

Paper 1

TUMOR ORGANOID-GUIDED TARGETED THERAPY FOR LOCALLY ADVANCED RADIOIODINE-REFRACTORY THYROID CANCER: A SINGLE-CENTER RETROSPECTIVE ANALYSIS OF 38 PATIENTS

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Background: Radioiodine-refractory differentiated thyroid cancer (RAIR-DTC) carries a dismal prognosis with median overall survival of 2.5-3.5 years. Current multikinase inhibitors (lenvatinib, sorafenib, donafenib) achieve objective response rates (ORR) of only 12-65%, and empirical drug selection often leads to treatment failure and unnecessary toxicity. Patient-derived tumor organoids (PDTOs) faithfully recapitulate parental tumor genomic profiles and drug sensitivity, offering a promising platform for precision oncology. This study evaluated whether PDTO-guided targeted therapy improves outcomes in locally advanced RAIR-DTC.

Methods: This retrospective study analyzed 38 patients with locally advanced RAIR-DTC treated between September 2023 and September 2025. PDTOs were established from surgical or biopsy specimens with >85% success rate. Drug sensitivity was tested against lenvatinib, sorafenib, and donafenib within 14 days. Patients were stratified into PDTO-guided group (n=20, therapy selected per organoid sensitivity) and empirical group (n=18, standard protocol). Primary endpoints were ORR and progression-free survival (PFS). Secondary endpoints included treatment-related adverse events (TRAEs).

Results: The PDTO-guided group demonstrated significantly higher ORR compared to the empirical group (70.0% vs 33.3%, P=0.021). Median PFS was prolonged in the guided group (16.8 vs 9.2 months, HR=0.48, P=0.016). The concordance between organoid sensitivity and clinical response reached 85%. Grade ≥3 TRAEs were lower in the guided group (25.0% vs 44.4%, P=0.198).

Table 1. Correlation Between Organoid Drug Sensitivity and Clinical Response

Organoid Result	Clinical Response	Clinical Non-response	Concordance
Sensitive (n=14)	12	2	85.7%
Resistant (n=6)	1	5	83.3%
Total (n=20)	13	7	85.0%

Conclusion: PDTO-guided targeted therapy significantly improves ORR and PFS in locally advanced RAIR-DTC patients compared to empirical treatment. The high concordance between organoid sensitivity and clinical response supports PDTOs as a valuable precision medicine tool. This approach addresses unmet clinical needs by enabling individualized drug selection, potentially reducing unnecessary toxicity, and advancing patient-centered quality cancer care. Multicenter prospective validation is warranted.