CASE REPORT · THORACIC & NEUROENDOCRINE ONCOLOGY

Durable Clinical and Radiographic Response to Tarlatamab in DLL3-High Metastatic High-Grade Neuroendocrine Carcinoma of Pulmonary Origin

Danielle Fogg, FNP[1], Corey Couto, MD[1], Arslan Babar, MD, MPH[1]

[1]Northern Light Cancer Care, Northern Light Eastern Maine Medical Center

Background

Delta-like ligand 3 (**DLL3**) is aberrantly surface-expressed in most small-cell lung cancers (SCLC) and across high-grade neuroendocrine carcinomas (NEC).

Tarlatamab, a DLL3×CD3 bispecific T-cell engager, improved overall survival versus chemotherapy in relapsed SCLC.[1,2]

13.6 vs 8.3
months median OS, DeLLphi-304

HR 0.60
overall survival vs chemotherapy

Emerging data suggest DLL3×CD3 engagers are active beyond SCLC — in DLL3-high pulmonary carcinoid (73% response), extrapulmonary NEC and LCNEC (obrixtamig), and DLL3+ neuroendocrine prostate cancer — but experience in non-SCLC high-grade NEC remains limited.[3–5]

Case Presentation

A **53-year-old man** with a **40 pack-year** smoking history (1 PPD × 40 years) presented with an enlarging left parietal scalp lesion (4.7 cm on CT) and a retroauricular nodule; the scalp lesion began as a "pimple" in 3/2025.

PATHOLOGY

Neck node, scalp and lumbar skin biopsies: metastatic high-grade NEC, probable pulmonary origin.

TTF-1+ · Synaptophysin+ · INSM1+ · Chromogranin focal+ · AE1/AE3+ · CAM5.2+ · Ki-67 ~15%, focally 80–90%

EXTENT OF DISEASE

Lungs, pleura, cervical/thoracic/abdominal nodes, liver, adrenals, pancreas, omentum, subcutaneous and muscle. Brain MRI negative.

NGS (TEMPUS XT CDX)

POTENTIALLY ACTIONABLE	
KRAS p.G12C	**53.6% VAF**
BIOLOGICALLY RELEVANT	
KEAP1 p.R470H	**74.3% VAF**
NF1 p.G638*	**53.7% VAF**
CDKN2A · CDKN2B · MTAP	**Copy number loss**
IMMUNOTHERAPY MARKERS	
TMB · MSI	**8.4 mut/Mb · Stable**
PD-L1	**TPS <1**

Conclusion

This case demonstrates a rapid, radiographically confirmed response to tarlatamab in DLL3-high, immunochemotherapy-refractory high-grade NEC, supporting **DLL3 immunohistochemistry as a selection biomarker** and prospective study in non-SCLC high-grade NEC.[1,5,6]

Clinical Course

- **Feb 2026** — Diagnosis of metastatic high-grade NEC; widespread disease on CT
- **3/16 – 5/19/26** — Carboplatin / etoposide / atezolizumab ×4
- **5/26 – 6/8/26** — Palliative RT to right neck and buttock
- **5/29/26** — **Progression**: liver, pancreas, omentum/mesentery, muscle, left kidney, adrenals. Repeat IHC: **DLL3 100%**
- **6/29/26** — **Tarlatamab C1D1** per DeLLphi-304: 1 mg → 10 mg C1D8/D15 → 10 mg every 2 weeks, with protocolized CRS/ICANS monitoring
- **8/12 – 8/14/26** — **Restaging CT and PET/CT: marked response**
- **9/23/26** — Brain MRI: no intracranial metastases
- **Oct 2026** — Continuing tarlatamab (C4D15)

Response to Tarlatamab

By **cycle 2**:

- Resolution of dyspnea
- **22-lb** weight gain
- Regression of cutaneous and nodal disease
- **No** documented CRS or ICANS

Restaging CT (8/12/26), ~6 weeks after C1D1:

- Resolved bilateral pleural effusions
- Smaller right infrahilar mass and mediastinal nodes
- Markedly improved hepatic metastases
- Smaller bilateral renal, adrenal and pancreatic lesions
- Peritoneal implants unchanged or regressed; no new disease
- Small pericardial effusion, slightly increased

Scalp Lesion on Tarlatamab



A Prior to C1 **B** C1D2 **C** C2D1 **D** C2D15

The scalp lesion rapidly evolved and crusted after cycle 1.

C4D15
still on tarlatamab as of Oct 2026

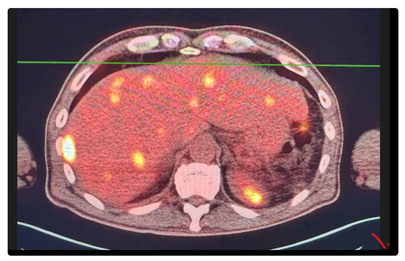
+22 lb
weight gain by cycle 2

None
documented CRS or ICANS

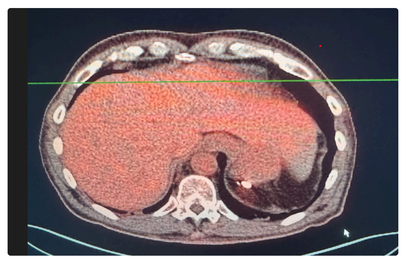
PET/CT: Before and On Tarlatamab

3/25/26 · PRE-TARLATAMAB | **8/14/26 · ON TARLATAMAB**

LIVER & RETROPERITONEUM

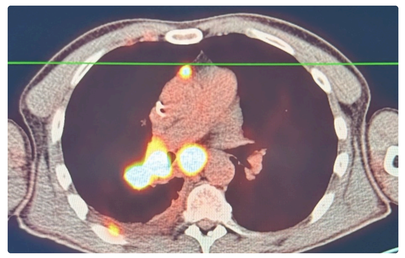


Multifocal hypermetabolic liver lesions and pancreatic head mass.

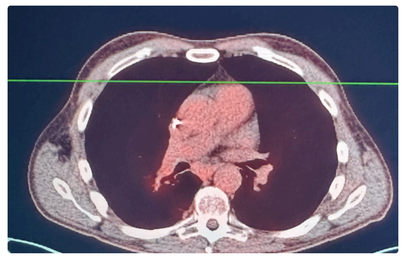


Almost complete resolution. Only residual uptake: left retroperitoneal nodules, 3.2 × 1.9 cm, SUV_{max} 1.5 (prev. 3.5 × 2.7 cm, 1.6).

HILAR, MEDIASTINAL & SUBCARINAL NODES

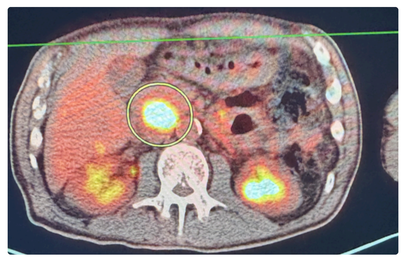


Hypermetabolic hilar, mediastinal and subcarinal nodes.

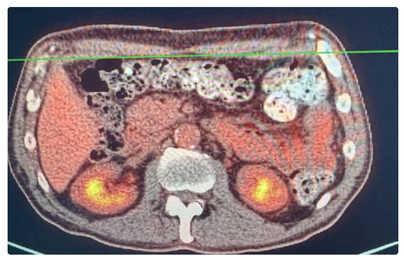


R paratracheal node 15 mm, SUV_{max} 3.1 (prev. 2 cm, 7.8). RLL nodule 13 mm, SUV_{max} 1.9 (prev. 3.7 × 2.8 cm mass, 9.2).

PANCREAS



Hypermetabolic pancreatic head mass.



Interval decrease in pancreatic head and body lesions.

References

1. Mountzios G, Sun L, Cho BC, et al. Tarlatamab in small-cell lung cancer after platinum-based chemotherapy. *N Engl J Med*. 2025;393(4):349-361. doi:10.1056/NEJMoa2502099
2. Rudin CM, Reck M, Johnson ML, et al. Emerging therapies targeting the delta-like ligand 3 (DLL3) in small cell lung cancer. *J Hematol Oncol*. 2023;16(1):66. doi:10.1186/s13045-023-01464-y
3. Wermke M, Gambardella V, Kuboki Y, et al. Phase I dose-escalation results for the DLL3/CD3 IgG-like T-cell engager obrixtamig (BI 764532) in patients with DLL3+ SCLC or neuroendocrine carcinomas. *J Clin Oncol*. 2025;43(27):3021-3031. doi:10.1200/JCO-25-00363
4. Ross JS, Lee J, Ortiz E, et al. Clinical responses to tarlatamab among patients with pulmonary carcinoid. *J Thorac Oncol*. 2026:104135. doi:10.1016/j.jtho.2026.104135
5. Aggarwal R, Rottey S, Bernard-Tessier A, et al. Safety and efficacy of tarlatamab in patients with neuroendocrine prostate cancer: results from the phase 1b DeLLpro-300 study. *Clin Cancer Res*. 2025. doi:10.1158/1078-0432.CCR-25-1211
6. Yao J, Bergsland E, Aggarwal R, et al. DLL3 as an emerging target for the treatment of neuroendocrine neoplasms. *Oncologist*. 2022;27(11):940-951. doi:10.1093/oncolo/oyac161