# SHR-4849 (IDE849), an ADC targeting delta-like ligand 3 (DLL3), in relapsed small cell lung carcinoma (SCLC) and other neuroendocrine carcinomas (NECs): long-term results from the phase 1 study

# BACKGROUND

- **Delta-like ligand 3 (DLL3)**, a protein that inhibits Notch signaling, is an attractive therapeutic target in small cell lung cancer (SCLC) and other neuroendocrine carcinomas (NECs) due to high expression in tumors of neuroendocrine lineage.[1-4]
- **SHR-4849 (IDE849*)** is an antibody-drug conjugate comprising a humanized anti-DLL3 IgG1 monoclonal antibody, linked to a DNA topoisomerase I inhibitor payload by a cleavable linker.
- We initiated a **first-in-human study** of SHR-4849 in relapsed or metastatic SCLC and other NECs. SHR-4849 at doses ranging from 0.8 to 4.2 mg/kg showed **a tolerable and manageable safety profile, favorable pharmacokinetic profile, and promising anti-tumor activity**.[5]

# METHODS

- **Study design**: a multicenter, phase 1 study (NCT06443489).
- **Key eligibility criteria**:
  - Histologically or cytologically confirmed relapsed or metastatic SCLC and other DLL3-expressing NECs.
    DLL3 positivity was defined as H-score >0.
  - Had progressive or recurrent disease after standard treatment(s).
  - Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.
  - Stable CNS metastases following local therapy.
- **Treatment**: Eligible patients received intravenous SHR-4849 at 0.8, 1.8, 2.4, 3.0, 3.5, and 4.2 mg/kg every 3 weeks.
- This report presents the **updated efficacy and safety data**.
  - Data cutoff: Aug 21, 2026.
  - Median follow-up duration: 12.1 months (IQR, 8.2–16.0).

# RESULTS

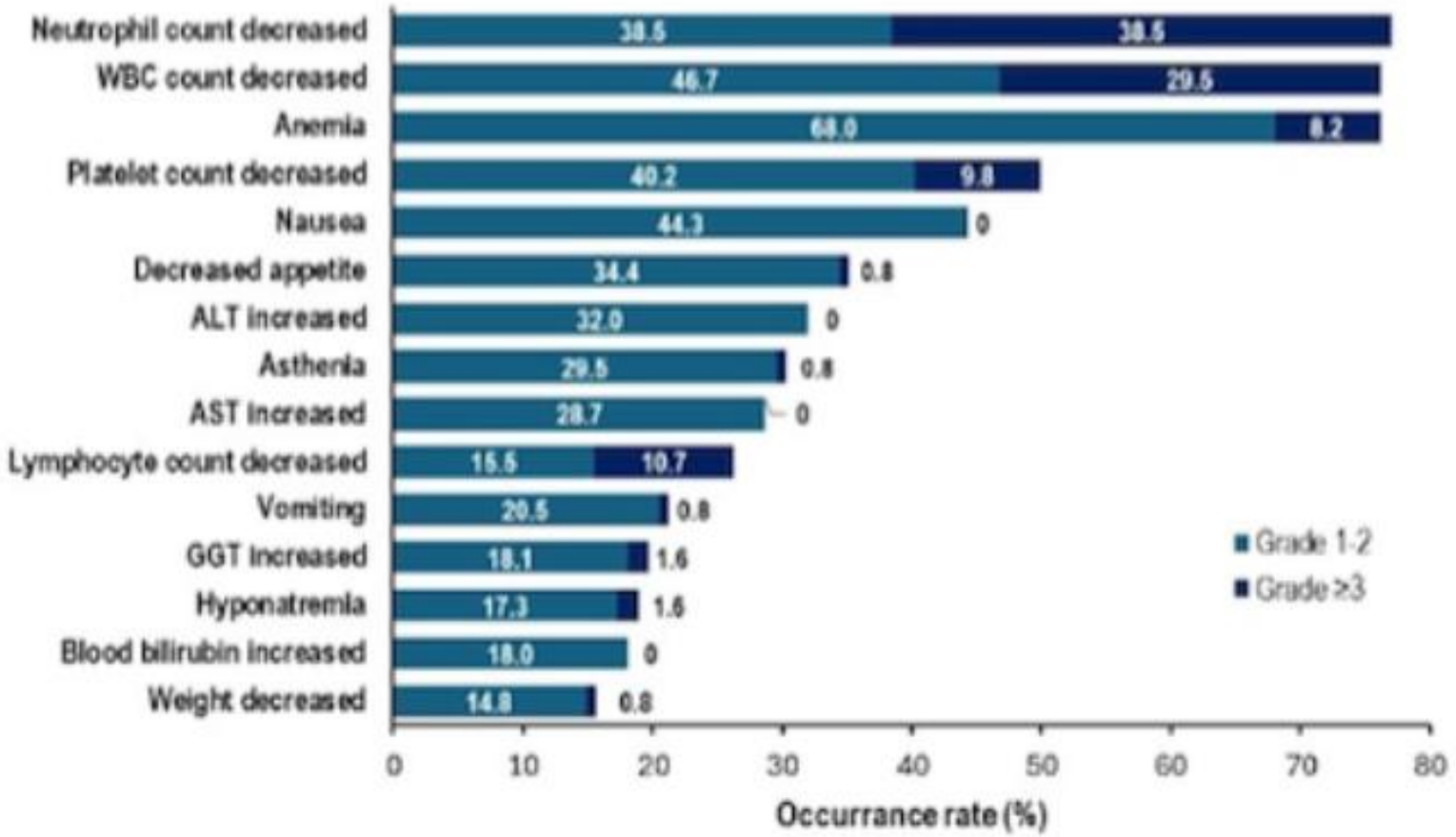



**Figure 1. TRAEs occurring in ≥15% of patients**

## Table 1. Patient characteristics

| | SCLC (N=103) | Other NECs (N=19) | Total (N=122) |
|---|---|---|---|
| **Sex** | | | |
| Male | 79 (76.7) | 9 (47.4) | 88 (72.1) |
| Female | 24 (23.3) | 10 (52.6) | 34 (27.9) |
| **Age**, years | 60 (36–75) | 59 (28–70) | 60.0 (28–75) |
| **ECOG performance status** | | | |
| 0 | 5 (4.9) | 2 (10.5) | 7 (5.7) |
| 1 | 98 (95.1) | 17 (89.5) | 115 (94.3) |
| **Clinical stage IV** | 89 (86.4) | 18 (94.7) | 107 (87.7) |
| **Brain metastases** | 27 (26.2) | 0 | 27 (22.1) |
| **Liver metastases** | 32 (31.1) | 9 (47.4) | 41 (33.6) |
| **Prior lines of therapy** | | | |
| 1 | 51 (49.5) | 12 (63.2) | 63 (51.6) |
| 2 | 35 (34.0) | 7 (36.8) | 42 (34.4) |
| ≥3 | 17 (16.5) | 0 | 17 (13.9) |
| **Prior immunotherapy** | 81 (78.6) | 11 (57.9) | 92 (75.4) |

Data are n (%) or median (range).
One (0.8%) patient had previously received T-cell-engaging therapy targeting DLL3.

**Table 2. Safety summary**

| | Total (N=122) |
|---|---|
| **Any TRAE** | 121 (99.2) |
| Grade ≥3 | 73 (59.8) |
| Leading to dose reduction | 23 (18.9) |
| Leading to treatment discontinuation | 3 (2.5) |
| Serious | 26 (21.3) |
| Leading to death | 1 (0.8) |

## Patients

- A total of 122 patients were enrolled, including 103 (84.4%) with SCLC and 19 (15.6%) with other NECs (**Table 1**).

## Safety

- The most common grade ≥3 treatment-related adverse events (TRAEs) were hematological toxicities (**Figure 1**).
- Occurrence of grade ≥3 TRAEs and serious TRAEs increased with dose; the rates in the 2.4, 3.0, and 3.5 mg/kg cohorts were:
  - Grade ≥3 TRAEs: 33.3%, 70.3%, and 76.2%;
  - Serious TRAEs: 15.2%, 24.3%, and 26.2%.
- Treatment-related interstitial lung disease occurred in 9 (7.4%) patients (grade 1–2: 8 [6.6%]; grade ≥3: 1 [0.8%]).
- Only 2.5% of patients discontinued SHR-4849 due to TRAEs (**Table 2**).
- One patient died due to TRAE (pneumonia).

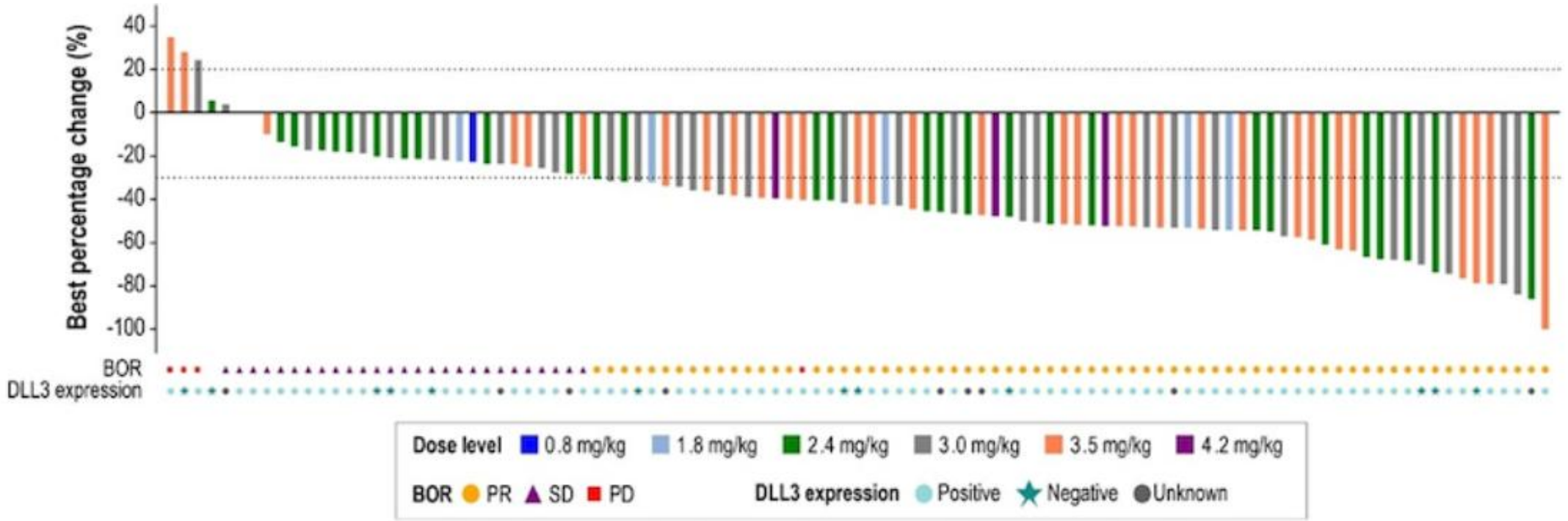



**Figure 2. Best percentage change in target lesions in SCLC patients**

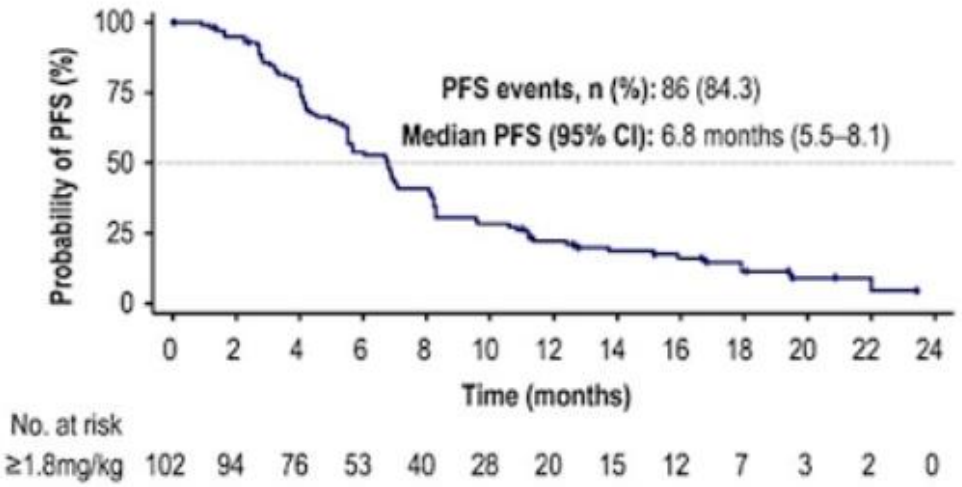



**Figure 3. PFS in SCLC**

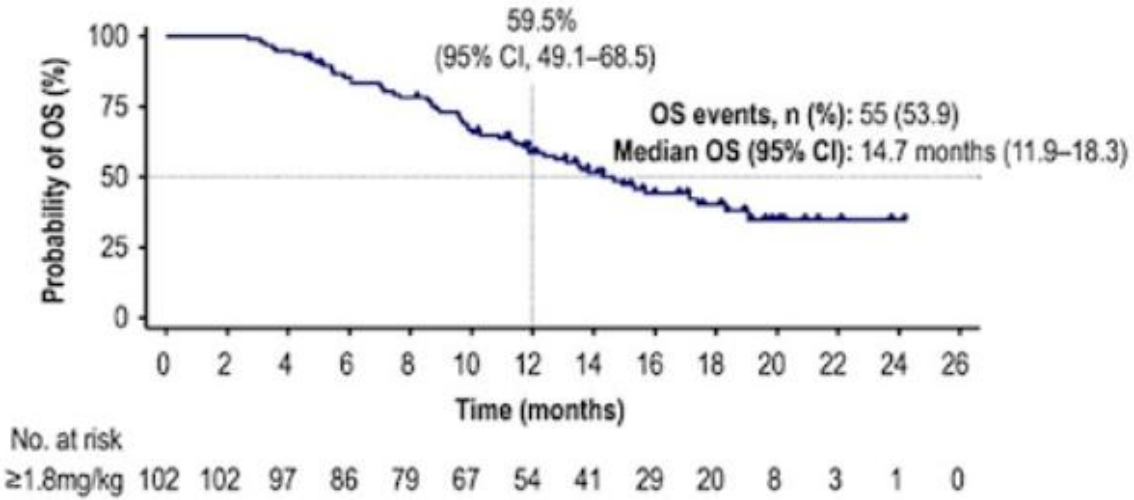



**Figure 4. OS in SCLC**

**Table 3. Antitumor activity**

| | SCLC (≥1.8 mg/kg) | | | | Other NECs (n=19) |
|---|---|---|---|---|---|
| | All (n=101) | 2L Setting (n=51) | 3L Setting (n=34) | With brain metastases (n=26) | |
| **ORR**, n (%; 95% CI) | 69 (68.3%; 58.3–77.2) | 37 (72.5%; 58.3–84.1) | 21 (61.8%; 43.6–77.8) | 20 (76.9%; 56.4–91.0) | 10 (52.6%; 28.9–75.6) |
| **Confirmed ORR**, n (%; 95% CI) | 55 (54.5%; 44.2–64.4) | 31 (60.8%; 46.1–74.2) | 17 (50.0%; 32.4–67.6) | 17 (65.4%; 44.3–82.8) | 7 (36.8%; 16.3–61.6) |
| **DCR**, n (%; 95% CI) | 94 (93.1%; 86.2–97.2) | 50 (98.0%; 89.6–100.0) | 32 (94.1%; 80.3–99.3) | 26 (100.0%; 86.8–100.0) | 16 (84.2%; 60.4–96.6) |

ORR, objective response rate. DCR, disease control rate.

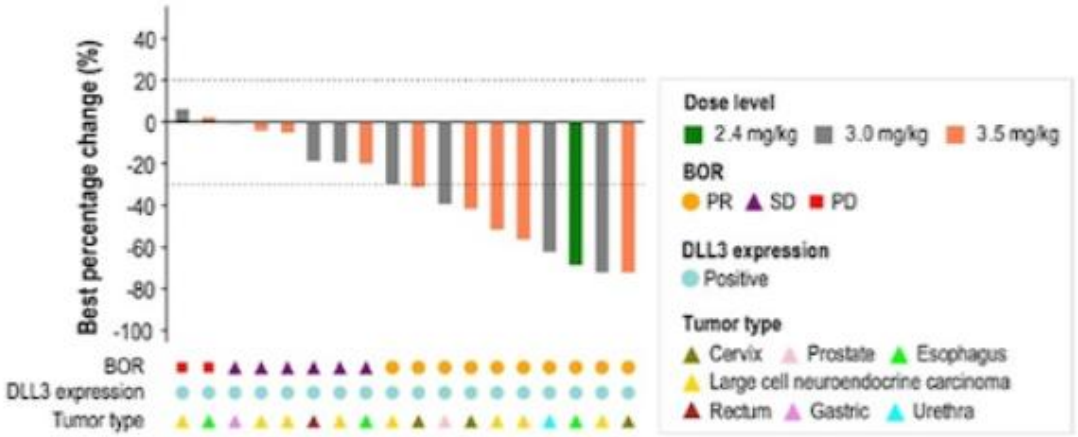



**Figure 5. The best percentage change in target lesions in other NECs**

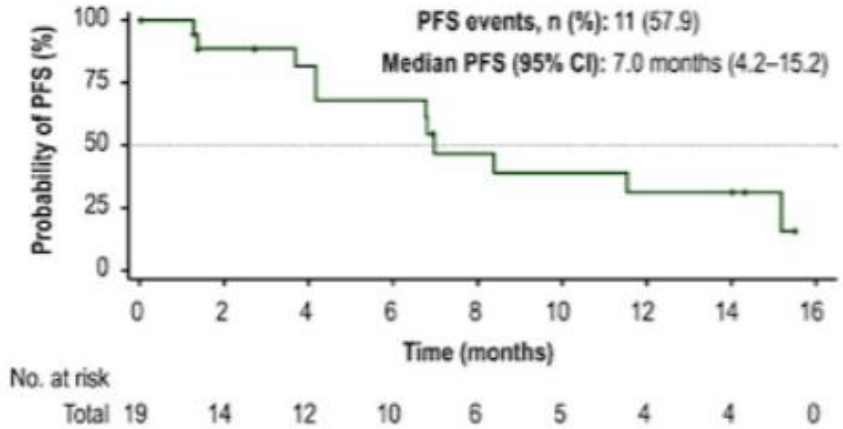



**Figure 6. PFS in other NECs**

**Efficacy in SCLC** (Table 3; Figures 2-5)

- **In patients receiving SHR-4849 at ≥1.8 mg/kg**:
  Confirmed ORR was 54.5%, and DCR was 93.1%;
  Median PFS was 6.8 months;
  Median OS was 14.7 months, and 12-month OS rate was 59.5%.
- **In patients in the 2L setting receiving SHR-4849 at ≥1.8 mg/kg:**
  Confirmed ORR was 60.8%, and DCR was 98.0%;
  Median PFS was 6.9 months (95% CI, 5.5–8.3);
  Median OS was 17.4 months (95% CI, 9.9–not reached), and 12-month OS rate was 60.0 (95% CI, 45.1–72.1).
- **In patients with brain metastases receiving SHR-4849 at ≥1.8 mg/kg:**
  Confirmed ORR was 65.4%, and DCR was 100.0%.

**Efficacy in other NECs** (Table 3; Figures 5-6)

- Confirmed ORR was 36.8%, and DCR was 84.2%;
- Median PFS was 7.0 months;
- 9-month OS rate was 82.4% (95% CI, 54.7–93.9).

## CONCLUSIONS

- SHR-4849 (IDE849) has promising efficacy in patients with relapsed SCLC and other NECs, with clinically meaningful ORR and DCR and encouraging PFS and OS results.
- The safety profile is favorable, with few treatment discontinuations.
- Registrational studies are planned in SCLC and other NECs.