2026 ASCO® ANNUAL MEETING

First-in-human trial of BH-30643, a novel macrocyclic, non-covalent, mutant selective OMNI-EGFR inhibitor, in *EGFR*-mutant (EGFRm) NSCLC

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Disclosures

Xiuning Le, M.D., Ph.D.

I have the following financial relationships to disclose:

- Consulting / advisory fees: AbbVie, Abion, Akeso, Allist, ArriVent, AstraZeneca, Avistone, Bayer, BioNTech, BlossomHill, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, Dizal, Eli Lilly, EMD Serono (Merck KGaA), Hengrui, Innovent, Johnson & Johnson (Janssen), Merck, Novartis, Pfizer, Regeneron, Summit, SystImmune, Taiho, Teligene
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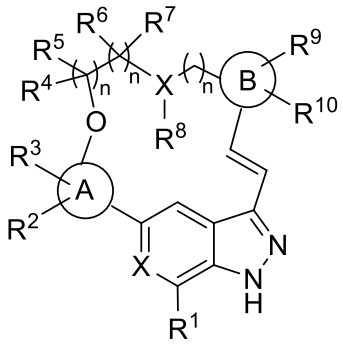
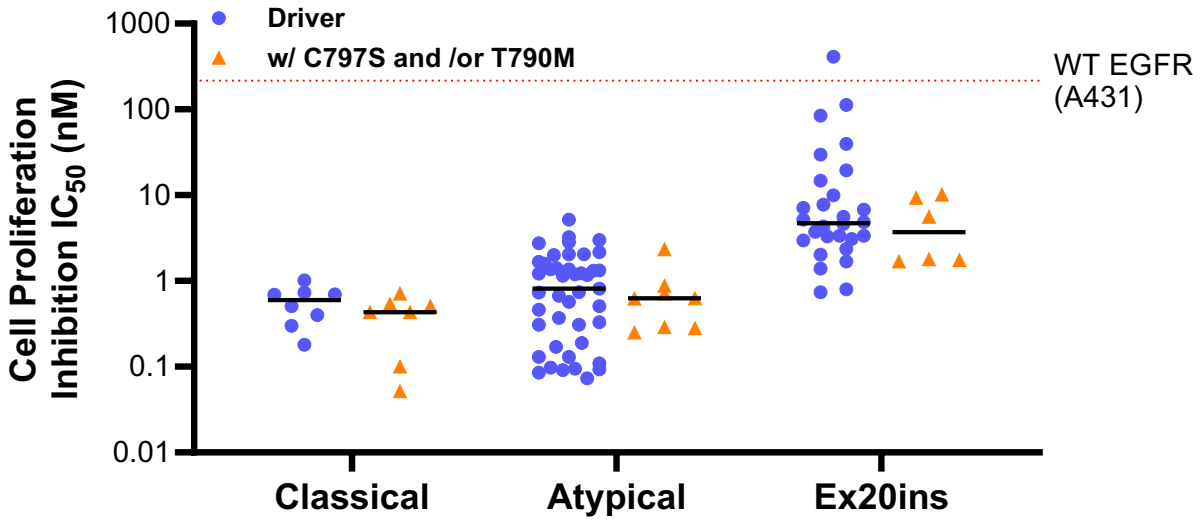
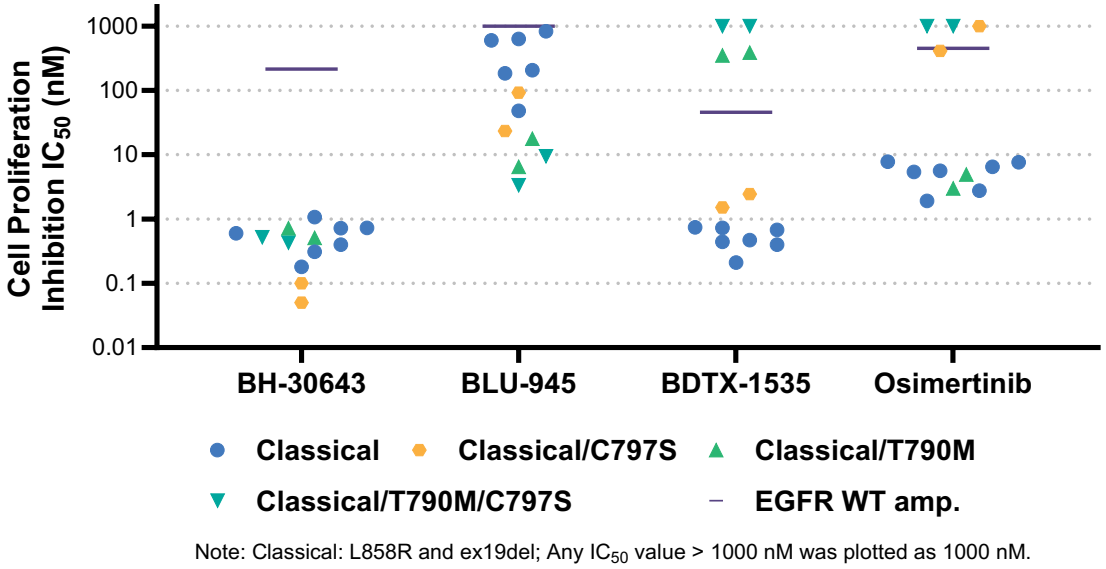
BH-30643 is a macrocyclic OMNI-EGFR inhibitor



BH-30643

- BH-30643 is a small molecule designed to target the common active state of mutant EGFR, allowing high potency across a wide range of EGFR mutations while sparing wildtype EGFR[1]
- BH-30643 is 10-fold more potent than osimertinib against classical mutations, and also maintains potency in the presence of on-target resistance mutations such as C797S and/or T790M[2]





Note: Classical: L858R and ex19del; Any IC_{50} value > 1000 nM was plotted as 1000 nM.

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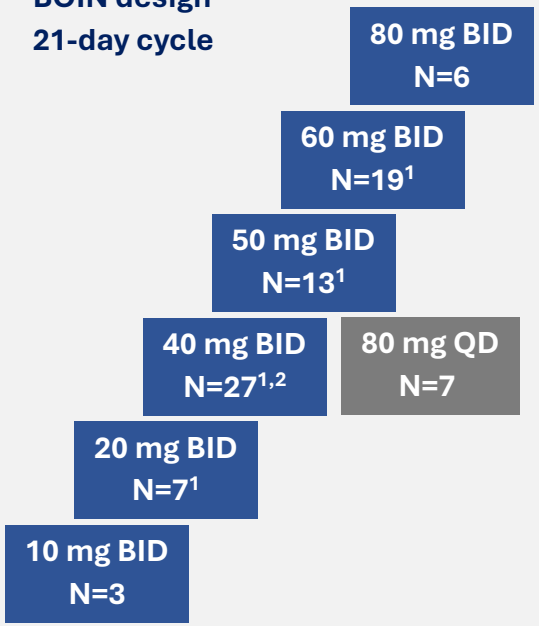
1. Cui et al, AACR 2025
2. Jiang et al, AACR 2026

SOLARA Phase 1 study design and patient characteristics

Phase 1 escalation / backfill enrolled a heavily pretreated and heterogeneous patient population, with a median of 3 prior lines of therapy, 66% with history of brain metastases, and 71% ECOG=1

Phase 1 Part 1A (Escalation & backfill)

BOIN design
21-day cycle



Endpoints:

- Primary: Selection of recommended doses for expansion (RDEs) and, if applicable, MTD
- Overall safety and tolerability
- PK characterization
- Preliminary antitumor activity

Key eligibility:

- Adults with advanced *EGFR* and/or *HER2* mutant NSCLC
- ECOG status 0-1
- Measurable disease by RECIST 1.1
- No limit on the number of prior therapy lines
- Untreated asymptomatic brain metastases allowed

Patients enrolled at 29 sites across North America and APAC

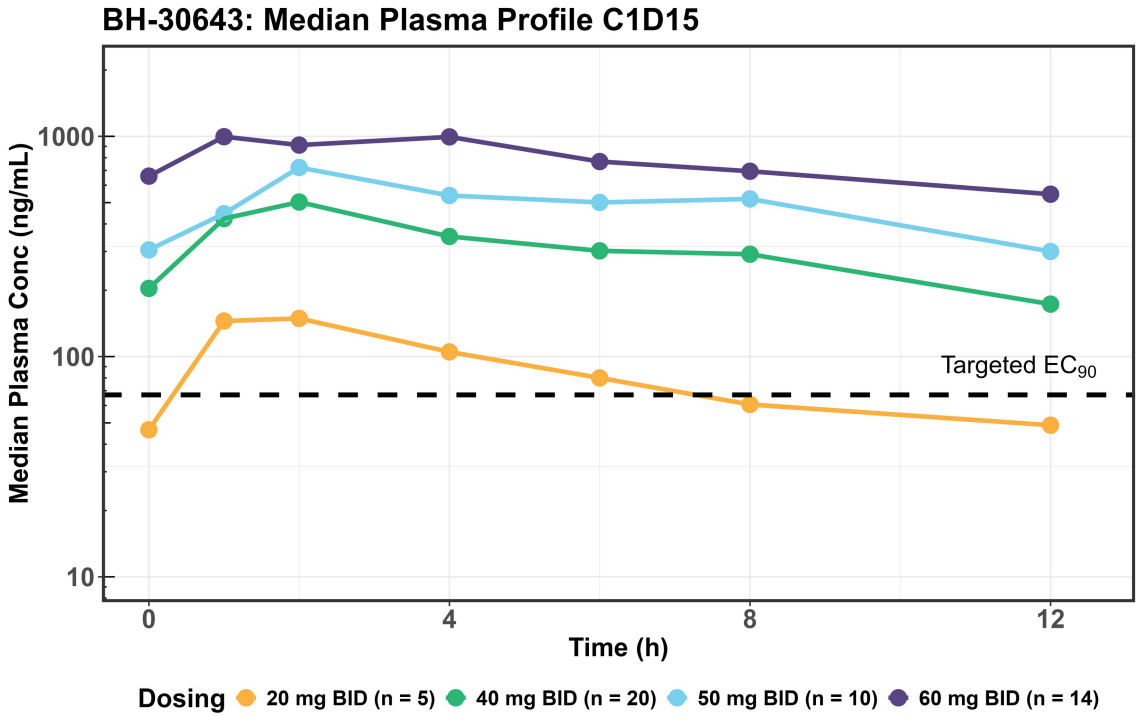
NCT06706076

Patients Baseline Characteristics	N=82[3]
Age (years), median (min, max)	61 (31, 81)
ECOG = 1, n (%)	58 (71%)
History of brain metastases, n (%)	54 (66%)
Prior lines of therapy, median (min, max)	3 (1, 12)
Prior 3rd Gen EGFR TKI	62 (76%)
Other prior EGFR targeted therapy	47 (57%)
Prior chemotherapy and/or ADC	58 (71%)
Prior immunotherapy	14 (17%)
***EGFR* or *HER2* driver mutation[4], n (%):**	
Classical *EGFR* (19del or indel, L858R)	54 (66%)
EGFR exon 20 insertion	16 (20%)
Atypical / other *EGFR*	10 (12%)
HER2 mutation	2 (2%)
Multiple *EGFR* mutations[4], n (%):	51 (62%)

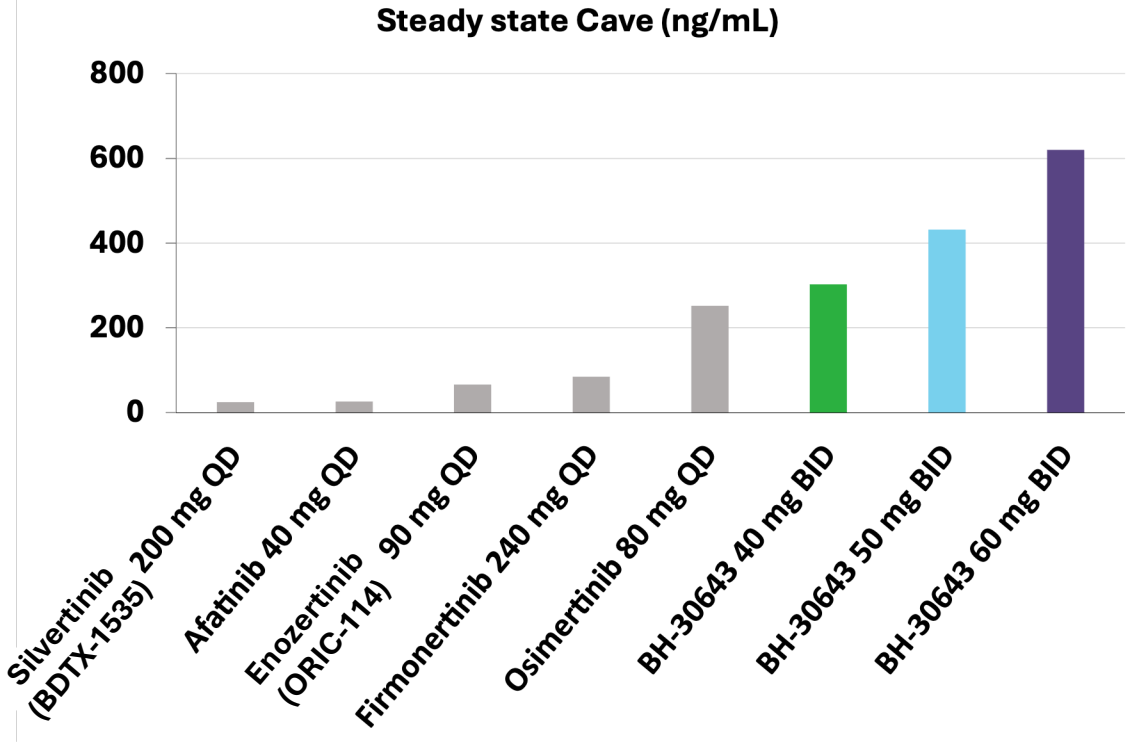
[1]Backfill cohorts enrolled at potentially efficacious doses based on PK and/or anti-tumor activity.
[2]Includes patients enrolled into pilot food effect sub study at 40mg BID.
[3]All data as of 2 March 2026 data cut, with efficacy follow-up through 29 April 2026 data cut.
[4]Includes historical and baseline molecular results.

Pharmacokinetics: Phase 1 escalation / backfill experience

- Median steady state plasma exposures at ≥40mg BID achieved high coverage over target EC90 and exceeded reported exposure levels of many contemporary EGFR TKIs
- At the steady state, trough Kp,uu of ~27% (CSF, primate) supports potential for CNS activity at ≥40mg BID in the setting of high plasma exposure



Includes BID dose levels with steady state data available from >2 patients.



Safety & tolerability: Phase 1 escalation / backfill experience

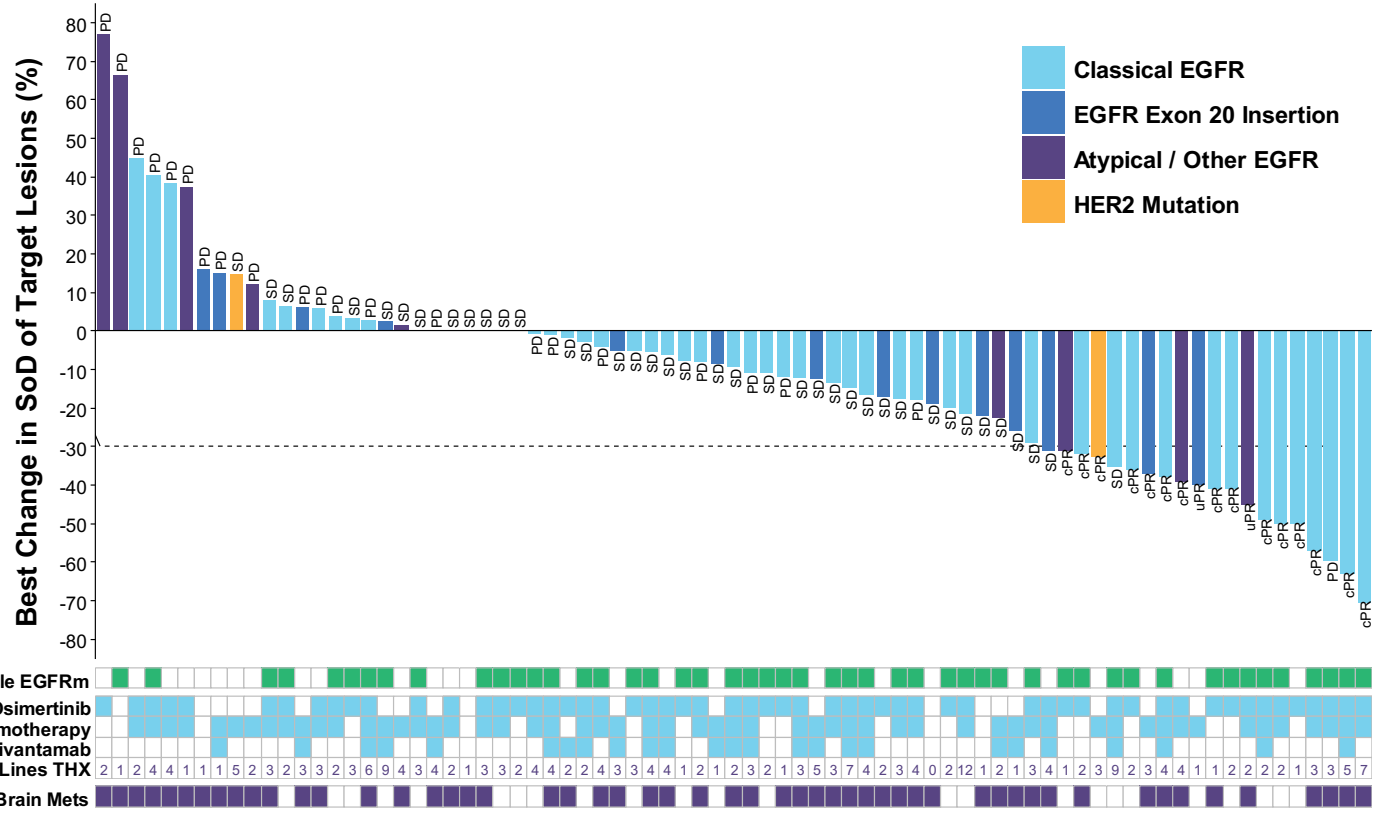
Safety Population (N=82)	TRAE				TEAE	
	Any Gr	Gr 1	Gr 2	Gr 3*	Any Gr	Gr 3+
Any AE, n (%)	71 (87)	34 (41)	21 (26)	16 (20)	80 (98)	33 (40)
EGFR wildtype-related AEs						
Diarrhea	30 (37)	22 (27)	8 (10)	0	35 (43)	0
Rash	30 (37)	20 (24)	7 (9)	3 (4)	34 (41)	3 (4)
Stomatitis	15 (18)	6 (7)	7 (9)	2 (2)	16 (20)	2 (2)
Dry skin	10 (12)	9 (11)	1 (1)	0	14 (17)	0
Paronychia	8 (10)	2 (2)	5 (6)	1 (1)	11 (13)	1 (1)
Additional TRAEs reported in ≥ 10% of patients						
Bilirubin increased	29 (35)	7 (9)	11 (13)	11 (13)	31 (38)	11 (13)
Fatigue	14 (17)	10 (12)	3 (4)	1 (1)	18 (22)	2 (2)
Nausea	10 (12)	4 (5)	6 (7)	0	14 (17)	0

Median duration of exposure was 2.8 months.
* The one grade 4 TRAE was ALT elevation, observed following recent immune-checkpoint inhibitor therapy, and recovered with dose interruption and steroids; no grade 5 TRAE were reported.

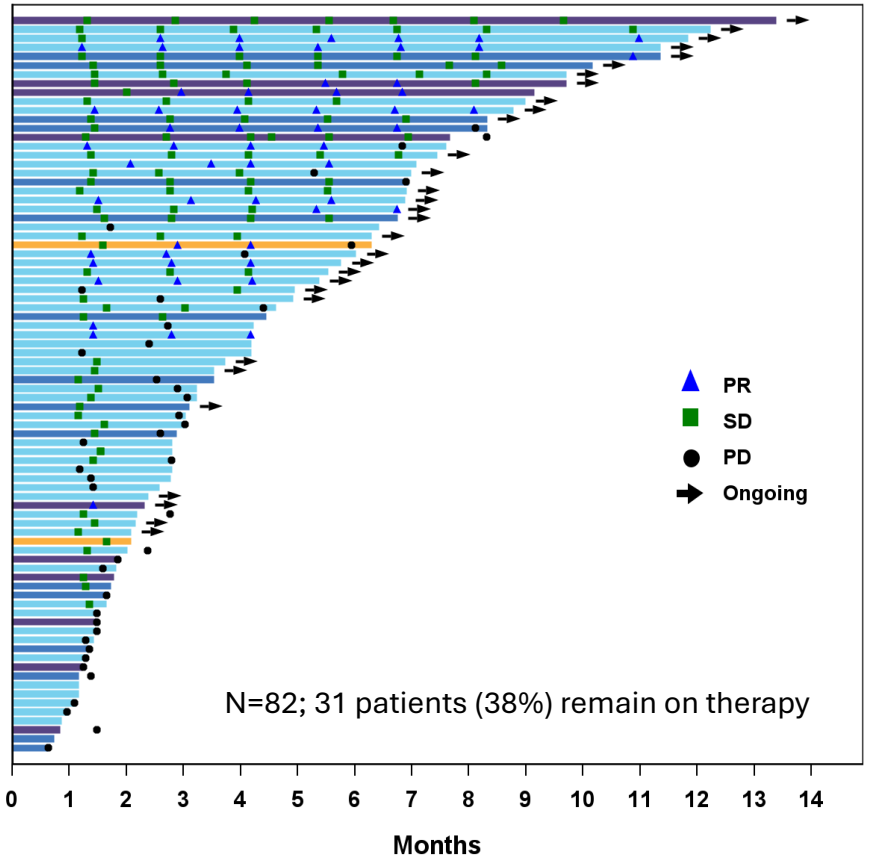
- 3 DLTs were reported, at 80mg BID (Gr. 3 mucositis, bilirubin increased) and at 60mg BID (Gr. 3 mucositis)
- Grade ≥2 EGFR-wildtype TRAEs reported in 27% of patients, more commonly at ≥60mg BID
- Bilirubin elevation has been predominately unconjugated and asymptomatic, and generally seen early on treatment due to exposure-dependent UGT1A1 inhibition (Gilbert's-like) by BH-30643
- Treatment-emergent ALT/AST elevations were observed in 12 patients (15%, two Gr. 3, one Gr. 4) with no cases of Hy's Law
- No clinically significant QTc prolongation or treatment-related cardiac effects
- TRAE leading to dose reduction in 13 patients (16%, most commonly bilirubin elevation), and discontinuation in 1 patients (1%)

Anti-tumor activity: Phase 1 escalation / backfill experience

- Responses and prolonged stable disease observed across diverse genotypes in this heavily pretreated cohort
- Responses in patients with multiple EGFR mutations suggest effective targeting of on-target resistance

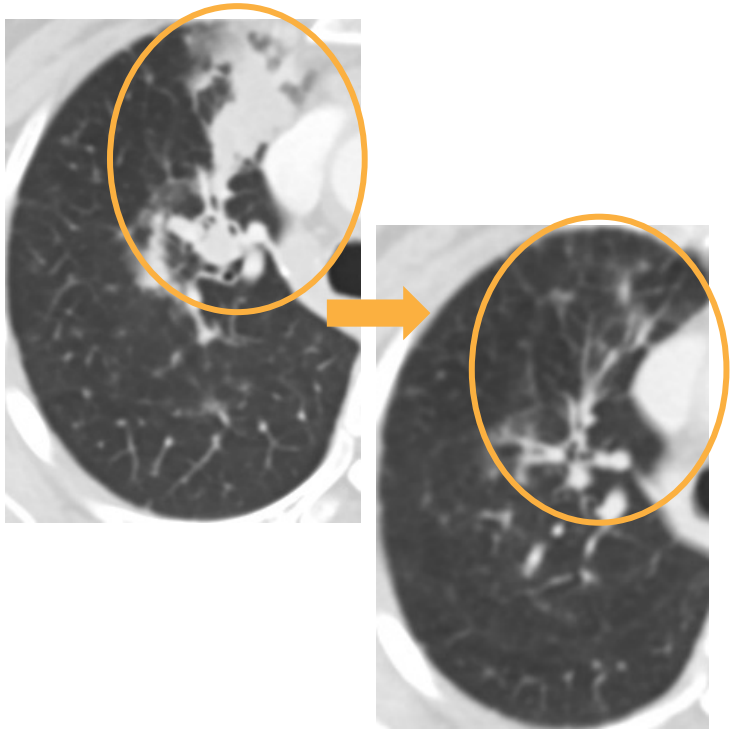


Waterfall represents 77 response evaluable patients with at least 1 post-baseline imaging assessment.
Median follow-up 6.9 months.

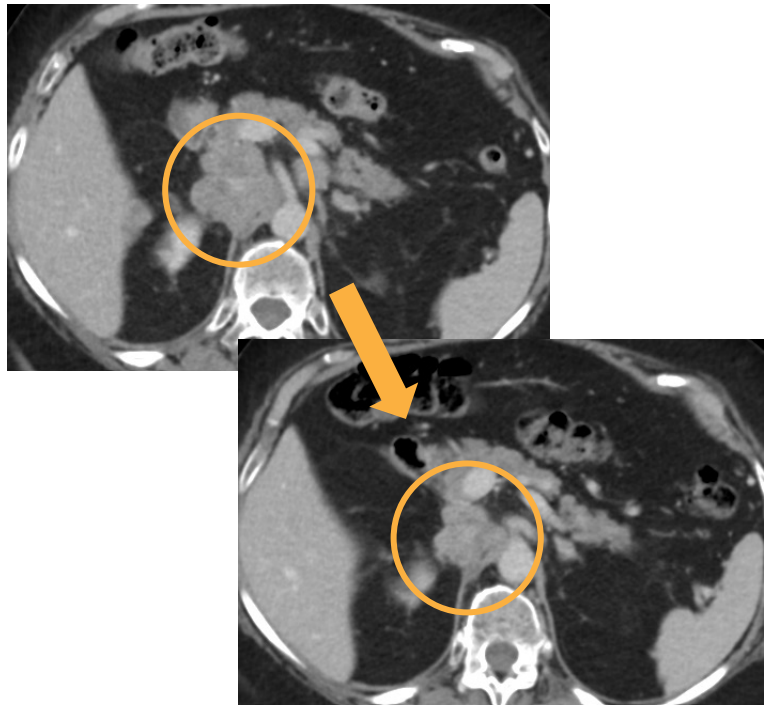


Case examples: Confirmed responses observed across diverse previously treated molecular contexts

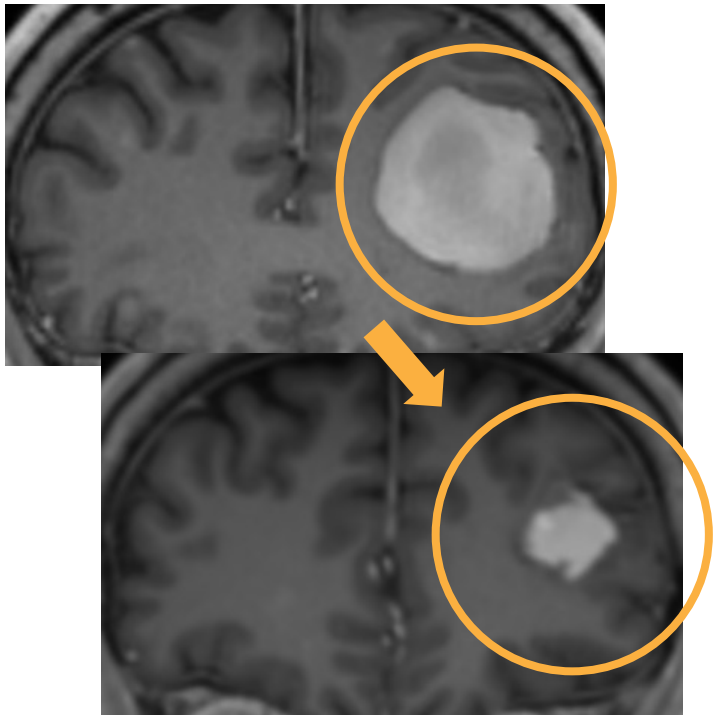
- 44 yo female, enrolled at 40mg BID
- EGFR **exon 19 deletion & C797S** detected after prior osimertinib, amivantamab and immunotherapy
- >11 months on treatment



- 68 yo female enrolled at 80mg QD
- EGFR **L861Q** previously treated with chemotherapy, erlotinib, osimertinib, mobocertinib
- 9 months on treatment

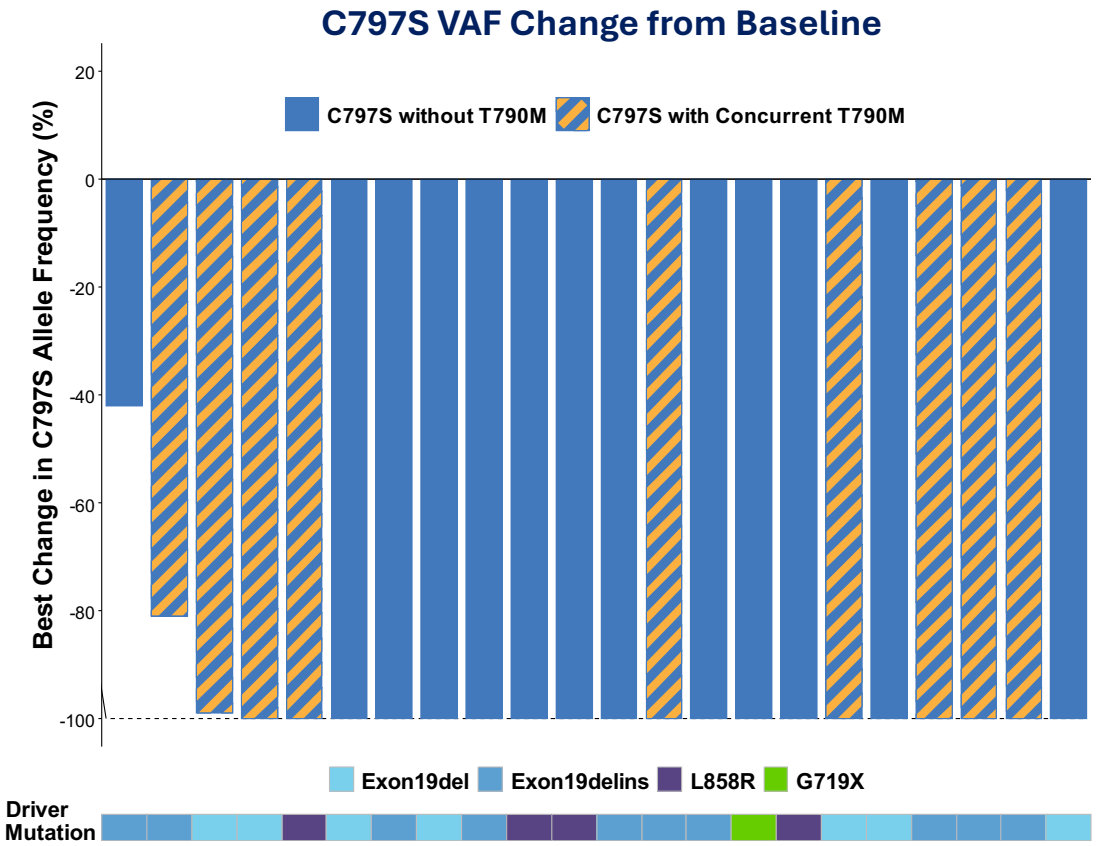


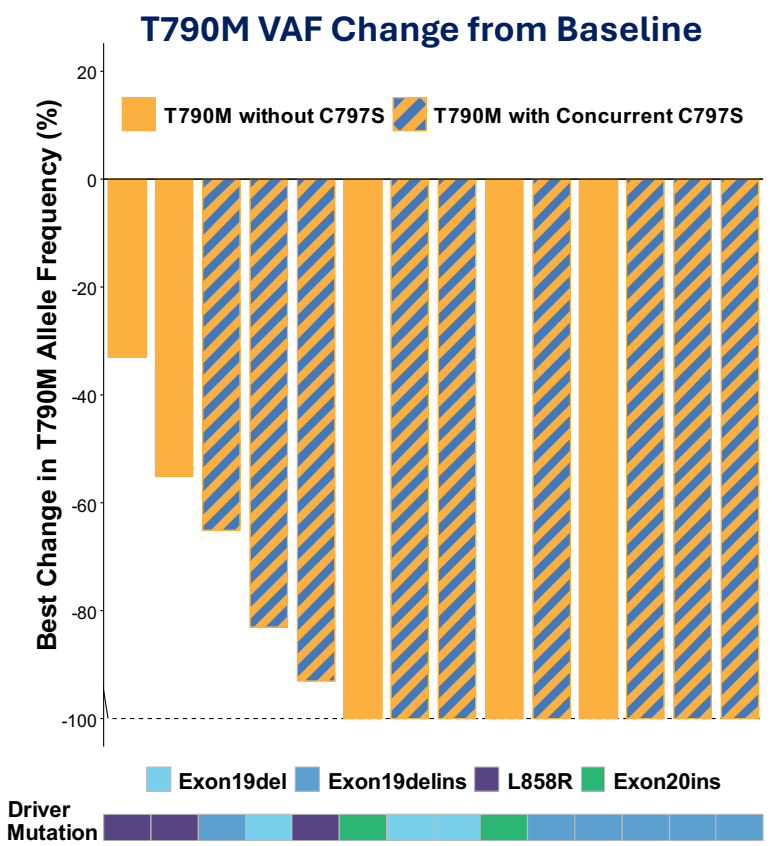
- 51 yo male enrolled at 80mg BID
- EGFR **exon 20 insertion** with 3 prior lines of chemotherapy
- No prior brain radiation or steroids
- 8 months on treatment



ctDNA response: Robust clearance of EGFR C797S and T790M

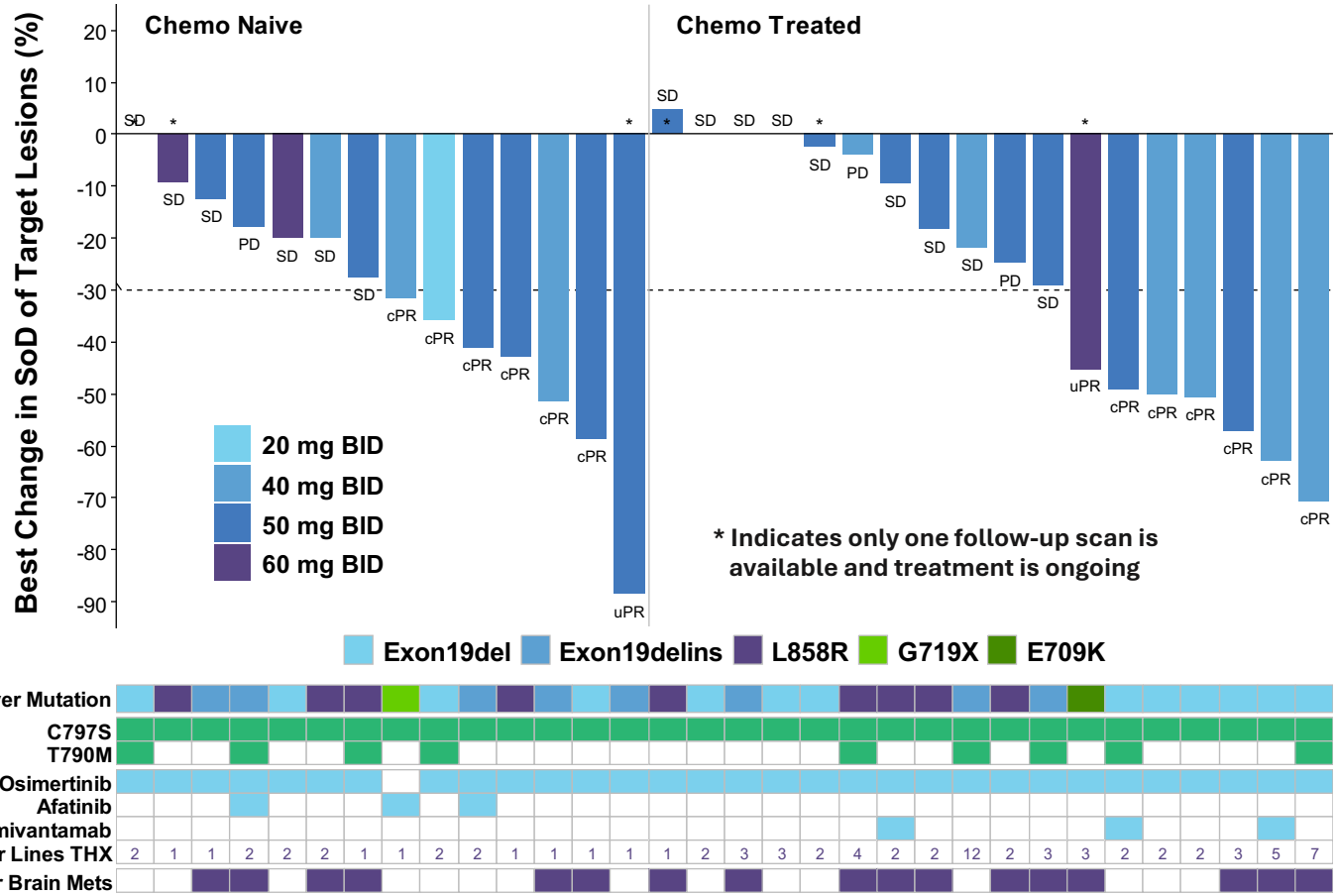
Studying 27 patients with ctDNA-detected C797S or T790M on central plasma NGS, clearance was observed for 86% of C797S mutations (19 of 22) and 64% of T790M mutations (9 of 14)





- Includes patients across escalation and expansion with plasma NGS at baseline and after 3-6 weeks on-treatment
- ctDNA clearance observed in the context of diverse EGFR driver mutations including exon 19 del or indel, L858R, G719X, and exon20ins
- 9 patients had concurrent C797S and T790M mutations with 5 showing clearance of both resistance mutations

Confirmed responses in EGFR C797S-positive NSCLC across dose levels and driver mutations



One patient enrolled at 20mg BID was escalated to 40mg BID after second cycle. Partial responses include those confirmed on a subsequent scan (cPR) and those that are ongoing pending confirmation (uPR). The target population excludes patients with concurrent driver alterations or who previously received a TKI specifically targeting a known C797S. Median follow-up was 4.9 months.

- 32 patients from the target C797S population were response evaluable across escalation and expansion cohorts
- ORR (confirmed or unconfirmed and ongoing) was 50% (7/14) in chemo naïve patients and 39% (7/18) in chemo pretreated patients
- Responses observed in the setting of concurrent T790M and prior history of brain metastases
- Clearance of ctDNA-detected *EGFR* primary driver mutations observed both in patients with SD (4/6) and with PR (4/7)

Conclusions

- Leveraging a novel macrocyclic scaffold, BH-30643 demonstrated promising clinical activity against diverse *EGFR* genotypes and on-target resistance in heavily pretreated patients with advanced *EGFR*-mutant NSCLC
- BH-30643 exposures exceeded target EC_{90} at 40mg BID and above
- BH-30643 was generally well tolerated with primarily low-grade EGFR wildtype toxicity as well as asymptomatic Gilbert's-like bilirubin elevation
- BH-30643 demonstrated promising efficacy in C797S-positive resistance, with or without concurrent T790M
- Phase 1 dose expansion is ongoing to determine RP2D and support further clinical development, initially focused on C797S-positive resistance

Expansion cohorts to inform Phase 2/3 development:

TKI resistance
- C797S detected after most recent therapy
- Atypical resistance mutations (L718X, G724X, etc.)

Targeted therapy naïve
- Classical mutations
- Atypical mutations (G719X, L861Q, S768I)
- Exon 20 insertions

Combination
- With platinum/pemetrexed following progression on 3rd-gen EGFR TKI