NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Selpercatinib for untreated advanced thyroid cancer with RET alterations

Draft scope

Draft remit/evaluation objective

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

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 (DTC). 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 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. 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.

The technology

Selpercatinib (Retevmo, Eli Lilly) does not currently have a marketing authorisation in the UK for treating people with untreated RET fusion-positive advanced thyroid cancer, or untreated RET mutation-positive advanced MTC. It is being 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 is also being studied in a clinical trial compared with cabozantinib and vandetanib in people with RET mutation-positive advanced MTC.

Selpercatinib currently has a marketing authorisation for the treatment of adults with advanced RET fusion-positive thyroid cancer who require systemic therapy following prior treatment with sorafenib and/or lenvatinib. It also has a marketing authorisation for the treatment of adults and adolescents 12 years and older with advanced RET-mutant MTC who require systemic therapy following prior treatment with cabozantinib and/or vandetanib.

Intervention(s)	Selpercatinib
Population(s)	• adults with untreated advanced RET-fusion positive thyroid cancer who require systemic therapy • adults and adolescents 12 years and older with untreated advanced RET-mutant MTC who require systemic therapy

Comparators	• For adults with untreated advanced RET-fusion positive thyroid cancer who require systemic therapy:
	  ○ Lenvatinib
	  ○ Sorafenib
	  ○ Best supportive care
	• For adults and adolescents 12 years and older with untreated advanced RET-mutant MTC who require systemic therapy:
	  ○ Cabozantinib (adults only)
	  ○ Best supportive 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out. 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 or 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:** Lenvatinib and sorafenib for treating differentiated thyroid cancer after radioactive iodine (2018). NICE Technology appraisal guidance 535. Review date to be confirmed.

	Vandetanib for treating medullary thyroid cancer (2018). NICE Technology appraisal guidance 550. Review date to be confirmed. Cabozantinib for treating medullary thyroid cancer (2018). NICE Technology appraisal guidance 516. Review date to be confirmed. Larotrectinib for treating NTRK fusion-positive solid tumours (2020) NICE Technology appraisal guidance 630. Review date to be confirmed. Selpercatinib for treating advanced thyroid cancer with RET alterations (2022). NICE Technology appraisal guidance 742. Review date 2024. **Related appraisals in development:** Cabozantinib for previously treated differentiated thyroid cancer unsuitable for or refractory to radioactive iodine NICE technology appraisal guidance [ID4046]. Publication expected July 2023. **Related Guidelines:** Thyroid disease: assessment and management (2019). NICE guideline 145. 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

Questions for consultation

Where do you consider selpercatinib will fit into the existing care pathway for advanced MTC/advanced thyroid cancer?

What is best supportive care for adults with advanced RET fusion-positive thyroid cancer and advanced RET mutation-positive MTC?

What is best supportive care for adolescents 12 years and older with advanced RET-mutant MTC (i.e. is it different to best supportive care for adults)?

Would selpercatinib be a candidate for managed access?

Do you consider that the use of selpercatinib can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which selpercatinib will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Macmillan Cancer Support (2017) Understanding thyroid cancer. Accessed June 2023.

2. International Agency for Research on Cancer (2021) United Kingdom. Accessed June 2023.

3. Dal Maso L, Tavilla A, Pacini F et al. (2017) Survival of 86,690 patients with thyroid cancer: A population-based study in 29 European countries from EUROCARE-5. European Journal of Cancer 1;77:140-152
4. American Thyroid Association (2020) Medullary thyroid cancer. Accessed June 2023.

5. Cancer Research UK (2018). Thyroid cancer – survival. Accessed June 2023.

6. Dal Maso L, Tavilla A, Pacini F et al. (2017). Survival of 86,690 patients with thyroid cancer: A population-based study in 29 European countries from EUROCARE-5. European Journal of Cancer 77, May 2017, 140-152.

7. National Institute of Health (2020) RET gene. Accessed June 2023.
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.