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ANTI-TUMOR ACTIVITY OF BH-30643, A NOVEL MACROCYCLIC EGFR TKI, IN PATIENTS WITH SECONDARY *EGFR* RESISTANCE MUTATIONS

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Background: Targeting C797S+ resistance

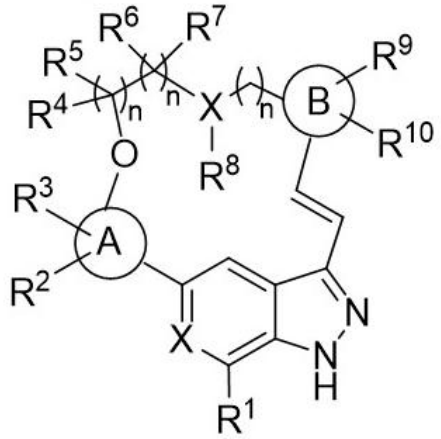
EGFR C797S+ resistance to 3rd-gen EGFR TKI

- Following progression on 3rd-gen EGFR TKIs, subsequent therapy options are limited for patients with *EGFR*-mutant NSCLC
  - Most patients receive chemotherapy-based combination regimens, which can have burdensome toxicity
- Precision approaches to target acquired resistance to 3rd-gen EGFR TKIs are a growing area of investigation
  - ~10-15% of patients develop secondary *EGFR* mutations (e.g. C797S), yet no targeted therapies are approved for this pattern of resistance

BH-30643 is a macrocyclic, mutant selective OMNI-EGFR TKI

- While macrocyclic ALK & ROS1 TKIs are used widely, no macrocyclic EGFR TKIs have regulatory approval
- BH-30643 was designed as a novel macrocyclic EGFR TKI to address on-target resistance
  - Sub-nM potency against *EGFR* classical, atypical & resistance mutations
  - Invulnerable to *EGFR* C797S or T790M resistance
  - Spares wildtype inhibition through targeting active conformation
  - High PK exposures
  - CNS penetrant

BH-30643



SOLARA: Global Phase 1/2 trial of BH-30643

- Phase 1 program spans more than 40 sites across 10 countries in North America & APAC[1]
- Expansion enrollment includes patients with *EGFR* C797S resistance after prior TKI

Study design[2]

Phase 1 Part 1: Dose escalation
BOIN escalation across 7 dose levels, with backfill at potentially active doses

Phase 1 Part 2: Dose expansion
Expansion cohorts target multiple molecularly defined subsets including TKI resistant and targeted therapy naïve

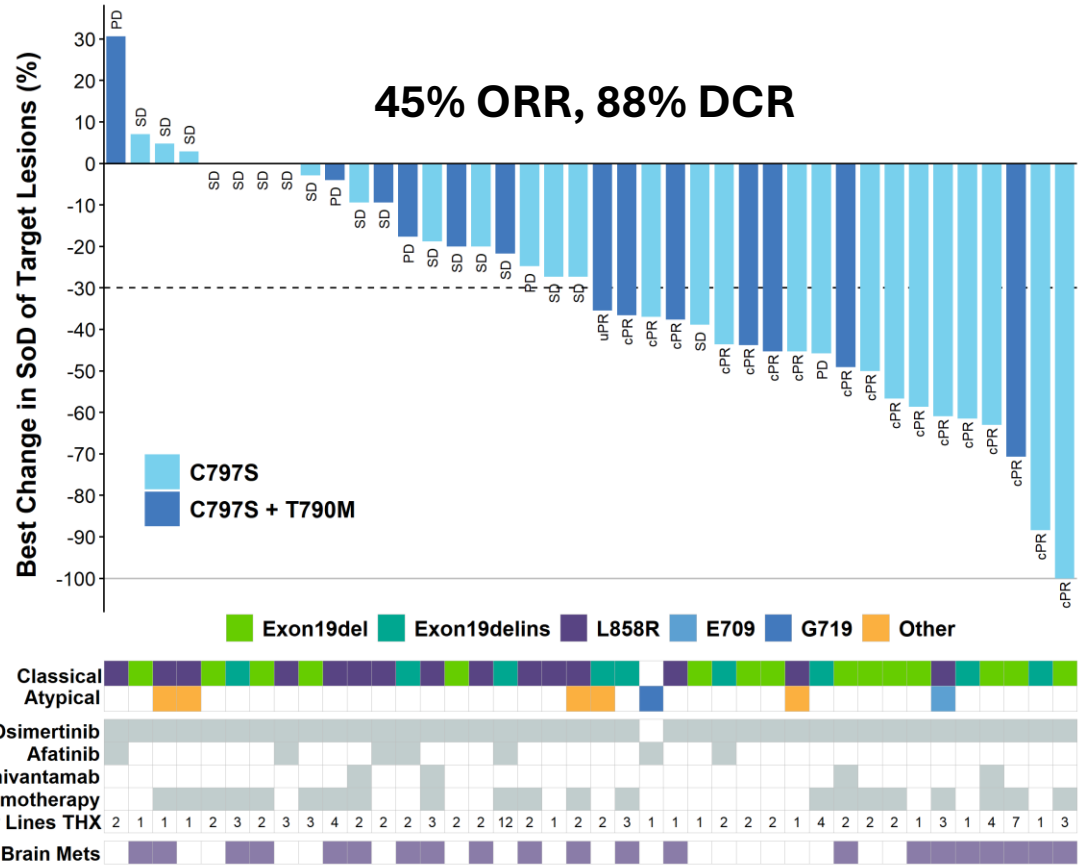
Expansion dose levels:
40 mg BID, 50 mg BID, 60 mg BID
(174 patients in total enrolled at these doses across Part 1 and Part 2)

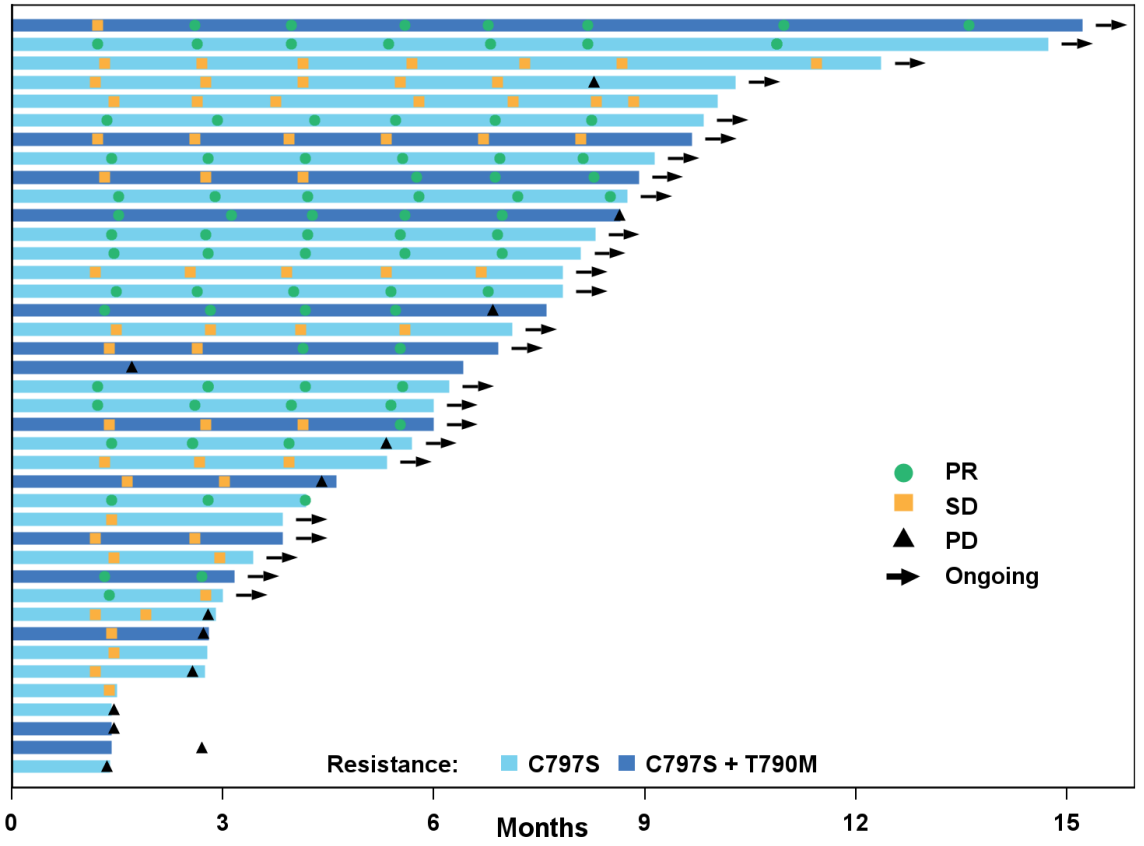
C797S target population (Part 1 and Part 2)[3]	N=40
Age (years), median (min, max)	64 (38, 82)
Asian, n (%)	26 (65%)
History of brain metastases, n (%)	21 (53%)
Prior lines of therapy, median (min, max)	2 (1,12)
Prior osimertinib	39 (98%)
Other prior EGFR targeted therapy	17 (43%)
Prior chemotherapy and/or ADC	21 (53%)
***EGFR* mutation, n (%):**	
Exon 19 deletion	24 (60%)
L858R	15 (38%)
Concurrent T790M	14 (35%)
Other atypical mutations[4]	7 (18%)

[1]12 May 2026 data cut off, with efficacy follow-up through 10 August 2026
[2]For additional study design details, see Le et al ASCO 2026 (NCT06706076)
[3]Target population excludes patients with concurrent driver alterations or who previously received an EGFR TKI specifically targeting a known C797S.
[4]Includes G719S, E709K, L718Q, L833V, R776H (x2), V834L

SOLARA: Efficacy in *EGFR* C797S+ resistance

- Responses in 18/40 (45% ORR, 95% CI 29%-62%)[1] in target population; disease control rate (DCR) of 88% (35/40)
- At median follow up of 6.9 months, 25 patients (63%) are still on therapy





[1]Responses include confirmed [cPR] or unconfirmed ongoing [uPR]. Efficacy follow-up through 10 August 2026; analysis does not include 14 patients enrolled after the data cut of 12 May 2026. One patient discontinued treatment due to an adverse event on day 6 and is not included in efficacy analysis set. ORR = objective response rate; SoD = sum of diameters; PR = partial response; SD = stable disease; PD = progressive disease.

SOLARA: Safety experience in expansion dose levels

Treatment-related adverse events (TRAE) in ≥ 10% patients[1]

Preferred Term, N (%)	40 mg, 50 mg, 60 mg BID N=174			
	All Grade	Grade 1	Grade 2	Grade 3/4[3]
Any TRAEs	**155 (89)**	**65 (37)**	**52 (30)**	**38 (22)**
Bilirubin elevation[2]	78 (45)	25 (14)	40 (23)	13 (7)
Rash[2]	75 (43)	60 (34)	11 (6)	4 (2)
Diarrhea	67 (39)	61 (35)	4 (2)	2 (1)
Dry skin	38 (22)	37 (21)	1 (1)	0 (0)
Stomatitis[2]	37 (21)	28 (16)	6 (3)	3 (2)
ALT increased	30 (17)	11 (6)	6 (3)	13 (7)
AST increased	29 (17)	11(6)	10 (6)	8 (5)
Fatigue	25 (14)	19 (11)	6 (3)	0 (0)
Nausea	20 (11)	13 (7)	7 (4)	0 (0)
Paronychia	20 (11)	8 (5)	11 (6)	1 (1)

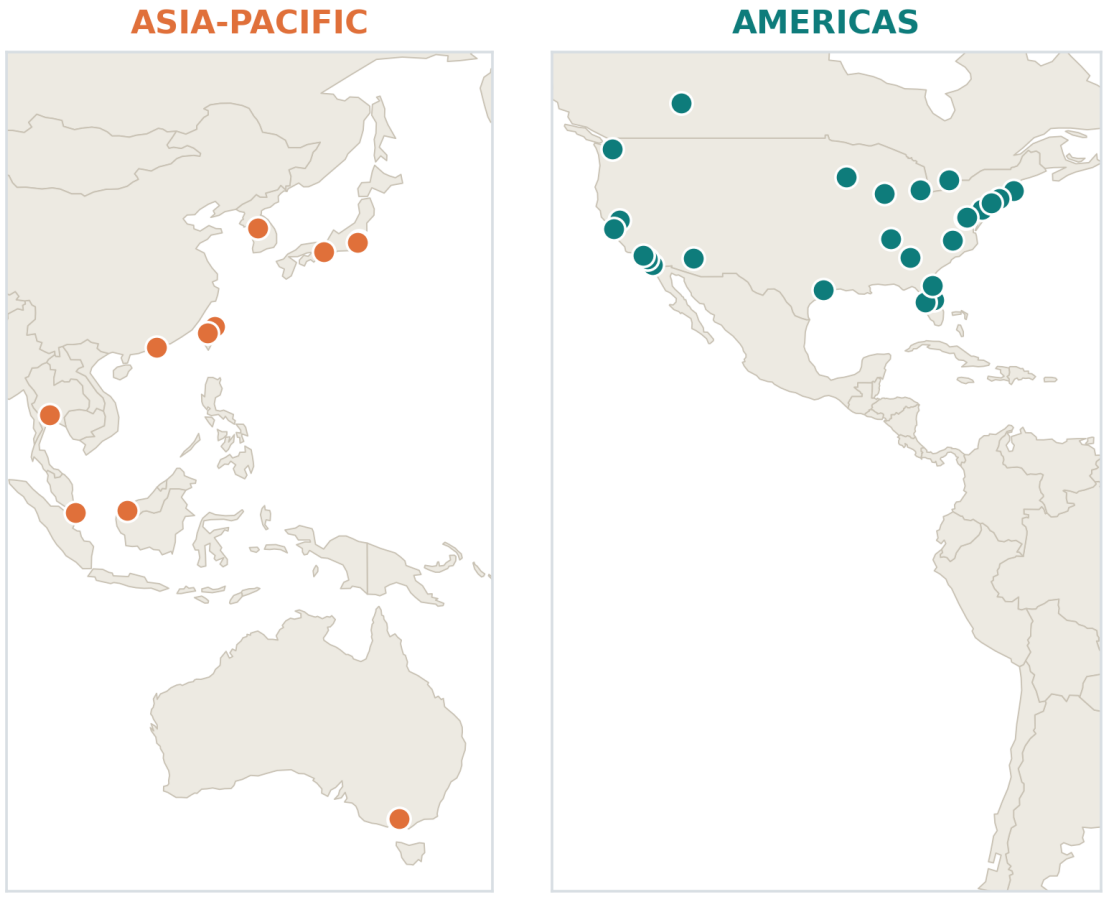
[1]12 May 2026 cut-off. Median duration of exposure of 3 months
[2]Grouped term
[3]No Grade 5 TRAE

- Dose reduction (9%) and treatment discontinuation (3%) due to TRAE are uncommon
- EGFR-wildtype associated TRAEs are mostly Grade 1
- Most common TRAE is bilirubin elevation:
  - "Gilbert's-like" pattern: usually asymptomatic and predominately unconjugated due to UGT1A1 inhibition by BH-30643
  - Exposure dependent: Reversible with dose modification or often tolerated without dose adjustment
- TRAE of Grade 3+ ALT / AST increase in 7% / 5% of patients, respectively, with no cases of Hy's law
- Rare pneumonitis (~1%)
- No clinically significant treatment-related cardiac effects or QTc prolongation

Summary & Next Steps

- BH-30643 demonstrated a 45% ORR in patients with *EGFR* C797S-positive resistance to prior TKI, with or without concurrent T790M
  - Fast Track Designation granted by US FDA for C797S-positive NSCLC after prior 3rd-gen TKI
- Safety notable for primarily low-grade EGFR wildtype toxicity as well as asymptomatic Gilbert's-like unconjugated bilirubin elevation
- Expansion cohorts are ongoing studying:
  - On-target resistance mutations
  - Targeted therapy naïve cohorts
  - Chemotherapy combination (dose escalation)
- Global Phase 2 study targeting C797S planned for Q1/2027

SOLARA enrollment ongoing in North America & APAC



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Study sites:

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Thank You.