

Targeted and Immunotherapy-Based Treatment Strategies for Anaplastic Thyroid Carcinoma: A Systematic Review



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Introduction

- Anaplastic thyroid carcinoma (ATC) is a rare, highly aggressive malignancy with historically poor survival.
- Molecular profiling has enabled increasingly targeted systemic therapies, including kinase inhibitors and immunotherapy-based regimens.
- Objective: To systematically review prospective clinical evidence evaluating targeted and immunotherapy-based treatment strategies in ATC.

Methods

- PRISMA-guided systematic review was performed.
- Eligible studies included prospective clinical trials and basket trials reporting ATC-specific clinical outcomes.
- Preclinical, non-therapeutic, and studies without ATC-specific outcomes were excluded.
- Extracted variables included molecular alteration, treatment regimen, sample size, overall survival (OS), progression-free survival (PFS), and overall response rate (ORR).
- Given substantial clinical and treatment heterogeneity, findings were synthesized qualitatively.

Results

- Five prospective studies evaluating targeted or immunotherapy-based treatment strategies were included.
- **BRAF V600E** was the most commonly represented molecular alteration.
- Dabrafenib + trametinib demonstrated **ORRs of 56–69%**, with reported **12-month OS of 51.7–80%** and **12-month PFS of 43.2–79%** across reports.
- In the multi-cohort immunotherapy study, median OS ranged from **6.21 to 43 months** and median PFS from **1.35 to 13.93 months**, with substantial variation by molecular cohort.
- Encorafenib + binimetinib demonstrated an **ORR of 80%**, **12-month OS of 81.8%**, and **12-month PFS of 75%** in a small BRAF V600E cohort.
- Across evaluated regimens, ORR ranged from **14% to 80%**.

Key Findings

- **BRAF-directed therapy:** Most consistent prospective response data
- **Molecular heterogeneity:** Outcomes varied substantially by alteration and regimen
- **Evidence limitations:** Small cohorts, heterogeneous treatments, and overlapping longitudinal reports

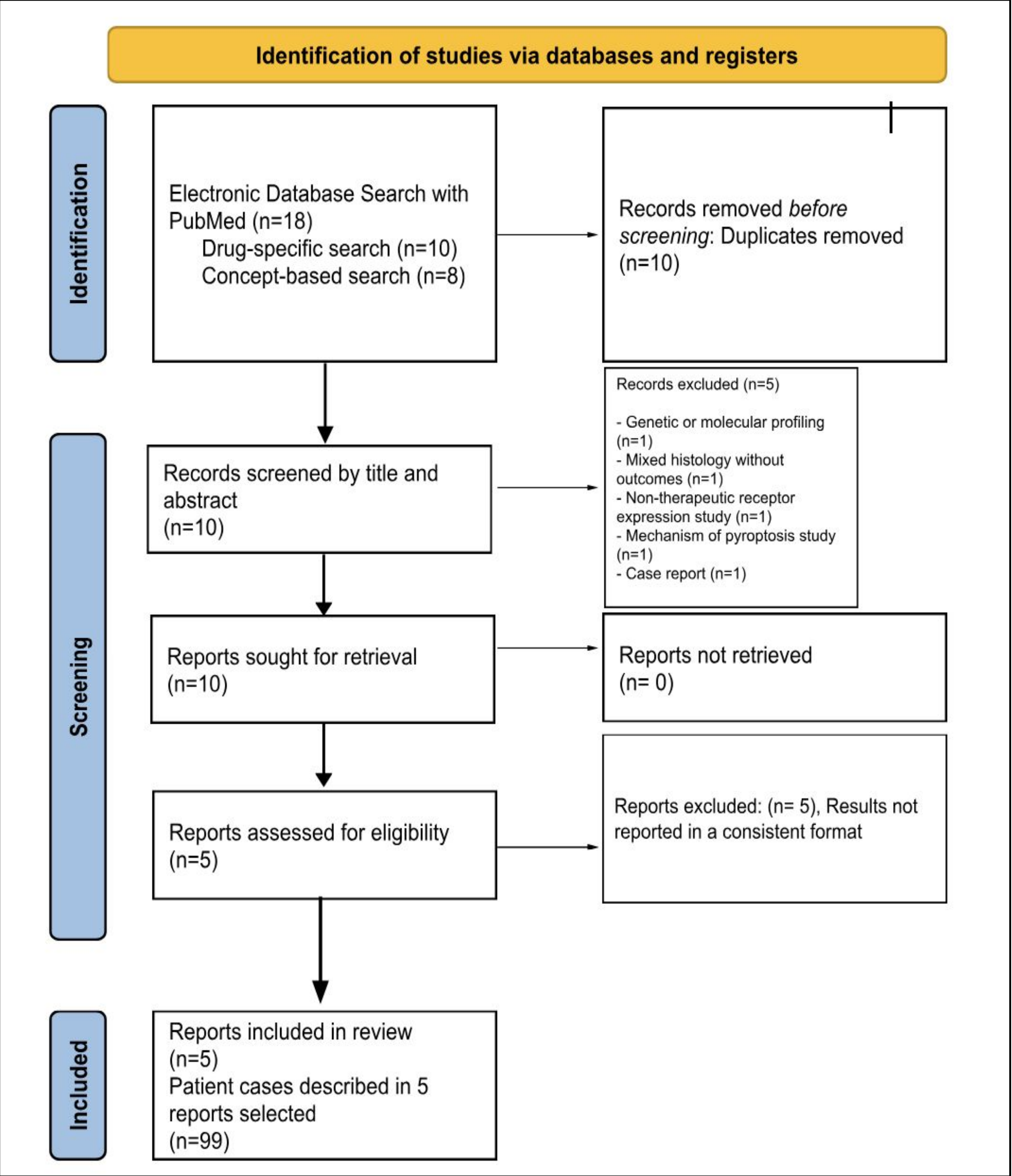


Figure 1: PRISMA protocol

Conclusion

- Targeted and immunotherapy-based regimens demonstrate **meaningful clinical activity** in ATC, although prospective evidence remains limited.
- **BRAF V600E-directed therapy currently has the most consistent prospective evidence**, with high response rates reported across multiple prospective reports.
- These findings support **early molecular testing and multidisciplinary treatment planning** while highlighting the need for larger prospective studies.

Table 1. Prospective targeted and immunotherapy-based studies in anaplastic thyroid carcinoma

Study	Population / Molecular Alteration	Treatment Regimen	Overall Survival	Progression-Free Survival	Overall Response Rate
Subbiah et al., 2017 Phase II, open-label	n=16 BRAF V600E Metastatic	Dabrafenib + trametinib	12-mo estimate: 80%	12-mo estimate: 79%	69% (11/16; 95% CI, 41–89%)
Subbiah et al., 2022 ROAR Phase II, open-label	n=36 BRAF V600E Unresectable or metastatic	Dabrafenib + trametinib	12-mo: 51.7% 24-mo: 31.5%	12-mo: 43.2%	56% (95% CI, 38.1–72.1%)
Subbiah et al., 2023 ROAR study	n=36 BRAF V600E Follow-up ROAR report	Dabrafenib + trametinib	14.5 mo (95% CI, 6.8–23.2)	6.7 mo (95% CI, 4.7–13.8)	56%
Cabanillas et al., 2024 Phase II, single-center	n=42 total C1: BRAF V600E (n=18) C2: RAS or NF1/2 (n=21) C3: Other (n=3)	C1: Vemurafenib + cobimetinib + atezolizumab C2: Cobimetinib + atezolizumab C3: Bevacizumab + atezolizumab	C1: 43 mo (95% CI, 16–NE) C2: 8.7 mo (95% CI, 5.1–37.0) C3: 6.21 mo (95% CI, 4.1–NE)	C1: 13.93 mo (95% CI, 6.6–64.13) C2: 4.80 mo (95% CI, 1.84–14.69) C3: 1.35 mo (95% CI, 1.35–NE)	C1: 50% (95% CI, 28.4–72.1%) C2: 14% C3: 33%
Tahara et al., 2024 Phase II, open-label, uncontrolled	n=5 BRAF V600E Metastatic	Encorafenib + binimetinib	12-mo: 81.8%	6- and 12-mo: 75%*	80% (95% CI, 28.4–99.5%)

[†] Subbiah 2022 and 2023 represent longitudinal follow-up reporting from the ROAR evidence base and should not be interpreted as independent patient cohorts.
^{*} PFS value for Tahara et al. should be verified before final submission.