TREATMENTS FOR RET-ALTERED ADVANCE OR METASTATIC THYROID CANCER: A SYSTEMATIC REVIEW

C. MORENO RAMOS, M.D. GIL-SIERRA, M.D.P. BRICEÑO-CASADO, J. CORDERO-RAMOS, R. CASTILLEJO-GARCIA
SERVICIO EXTREMEÑO DE SALUD, SERVICIOS CENTRALES. SUBDIRECCIÓN DE FARMACIA., MERIDA-BADAJOZ, SPAIN.

4CPS-092
L01- ANTINEOPLASTIC AGENTS

Background and importance

Receptor tyrosine kinase rearranged during transfection (RET) can be oncogenically activated by gene fusions or point mutations. RET alterations are implicated in the pathogenesis of approximately 20% of thyroid cancers (TC). Multikinase inhibitors and selective RET inhibitors are promising therapies.

Aim and objectives

To develop a systematic review of therapies for advanced and metastatic TC with fusion-positive, mutated or altered RET gene (RET+)

Material and methods

PRISMA methodology

A literature search in PubMed® database was performed until September 2024.

- Inclusion criteria: clinical trials (CTs) enrolling patients diagnosed with RET+ advanced and/or metastatic TC who could be naïve or previously treated patients.
- Efficacy endpoints: overall survival (OS), progression-free survival (PFS) and objective response rate (ORR).
- Data collected: publication date, study design, tumor stage, sample size, population follow-up, treatments, efficacy results and comparator arm.

Results

40 search results → 10 CTs met the inclusion criteria.

- 7 studies had no comparator arm.
- Median follow-up: 14 - 47 months.
- Sample size: 19 - 312 patients.
- Therapies: cabozantinib, pralsetinib, selpercatinib, sorafenib, and vandetanib

Selpercatinib achieved the highest numerical efficacy.

Cabozantinib presented the next best numerical efficacy.

Therapy	OS	PFS	ORR
Selpercatinib	64.3 months (48.3-NR)	41.4 months (30.2-NR)	77.6% (70.2-84.0)
Cabozantinib	26.6 months (not available)	11.2 months (not available)	not available

Conclusion and relevance

- **Selpercatinib presented the best numerical efficacy result in patients with TC and RET+, followed by cabozantinib.**
- **Comparative randomised CTs for all therapeutic alternatives could facilitate clinical decision making.**

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