NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Selpercatinib for treating advanced thyroid cancer with RET alterations (managed access review of TA742)

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of selpercatinib within its marketing authorisation for treating advanced RET fusion-positive thyroid cancer and advanced RET mutation-positive medullary thyroid cancer (MTC).

Background

Cancer of the thyroid, a small gland at the base of the neck, can cause pain and difficulties in swallowing and breathing. The most common types of thyroid cancer are papillary and follicular, and these are sometimes referred to as differentiated thyroid cancer Differentiated thyroid cancer cells retain the appearance of normal thyroid cells and do not spread as quickly as undifferentiated cancer cells. Rarer types of thyroid cancer include medullary thyroid cancer (MTC) and anaplastic thyroid cancer.[1]

Thyroid cancer is uncommon and accounted for 1.2% of all new cases of cancer in the UK in 2020.[2] There was a 5-year prevalence of 21,306 people with thyroid cancer in the UK in 2020.[2] Differentiated thyroid cancers account for approximately 90% of all cases.[1] Differentiated thyroid cancers are typically curable, with 10-year survival typically around 85%.[3] MTC arises from a different type of cell than other thyroid cancers. It can run in families, frequently spreads to lymph nodes in the neck, and typically has poorer long-term outcomes.[4] For example, UK 5-year survival for MTC is 75% in males compared to 90% for papillary thyroid cancer (90% and 95% respectively in females).[5,6]

Some thyroid cancers can be caused by alterations in the RET (or 'rearranged during transfection') gene, which can lead to uncontrolled cell growth. Mutations in the RET gene are present in many MTC cases (RET mutation-positive), and chromosomal rearrangements (or 'fusions') involving the RET gene can cause papillary thyroid cancer (RET fusion-positive).[7,8]

Thyroid cancer is usually treated by partial or total thyroidectomy. The choice of surgery depends on the type and size of cancer amongst other factors. Surgery may be followed by adjuvant treatments. Primarily, this is radioactive iodine which is used to destroy any residual thyroid tissue and any remaining cancer cells. External beam radiotherapy or palliative chemotherapy can also be used. The British Thyroid Association's 'Guidelines for the management of thyroid cancer' notes that the use of external beam radiotherapy and chemotherapy in palliative care has begun to be superseded by targeted therapy.[9] In clinical practice, best supportive care or monitoring is offered until the disease starts to progress and symptoms occur, or there is rapid progression that is likely to become symptomatic.

For residual or recurrent disease, targeted therapy (tyrosine kinase inhibitors) may be used. NICE technology appraisal 535 recommends lenvatinib and sorafenib, which

inhibit multiple receptor tyrosine kinases including vascular endothelial growth factor (VEGF) receptors, as options for treating differentiated thyroid cancer after radioactive iodine. NICE technology appraisal 516 recommends cabozantinib as an option for treating advanced MTC in adults. NICE technology appraisal 630 recommends larotrectinib for use within the Cancer Drugs Fund as an option for treating for treating NTRK fusion-positive solid tumours. There is no currently NICE-recommended systemic treatment for people under the age of 18 with advanced RET-altered thyroid cancer.

NICE technology appraisal 742 recommends selpercatinib for use within the Cancer Drugs Fund as an option for treating advanced RET fusion-positive thyroid cancer in adults who need systemic therapy after sorafenib or lenvatinib, and for treating advanced RET-mutant medullary thyroid cancer in people 12 years and older who need systemic therapy after cabozantinib or vandetanib.

This review of technology appraisal guidance 742 covers the population eligible for treatment according to selpercatinib's marketing authorisation.

The technology

Selpercatinib (Retsevmo, Eli Lilly) has a marketing authorisation in the UK for treating adults with advanced RET fusion-positive thyroid cancer who require systemic therapy following prior treatment with sorafenib and/or lenvatinib. Selpercatinib does not currently have a marketing authorisation in the UK for people aged 12-18 years with advanced RET fusion-positive thyroid cancer who require systemic therapy following prior treatment with sorafenib and/or lenvatinib. It has been studied in a single-arm basket trial (study designed to test the effect of a single drug across multiple cancer populations) in people with advanced solid tumours with RET alterations. The trial included people with thyroid cancer. It also has a marketing authorisation in the UK for treating adults and adolescents 12 years and older with advanced RET-mutant MTC.

Intervention(s)	Selpercatinib
Population(s)	• People with advanced RET fusion-positive thyroid cancer who require systemic therapy after sorafenib or lenvatinib • People with advanced RET mutation-positive medullary thyroid cancer (MTC) who require systemic therapy after cabozantinib or vandetanib

Subgroups	If the evidence allows, subgroups based on the following will be considered: • Type of thyroid cancer within advanced RET fusion-positive thyroid cancer (such as papillary carcinoma, follicular carcinoma, poorly differentiated carcinoma and anaplastic carcinoma) • Specific type of RET alteration (within RET fusion-positive thyroid cancer or RET-mutation positive MTC) may need to be considered, as some types of RET genetic alteration may be more or less sensitive to selpercatinib
Comparators	• For advanced RET fusion-positive thyroid cancer which has progressed following prior treatment: o best supportive care or palliative care • For advanced RET mutation-positive MTC which has progressed following prior treatment: o best supportive care or palliative care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • adverse effects of treatment • health-related quality of life.

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The use of selpercatinib is conditional on the presence of RET mutation or fusion. The economic modelling should include the costs associated with diagnostic testing for RET mutation/fusion in people with advanced MTC/advanced thyroid cancer who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related Technology Appraisals:** Cabozantinib for previously treated differentiated thyroid cancer unsuitable for or refractory to radioactive iodine (2023). NICE technology appraisal guidance 928. Selpercatinib for treating advanced thyroid cancer with RET alterations (2022). NICE Technology appraisal guidance 742. Vandetanib for treating medullary thyroid cancer (2018). NICE Technology appraisal guidance 550. Lenvatinib and sorafenib for treating differentiated thyroid cancer after radioactive iodine (2018). NICE Technology appraisal guidance 535. Cabozantinib for treating medullary thyroid cancer (2018). NICE Technology appraisal guidance 516. **Related appraisals in development:** Selpercatinib for untreated advanced thyroid cancer with RET alterations NICE technology appraisal guidance [ID6132]. Publication expected June 2024.

	Related Guidelines: Thyroid cancer: assessment and management (2022) NICE guideline 230. **Related interventional Procedures:** Minimally invasive video-assisted thyroidectomy (2014). NICE interventional procedures guidance 499. Intraoperative nerve monitoring during thyroid surgery (2008) NICE interventional procedures guidance 255.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019), chapters 9, 12, 105, 106

References

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2. International Agency for Research on Cancer (2021) United Kingdom. Accessed February 2024.
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8. Li AY, McCusker MG, Russo A et al. (2019) RET fusions in solid tumors. Cancer Treatment Reviews 81, 101911.
9. Perros P, Colley S, Boelaert K et al. (2014) Guidelines for the management of thyroid cancer. Clinical Endocrinology: 81;s1.