

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Selpercatinib for treating advanced thyroid cancer with RET alterations

Final scope

Final remit/appraisal 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.¹ There are several types of thyroid cancer, including the most common, papillary and follicular, as well as the rarer medullary thyroid cancer (MTC) and anaplastic thyroid cancer.

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).^{2,3}

Thyroid cancer is uncommon and can occur at any age, but is most often diagnosed in people from their 20s through to their 60s. Between 2013 and 2017, more than 15,000 people in England were diagnosed with thyroid cancer,⁴ and it is around three times more common in women than in men.⁵ The ‘differentiated’ thyroid cancers (papillary and follicular) represent 90% of all thyroid cancers.⁶ MTC is rarer, and accounts for approximately 3% (adult) to 10% (paediatric) of thyroid cancers.⁷ 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.⁸ 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).^{9,10}

British Thyroid Association guidelines indicate that usual treatment for thyroid cancer in the UK is surgery to remove part or all of the thyroid.⁷ Surgery may be followed by a number of systemic and non-systemic treatments, according to the size and type of cancer and factors such as evidence of local or distant disease.⁷ Treatment options may include radioactive iodine, external beam radiotherapy, or targeted drugs.⁷ These drugs inhibit proteins that are involved in signalling within cells, in order to stop thyroid cancer growing and spreading.

For differentiated thyroid cancer, surgery followed by radioactive iodine is the most common treatment approach. If the cancer doesn’t respond to radioactive iodine, then lenvatinib or sorafenib (multi-kinase inhibitors) are recommended options (technology appraisal [535](#)) for adults. They represent possible systemic treatments for some people with advanced RET fusion-positive thyroid cancer whose disease has progressed following prior treatment.

Cabozantinib (a tyrosine kinase inhibitor) is recommended for progressive medullary thyroid cancer in adults with unresectable, locally advanced or metastatic disease (technology appraisal [516](#)). At the time of that appraisal, it was not appropriate to make a recommendation based on RET mutation tumour status, as the required test was not routinely carried out. Vandetanib is not recommended for medullary thyroid cancer (technology appraisal [550](#)), although some people under the age of 18 access it via an individual patient funding request, due to cabozantinib not being recommended for the paediatric population. This means cabozantinib is the only currently recommended systemic treatment for adults with advanced MTC who can't have surgery, regardless of whether or not their cancer is RET-mutation positive.

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) is a small molecule inhibitor of the rearranged during transfection (RET) receptor tyrosine kinase. Chromosomal rearrangements involving fusions of RET with various partners can result in the growth of cancer cells. Point mutations in RET can also result in irregular RET proteins that can promote the growth of cancer cells. Administration of selpercatinib can target RET cancers and inhibit growth of tumour cells. It is administered orally as a capsule.

Selpercatinib does not have a marketing authorisation in the UK for treating people with RET fusion-positive advanced thyroid cancer, or 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.

Intervention(s)	Selpercatinib
Population(s)	<ul style="list-style-type: none"> • People with advanced RET fusion-positive thyroid cancer who require systemic therapy and whose disease has progressed following prior treatment • People with advanced RET mutation-positive medullary thyroid cancer (MTC) who require systemic therapy
Comparators	<ul style="list-style-type: none"> • For advanced RET fusion-positive thyroid cancer which has progressed following prior treatment: <ul style="list-style-type: none"> ○ lenvatinib or sorafenib for differentiated thyroid cancer which did not respond to radioactive iodine (adults only) ○ best supportive care or palliative care • For advanced RET mutation-positive MTC: <ul style="list-style-type: none"> ○ cabozantinib (adults only) ○ best supportive care or palliative care

<p>Outcomes</p>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rate • adverse effects of treatment • health-related quality of life
<p>Economic analysis</p>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account.</p> <p>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 5.9 of the Guide to the Methods of Technology Appraisals.</p>

<p>Other considerations</p>	<p>If the evidence allows, subgroups based on the following will be considered:</p> <ul style="list-style-type: none"> • 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 • Line of treatment (position in pathway) <p>The availability and cost of biosimilar and generic products should be taken into account.</p> <p>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.</p>
<p>Related NICE recommendations and NICE Pathways</p>	<p>Related Technology Appraisals:</p> <p>Cabozantinib for treating medullary thyroid cancer (2018). NICE Technology Appraisal 516. Review date 2020.</p> <p>Lenvatinib and sorafenib for treating differentiated thyroid cancer after radioactive iodine (2018). NICE Technology Appraisal 535. Review date 2021.</p> <p>Vandetanib for treating medullary thyroid cancer (2018). NICE Technology Appraisal 550. Review date 2021.</p> <p>Guidelines in development:</p> <p>Thyroid cancer: assessment and management. Publication expected April 2022.</p> <p>Related Interventional Procedures:</p> <p>Minimally invasive video-assisted thyroidectomy (2014). NICE interventional procedures guidance 499.</p> <p>Intraoperative nerve monitoring during thyroid surgery (2008). NICE interventional procedures guidance 255.</p> <p>Related NICE Pathways:</p> <p>Endocrine cancers (2018) NICE pathway https://pathways.nice.org.uk/pathways/endocrine-cancers</p>
<p>Related National Policy</p>	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan</p> <p>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapter 9 Adult specialist</p>

	<p>endocrinology services, Chapter 109 Specialist endocrinology and diabetes services for children.</p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 4. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</p>
--	--

References

- 1 Macmillan Cancer Support (2017) [Understanding thyroid cancer](#). Accessed April 2020.
- 2 National Institute of Health (2020) [RET gene](#). Accessed April 2020.
- 3 Li AY, McCusker MG, Russo A et al. (2019) [RET fusions in solid tumors](#). Cancer Treatment Reviews 81, 101911.
- 4 Office for National Statistics (2019) [Cancer survival in England - adults diagnosed](#). Accessed May 2020.
- 5 National Cancer Intelligence Network (2020) [Thyroid cancer – trends by sex, age and histological type](#). Accessed April 2020.
- 6 Cancer Research UK (2018) [Types of thyroid cancer](#). Accessed April 2020.
- 7 British Thyroid Association (2014). [Guidelines for the management of thyroid cancer](#). Clinical Endocrinology 81: Suppl 1.
- 8 American Thyroid Association (2020) [Medullary thyroid cancer](#). Accessed May 2020.
- 9 Cancer Research UK (2018). [Thyroid cancer – survival](#). Accessed May 2020.
- 10 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.