NICE National Institute for Health and Care Excellence

Selpercatinib for treating advanced thyroid cancer with RET alterations [ID3744]

Lead team presentation

Lead team: Sofia Dias, Bernard Khoo, Rebecca Harmston

ERG: Kleijnen Systematic Reviews

Technical team: Gary McVeigh, Luke Cowie, Vicky Kelly, Jasdeep Hayre

Company: Eli Lilly

17th June 2021

Thyroid cancer

Overview of thyroid cancer:

- Thyroid cancer (TC) accounts for 1% of all new cancer cases and 3700 patients are diagnosed per year in the UK.
- Papillary thyroid cancer (PTC) and follicular thyroid cancer are classified as differentiated thyroid cancers (DTC) and account for around 90% of all TCs.
- Medullary thyroid cancer (MTC) develops in non-follicular cells and accounts for approximately 3% (adult) to 10% (paediatric) of TCs.
- TC is associated with generally good prognosis. Metastatic TCs, accounting for 4–15%, are associated with higher mortality.

Rearranged during transfection (RET):

- RET fusions, alterations, or mutations can occur in histological subtypes (e.g. MTC & PTC).
- RET alterations vary in prevalence by histological subtype, between 5–40% in PTC and uncommon in other types of follicular TCs.
- In RET-fusion positive PTC (approximately 25% of all cases), RET alterations are typically acquired during the initial formation of tumours.
- Around 25% of MTC cases are hereditary and are predominantly associated with the RET mutations.
- RET diagnosis using single gene fluorescence in-situ hybridisation (FISH) testing anticipated to be replaced by next generation sequencing (NGS) in Genomic Hubs.

Selpercatinib

Marketing authorisation (granted February 2021)	Selpercatinib as monotherapy is indicated for the treatment of adults with: • advanced RET fusion-positive thyroid cancer who require systemic therapy following prior treatment with sorafenib and/or lenvatinib Selpercatinib as monotherapy is indicated for the treatment of adults and adolescents 12 years and older with: • advanced RET-mutant medullary thyroid cancer (MTC) who require systemic therapy following prior treatment with cabozantinib and/or vandetanib.
Mechanism of action	Selpercatinib is a selective small molecule inhibitor of the rearranged during transfection (RET) receptor tyrosine kinase.
Oral dose	The recommended dose of selpercatinib based on body weight is: • For adults ≥50 kg: 160 mg orally (2 x 80 mg capsules) twice daily (BID) • For adults <50 kg: 120 mg orally BID. Treatment should be continued until disease progression or unacceptable toxicity.
Price	• The cost of a 28-day cycle of selpercatinib is £8,736.00 • There is a simple discount PAS for selpercatinib.

Background (1)

- LIBRETTO-001: multicentre, single-arm, open-label, Phase I/II study in patients with advanced solid tumours, with RET activations.
- Data cut: Dec 2019. March 2020 data cut provided but not used in analyses.

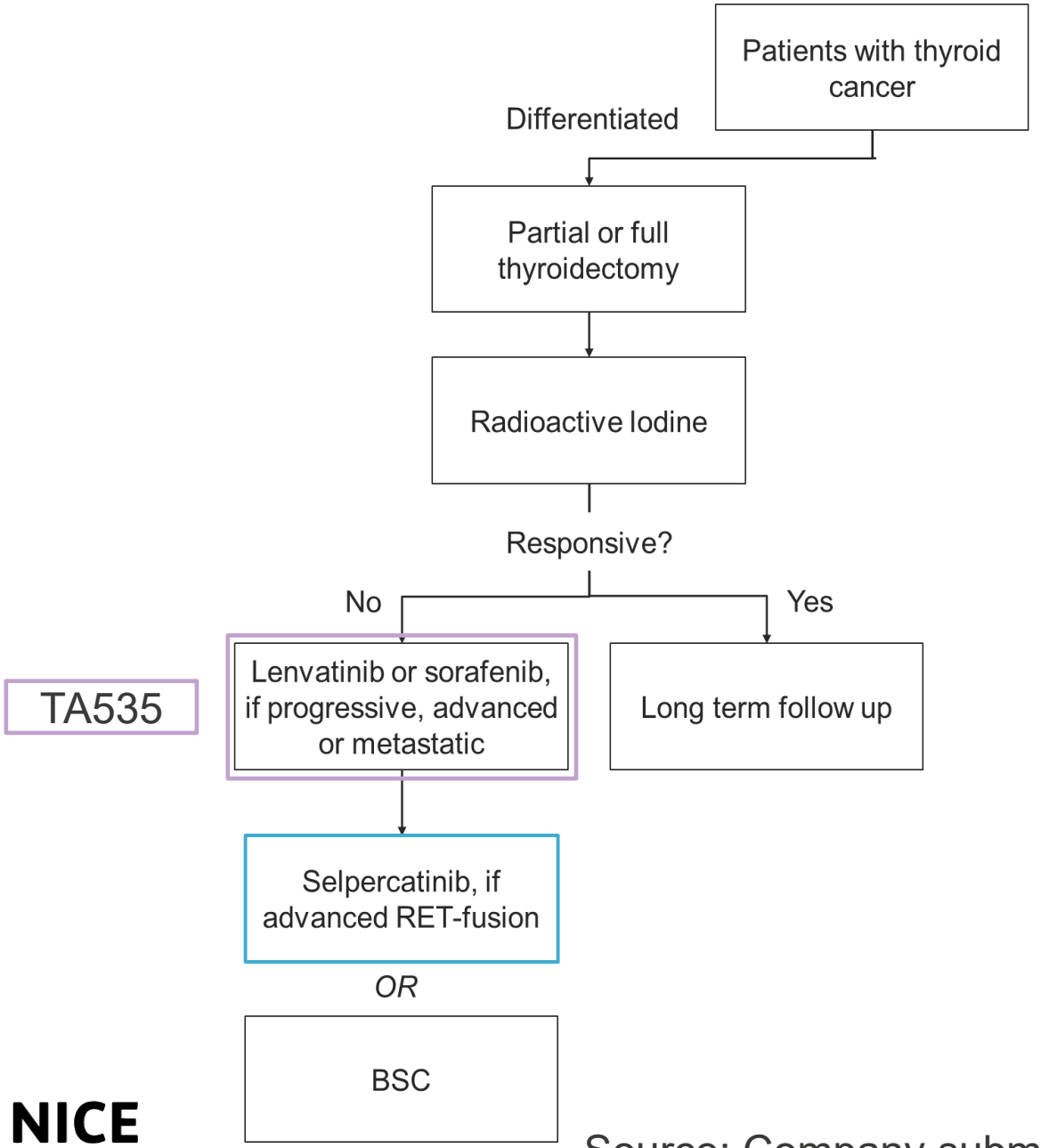
Populations	**Advanced RET fusion-positive thyroid cancer**			**Advanced RET mutation-positive MTC**		
Analysis set	Previously treated n=19	Systemic therapy naïve n=8	RET fusion-positive TC n=27	PAS (subset of IAS), n=55	IAS (≥1 lines of cabo. or vand.) n=124	SAS1 (cabo. and vand. naïve) n=88
ORR, n(%)	15 (78.9)	[redacted]	[redacted]	38 (69.1)	[redacted]	64 (72.7)
PFS (median)	20.07	[redacted]	[redacted]	[redacted]	[redacted]	23.56
PFS; % alive without disease progression	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
OS (median)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Survival status (deaths)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

PAS; Primary analysis set, IAS; Integrated analysis set, SAS1; supplementary analysis set

Background (2)

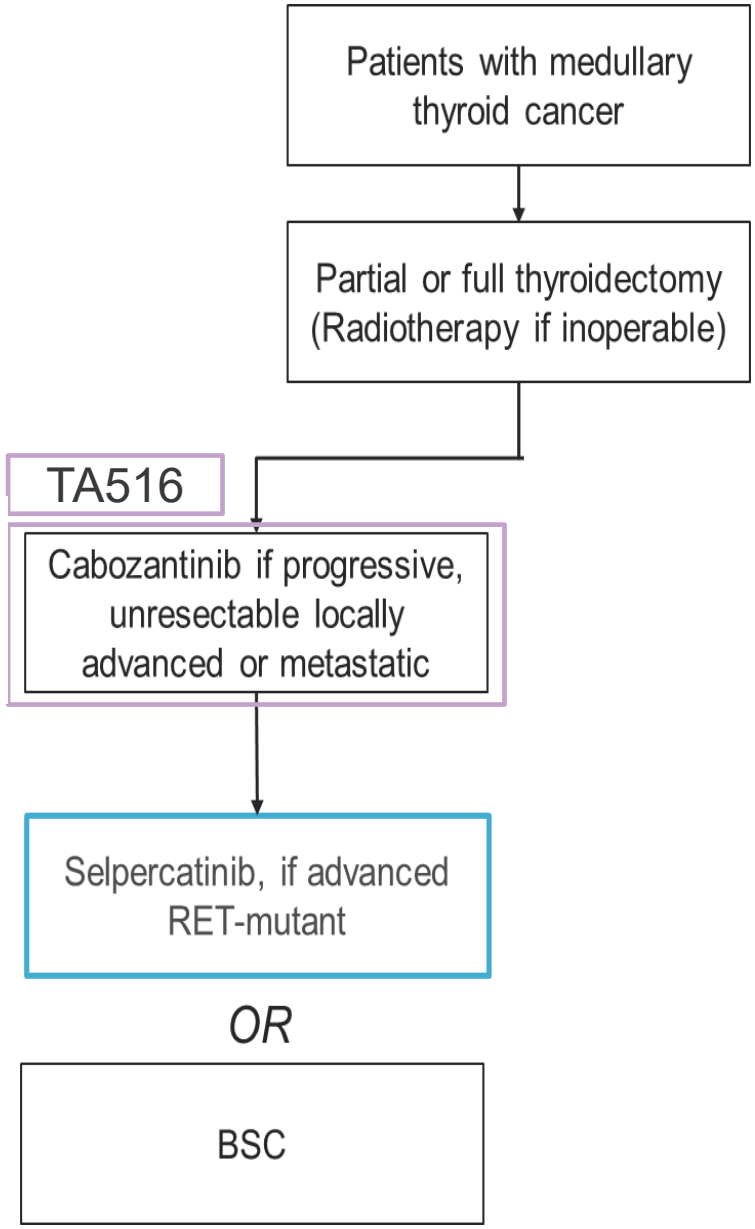
Populations	Advanced RET fusion-positive TC	Advanced RET mutation-positive MTC
Indirect comparisons	• Comparison with BSC • Naïve (unanchored) indirect comparison • Data from previously treated population of LIBRETTO-001 trial for selpercatinib and SELECT trial for BSC	• Comparison with BSC • Unanchored MAIC • Data from any line (n=212) LIBRETTO-001 trial for selpercatinib and EXAM trial for BSC
Trials for indirect comparisons	SELECT: Phase III, double-blind RCT comparing lenvatinib with placebo. 20.6% had received at least one prior therapy	EXAM: Phase III, double-blind RCT comparing cabozantinib with placebo. Included both pre treated & treatment naïve patients
Key results	• Median PFS: 20.07 (95% CI: 9.4, NE) months • Compares with median PFS of 3.6 (95% CI: 1.9, 3.7) in pre-treated subgroup of SELECT trial.	• Differences between treatments in PFS [redacted] versus placebo (BSC) ([redacted]; HR: [redacted]; 95% CI: [redacted], [redacted]). • Differences between treatments in OS [redacted] versus placebo ([redacted]; HR: [redacted]; 95% CI: [redacted], [redacted]).

Treatment pathway (RET-fusion TC)



Source: Company submission

Treatment pathway (RET-mutant MTC)



Source: Company submission

Patient and carer perspective (RET mutation-positive MTC)

- Can be devastating for families due to the inherited nature of the condition. Both children diagnosed, at ages 5 and 6.
- Daughter was diagnosed with advanced metastatic disease age 6, and at that time (2018) surgery was the only option, with no clear 2nd line treatment options.
- Surgery was extensive and damaging, causing long-term and permanent adverse effects.
- Cabozantinib not licensed for children, not a targeted TKI for RET alterations and often difficult to tolerate.
- Selpercatinib is currently working well at suppressing their tumours and therefore any disease-related effects.
- For the children, the greatest advantage to them has been their ability to seem just like their peers. Liken it to other long term conditions with daily medication, such as epilepsy or diabetes.

If selpercatinib had been available at the time of diagnosis, my daughter could have had limited surgery rather than the extensive surgery which resulted in her post-operative complications, one of which has affected her appearance permanently, her self-confidence and is a daily reminder of everything she has been through.

Selpercatinib has radically improved our quality of life, both directly for the children and indirectly for us as parents. It is easy to administer as it is taken orally, as capsule or liquid.

Clinical and professional orgs. submissions

Society for Endocrinology, NCRI-ACP-RCP-RCR, Thyroid Cancer Forum-UK, Kate Garcez

- Main aim of treating advanced thyroid cancer is to delay disease progression, to improve symptoms and quality of life and to reduce related morbidity and mortality.
- Current treatments are limited. Very different situation to many of the commoner cancers where multiple lines of therapy are available.
- All currently available treatments have significant toxic adverse effects. Selpercatinib would provide an alternative treatment option which may be better tolerated and more effective for patients with a RET alteration.
- Unlike other tyrosine kinase inhibitors, selpercatinib does not have vascular endothelial growth factor activity - may be a better option for patients at risk of bleeding or other vascular complications.
- Molecular testing for RET fusions and RET mutations is crucial, in order to identify patients who may be suitable for treatment with selpercatinib.

Company's model structure

- Partitioned survival model consisting of three mutually exclusive health states: (i) progression-free (PF), (ii) progressed disease (PD), and (iii) death.
- Consistent with model used in NICE appraisals in thyroid cancer (TA516 & TA535).
- The model cycle length is 7 days and no half-cycle correction is applied.
- Patients are tracked over their lifetime (25 years).
- Health-state utility estimates reported by Fordham et al. (2015) were accepted by the NICE appraisal committee in TA516 and TA535.

Key Issues (1)

Issue	Question for committee	Technical team
1: Appropriateness of cabozantinib as a comparator	Is cabozantinib a relevant comparator for the RET mutation-positive MTC population?	The final licence for selpercatinib suggests that cabozantinib is not a relevant comparator.
2: Immaturity of effectiveness data	Is the data from LIBRETTO-001 suitable for decision making?	Some additional efficacy data from a March 2020 data cut was provided* but not used in the ITCs/model.
3: Reliability of the MAIC for the RET-mutant MTC population	Are the results of the MAIC suitable for decision making?	Noted limitations in the comparison increase uncertainty.
4: Reliability of the naïve indirect comparison for the RET fusion-positive TC population	Are the results of the ITC suitable for decision making?	Noted limitations in the comparison increase uncertainty.

High priority Lower priority Resolved

* No formal TE stage: company responded to ERG key issues. ERG provided critique of this.

RET = rearranged during transfection; MTC = Medullary thyroid cancer; MAIC = matched adjusted indirect comparison; TC = thyroid cancer; TE = technical engagement

Key Issues (2)

Issue	Question for committee	Technical team
5: Extrapolations of survival data	What are the most plausible survival extrapolations for PFS and OS?	Choice of OS and PFS has a large impact on the ICERs
6: Source of health state utility values	What are the most plausible health state utility values?	ICERs are somewhat sensitive to changes to the progressed utility value
7: Inclusion of genetic testing costs	Should the costs of genetic testing be included?	Updated costs were provided by the company at TE.
8: Time on treatment	Should time on treatment be modelled in line with data from LIBRETTO-001?	Company have aligned with the ERG's preference regarding the modelling of ToT
Other: EOL	Does selpercatinib meet the end of life criteria?	Uncertain due to immature data
Other: CDF	Does selpercatinib meet the criteria for Cancer Drugs Fund?	Uncertain

High priority Lower priority Resolved

NICE

OS = overall survival; PFS = progression free survival; ICER = Incremental cost-effectiveness ratio; TE = technical engagement; ToT = time on treatment

Issue 2: Immaturity of effectiveness data

Is the data from LIBRETTO-001 suitable for decision making?

ERG comments:

- Single arm phase I/II study with median follow up of xxx months at the December 2019 data cut-off.
- Progression-free survival, overall survival and duration of response are immature (e.g. inability to evaluate confidence intervals).
- This limits the analysis regarding the potential effect of selpercatinib.

Company response:

- Since the original submission (December 2019 data cut), additional efficacy data from a March 2020 data cut have become available.
- March 2020 data cut provide additional 9.5 months of follow up.
- For pre-treated RET fusion-positive TC, population increases from 19 to xxx.
- For RET-mutant MTC, IAS population (MKI experienced) increases from 124 to xxx, SAS1 population (MKI naïve) increases from 88 to xxx.
- No difference in efficacy between these 2 data cut-offs.
- New data have not been used to conduct additional MAICs and naïve ITCs for the RET-mutant MTC and RET fusion-positive TC populations, respectively, nor to inform the revised base case.

IAS: Integrated analysis set; MKI: multi-kinase inhibitor; SAS1: supplementary analysis set; MAIC: matching-adjusted indirect comparison; ITC: indirect treatment comparison

Issue 3: Reliability of the MAIC for the RET-mutant MTC population (1)

Are the results of the MAIC suitable for decision making?

ERG comments:

- Major limitations in availability and baseline similarity of data for comparator.
- EXAM study did not report separate results for treatment-naïve and pre-treated patients: any-line pooled population from the LIBRETT0-001 trial was used for closer matching to characteristics of RET-mutant subgroup of EXAM trial.
- 80% of patients in EXAM were naive to a prior MKI. Of the patients who received prior MKIs, 44% had both cabozantinib and vandetanib.
- MAIC results now apply to EXAM population rather than LIBRETTO-001 population → not relevant population: includes pre treated and treatment naïve.
- Baseline characteristics of RET-mutant subgroups not available for placebo arm of EXAM study: baseline characteristics of cabozantinib group used instead.
- MAIC only included prognostic factors & effect modifiers which reported by both studies; risk of unobserved confounding.
- OS data were not available for the RET-mutant MTC population and had to be estimated using the results for the RET M918-positive population.
- No discussion on likely amount of residual systematic error in MAIC.

MAIC: matching-adjusted indirect comparison; MKI: multi-kinase inhibitor; OS: overall survival

Issue 3: Reliability of the MAIC for the RET-mutant MTC population (2)

ERG comments (cont.):

- Placebo arm in ZETA trial (comparing vandetanib with placebo) provides improved PFS results for BSC than placebo arm in EXAM trial.
- It is unclear which trial is the better match for LIBRETTO-001, but actual PFS might lie somewhere between results of a MAIC using EXAM and one using ZETA → company did not include this in its analyses as ZETA included vandetanib which is not used in clinical practice.

Company response:

- Limitations relating to potential differences between trials included in MAIC cannot be resolved. Company ask Committee to consider this uncertainty in their decision-making.

PFS: progression-free survival; BSC: best supportive care; MAIC: matching-adjusted indirect comparison

Issue 4: Reliability of the naïve ITC for the RET fusion-positive TC population

Are the results of the ITC suitable for decision making?

ERG comments:

- Comparator arms only included patients with differentiated thyroid cancer. Higher % of patients had performance status 1 or 2 in LIBRETTO-001 trial than in SELECT and DECISION trials. Also, 100% of patients are RET fusion-positive in LIBRETTO-001 but unknown in SELECT trial; and 100% of LIBRETTO-001 and 20.6% of SELECT had received at least one prior therapy.
- Subgroup results by line of therapy not reported for OS for the comparator arm. OS also affected by patient crossover in the comparator trials.
- Because analysis based on small patient numbers and comparison of single arms without adjustments to balance patient groups, PFS results also uncertain.

Company response:

- Limitations relating to the potential differences between trials included in the naïve comparison cannot be resolved. Company ask Committee to consider this uncertainty in their decision-making.

Issue 5: Extrapolations of survival data (1)

What are the most plausible survival extrapolations for PFS and OS?

ERG comments:

- Limitations of MAIC and ITC mean that survival extrapolations highly uncertain.
- RET fusion-positive TC:
  - PFS: agree with stratified Weibull based on clinical expert opinion.
  - OS: (high degree of uncertainty due to low sample size and immature data), agree piecewise exponential function fitted to data from 0 to six months and from six months onwards is appropriate for BSC and selpercatinib (but a different approach for selpercatinib may be more appropriate once additional data cut available from LIBRETTO-001).
- RET-mutant MTC:
  - PFS: agree with loglogistic (but important to explore uncertainty).
  - OS: consider Weibull overly optimistic for selpercatinib, with over xxxx of patients still alive after 25 years. Preferred stratified Weibull.
- Different survival extrapolations lead to vastly different ICERs (explored in scenario analyses).

Company response:

- Company received additional clinical expert feedback on OS for the RET-mutant MTC population: stratified gamma selected to replace Weibull in company base case (ERG responded that it has no reason to object to this clinical opinion and adopted the stratified gamma in its base case).

Issue 5: Extrapolations of survival data (2)

Progression free survival for selpercatinib, RET fusion-positive TC

Issue 5: Extrapolations of survival data (3)

Overall survival for selpercatinib, RET fusion-positive TC

Issue 5: Extrapolations of survival data (4)

Progression free survival for selpercatinib, RET-mutant MTC

Issue 5: Extrapolations of survival data (5)

Overall survival for selpercatinib, RET-mutant MTC

Issue 5: Extrapolations of survival data (6)

Predicted long-term survival estimates for the RET-mutant MTC population using stratified Log-logistic, stratified Gamma and stratified Weibull

	Median PFS (months)	Median OS (months)	5-year	10-year	25-year
Stratified Log-logistic, mean LY = [redacted]					
BSC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Selpercatinib	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Stratified Gamma *(used in company & ERG base case)*, mean LY = [redacted]					
BSC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Selpercatinib	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Stratified Weibull , mean LY = [redacted]					
BSC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Selpercatinib	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Issue 6: Source of health state utility values

What are the most plausible health state utility values?

ERG:

- No EQ-5D data were available from LIBRETTO-001 → mapping from the EORTC QLQ-C30 to EQ-5D resulted in implausible results.
- Uncertain how reflective the health state utility values obtained from the literature would be for RET-mutation populations.
- Fordham et al. (2015): vignette study in people with radioactive iodine-refractory differentiated TC (not directly measured so may not meet NICE reference case).
- ERG did not change base-case utility values from Fordham (PFS=0.8, PD=0.5) due to uncertainties relating to alternative utility value sources.
- Progressed value most uncertain.
- Utility value scenario analyses provided on slide 32.

TA516 cabozantinib	**TA535 sorafenib & lenvatinib**	**SMC Cabozantinib**	**SMC Sorafenib**
Fordham et al. (2015): 0.8, 0.5	DECISION study for BSC, sorafenib & lenvatinib: PD=0.64	PFS = 0.796, PD = 0.624	PFS=0.8, PD=0.64

Company response:

- Company maintain that progressed disease utility value reported by Fordham et al. (2015) is most appropriate, but recognise some uncertainty.

Issue 7: Inclusion of genetic testing costs

Should the costs of genetic testing be included? If so, what are the correct costs?

ERG comments:

- Company initially excluded genetic testing costs on assumption that all patients would receive testing as part of standard practice: transition to next generation sequencing testing, completed at Genomic Hubs, will include routine RET testing and so no additional costs to healthcare system.
- Since number of patients receive routine genetic testing would be almost zero at time of appraisal, ERG preferred to include costs of genetic testing in their base case analysis.
- Agree with updated costs provided by NHS England, outlined below.

Company response:

- NHS England provided a cost of xxxx per test specifically attributed to the RET-fusion or RET-mutant portion of a multi-gene testing NGS panel, which has been included in the revised model.
- Diagnostic costs of xxxx per advanced RET-mutant MTC patient, and xxxx per advanced RET fusion-positive TC patient have been applied.

Other issues: End-of-life (1)

Does selpercatinib meet the criteria for end-of-life?

ERG comments:

- Criterion of short life expectancy, normally less than 24 months: company refers to evidence from the EXAM and SELECT trials.
- In both TA516 (EXAM) and TA535 (SELECT) committee concluded that the interventions did not meet the criterion for short life expectancy, and therefore the end-of-life criteria did not apply. The committee came to the same conclusion in the appraisal of vandetanib (TA550).
- But in the previous appraisals the population included in the scope was different from the population in this appraisal.
- Criterion of extension to life of at least three months: company relies on evidence from the economic model that is based on results from highly uncertain MAIC analyses.

Company response:

- OS data for patients receiving placebo in EXAM and SELECT trials are best proxy for BSC, but may overestimate survival of pre-treated patients (largely because OS based on mixed pre-treated & treatment naïve populations).
- March 2020 data cut of LIBRETTO-001 addresses some MAIC uncertainty: evidence suggests that selpercatinib offers significantly greater than three months extension to life compared with current NHS treatment.

Other issues: End-of-life (2)

- **RET-mutant MTC**

EXAM trial RET M918T subpopulation		Company model prediction		
RET M918T pop. median OS (n=45)	ITT pop. median OS (n=111)	BSC mean LYs (undiscounted)	BSC median OS	Selpercatinib median OS
18.9	21.1	[redacted]	[redacted]	[redacted]

  - Company noted that EXAM trial includes majority of patients naïve to MKIs. RET mutant-positive MTC patients may have worse prognosis than ITT in EXAM trial.

- **RET fusion-positive TC**

SELECT trial	Company model prediction		
ITT population median OS	BSC mean LYs (undiscounted)	BSC median OS	Selpercatinib median OS
Not reached	[redacted]	[redacted]	[redacted]

  - Company noted the SELECT population included predominantly (79.4%) patients naïve to tyrosine kinase. Therefore, may overestimate survival of pre-treated population.

Other issues: End-of-life (3)

Recap on 'life-extending treatment at the end of life', from NICE Guide to the Methods of Technology Appraisal 2013

Section 6.2.10:
In the case of a 'life-extending treatment at the end of life', the Appraisal Committee will satisfy itself that all of the following criteria have been met:

- the treatment is indicated for patients with a short life expectancy, normally less than 24 months and
- there is sufficient evidence to indicate that the treatment has the prospect of offering an extension to life, normally of a mean value of at least an additional 3 months, compared with current NHS treatment.

In addition, the Appraisal Committees will need to be satisfied that:

- the estimates of the extension to life are sufficiently robust and can be shown or reasonably inferred from either progression-free survival or overall survival (taking account of trials in which crossover has occurred and been accounted for in the effectiveness review) and
- the assumptions used in the reference case economic modelling are plausible, objective and robust.

Other issues: Cancer Drugs Fund

Would further data collection reduce uncertainty?

Limitations of the clinical evidence base:

- Patients in LIBRETTO-001 relatively heavily pre-treated, specifically with MKIs. In UK practice, since cabozantinib is only NICE approved MKI for treatment of progressive, advanced or metastatic MTC, patients are comparatively unlikely to have received more than one MKI prior to selpercatinib.
- No head-to-head randomised clinical trial evidence was available, single-arm LIBRETTO-001 trial represents primary source of evidence for selpercatinib.
- Relative efficacy is based on unanchored population-adjusted and naïve indirect comparisons, which may be subject to selection bias and confounding.
- Sample sizes are small across the LIBRETTO-001 and comparator trials, especially for RET-fusion positive TC patient population, and OS data are immature. This leads to uncertainty in the long-term estimates of treatment efficacy in the model.

Company's ongoing trials:

- LIBRETTO-001: end date 2023.
- LIBRETTO-531: recruiting. RET-mutant MTC population, but inclusion criteria specifies ‘kinase-inhibitor naïve’ whereas licence now includes ‘prior cabozantinib’.

Company and ERG base case*

	Selpercatinib		BSC		Inc. Costs (£)	Inc. QALYs	ICER (£ / QALY)
	Total Costs (£)	Total QALYs	Total Costs (£)	Total QALYs			
RET-mutant MTC							
Deterministic	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	54,527
Probabilistic **	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	54,942
RET fusion-positive TC							
Deterministic	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	62,588
Probabilistic	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	61,710

BSC = best supportive care; ICER = incremental cost effectiveness ratio; Inc. = incremental; MTC = medullary thyroid cancer; QALY(s) = quality-adjusted life year(s); RET = rearranged during transfection; TC = thyroid cancer.

*ERG base case is same as updated company base-case.
** ERG corrected errors in company's probabilistic model for RET-mutant MTC

Overall survival scenarios

Selpercatinib extrapolations

- **ERG comments**: In the RET fusion-positive TC population, the only alternative extrapolation which did not result in crossing curves was the stratified gamma, for which the selpercatinib extrapolation was much less optimistic than the base-case piecewise exponential.
- In the RET mutant MTC several curves including the stratified Weibull were plausible.

RET fusion-positive TC	Pairwise ICER (£/QALY)
Base case (Piecewise exponential)	62,588
Stratified Gamma	111,393

RET-mutant MTC	Pairwise ICER (£/QALY)
Base case (Stratified Gamma)	54,527
Stratified Weibull (ERG suggested alternative)	67,346
Weibull	32,907
Stratified log-logistic	53,076
Stratified Spline 1 knot	76,528

Progression free survival scenarios

RET-mutant MTC

- **ERG**: Uncertainty towards the end of the KM curve generates a much broader potentially plausible range for selpercatinib from £42,636 - £79,477.

RET mutant - MTC	Pairwise ICER (£/QALY)
Base case (log logistic)	54,527
Exponential	79,477
Stratified spline 3 knot	62,423
Stratified spline 1 knot	65,505
Lognormal	56,056
Gamma	53,107
Weibull	52,207
Stratified Spline 2 knot	52,655
Stratified Gompertz	51,127
Spline 2 knot	44,200
Gompertz	42,636

RET-fusion positive TC

- **ERG**: Uncertainty on which extrapolations however this parameter has less of an impact on results → all curves were considered.

RET-fusion positive TC	Pairwise ICER (£/QALY)
Base case (stratified Weibull)	62,588
Stratified lognormal	67,545
Stratified loglogistic	68,229
Stratified gamma	63,063
Stratified Gompertz	62,030

Company scenario analysis

- Utility values (base case PFS=0.8; PD=0.5)
- Diagnostic testing

	Incremental costs (£)	Incremental QALYs	Pairwise ICER (£/QALY)
RET-mutant MTC			
Base case	[redacted]	[redacted]	54,527
Utilities, progression-free values for sorafenib, PF: 0.72, PD: 0.64	[redacted]	[redacted]	54,091
Utilities, SMC cabozantinib PF: 0.796, PD: 0.624	[redacted]	[redacted]	51,102
No diagnostic testing costs	[redacted]	[redacted]	54,506
RET fusion-positive TC			
Base case	[redacted]	[redacted]	62,588
Utilities, progression-free values for sorafenib, PF: 0.72, PD: 0.64	[redacted]	[redacted]	62,936
Utilities, SMC cabozantinib PF: 0.796, PD: 0.624	[redacted]	[redacted]	59,149
No diagnostic testing costs	[redacted]	[redacted]	62,411

Equalities and Innovation

Are there any equalities issues or innovation the committee should consider?

Equalities:

- At scoping stage, access to RET alteration testing was not uniform across the country, but was expected to be managed in specialist centres within the year.
- Committee should seek information from clinical and commissioning experts on whether changes to testing practices that were proposed/ongoing at the time of scoping have been implemented within the NHS by the time of decision-making for this topic.

Innovation:

- Current treatments for differentiated TC and MTC have non-selective mechanisms of action and are associated with poor tolerability. The highly selective targeting of selpercatinib on the RET receptor allows for a potent anti-tumour response with minimal off target effects.