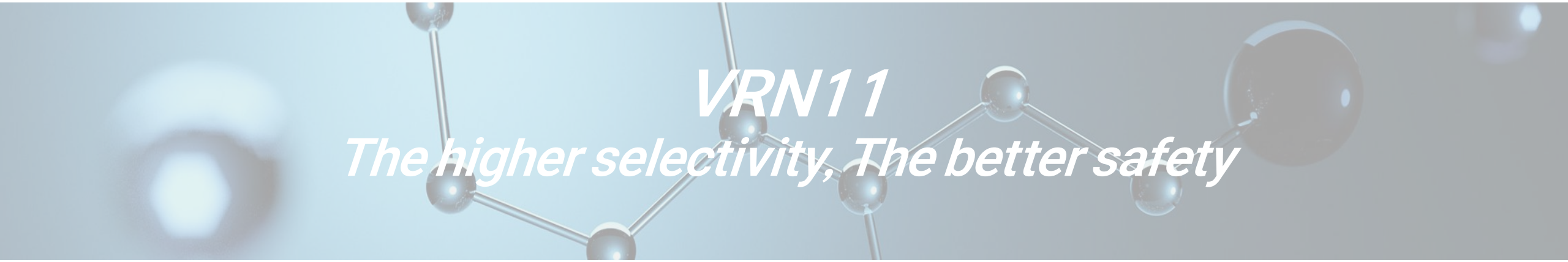


PFS 와 Depth of Response 간의 상관관계(ALK, EGFR)

ALK 사례에서도 Target Engagement가 높을 수록 종양 감소 폭이 크고, 결과적으로 PFS가 길어지는 현상 확인







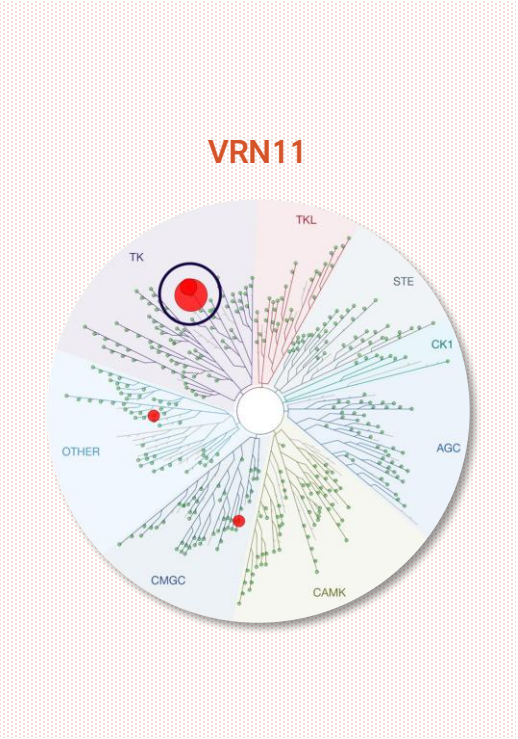
VRN11

The higher selectivity, The better safety

Safety Profile

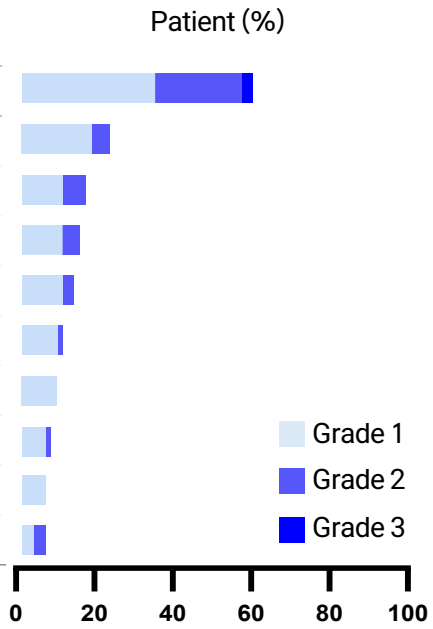
Grade 3 이상의 약물 관련 부작용 3%로 뛰어난 내약성 확인
약물 관련 부작용으로 인한 영구 투여 중단(Permanent discontinuation) 사례 없음

VRN11 선택성(Selectivity)



임상 1상에서 양호한 안전성 및 내약성 확인

VRN11 10 – 480 mg (n=67)	Treatment-Related Adverse Events (> 5%)	
	Any Grade	≥ Grade 3
Discontinuation	0%	
Dose reduction	6%	
Any AE	60%	3%
Rash	22%	-
Pruritus	16%	-
Diarrhea	15%	-
Dry skin	13%	-
AST increase	10%	-
ALT increase	9%	-
Nausea	8%	-
Anorexia	6%	-
Paronychia	6%	-



- ✓ 용량제한독성(DLT)이 관찰되지 않아 최대 내약용량(MTD)에 도달하지 않음.
- ✓ 치료 관련 부작용(TRAE)으로 인한 영구적 투여 중단 사례 없음
- ✓ 대부분의 치료 관련 부작용은 경증이었으며, EGFR 억제로 인한 On-target 부작용으로 확인

Kinase profiles were analyzed against 486 human kinases, and S10 kinases were indicated as a red dot.
Data cut-off July 2, 2026

경쟁 약물의 안전성 프로파일 및 실제 임상 투여 현황(Osimertinib)

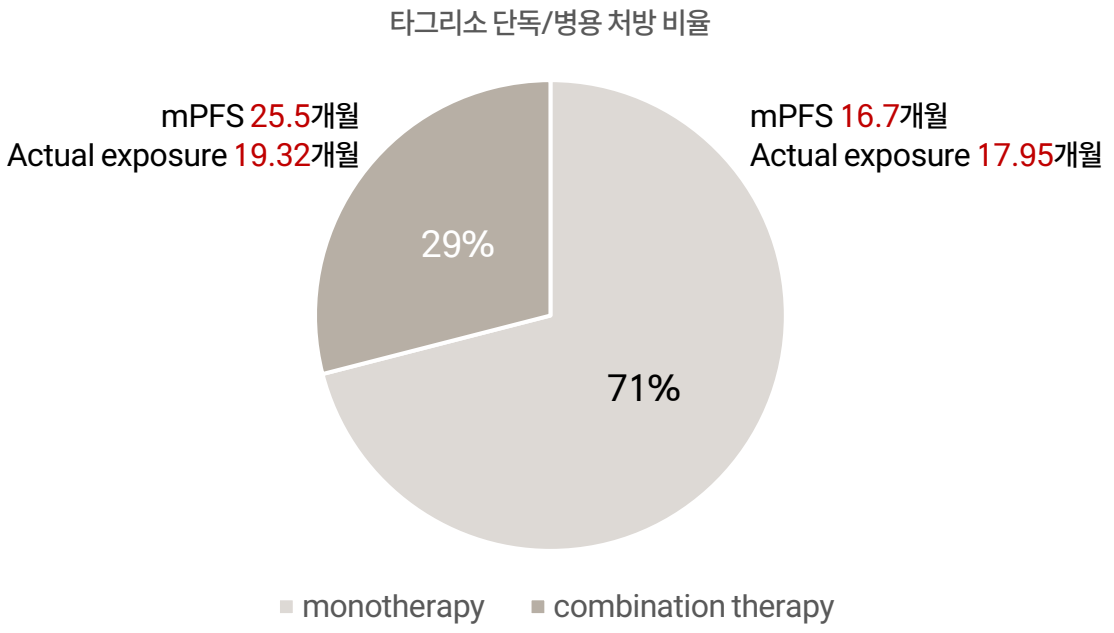
Osimertinib 병용요법의 경우, 높은 부작용으로 인해 실제 투여 기간이 무진행생존기간 대비 감소하고 처방률이 저하됨

Adjuvant		
ADAURA	대조군	Osimertinib
	재발율	DFS
2년	45%	
3년		84%
4년	62%	
5년		53%

Osimertinib 주요 임상별 안전성 프로파일 비교[1,2,3]

	ADAURA	AURA3	FLAURA2	
	단독	단독	단독	병용
Grade ≥3 AE any cause	23%	23%	34%	70%
Serious AE	20%	18%	19%	38%
Discontinuation due to AE	13%	7%	7%	12%
Dose interruption	27%	~19%	19%	44%
Dose reduction	12%	3%	3%	10%

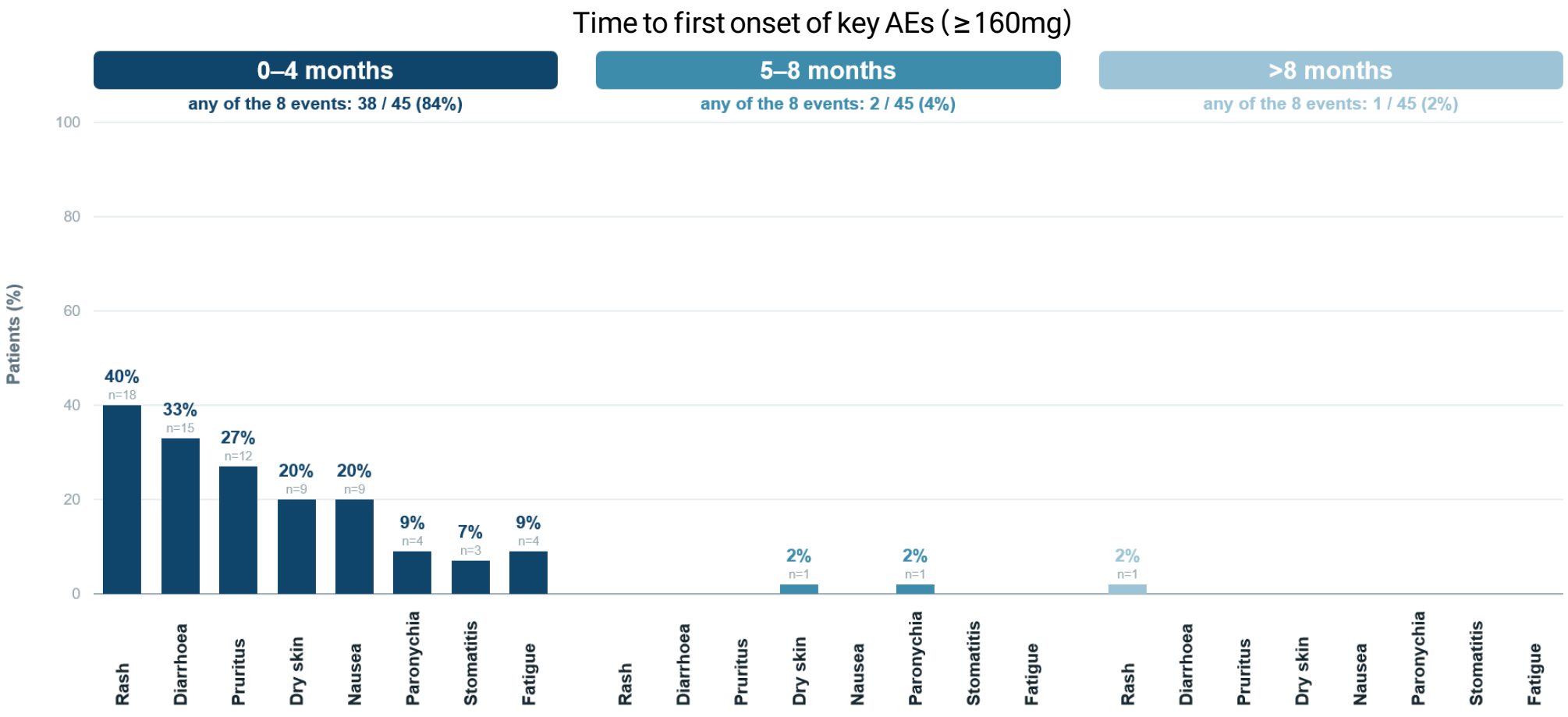
높은 부작용에 따른 병용 요법의 낮은 처방비율 및 실질 투여기간 단축[4,5]



Source: [1]Herbst RS, et al. J Clin Oncol. 2023 Apr 1;41(10):1830-1840, [2]Mok TS, et al. N Engl J Med. 2017 Feb 16;376(7):629-640. [3]Jänne PA, et al. N Engl J Med. 2026 Jan 1;394(1):27-38, [4]Santos E, et al. Journal of Thoracic Oncology, 20S474, [5]Osimertinib (Tagrisso): Therapeutic area: Non-small cell lung cancer: Reimbursement Review [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2025 Jan. Clinical Review.

Safety Profile: Onset Adverse Events

주요 이상반응은 대부분 투여 초기(0~4개월)에 발생하며, 후기 발생은 드묾

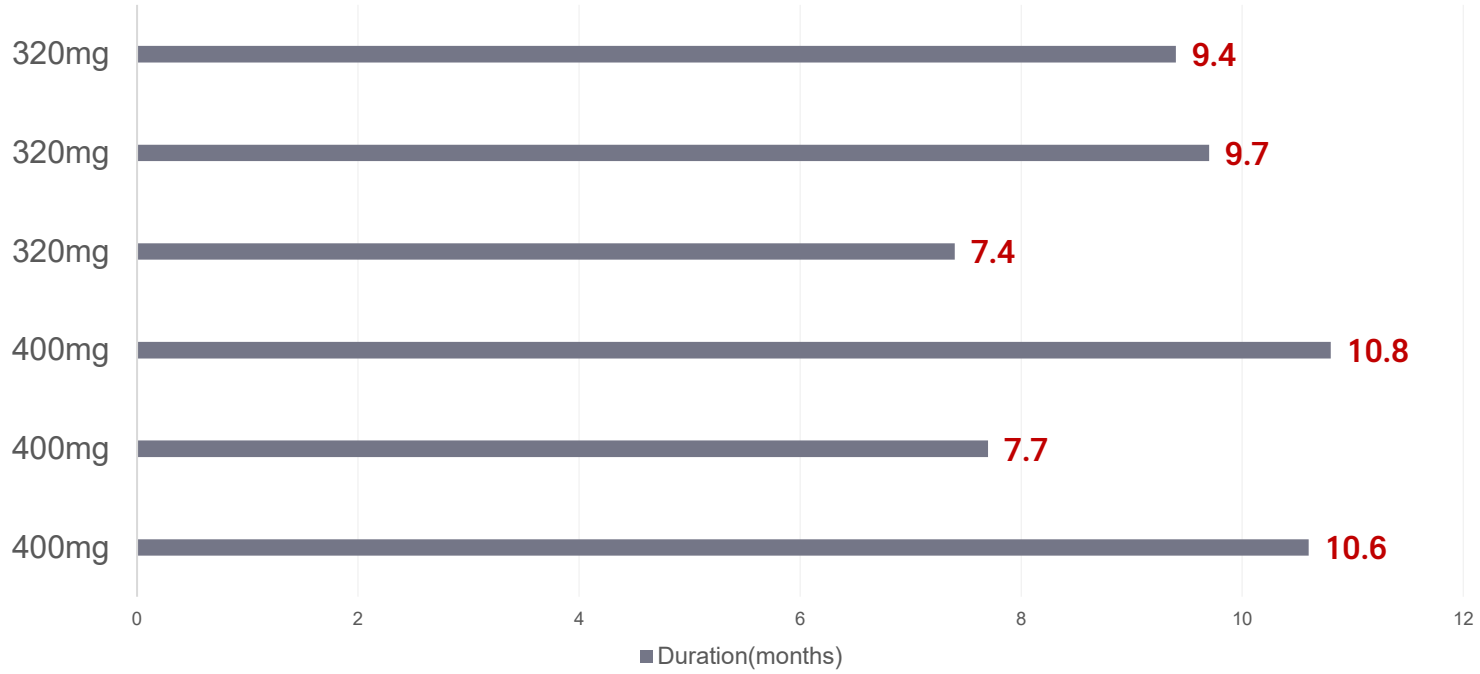


Data cut-off July 2, 2026

Safety Profile: Long-Term Exposure

320mg, 400mg을 6개월 이상 투약한 환자에서도 대부분 Grade 1 이상반응만 관찰되었으며, 중대한 이상반응은 없음

Long-duration treated patients (> 6 months)



CTCAE Grade	
Grade 1	
Grade 1	
Grade 1	
Grade 1	
Grade 1	
Grade 1	
Grade 2	- Grade 2 diarrhea resolved within 1 day

✓ 320 mg cohort (n=9): 3 pts treated for > 6 months.
3 pts remain on treatment.

✓ 400 mg cohort (n=8): 3 pts treated for > 6 months.
5 pts remain on treatment.

Data cut-off July 2, 2026

우수한 안전성을 기반으로 EGFR Resistance-Negative(unknown) 치료 패러다임 재편

우수한 안전성 프로파일을 기반으로 한 다양한 병용 가능성 존재

표준 치료요법 내성/불응 환자 대상 임상 시험 비교 [1,2,3,4]

EGFR 2L+환자 기본 옵션 (expected)

	VRN11		Dato-Dxd	Chemotherapy	Chemotherapy, Pembrolizumab	Chemotherapy, Amivantamab	Chemotherapy, Amivantamab, Lazertinib	VRN11 +Chemotherapy	
	뇌전이	뇌전이X						뇌전이	뇌전이X
mPFS (months)	≥9	7.3	4.4	4.2	5.6	6.3	8.3	≥ 13.2	11.5
≥ Grade 3 TRAE	3%		25.6%	35%	43.7%	67%	87%	38%	

EGFR 표준 치료 불응 환자 대상으로 VRN11과 세포독성항암제(chemotherapy) 와의 병용요법 진행

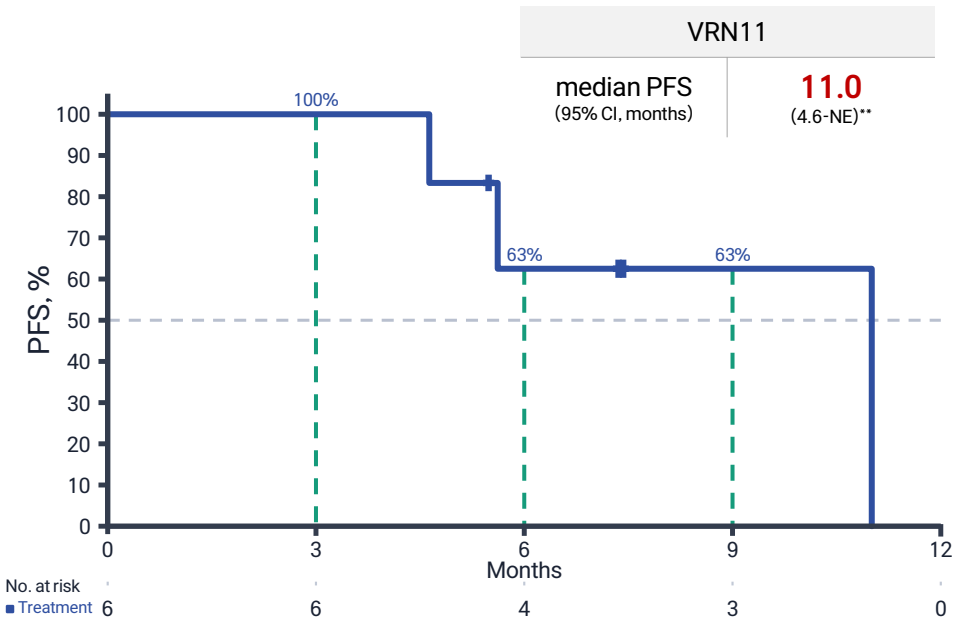
Source: [1]Passaro, A. et al. Annals of Oncology, Volume 35, Issue 1, 77 - 90, [2]Jänne PA, et al. N Engl J Med. 2015;372(18):1689-1699, [3]Myung-Ju Ahn et al. J Clin Oncol 43, 260-272(2025), [4]James Chih-Hsin Yang et al., JCO 42, 4029-4039(2024)
PFS, progression-free survival; TRAE, treatment-related adverse event; DCR, disease control rate ※VRN11 병용의 수치의 경우, 두 약물의 단순 합산값

VRN11
EGFR C797S

EGFR C797S 변이 환자에서의 치료 효과

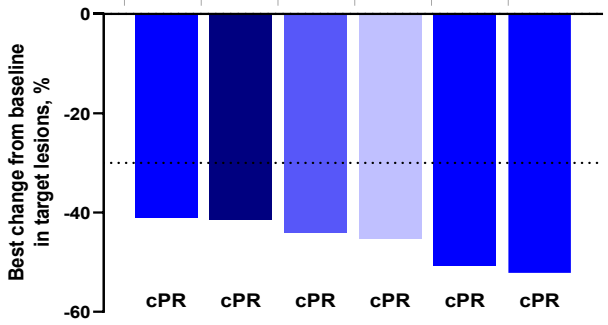
유효용량 (≥160mg)을 투약한 모든 EGFR C797S 변이 환자군에서 **무진행 생존기간 11개월** 및 **객관적 반응률 100%** 확인(6/6, Partial Response)

Progression-Free Survival



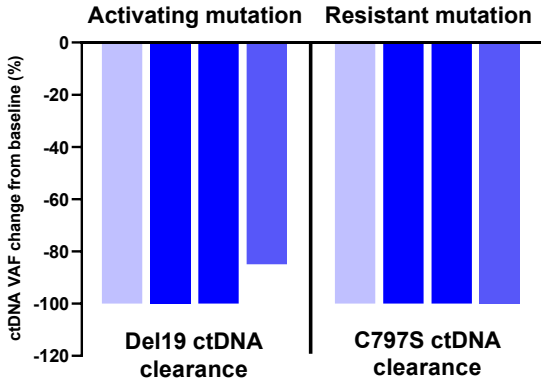
Best Response

ctDNA marker	DC	DC*	DC	DC	DC	LC*
Dose(mg)	320	400	240	160	320	320
No. prior Tx	2	2	2	2	1	4
BM	X	X	O	O	O	X



160mg 이상 투여한 C797S 변이 환자 6명에서
- ✓ ORR 100% 확인(6/6)
- ✓ Baseline 대비 40% 이상 종양 감소 관찰

ctDNA Clearance



모든 환자에서 C797S ctDNA 소실 확인
이 중 3명에서 Del19 ctDNA 소실 확인

BM, brain metastasis; cPR, confirmed partial response; ctDNA, circulating tumor DNA; mo, months; NE, not estimable; ORR, objective response rate; PFS, progression-free survival; Tx, treatment; uPR, unconfirmed partial response.
* Patients with C797S undetected on screening ctDNA, pre-biomarker for inclusion required tumor tissue NGS confirmation of C797S within 3 months prior to C1D1.
** Preliminary data as of July 02, 2026; n=6, 3 PFS events. Median PFS estimate is not mature and subject to change with longer follow-up.

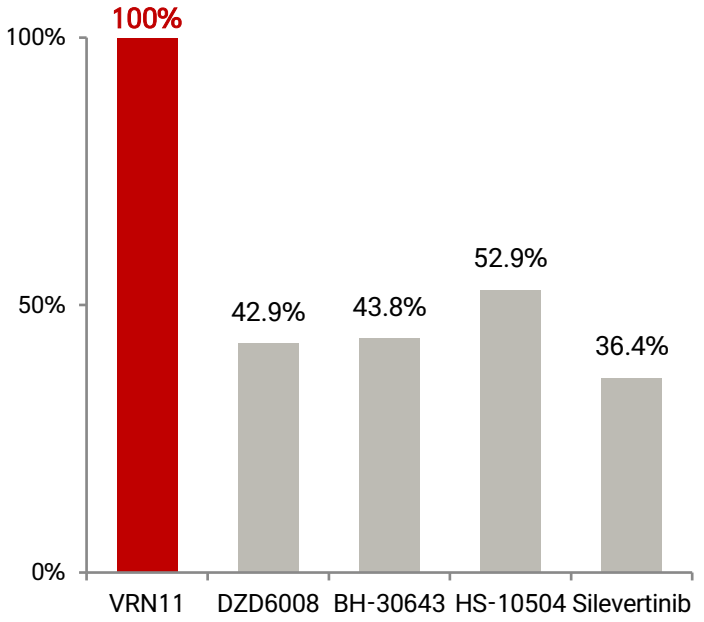
EGFR C797S Competitive Landscape

높은 객관적 반응률(ORR)과 낮은 부작용(Grade≥3)을 통해 효능과 안전성 측면에서 경쟁력 입증

	VRN11	DZD6008	BH-30643	HS-10504		Silevertinib (BDTX-1535)
Clinical study	Ph1	Ph1	Ph1	Ph1		Ph2
ORR	100% (6/6)	42.9% (9/21) (60mg)	43.8% (14/32)	300mg	400mg(RP2D)	36.4% (12/33) (200mg)
				31.8%	52.9%	
≥G3 TRAE	3%	*Not reported*	20%	35.3%	65.7%	35%
Dose reduction	6%	*Not reported*	16%	0%	42.9%	32%

✓ DZD 6008 Grade ≥3 TRAE: Lymphocyte count decreased 8.3%, Anemia 4.2%, Malaise 4.2%, Fatigue 4.2%, Amylase increased 4.2%
✓ BH-30643 Grade ≥3 TRAE: Bilirubin increased 13%

C797S ORR: VRN11 100%
>2 fold higher efficacy
compared to competitors



Sources: Silevertinib: ASCO2026, DZD6008: Wang et al. ASCO 2025 abstract 8616, ASCO2026, NCT06905197. HS-10504: AACR2026, BH-30643: BlossomHill JPM 2026, ASCO 2026, NCT06706076. VRN11: Voronoi internal & WCLC 2026.

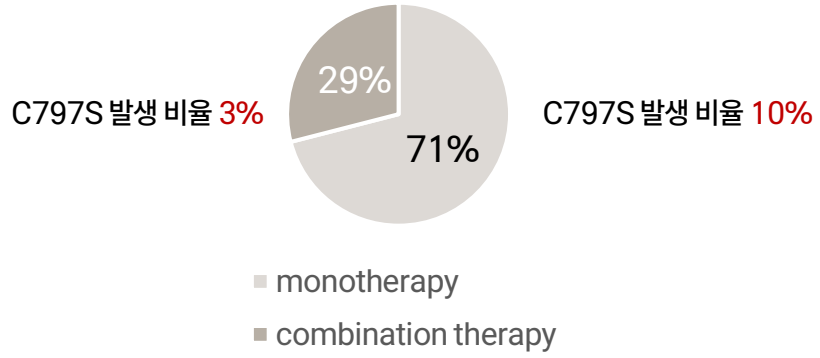
EGFR Resistance-Positive(C797S) 가속승인 전략

승인된 표적 치료제가 없는 EGFR C797S 변이 영역에서 VRN11의 독보적 효능 및 내약성 기반 가속승인 추진
3% 수준의 Driver 변이로 USD 1B 글로벌 매출 예상

EGFR C797S 변이 발생 비율[1,2]

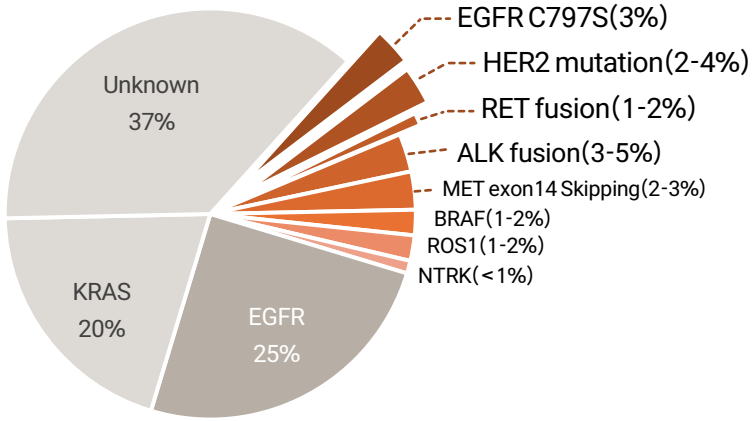
✓ 1차 치료 이후 C797S 발생 비율

타그리소 단독/병용 처방 비율



✓ 1차 치료 이후 뿐 아니라,
2차 이상(2L+) 후속 치료 라인에서도 C797S 변이 지속 발생

비소세포폐암 희귀 Driver 변이 표적 TKI 상업성 비교(Commercial Potential)



표적	발생 비율	대표 약물명	가속 승인 연도	Annual Sales
EGFR C797S	3%	VRN11	2027-2028 (expected)	$1B(expected)
HER2 mutation	2-4%	Zongertinib (Hernexeos)	2025	$1B(estimated)
ALK fusion	3-5%	Lorlatinib (Lorbrena)	2015	$1.2B
RET fusion	1-2%	Selpercatinib (Retevmo)	2020	~$0.5B

Source: [1]Santos E, et al. Journal of Thoracic Oncology, 20S474, [2]WCLC2024

VRN11
Clinical Development Strategy

VRN11 임상 개발 전략

우수한 효능·안전성·뇌 투과율 데이터를 바탕으로, EGFR 변이 폐암 전반의 미충족 의료 수요 해결을 목표로 하는 임상 개발 전략

2차 치료(2L+) 데이터에 기반한 1차 치료(1L)로의 진입/확장

1차 치료(1L) 패러다임의 전환

	VRN11 (expected)	Osimertinib[1,2]
Depth of response	≥-60%(Low) ≥-70%(High)	-50%
CNS CR	≥70%	16%
PFS	40~60m(Low) ≥7y(High)	18.9
≥Grade 3 TRAEs	Low	13%

가속승인 기대(2L+)

Brain Metastasis

Osimertinib* 대비 우월한 임상 데이터 확인:
- Kp,uu,CSF : 0.2 vs 2.0
- CNS PFS: 3.5 vs Not Reached(**≥9**개월)

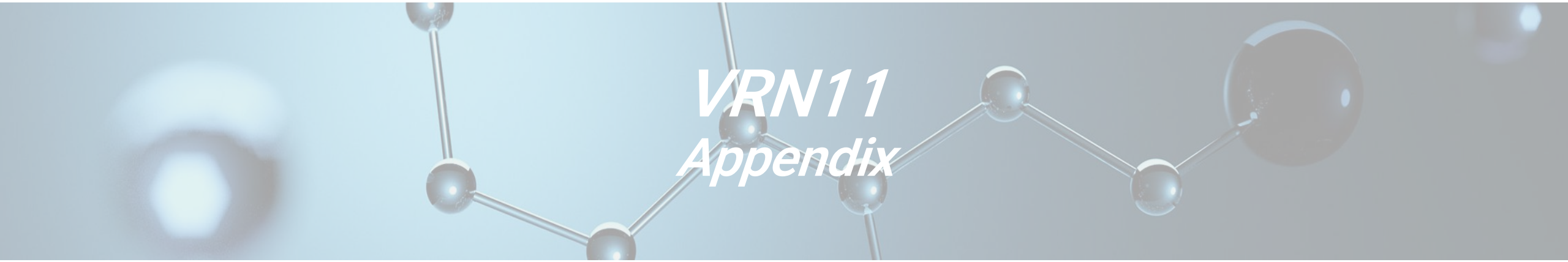
Resistance Positive(+)
C797S

ORR **100%** (6/6, ≥160mg)
PFS **11months**

Resistance Negative(-)
Unknown Resistance

PFS **7.3** 개월
압도적 안전성 확인(≥Grade 3 TRAEs **3%**)

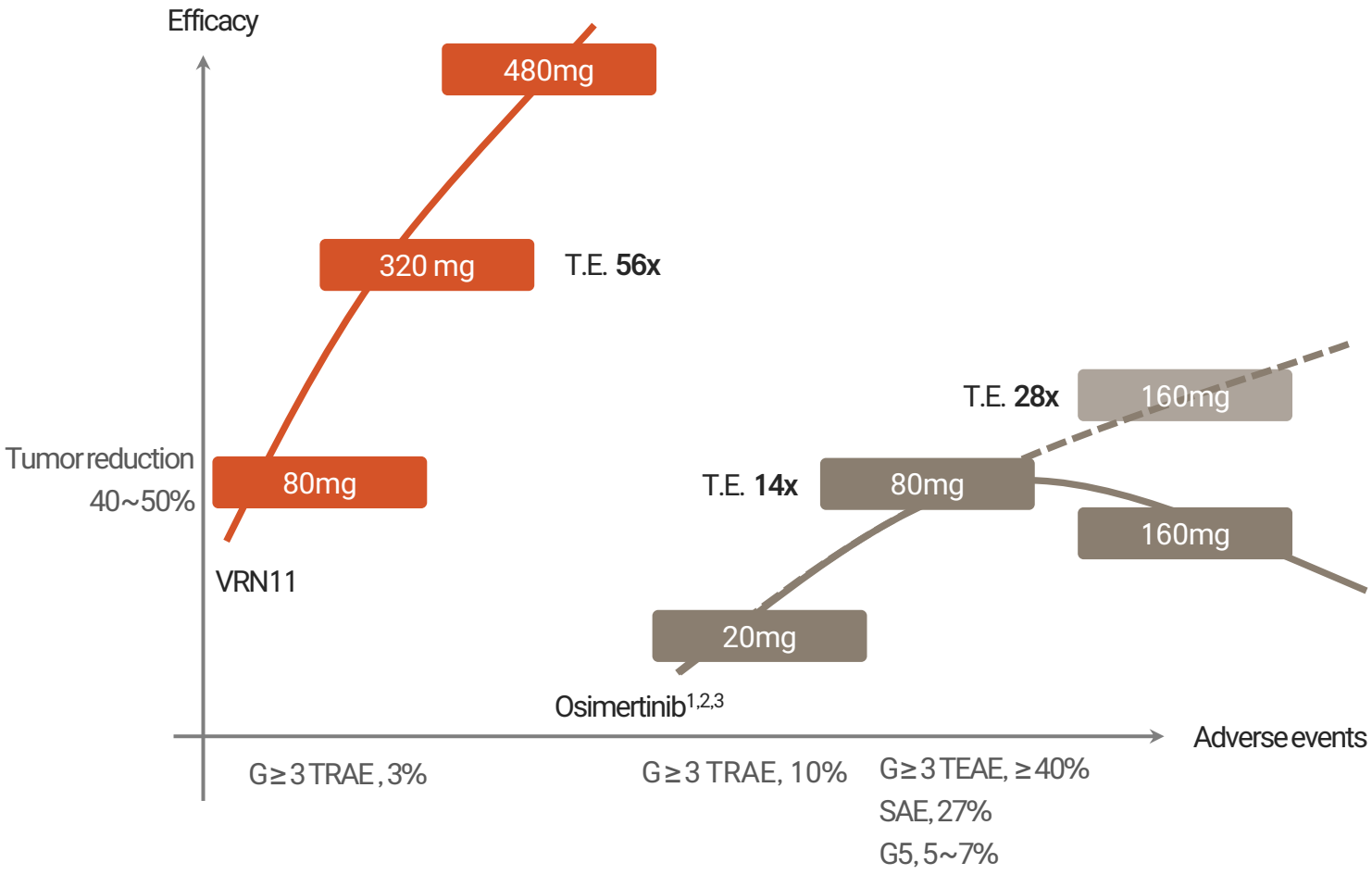
Data cutoff July 2,2026
Source: [1]Soria JC, et al. N Engl J Med. 2018 Jan 11;378(2):113-125. [2]Jänne PA, et al. J Clin Oncol. 2024 Mar 1;42(7):808-820.



VRN11
Appendix

[Appendix] VRN11-Osimertinib 비교 효능 및 안전성

VRN11, Osimertinib 대비 더 낮은 부작용 / 더 높은 치료효과 확인



Osimertinib[4]	80mg	160mg
Target engagement	14x	28x
ORR	67%	87%
Best % change in Target lesion size(mean)	-42%	-54%
G≥3 TEAE	60%	63%
G≥3 TRAE	13%	23%
Any AE leading to Dose reduction	10%	53%
mDoR(mo)	19.3	16.7
mPFS(mo)	22.1	19.3

Source: [1]Jänne PA, et al., N Engl J Med. 2015;372(18):1689-1699, [2]S.S. Ramalingam, et al.,N Engl J Med 2020;382, [3]ESMO2023, [4]Ramalingam SS, et al., J Clin Oncol 36:841-849.

Creating Novel Therapeutics
For patients with Excellent Experts
In Drug Design

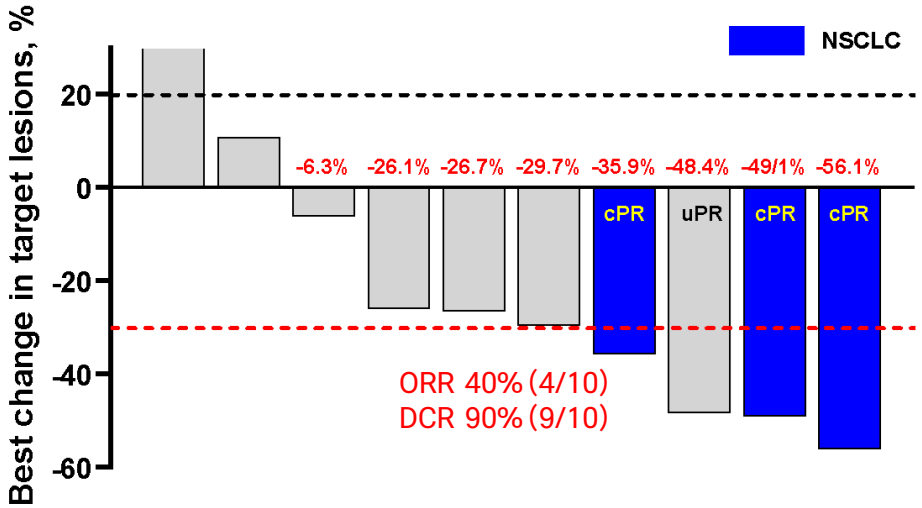
VRN10
HER2 Targeted Therapy

HER2 변이 환자에서의 치료 효과

Best-in-class 약물 가능성 확인: HER2 변이 비소세포폐암 환자 대상 **ORR 100%** (vs. Zongertinib 35%)
HER2 ADC와 TKI 치료 이후 환자에서 100% 부분관해(PR) 확인

[VRN10-Zongertinib 비교] Phase 1a Dose-Escalation Study

VRN10

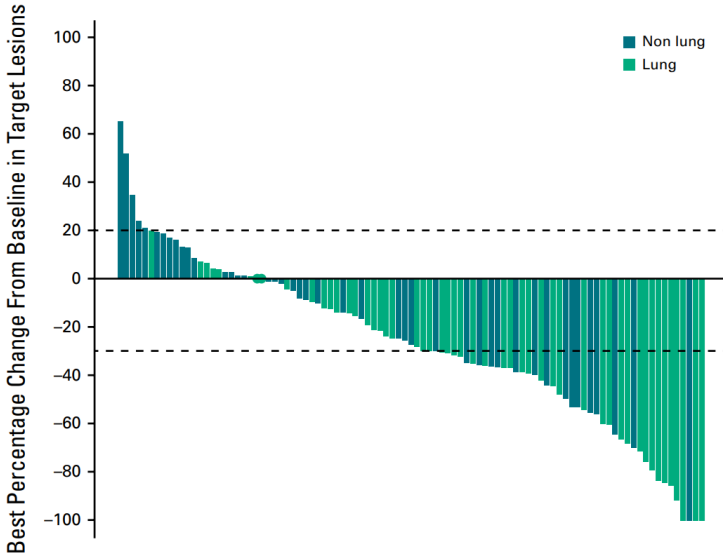


HER2 mutant	R678Q	G727A	S310Y	L755S	S310F	V777L	L755P	V659E	S310Y	YVMA
No. Prior TX	2	4	1	2	3	7	3	2	3	7
Prior HER2 TKI	N	N	N	N	Y	N	N	N	Y	Y
Prior T-DXd	N	N	N	N	N	Y	Y	N	Y	Y

* Shown are response-evaluable patients (with ≥1 post-baseline tumor assessment; n=10/12).

Efficacy	VRN10 (n=10)		Zongertinib (n=54)
	All	NSCLC	NSCLC
CR (%)	0%	0%	0%
PR (%)	40%	100%	35%
SD (%)	50%	0%	57%
PD (%)	10%	0%	2%
ORR (%)	40%	100%	35%
DCR (%)	90%	100%	93%

Zongertinib



Source: Heymach JV et al., J Clin Oncol. 2025 Apr 10;43(11):1337-1347.

Case Report: HER2-Mutant Patients(1)

T-DXd 치료 후 환자 4/5명 및 HER2 TKI 치료 후 환자 3/5명 포함. 이 중 Baseline 기준 뇌전이 환자 3/5명으로, 앞서 다수의 치료를 경험한 환자군 대상 임상

Patient Characteristics

	Patient A	Patient B	Patient C	Patient D	Patient E
Age/Sex	56/F	60/M	46/F	72/M	62/F
ECOG	0	1	0	0	0
Dose (mg)	160	320	160	80	240
HER2 mutation	S310Y	L755P	V777L	S310F	A775_G776insYVMA
HER2 domain	ECD	TKD	TKD	ECD	TKD
Primary site	Lung	Lung	Breast	Pancreas	Lung
Metastatic site	Lymph Nodes, Brain, LT.PLEURAL	Lymph Nodes, Bone, Brain, Pleural seeding	Liver, Lung, Pleura	Gastric, Lymph node	Lung, Lymph Nodes, Brain
Prior HER2 Tx	trastuzumab, neratinib, T-DXd	T-DXd	T-DXd	trastuzumab, tucatinib	sevabertinib, ELVN-002, T-DXd
Prior Systemic Tx	3	3	7	3	7

ECD, Extracellular Domain; TKD, Tyrosine Kinase Domain

Case Report: HER2-Mutant Patients(2)

Patient A

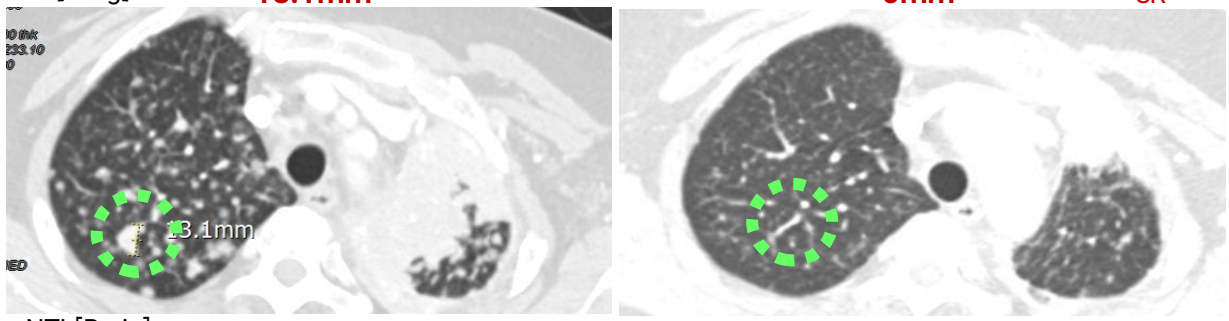
56 Female · 160 mg · Lung Cancer

HER2 S310Y

pembrolizumab+pemetrexed+cisplatin SD → **trastuzumab+neratinib** SD → **T-DXd** SD → **VRN10 PR**

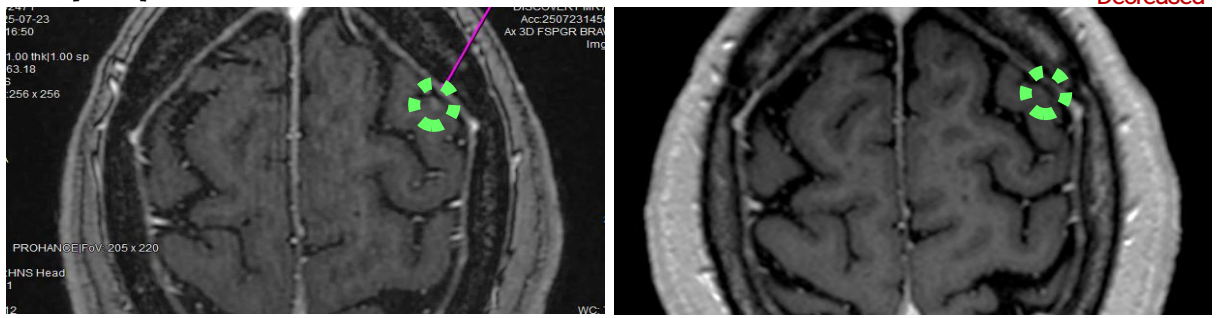
TL[Lung]

Baseline **13.1mm** → C3D1 **0mm** "CR"



NTL[Brain]

"Decreased"



- Prior therapies, including T-DXd, all reached only stable disease
- Achieved PR at C5D1 with continued response by -49.1% at C14D1
- Overall PR with sequential CR in TLs; Lung at C3D1 and Breast at C14D1

Patient C

46 Female · 160 mg · Breast Cancer

HER2 V777L

palbociclib+letrozole **PR** → fulvestrant Unknown → fulvestrant+alpelisib **PD** → everolimus+exemestane **SD** → capecitabine **PR** → paclitaxel **PR** → T-DXd **PR** → **VRN10 SD**

- Anti-Tumor activity in heavily pre-treated setting (≥7 prior Tx)
- Tumor response by RECIST v1.1: **SD** (-29.7% in Liver TL at C5D1)
- Discontinued due to non-TL PD

Patient D

72 Male · 80 mg · **Pancreatic** Cancer

HER2 S310F

FOLFIRINOX Unknown → nab-paclitaxel+gemcitabine Unknown → trastuzumab+tucatinib **SD** → **VRN10 SD**

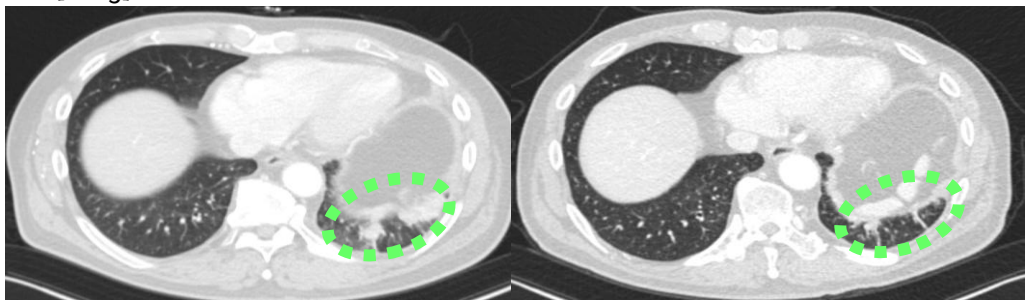
- Tumor response by RECIST v1.1: SD (-26.7% shrinkage in Stomach at C3D1)
- Tx interrupted for ~3 weeks due to underlying disease
- Discontinued to **subject withdrawal**

Case Report: HER2-Mutant Patients(3)

Patient B 60 Male · 320 mg · Lung Cancer **HER2 L755P**

MEDI5752(anti-PD-1xCTLA-4 bispecific antibody)+pemetrexed+carboplatin SD → pembrolizumab+ pemetrexed+carboplatin **PD** → T-DXd **PR** → **VRN10 PR**

TL[Lung] Baseline C5D1

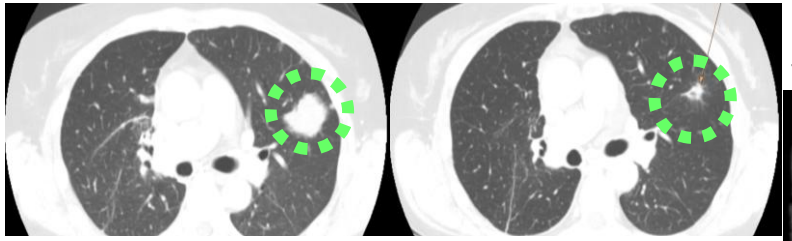


- PR maintained with VRN10 following prior T-DXd (17 months)
- Overall PR with -35.8% tumor reduction in 2 Lung TL at C5D1
- **G3 diarrhea resolved** within a week via anti-diarrheal regimen

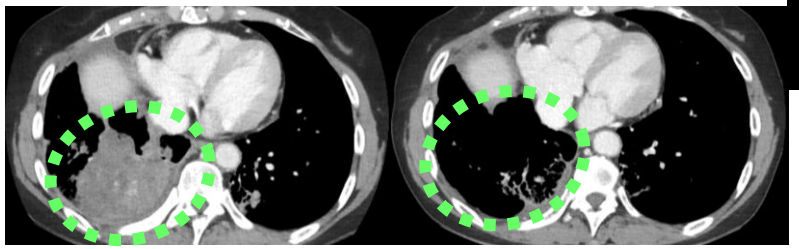
Patient E 62 Female · 240 mg · Lung Cancer **HER2 A775_G776insYVMA**

pemetrexed+cisplatin **PD** → atezolizumab **PD** → sevabertinib **PR** → ELVN-002(HER2 TKI) **SD** → gemcitabine **SD** → docetaxel **PD** → T-DXd **PR** → **VRN10 PR**

TL[Lung] Baseline **34mm** → C3D1 **13mm**

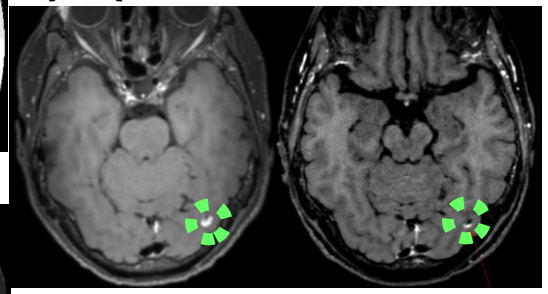


NTL[Lung]



Baseline C3D1

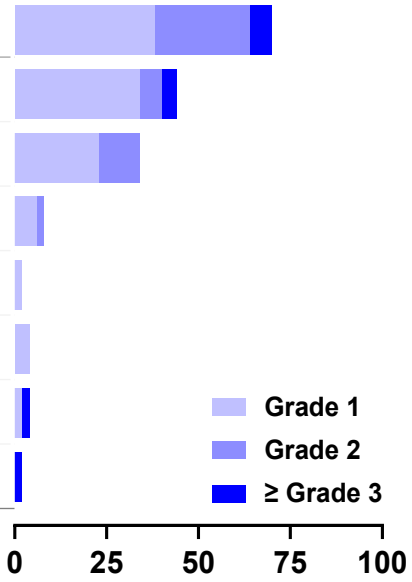
TL[Brain]



- 2 Lung TL PR achieved at first tumor assessment of -56.1%
- Deep partial response following relapse on sevabertinib, ELVN-002, and T-DXd
- **Brain NTL also decreased**

Safety Profile

Drug-related AE	VRN10, 80 – 480mg (n=47)	
	All	≥ Grade 3
Any	70%	6%
Diarrhea	45%	4%
Nausea	34%	-
Rash	9%	-
Dry skin	2%	-
Pruritus	4%	-
AST increased	2%	2%
ALT increased	4%	2%



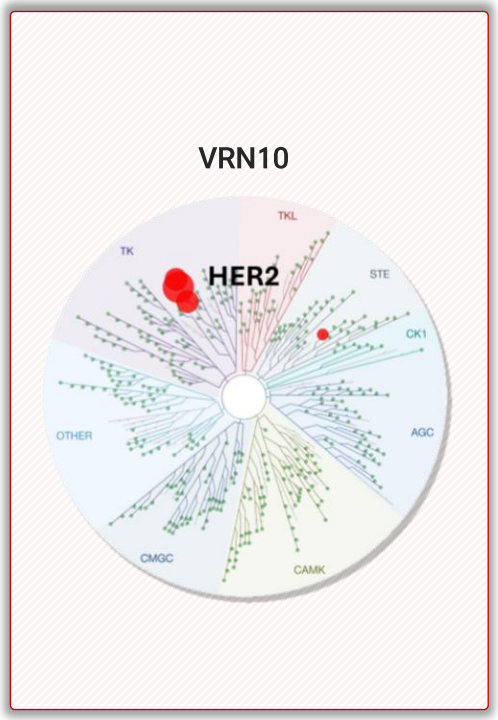
- 모든 용량 수준에서 전반적으로 양호하고 관리 가능한 안전성 프로파일 확인
- 설사 발생 시 로페라미드(loperamide)를 필요에 따라 투여하여 효과적으로 관리 가능
- 약물 관련 Grade 3 AST/ALT 상승은 1명에서 발생함.
- 약물 관련 간질성 폐질환(ILD) 또는 폐렴 발생 사례 없음.
- 최대내약용량(MTD)에 도달하지 않음

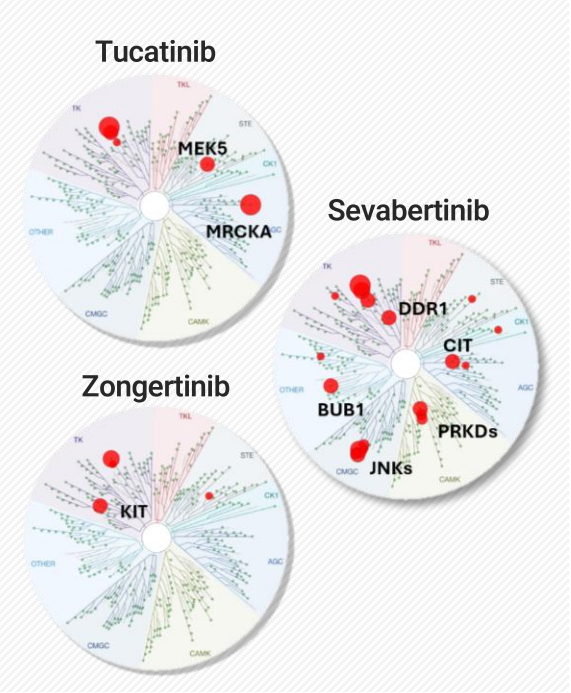
Combined term, includes rash, rash maculopapular, exfoliative rash
Abbreviations: adverse event; TRAE; AE, adverse event; AST, Aspartate Aminotransferase; ALT, Alanine Aminotransferase.

경쟁 약물 대비 뛰어난 선택성

경쟁 약물 대비 뛰어난 선택성으로, 간독성 및 심독성 발생 우려 낮음

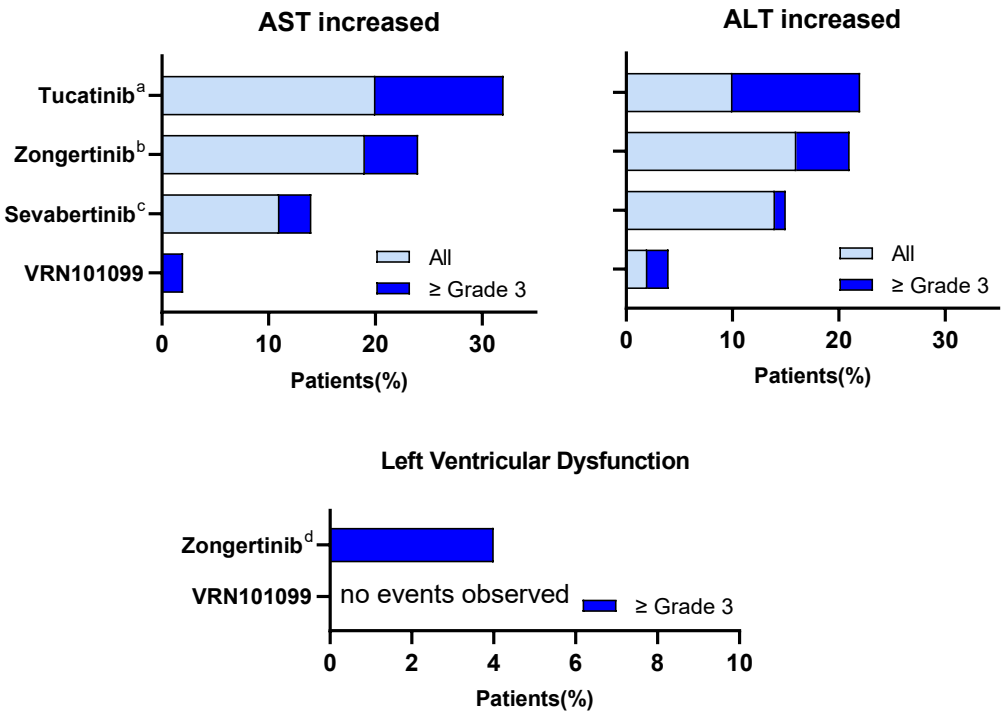
VRN10 선택성(Selectivity)





✓ Shared hepatotoxicity, divergent off-target toxicities
: a selectivity issue across HER2 TKIs.

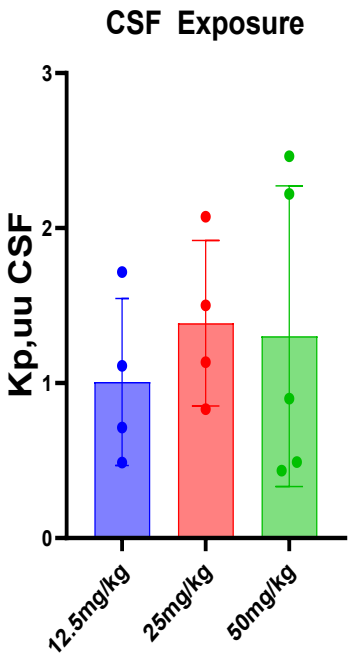
경쟁약물 대비 낮은 간독성 및 심독성

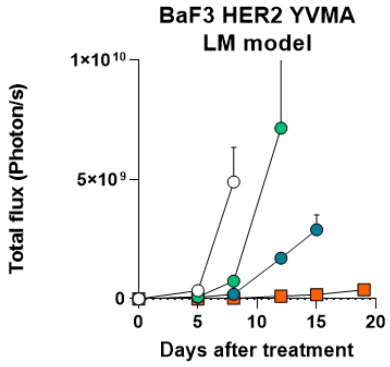


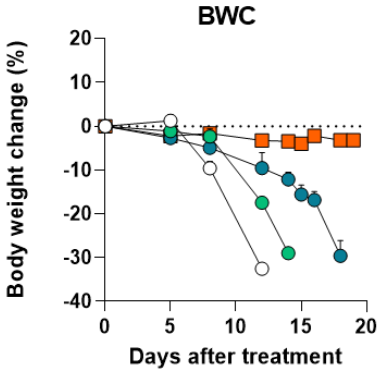
Source: a. Borges VF, Ferrario C, Aucoin N, et al. Tucatinib Combined With Ado-Trastuzumab Emtansine in Advanced ERBB2/HER2-Positive Metastatic Breast Cancer: A Phase 1b Clinical Trial. JAMA Oncol. 2018;4(9):1214-1220. doi:10.1001/jamaoncol.2018.1812
b. Heymach JV, Ruiter G, Ahn MJ, et al. Zongertinib in Previously Treated HER2-Mutant Non-Small-Cell Lung Cancer. N Engl J Med. 2025;392(23):2321-2333. doi:10.1056/NEJMoa2503704
c. Le X, Kim TM, Loong HH, et al. Sevabertinib in Advanced HER2-Mutant Non-Small-Cell Lung Cancer. N Engl J Med. 2025;393(18):1819-1832. doi:10.1056/NEJMoa2511065
d. Heymach JV, Opdam F, Barve M, et al. HER2-Selective Tyrosine Kinase Inhibitor, Zongertinib (BI 1810631), in Patients With Advanced/Metastatic Solid Tumors With HER2 Alterations: A Phase Ia Dose-Escalation Study. J Clin Oncol. 2025;43(11):1337-1347. doi:10.1200/JCO-24-01727

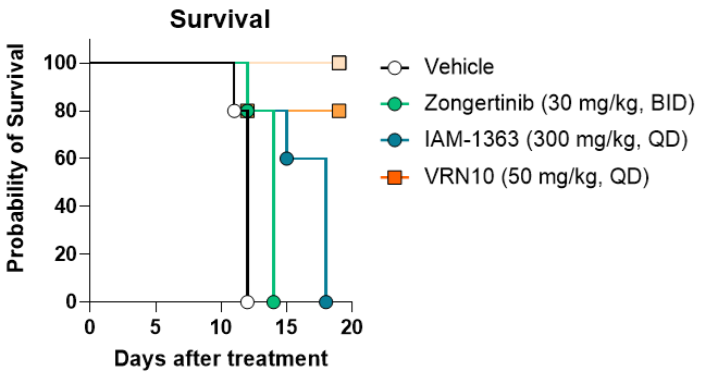
CNS Activity: HER2 YVMA Intracranial Model (Leptomeningeal metastasis)

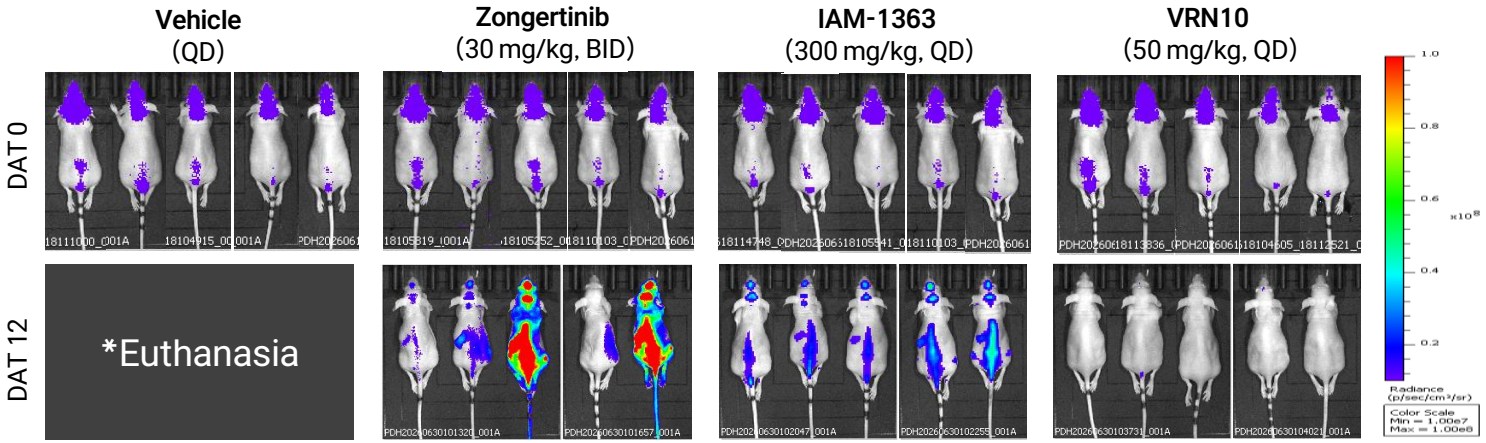
VRN10, 마우스에서 **우수한 뇌 투과력** 확인(Kp,uu,CSF ~1)
HER2 변이 비소세포폐암의 대부분을 차지하는 YVMA 변이 두개내 모델에서 경쟁 약물 대비 뛰어난 항종양 효능 확인









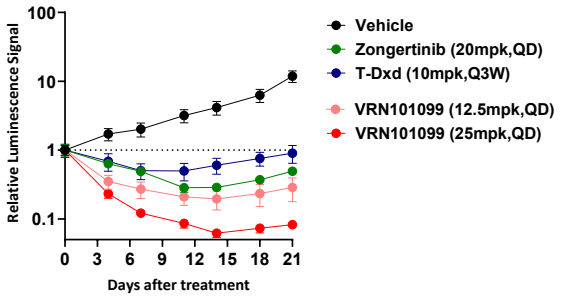


CNS Activity: A Case Report with Preclinical Data

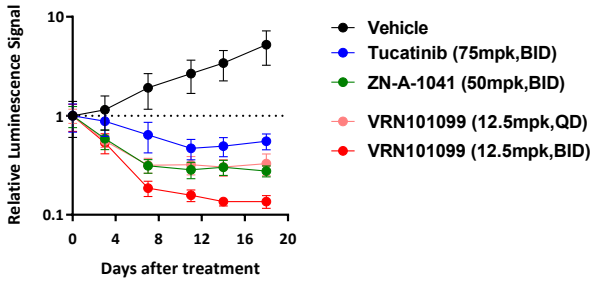
임상에서 두개내 항종양 효과 확인

[Preclinical] BT474 (HER2+ BC) Intracranial model

Comparison to Zongertinib and T-DXd



Comparison to Tucatinib and ZN-A-1041

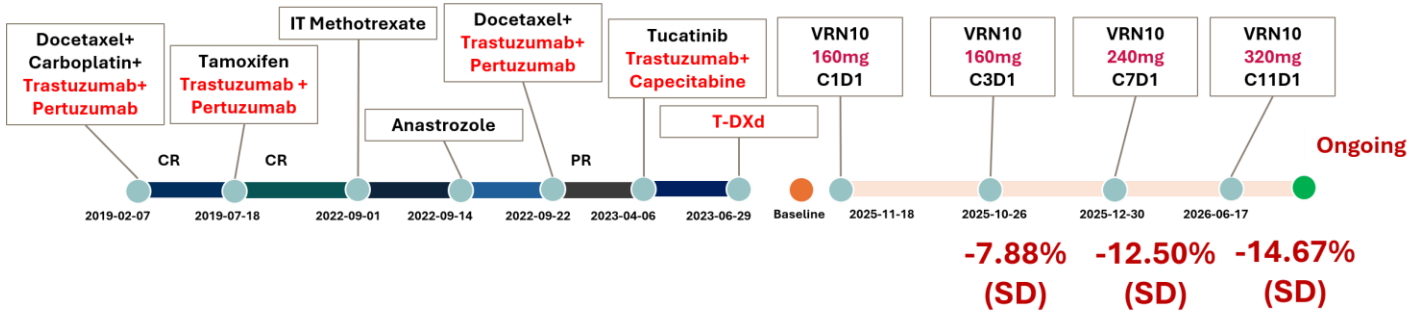


VRN10 showed superior intracranial activity vs comparators in a HER2-positive breast cancer brain metastasis model

[Clinical] Phase 1 Case Report

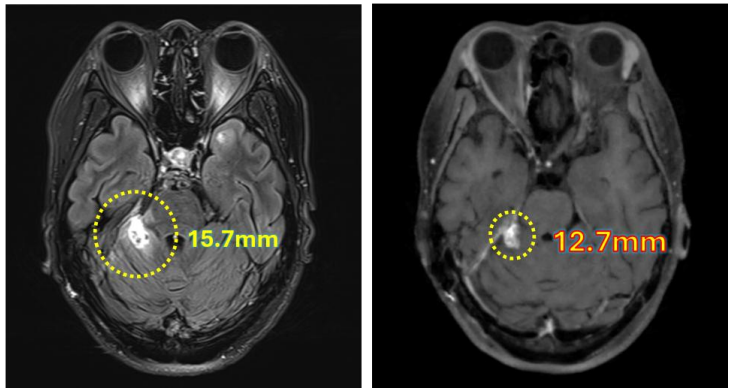
Patient X Female · 160 mg · Breast Cancer

HER2 positive



Baseline **C3D1**

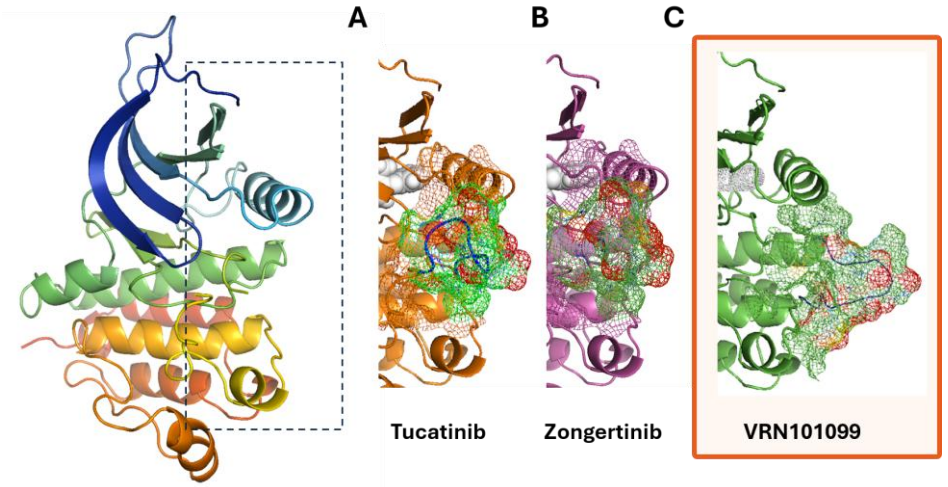
TL (Brain)

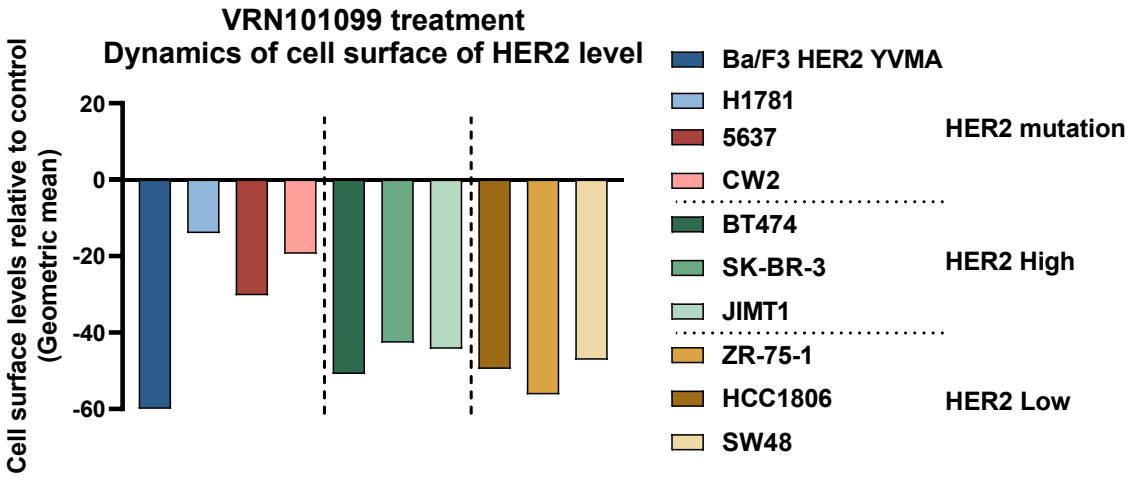


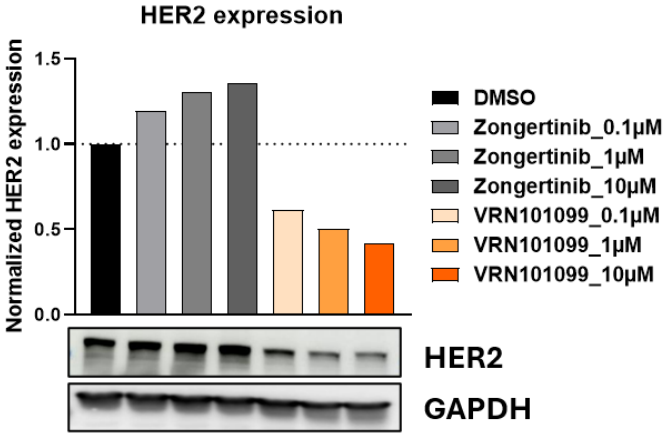
- Heavily pretreated: 8 prior systemic regimens, including 5 HER2-directed therapies (prior T-DXd)
- Reduction in brain target lesions and non-target lesion was stable
- Duration of treatment: 9.7 months (ongoing)

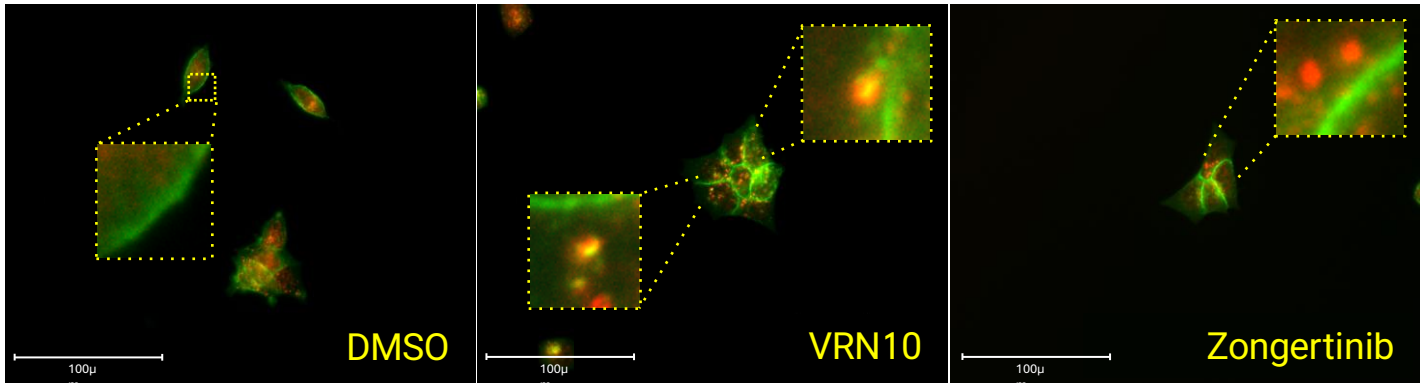
Unique Binding Mode and On-Target Degradation

차별화된 결합을 통해 HER2 수용체의 세포 내재화 및 분해 유도



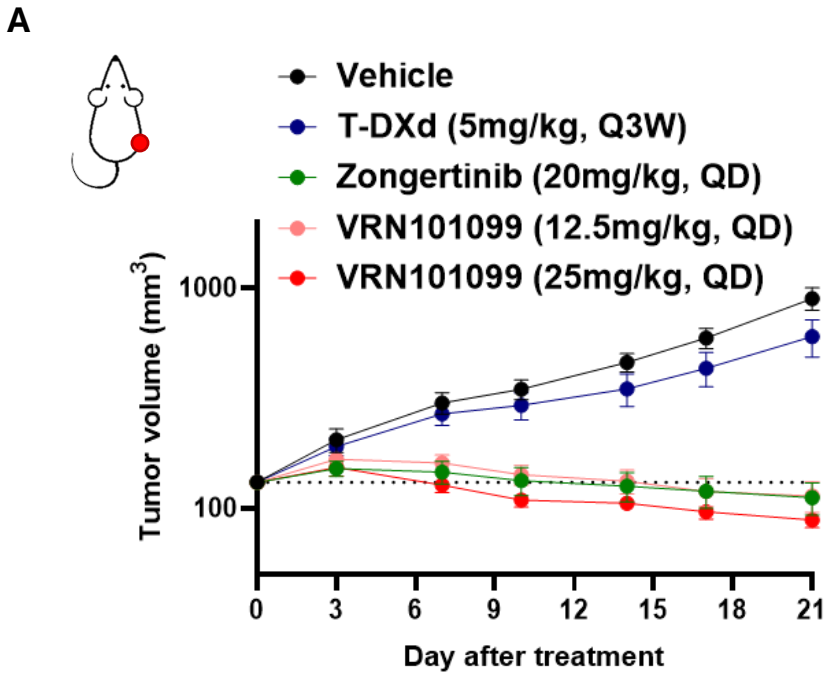


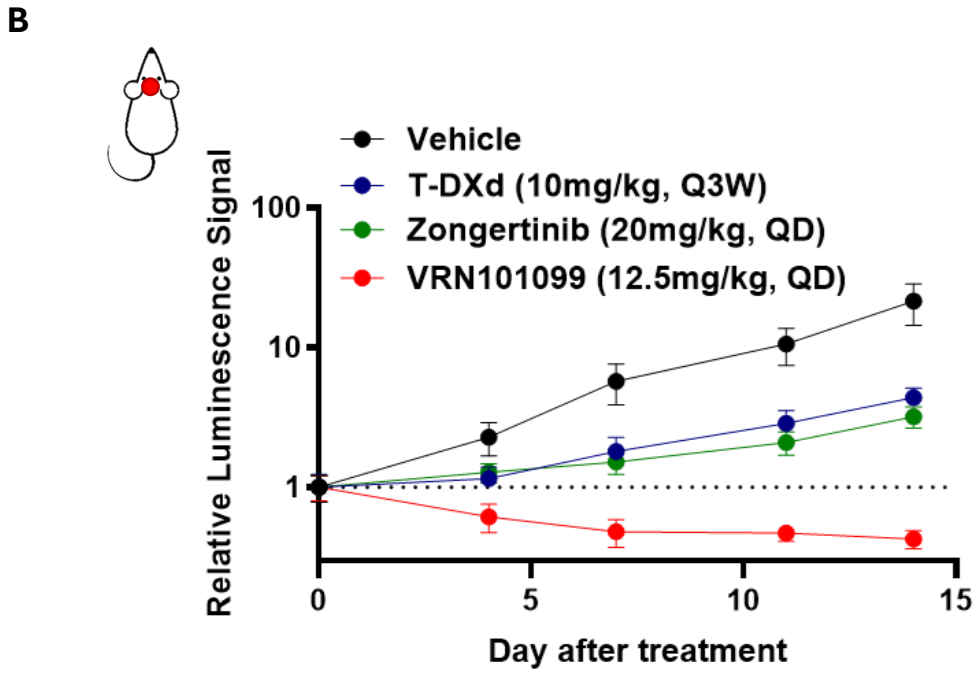




In vivo anti-tumor efficacy in T-DXd resistance model

T-DXd 내성 종양 세포 기반의 두개내(Intracranial , IC) 및 피하(Subcutaneous , SC)모델에서 효능 확인



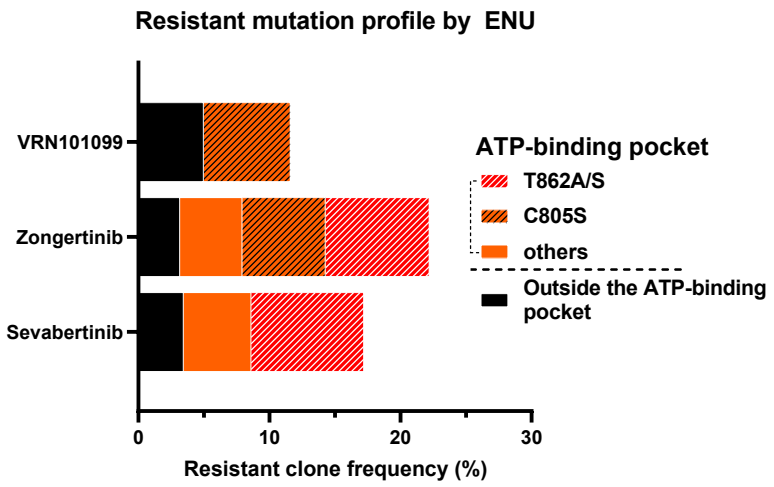


(A) Subcutaneous (SC) NCI-N87 _ TR anti-tumor activity. (B) Intracranial SK-BR-3 _ TR CNS activity.

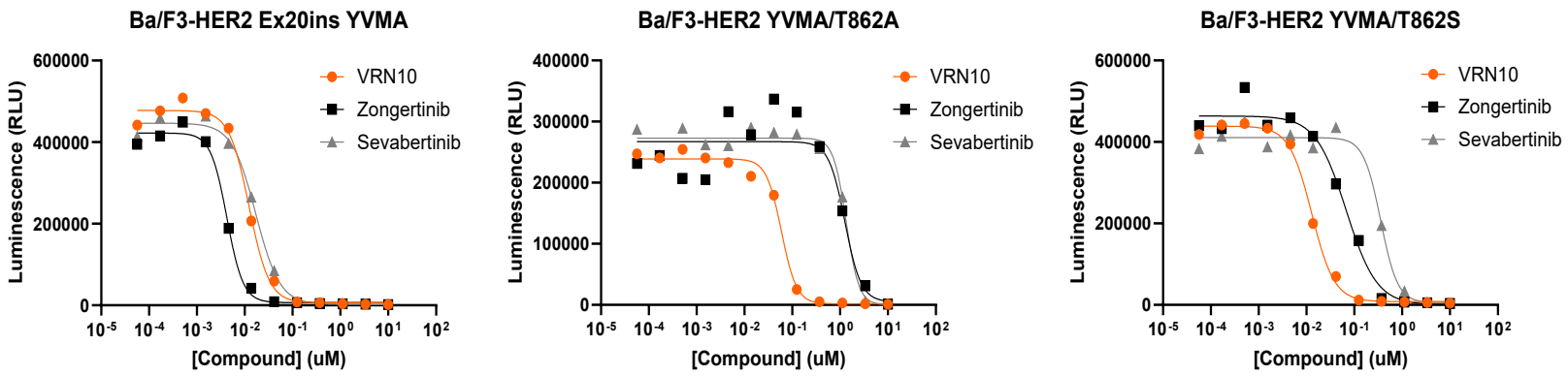
Evaluation of resistance in ENU-induced mutants

(A)ENU-induced drug-resistant mutation profiles.
(B)GI50 values in YVMA and YVMA with secondary mutations (YVMA+mutation) (n = 3)
(C)Fold changes of GI50 shifts in YVMA mutation models.

A



B



C

	ENU-induced mutation / YVMA GI_{50} shifting	
	T862S	T862A¶
VRN10	1.0	4.8
Zongertinib	16.1	299
Sevabertinib	19.8	78.4

¶: HER2 T862A also confers cross-resistance to competing agents like zongertinib and sevabertinib (Yuji Shibata et al., 2026 AACR).

Creating Novel Therapeutics
For patients with Excellent Experts
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Thank You