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### **Efficacy and Safety of HLX43, a PD-L1-Targeting ADC, in Pretreated Advanced Thymic Squamous Cell Carcinoma: Results from a Phase I Trial**

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# Background and study design

An open-label, first-in-human, phase 1 clinical trial (NCT06115642)



- Thymic squamous cell carcinoma (TSCC) is an ultra-rare, highly progressive thoracic tumor for which platinum-based chemotherapy constitutes the only established first-line regimen<sup>1</sup>.

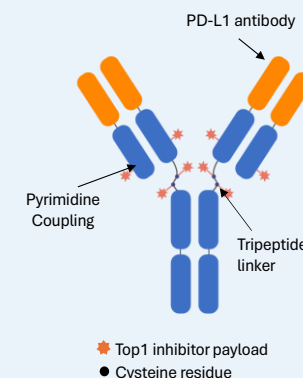


- Owing to its low incidence, large-scale prospective trials validating effective post-platinum therapies have been challenging to conduct; single-agent ICIs achieve only limited tumor control while conferring an elevated risk of severe immune-mediated toxicities<sup>2,3</sup>.



- HLX43 is the first PD-L1-targeting ADC to be investigated in TSCC.

## Molecular components of HLX43



### Key Features

- High-affinity, internalizable PD-L1 antibody
- Highly stable linker in circulating blood
- Cleavable and **TME-activatable tripeptide linker**
- Potent cytotoxic payload Top1 inhibitor (DAR=8)

### Key inclusion criteria:

- Age ≥18 years;
- ECOG PS of 0 or 1;
- For **phase 1a**, histologically or cytologically confirmed advanced malignant **solid tumors**;
- For **phase 1b cohort 2**, histologically or cytologically confirmed advanced **TSCC** refractory or not amenable to standard therapy;

3.0 mg/kg Q3W  
N=11

2.5 mg/kg Q3W  
N=12

2.0 mg/kg Q3W  
N=11



Further dose exploration, including step-down dosing, and expansion at the recommended dose are ongoing and will be reported separately.

### Primary endpoints

- BICR-ORR

### Secondary endpoints

- INV-ORR
- Safety
- OS
- Immunogenicity
- Biomarker exploration
- DCR
- DoR
- PFS

**Given the rarity of TSCC, patients with TSCC enrolled in phase 1a were combined with the phase 1b cohort 2 for a pooled analysis.**

1. Riely, et al. J Natl Compr Canc Netw. 2025; 23(6):255-269. 2. Arunachalam, et al. Lung Cancer. 2023; 176:132-139. 3. Cho, et al. J Clin Oncol. 2019; 37(24):2162-2170.

ADC, antibody-drug conjugate; BICR, blinded independent central review; DAR, drug-to-antibody ratio; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ICIs, immune checkpoint inhibitors; INV, investigator; N, number; ORR, objective response rate; OS, overall survival; PD-L1, programmed cell death 1-ligand 1; PFS, progression-free survival; Q3W: every 3 weeks; TME, tumor microenvironment; Top1, topoisomerase 1; TSCC, thymic squamous cell carcinoma.

# Baseline demographics and disease characteristics

Here we present results in the TSCC patients

Data cutoff: June 01, 2026

Median follow-up:

2.0mg/kg: 11.1 months

2.5mg/kg: 11.4 months

3.0mg/kg: 6.9 months

ITT: N=34

SS: N=34

RES: N=33<sup>#</sup>

|                                 | HLX 43<br>2.0mg/kg<br>(n = 11) | HLX43<br>2.5mg/kg<br>(n = 12) | HLX43<br>3.0mg/kg<br>(n = 11) | Total<br>(n = 34) |
|---------------------------------|--------------------------------|-------------------------------|-------------------------------|-------------------|
| Median age (range), years       | 61 (43–70)                     | 53 (34–69)                    | 55 (39–64)                    | 56 (34–70)        |
| Male, n (%)                     | 5 (45.5)                       | 7 (58.3)                      | 6 (54.5)                      | 18 (52.9)         |
| ECOG PS, n (%)                  |                                |                               |                               |                   |
| 0                               | 0                              | 5 (41.7)                      | 6 (54.5)                      | 11 (32.4)         |
| 1                               | 11 (100)                       | 7 (58.3)                      | 5 (45.5)                      | 23 (67.6)         |
| Site of metastasis, n (%)       |                                |                               |                               |                   |
| Lung                            | 7 (63.6)                       | 7 (58.3)                      | 7 (63.6)                      | 21 (61.8)         |
| Liver                           | 6 (54.5)                       | 4 (33.3)                      | 2 (18.2)                      | 12 (35.3)         |
| Brain                           | 1 (9.1)                        | 1 (8.3)                       | 1 (9.1)                       | 3 (8.8)           |
| PD-L1 expression by TPS*, n (%) |                                |                               |                               |                   |
| TPS < 1%                        | 4 (36.4)                       | 3 (25.0)                      | 2 (18.2)                      | 9 (26.5)          |
| 1% ≤ TPS < 50%                  | 5 (45.5)                       | 3 (25.0)                      | 3 (27.3)                      | 11 (32.4)         |
| TPS ≥ 50%                       | 1 (9.1)                        | 3 (25.0)                      | 4 (36.4)                      | 8 (23.5)          |
| Not available                   | 1 (9.1)                        | 3 (25.0)                      | 2 (18.2)                      | 6 (17.6)          |

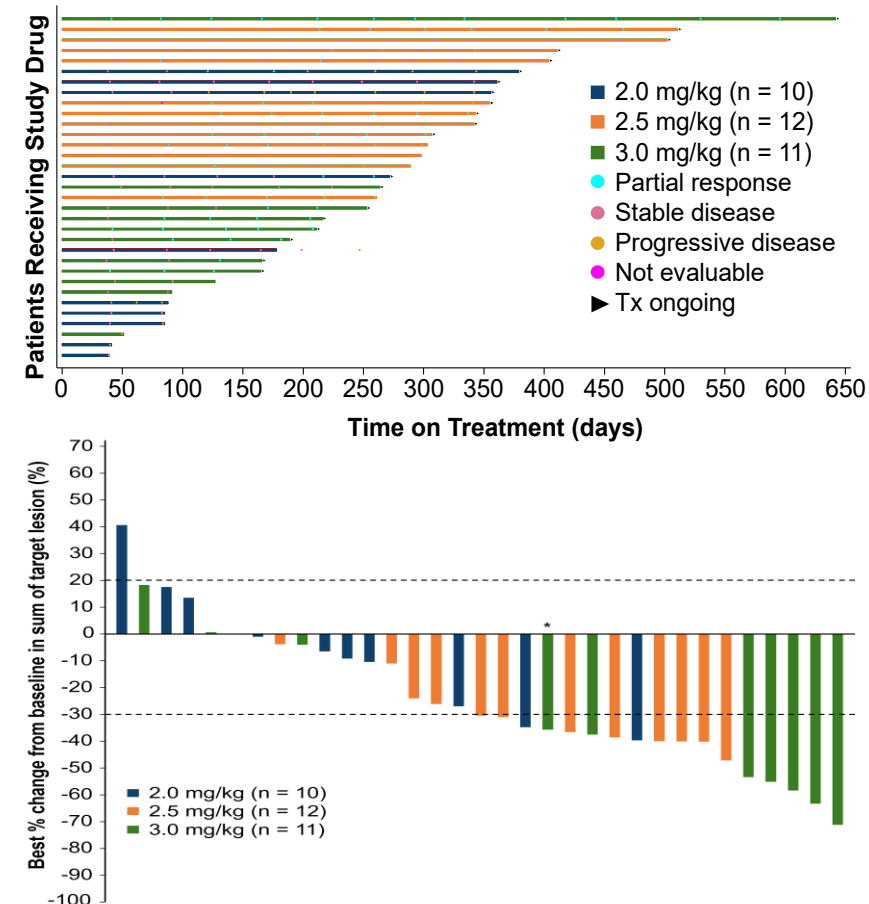
|                             | HLX 43<br>2.0mg/kg<br>(n = 11) | HLX43<br>2.5mg/kg<br>(n = 12) | HLX43<br>3.0mg/kg<br>(n = 11) | Total<br>(n = 34) |
|-----------------------------|--------------------------------|-------------------------------|-------------------------------|-------------------|
| Prior antitumor therapy     | 11 (100)                       | 12 (100)                      | 11 (100)                      | 34 (100)          |
| Chemotherapy                | 11 (100)                       | 12 (100)                      | 11 (100)                      | 34 (100)          |
| Immunotherapy               | 8 (72.7)                       | 10 (83.3)                     | 7 (63.6)                      | 25 (73.5)         |
| Targeted therapy            | 6 (54.5)                       | 4 (33.3)                      | 5 (45.5)                      | 15 (44.1)         |
| Prior lines of therapy      |                                |                               |                               |                   |
| 1                           | 2 (18.2)                       | 2 (16.7)                      | 5 (45.5)                      | 9 (26.5)          |
| 2                           | 3 (27.3)                       | 3 (25.0)                      | 2 (18.2)                      | 8 (23.5)          |
| 3                           | 3 (27.3)                       | 4 (33.3)                      | 1 (9.1)                       | 8 (23.5)          |
| ≥ 4                         | 3 (27.3)                       | 3 (25.0)                      | 3 (27.3)                      | 9 (26.5)          |
| Median no. of lines (range) | 3.0 (1–7)                      | 3.0 (1–4)                     | 2.0 (1–6)                     | 3.0 (1–7)         |

<sup>#</sup> One patient in the 2.0mg/kg group did not have any post-baseline tumor assessments were excluded from RES. \* Detected with SP263.

CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; ITT, intent-to-treat; no., number; PD-L1, programmed cell death 1-ligand 1; RES, response-evaluable set; SS, safety set; TPS, tumor proportion score; TSCC, thymic squamous cell carcinoma.

# BICR-assessed confirmed tumor response in TSCC patients

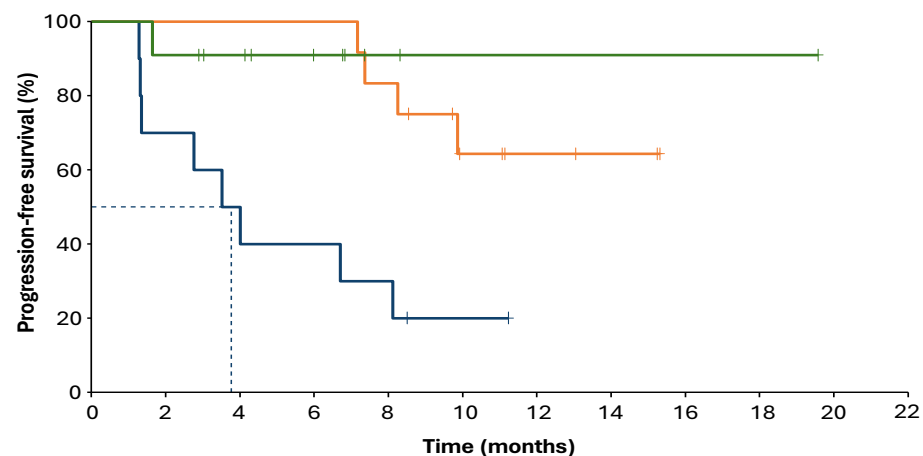
| Confirmed tumor response <sup>#</sup> | HLX 43<br>2.0mg/kg<br>(n = 10) | HLX43<br>2.5mg/kg<br>(n = 12) | HLX43<br>3.0mg/kg<br>(n = 11) | Total<br>(n = 33)   |
|---------------------------------------|--------------------------------|-------------------------------|-------------------------------|---------------------|
| CR                                    | 0                              | 0                             | 0                             | 0                   |
| PR                                    | 2 (20.0)                       | 7 (58.3)                      | 6 (54.5)                      | 15 (45.5)           |
| SD                                    | 5 (50.0)                       | 5 (41.7)                      | 4 (36.4)                      | 14 (42.4)           |
| PD                                    | 3 (30.0)                       | 0                             | 1 (9.1)                       | 4 (12.1)            |
| ORR,<br>% (95% CI)                    | 20.0<br>(2.5–55.6)             | 58.3<br>(27.7–84.8)           | 54.5<br>(23.4–83.3)           | 45.5<br>(28.1–63.6) |
| DCR,<br>% (95% CI)                    | 70.0<br>(34.8–93.3)            | 100.0<br>(73.5–100)           | 90.9<br>(58.7–99.8)           | 87.9<br>(71.8–96.6) |
| mDoR, months<br>(95% CI)              | 2.8<br>(NE–NE)                 | NR<br>(4.3–NE)                | NR<br>(NE–NE)                 | NR<br>(4.3–NE)      |



Data is presented as n (%) unless otherwise specified. <sup>#</sup> Confirmed tumor response among the 33 response-evaluable patients as assessed by BICR per RECIST v1.1; one patient in the 2.0mg/kg group did not have post-baseline tumor assessment and were excluded in efficacy analysis. \* Had a best overall response of stable disease based on BICR assessment.

BICR, blinded independent central review; CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, median duration of response; m, median; NE, not evaluable; NR, not reached; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; Tx, treatment.

# BICR-assessed PFS and subgroup analysis of efficacy



| Number at risk |    |    |    |    |   |   |   |   |   |   |   |
|----------------|----|----|----|----|---|---|---|---|---|---|---|
| 10             | 7  | 5  | 4  | 3  | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 12             | 12 | 12 | 12 | 10 | 5 | 3 | 2 | 0 | 0 | 0 | 0 |
| 11             | 10 | 8  | 5  | 2  | 1 | 1 | 1 | 1 | 1 | 0 | 0 |

|                                  | HLX43<br>2.0mg/kg<br>(n = 10) | HLX43<br>2.5mg/kg<br>(n = 12) | HLX43<br>3.0mg/kg<br>(n = 11) | Total<br>(n = 33)   |
|----------------------------------|-------------------------------|-------------------------------|-------------------------------|---------------------|
| Median PFS, months<br>(95% CI)   | 3.8<br>(1.3–8.1)              | NR<br>(7.4–NE)                | NR<br>(NE–NE)                 | NR<br>(7.4–NE)      |
| 6-month PFS rate, %<br>(95% CI)  | 40.0<br>(12.3–67.0)           | 100.0<br>(100–100)            | 90.9<br>(50.8–98.7)           | 78.3<br>(59.8–89.0) |
| 12-month PFS rate, %<br>(95% CI) | NE<br>(NE–NE)                 | 64.3<br>(29.8–85.1)           | 90.9<br>(50.8–98.7)           | 51.1<br>(29.5–69.1) |

| Potential recommended<br>phase 2 dose | HLX43<br>2.5mg/kg   | HLX43<br>3.0mg/kg   | HLX43<br>2.5mg/kg   | HLX43<br>3.0mg/kg   |
|---------------------------------------|---------------------|---------------------|---------------------|---------------------|
| Prior immunotherapy                   | Yes,<br>n = 10      | Yes,<br>n = 7       | No,<br>n = 2        | No,<br>n = 4        |
| Confirmed ORR,<br>% (95% CI)          | 60.0<br>(26.2–87.8) | 28.6<br>(3.7–71.0)  | 50.0<br>(1.3–98.7)  | 100.0<br>(39.8–100) |
| Confirmed DCR,<br>% (95% CI)          | 100.0<br>(69.2–100) | 85.7<br>(42.1–99.6) | 100.0<br>(15.8–100) | 100.0<br>(39.8–100) |
| PD-L1 expression <sup>#</sup>         | Positive,<br>n = 6  | Positive,<br>n = 7  | Negative,<br>n = 3  | Negative,<br>n = 2  |
| Confirmed ORR,<br>% (95% CI)          | 66.7<br>(22.3–95.7) | 57.1<br>(18.4–90.1) | 66.7<br>(9.4–99.2)  | 0                   |
| Confirmed DCR,<br>% (95% CI)          | 100.0<br>(54.1–100) | 100.0<br>(59.0–100) | 100.0<br>(29.2–100) | 50.0<br>(1.3–98.7)  |

<sup>#</sup> PD-L1 expression was not available in three patients in the 2.5mg/kg group and two in the 3.0mg/kg group.

BICR, blinded independent central review; CI, confidence interval; DCR, disease control rate; n, number; NE, not evaluable; NR, not reached; ORR, objective response rate; PD-L1, programmed cell death 1-ligand 1; PFS, progression-free survival.

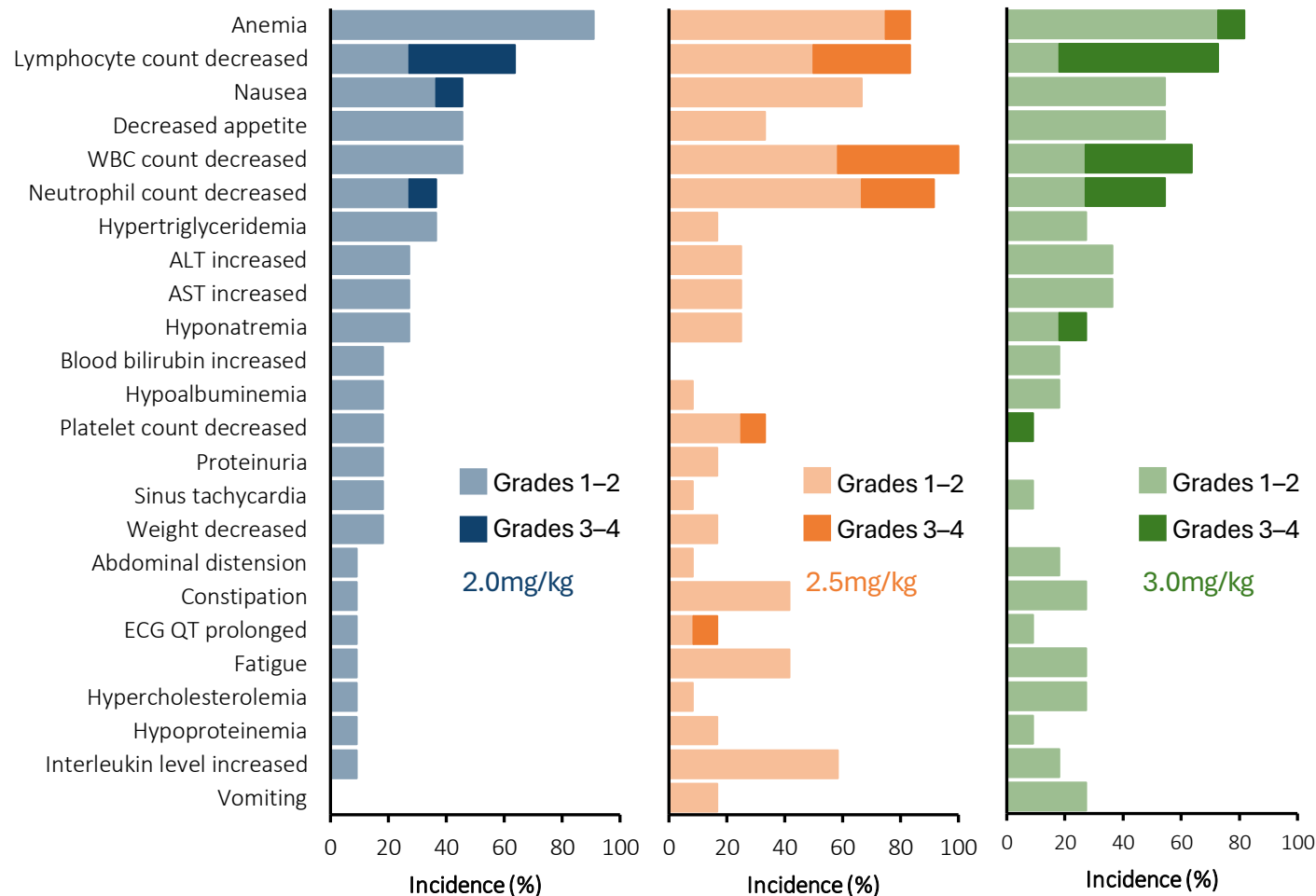
# Safety and tolerability

| n (%)                         | HLX 43<br>2.0mg/kg<br>(n = 11) | HLX43<br>2.5mg/kg<br>(n = 12) | HLX43<br>3.0mg/kg<br>(n = 11) | Total<br>(n = 34) |
|-------------------------------|--------------------------------|-------------------------------|-------------------------------|-------------------|
| Any TEAE                      | 11 (100)                       | 12 (100)                      | 11 (100)                      | 34 (100)          |
| Grade ≥3 TEAE                 | 6 (54.5)                       | 9 (75.0)                      | 8 (72.7)                      | 23 (67.6)         |
| Serious                       | 3 (27.3)                       | 0                             | 3 (27.3)                      | 6 (17.6)          |
| Leading to Tx interruption    | 5 (45.5)                       | 11 (91.7)                     | 7 (63.6)                      | 23 (67.6)         |
| Leading to Tx discontinuation | 1 (9.1)                        | 0                             | 1 (9.1)                       | 2 (5.9)           |
| Leading to dose reduction     | 0                              | 2 (16.7)                      | 6 (54.5)                      | 8 (23.5)          |
| Leading to death              | 0                              | 0                             | 0                             | 0                 |
| Any TRAE                      | 11 (100)                       | 12 (100)                      | 11 (100)                      | 34 (100)          |
| Grade ≥3 TRAE                 | 5 (45.5)                       | 9 (75.0)                      | 8 (72.7)                      | 22 (64.7)         |
| Serious                       | 3 (27.3)                       | 0                             | 2 (18.2)                      | 5 (14.7)          |
| Leading to Tx interruption    | 5 (45.5)                       | 11 (91.7)                     | 5 (45.5)                      | 21 (61.8)         |
| Leading to Tx discontinuation | 1 (9.1)                        | 0                             | 1 (9.1)                       | 2 (5.9)           |
| Leading to dose reduction     | 0                              | 2 (16.7)                      | 6 (54.5)                      | 8 (23.5)          |
| Leading to death              | 0                              | 0                             | 0                             | 0                 |
| Any irAE                      | 2 (18.2)                       | 2 (16.7)                      | 0                             | 4 (11.8)          |
| Grade ≥3 irAE <sup>#</sup>    | 1 (9.1)                        | 0                             | 0                             | 1 (2.9)           |

<sup>#</sup> Immune-mediated lung disease of grade 3 in severity. <sup>\*</sup> Occurring in at least 10% of all enrolled patients.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ECG, electrocardiogram; irAE, immune-related adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; Tx, treatment; WBC, white blood cell.

## Most common TRAEs (≥10%)\*

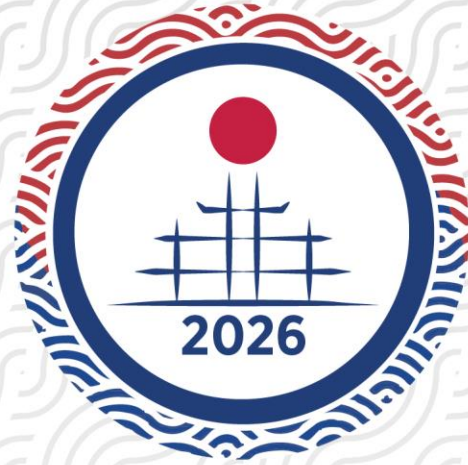


# Conclusions

- **Promising efficacy in TSCC (median prior therapy  $\geq$  3L)**
  - ✓ **At potential RP2D of 2.5 mg/kg and 3.0 mg/kg,**
    - ✓ cORR: 58.3% and 54.5%; cDCR: 100.0% and 90.9%
    - ✓ mDoR: not reached
    - ✓ mPFS: not reached
  - ✓ **Favorable safety profile with low hematologic toxicities**
    - ✓ Tx discontinuation due to TRAEs: 5.9%
    - ✓ Death due to TRAEs: 0%



HLX43 demonstrated promising efficacy, particularly at 2.5 mg/kg and 3.0 mg/kg, with manageable safety in heavily pretreated TSCC. Further investigation of HLX43 for this disease indication is warranted.



# Thank You.