



Topic Brief: Systemic Treatments of Advanced Thyroid Cancer

Date: 8/1/2022

Nomination Number: 0982

Purpose: This document summarizes the information addressing a nomination submitted on May 10, 2022, through the Effective Health Care Website. This information was used to inform the Evidence-based Practice Center (EPC) Program decisions about whether to produce an evidence report on the topic, and if so, what type of evidence report would be most suitable.

Issue: Due to increasing incidence and diagnosis of thyroid disease, paired with recent advancements in the therapeutic landscape, the nominators of this topic seek a guideline that would inform medical oncologists about best practices regarding the treatment of advanced thyroid cancer.

Findings:

We found a systematic review addressing Key Question (KQ) 1, and very limited evidence for KQs 2-3. The EPC Program will not develop a new systematic review at this time.

Background

According to data from the World Health Organization and American Cancer Society databases, in 2018 thyroid cancer was the tenth most common cancer type in the United States and one of the most survivable cancers. This data shows 0.411 million people with thyroid cancer in 2018, and that seven percent of all people with thyroid cancer up to age 74 died due to their illness at that time.¹ The estimated number of new cases and deaths in the U.S. in 2022 is 43,800 and 2,230, respectively.² The financial burden of thyroid cancer in the U.S. is higher than for other cancers, with estimated out-of-pocket cost of initial thyroid cancer diagnosis and treatment ranging from \$1,425-\$17,000.³

Thyroid cancer types can be broken down into differentiated and undifferentiated thyroid cell types. Most cancers are the differentiated type. Differentiated cell types reported by the American Cancer Society include papillary (80%), follicular (10%), Hurthle cell (3%), and medullary (4%). The medullary cancers are broken down between 80% sporadic type and 20 percent familial type. The familial type can be part of a genetic multiple endocrine cancer syndrome as one of several cancers that present in an individual.⁴

Most thyroid cancers are curable if found and treated early. Thyroid cancers are treated with multimodalities depending on the staging. These modalities could include surgery, radioactive iodine uptake when appropriate, external beam radiation, chemotherapy, and in some cases targeted therapy chemotherapy. When thyroid cancers do not respond to standard therapies or are

undifferentiated or widespread, targeted therapies to known genetic mutations or genetic markers may be used to consider new chemotherapies and targeted treatments. There have been recent shifts to the therapeutic landscape with changes to Federal Drug Administration (FDA) approvals for therapeutic agents. For example, in May 2020, the FDA granted approval to selpercatinib for use as systemic treatment for thyroid cancer.⁵ A new systematic review would facilitate consistency in practice in the face of such changes.

Scope

1. What is the effectiveness and harms of multi-kinase tyrosine kinase inhibitors (TKIs) in radioactive iodine refractory thyroid cancer?
 - a. How do outcomes vary by factors such as patient characteristics (e.g., age, sex, race) and cancer characteristics (e.g., thyroid cancer histologic subtypes, stage)?
2. What is the effectiveness, comparative effectiveness, and harms of different sequencing of TKIs?
3. What is the comparative effectiveness and harms of genomically targeted agents compared to FDA-approved TKIs in thyroid cancer?

Table 1. Questions and PICO (population, intervention, comparator, outcome)

| | | | |
|----------------------|--|--|---|
| Questions | 1. Effectiveness and harms of multi-kinase TKIs | 2. Effectiveness, comparative effectiveness, and harms of different sequencing of TKIs | 3. Comparative effectiveness and harms of genomically targeted agents vs. TKIs |
| Population | Adults (≥ 18) with radioiodine-refractory differentiated thyroid cancer | Adults (≥ 18) with radioiodine-refractory differentiated thyroid cancer | Adults (≥ 18) with radioiodine-refractory differentiated thyroid cancer |
| Interventions | Multi-kinase TKIs (e.g., lenvatinib, sorafenib) | Sequencing patterns of TKIs with other treatment | BRAF inhibitors (e.g., vemurafenib, dabrafenib, encorafenib), NTRK fusions (e.g., larotrectinib, entrectinib), ALK inhibitors (e.g., crizotinib, alectinib, brigatinib, lorlatinib) |
| Comparators | Treatment as usual, other treatments, placebo | Other sequencing patterns with TKIs | FDA-approved TKIs (e.g., cabozantinib, larotrectinib, entrectinib) |
| Outcomes | Progression-free survival, objective response (e.g., RECIST, duration of the response) Harms (e.g., toxicity) | Progression-free survival, objective response (e.g., RECIST, duration of the response) Harms (e.g., toxicity) | Progression-free survival, objective response (e.g., RECIST, duration of the response) Harms (e.g., toxicity) |

Abbreviations: FDA=United States Food and Drug Administration; RECIST=response evaluation criteria in solid tumors; TKIs=tyrosine kinase inhibitors.

Assessment Methods

See Appendix A.

Summary of Literature Findings

We found one systematic review that addresses KQ 1 and very little to no evidence addressing KQs 2 and 3.

The systematic review and meta-analysis that covers KQ 1 examined the efficacy and safety of multi-kinase inhibitors in patients with radioiodine-refractory differentiated thyroid cancer. The review was published in July 2022, and the search for evidence included studies through December 2021. The authors report that multi-kinase inhibitors significantly improved progression-free survival and overall survival, but that adverse events were higher than in the control group.⁶

For KQ 2, we did not find any systematic reviews, and found one study that evaluated the axitinib as first, second, and third/fourth line treatment.⁷ For KQ 3, we did not find any systematic reviews or primary studies.

We note that a recent ESMO guideline (which was not underpinned by a systematic review) included 23 studies on treatment of radioiodine refractory thyroid cancer. None of which were identified in our targeted scan for the following reasons: 10 were published before July 2017; one was a systematic review; and the remaining studies lacked a comparison group.

Table 2. Literature identified for each Key Question

| Question | Systematic reviews (7/2019-7/2022) | Primary studies (7/2017-7/2022) |
|--|---|--|
| Question 1: Effectiveness and harms of multi-kinase TKIs | Total: 1 <ul style="list-style-type: none"> • Cochrane: 0 • AHRQ: 0 • Other: 1⁶ | Not assessed |
| Question 2: Effectiveness, comparative effectiveness, and harms of different sequencing TKIs | Total: 0 | Total: 1 <ul style="list-style-type: none"> • Observational: 1⁷ Clinicaltrials.gov Recruiting: 0 |
| Question 3: Comparative effectiveness and harms of genomically targeted agents vs. TKIs | Total: 0 | Total: 0 |

Abbreviations: AHRQ=Agency for Healthcare Research and Quality; TKIs=tyrosine kinase inhibitors.

See Appendix B for detailed assessments of all EPC selection criteria.

Summary of Selection Criteria Assessment

Despite an increase in the incidence of thyroid cancer, guidelines on treatment are lacking. While the nominators would plan to develop a guideline using a new systematic review, we did not find the evidence base needed to conduct one. We found a systematic review that addresses the effectiveness and harms of multi-kinase TKIs in radioactive iodine refractory thyroid cancer, and very limited to no evidence addressing the effectiveness and harms of different sequencing of TKIs, and the comparative effectiveness and harms of genomically-targeted agents, respectively.

Please see Appendix B for detailed assessments of individual EPC Program selection criteria.

References

1. Camilla M, Giuseppe L. Current Cancer Epidemiology. Journal of Epidemiology and Global Health. 2019 2019/10/17;9(4):217-22. doi: <https://doi.org/10.2991/jegh.k.191008.001>.

2. Thyroid Cancer in Treatment (Adult) Health Professional Version. NIH National Cancer Institute. doi: <https://www.cancer.gov/types/thyroid/hp/thyroid-treatment-pdq>.
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 4. What is Thyroid Cancer? American Cancer Society. doi: <https://www.cancer.org/cancer/thyroid-cancer/about/what-is-thyroid-cancer.html>.
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 6. Su J, Wang M, Fu Y, et al. Efficacy and safety of multi-kinase inhibitors in patients with radioiodine-refractory differentiated thyroid cancer: a systematic review and meta-analysis of clinical trials. *Expert Review of Anticancer Therapy*. 2022 Jul 20:1-10. doi: <https://dx.doi.org/10.1080/14737140.2022.2102000>. PMID: 35833358.
 7. Capdevila J, Trigo JM, Aller J, et al. Axitinib treatment in advanced RAI-resistant differentiated thyroid cancer (DTC) and refractory medullary thyroid cancer (MTC). *European Journal of Endocrinology*. 2017 Oct;177(4):309-17. doi: <https://dx.doi.org/10.1530/EJE-17-0243>. PMID: 28687563.
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Conflict of Interest: None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

Acknowledgements

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This report was developed by the Scientific Resource Center under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. HHS 290-2017-00003C). The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. No statement in this article should be construed as an official position of the Agency for Healthcare Research and Quality or of the U.S. Department of Health and Human Services.

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Appendix A: Methods

We assessed nomination for priority for a systematic review or other AHRQ Effective Health Care report with a hierarchical process using established selection criteria. Assessment of each criteria determined the need to evaluate the next one. See Appendix B for detailed description of the criteria.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance.

Desirability of New Review/Absence of Duplication

We searched for high-quality, completed or in-process evidence reviews published in the last three years July 2019-July 2022 on the questions of the nomination from these sources:

- AHRQ: Evidence reports and technology assessments
 - AHRQ Evidence Reports <https://www.ahrq.gov/research/findings/evidence-based-reports/index.html>
 - EHC Program <https://effectivehealthcare.ahrq.gov/>
 - US Preventive Services Task Force <https://www.uspreventiveservicestaskforce.org/>
 - AHRQ Technology Assessment Program <https://www.ahrq.gov/research/findings/ta/index.html>
- US Department of Veterans Affairs Products publications
 - Evidence Synthesis Program <https://www.hsrd.research.va.gov/publications/esp/>
 - VA/Department of Defense Evidence-Based Clinical Practice Guideline Program <https://www.healthquality.va.gov/>
- Cochrane Systematic Reviews <https://www.cochranelibrary.com/>
- PROSPERO Database (international prospective register of systematic reviews and protocols) <http://www.crd.york.ac.uk/prospetro/>
- PubMed <https://www.ncbi.nlm.nih.gov/pubmed/>
- Joanna Briggs Institute <http://joannabriggs.org/>
- WHO Health Evidence Network <http://www.euro.who.int/en/data-and-evidence/evidence-informed-policy-making/health-evidence-network-hen>
- Epistemonikos <https://www.epistemonikos.org/>

Impact of a New Evidence Review

The impact of a new evidence review was qualitatively assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether it was possible for this review to influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.).

Feasibility of New Evidence Review

We conducted a limited literature search in PubMed from the last five years, July 2017-July 2022, on parts of the nomination scope not addressed by earlier identified systematic reviews. We reviewed all identified titles and abstracts for inclusion and classified identified studies by question and study design to estimate the size and scope of a potential evidence review.

Search strategy

Ovid MEDLINE ALL 1946 to July 20, 2022

Date searched: July 21, 2022

- 1 Thyroid Neoplasms/ or Thyroid Cancer, Papillary/ or Thyroid Nodule/ or thyroid\$3.ti,ab,kf. (210564)
- 2 (iodine or radioiodine or radio-iodine or RAI or RAIR or RR-DTC).ti,ab,kf. (68801)
- 3 (advanced or metastati* or refractor* or resist* or (stage adj2 ("4" or four or "IV" or late)) or (BRAF\$4 or gene\$3 or genom\$3 or MEK1 or MEK2 or molecular\$2 or mutant\$1 or mutat\$1 or NTRK or oncogene* or RET)).ti,ab,kf. (7067746)
- 4 and/1-3 (5173)
- 5 Angiogenesis Inhibitors/ or (antiangiogene* or anti-angiogene* or ((angiogene* or neovascular* or neo-vascular*) adj3 (agent\$1 or antagonist\$1 or drug\$1 or inhibit* or pharma*)) or multikinase or multi-kinase or TKI\$1 or tyrosine).ti,ab,kf. (226200)
- 6 (Axitinib or Inlyta\$1 or Bevacizumab or Avastin\$1 or Cabozantinib or Cabometyx\$1 or Cometriq\$1 or Dabrafenib or Tafinlar\$1 or Entrectinib or Rozlytrek\$1 or Everolimus or Afinitor\$1 or Larotrectinib or Vitrakvi\$1 or Lenalidomide or Revlimid\$1 or Lenvatinib or Lenvima\$1 or Pazopanib or Votrient\$1 or Ramucirumab or Cyramza\$1 or Regorafenib or Stivarga\$1 or Selpercatinib or Retevmo\$1 or Sorafenib or Nexavar\$1 or Sunitinib or Sutent\$1 or Thalidomide or Synovir\$1 or Thalomid\$1 or Trametinib or Mekinist\$1 or Vandetanib or Caprelsa\$1 or Ziv-aflibercept or Zaltrap\$1).ti,ab,kf. (59504)
- 7 or/5-6 (268208)
- 8 and/4,7 (624)
- 9 limit 8 to english language (595)
- 10 9 not ((Animals/ not Humans/) or (animal\$1 or canine or cat\$1 or dog\$1 or feline or mice or mouse or rat\$1 or rattus or rodent\$2).ti.) (580)
- 11 (meta-analysis or "systematic review").pt. or (meta-anal* or metaanal* or ((evidence or scoping or systematic or umbrella) adj3 (review or synthesis))).ti. (362841)
- 12 and/10-11 (18)
- 13 limit 12 to yr="2019 -Current" (11)
- 14 ("controlled clinical trial" or "randomized controlled trial").pt. or (control\$3 or random* or placebo or trial).ti. (1283869)
- 15 and/10,14 (48)
- 16 limit 15 to yr="2017 -Current" (32)
- 17 exp cohort studies/ or exp epidemiologic studies/ or exp evaluation studies as topic/ or Observational Studies as Topic/ or "observational study".pt. or (cohort\$1 or comparative or cross-sectional or evaluation or follow-up or longitudinal\$3 or observational or program\$2 or prospective\$2 or retrospective\$2).ti,ab,kf. (7105735)
- 18 and/10,17 (208)
- 19 limit 18 to yr="2017 -Current" (137)

Ovid EBM Reviews - Cochrane Central Register of Controlled Trials June 2022

Date searched: July 21, 2022

- 1 Thyroid Neoplasms/ or Thyroid Cancer, Papillary/ or Thyroid Nodule/ or thyroid\$3.ti,ab. (8359)
- 2 (iodine or radioiodine or radio-iodine or RAI or RAIR or RR-DTC).ti,ab. (5106)
- 3 (advanced or metastati* or refractor* or resist* or (stage adj2 ("4" or four or "IV" or late)) or BRAF\$4 or gene\$3 or genom\$3 or MEK1 or MEK2 or molecular\$2 or mutant\$1 or mutat\$1 or NTRK or oncogene* or RET).ti,ab. (316610)
- 4 and/1-3 (319)
- 5 Angiogenesis Inhibitors/ or (antiangiogene* or anti-angiogene* or ((angiogene* or neovascular* or neo-vascular*) adj3 (agent\$1 or antagonist\$1 or drug\$1 or inhibit* or pharma*)) or multikinase or multi-kinase or TKI\$1 or tyrosine).ti,ab. (8032)

6 (Axitinib or Inlyta\$1 or Bevacizumab or Avastin\$1 or Cabozantinib or Cabometyx\$1 or Cometriq\$1 or Dabrafenib or Tafinlar\$1 or Entrectinib or Rozlytrek\$1 or Everolimus or Afinitor\$1 or Larotrectinib or Vitrakvi\$1 or Lenalidomide or Revlimid\$1 or Lenvatinib or Lenvima\$1 or Pazopanib or Votrient\$1 or Ramucirumab or Cyramza\$1 or Regorafenib or Stivarga\$1 or Selpercatinib or Retevmo\$1 or Sorafenib or Nexavar\$1 or Sunitinib or Sutent\$1 or Thalidomide or Synovir\$1 or Thalomid\$1 or Trametinib or Mekinist\$1 or Vandetanib or Caprelsa\$1 or Ziv-aflibercept or Zaltrap\$1).ti,ab. (19409)

7 or/5-6 (25265)

8 and/4,7 (182)

9 limit 8 to yr="2017 -Current" (84)

EPISTEMONIKOS

Date searched: July 21, 2022

(title:((title:(thyroid* AND (iodine OR radioiodine OR radio-iodine OR RAI OR RAIR OR RR-DTC) AND (advanced OR metastati* OR refractor* OR resist* OR (stage AND ("4" OR four OR "IV" OR late)) OR BRAF OR gene* OR genom* OR MEK1 OR MEK2 OR molecul* OR mutant* OR mutat* OR NTRK OR oncogene* OR RET)) OR abstract:(thyroid* AND (iodine OR radioiodine OR radio-iodine OR RAI OR RAIR OR RR-DTC) AND (advanced OR metastati* OR refractor* OR resist* OR (stage AND ("4" OR four OR "IV" OR late)) OR BRAF OR gene* OR genom* OR MEK1 OR MEK2 OR molecul* OR mutant* OR mutat* OR NTRK OR oncogene* OR RET))) AND (title:((antiangiogene* OR anti-angiogene* OR ((angiogene* OR neovascular* OR neo-vascular*) AND (agent* OR antagonist* OR drug OR drugs OR inhibit* OR pharma*)) OR multikinase OR multi-kinase OR TKI OR tyrosine) OR (Axitinib OR Inlyta OR Bevacizumab OR Avastin OR Cabozantinib OR Cabometyx OR Cometriq OR Dabrafenib OR Tafinlar OR Entrectinib OR Rozlytrek OR Everolimus OR Afinitor OR Larotrectinib OR Vitrakvi OR Lenalidomide OR Revlimid OR Lenvatinib OR Lenvima OR Pazopanib OR Votrient OR Ramucirumab OR Cyramza OR Regorafenib OR Stivarga OR Selpercatinib OR Retevmo OR Sorafenib OR Nexavar OR Sunitinib OR Sutent OR Thalidomide OR Synovir OR Thalomid OR Trametinib OR Mekinist OR Vandetanib OR Caprelsa OR Ziv-aflibercept OR Zaltrap)) OR abstract:((antiangiogene* OR anti-angiogene* OR ((angiogene* OR neovascular* OR neo-vascular*) AND (agent* OR antagonist* OR drug OR drugs OR inhibit* OR pharma*)) OR multikinase OR multi-kinase OR TKI OR tyrosine) OR (Axitinib OR Inlyta OR Bevacizumab OR Avastin OR Cabozantinib OR Cabometyx OR Cometriq OR Dabrafenib OR Tafinlar OR Entrectinib OR Rozlytrek OR Everolimus OR Afinitor OR Larotrectinib OR Vitrakvi OR Lenalidomide OR Revlimid OR Lenvatinib OR Lenvima OR Pazopanib OR Votrient OR Ramucirumab OR Cyramza OR Regorafenib OR Stivarga OR Selpercatinib OR Retevmo OR Sorafenib OR Nexavar OR Sunitinib OR Sutent OR Thalidomide OR Synovir OR Thalomid OR Trametinib OR Mekinist OR Vandetanib OR Caprelsa OR Ziv-aflibercept OR Zaltrap)))) OR abstract:((title:(thyroid* AND (iodine OR radioiodine OR radio-iodine OR RAI OR RAIR OR RR-DTC) AND (advanced OR metastati* OR refractor* OR resist* OR (stage AND ("4" OR four OR "IV" OR late)) OR BRAF OR gene* OR genom* OR MEK1 OR MEK2 OR molecul* OR mutant* OR mutat* OR NTRK OR oncogene* OR RET)) OR abstract:(thyroid* AND (iodine OR radioiodine OR radio-iodine OR RAI OR RAIR OR RR-DTC) AND (advanced OR metastati* OR refractor* OR resist* OR (stage AND ("4" OR four OR "IV" OR late)) OR BRAF OR gene* OR genom* OR MEK1 OR MEK2 OR molecul* OR mutant* OR mutat* OR NTRK OR oncogene* OR RET))) AND (title:((antiangiogene* OR anti-angiogene* OR ((angiogene* OR neovascular* OR neo-vascular*) AND (agent* OR antagonist* OR drug OR drugs OR inhibit* OR pharma*)) OR multikinase OR multi-kinase OR TKI OR tyrosine) OR (Axitinib OR Inlyta OR Bevacizumab OR Avastin OR Cabozantinib OR Cabometyx OR Cometriq OR Dabrafenib OR Tafinlar OR Entrectinib OR Rozlytrek OR

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PROSPERO

Date searched: July 21, 2022

thyroid* AND (iodine OR radioiodine OR radio-iodine OR RAI OR RAIR OR RR-DTC) AND (advanced OR metastati* OR refractor* OR resist* OR (stage AND ("4" OR four OR "IV" OR late)) OR BRAF OR gene* OR genom* OR MEK1 OR MEK2 OR molecu* OR mutant* OR mutat* OR NTRK OR oncogene* OR RET) AND (antiangiogene* OR anti-angiogene* OR ((angiogene* OR neovascular* OR neo-vascular*) AND (agent* OR antagonist* OR drug OR drugs OR inhibit* OR pharma*)) OR multikinase OR multi-kinase OR TKI OR tyrosine) OR (Axitinib OR Inlyta OR Bevacizumab OR Avastin OR Cabozantinib OR Cabometyx OR Cometriq OR Dabrafenib OR Tafinlar OR Entrectinib OR Rozlytrek OR Everolimus OR Afinitor OR Larotrectinib OR Vitrakvi OR Lenalidomide OR Revlimid OR Lenvatinib OR Lenvima OR Pazopanib OR Votrient OR Ramucirumab OR Cyramza OR Regorafenib OR Stivarga OR Selpercatinib OR Retevmo OR Sorafenib OR Nexavar OR Sunitinib OR Sutent OR Thalidomide OR Synovir OR Thalomid OR Trametinib OR Mekinist OR Vandetanib OR Caprelsa OR Ziv-aflibercept OR Zaltrap) AND (Systematic Review OR Meta-Analysis OR IPD OR PMA OR Network meta-analysis OR Review of reviews):RT WHERE CD FROM 21/07/2019 TO 21/07/2022 (3)

[Clinical Trials.gov](https://www.clinicaltrials.gov)

Appendix B. Selection Criteria Assessment

| Selection Criteria | Assessment |
|---|---|
| 1. Appropriateness | |
| 1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the United States? | Yes. |
| 1b. Is the nomination a request for an evidence report? | Yes. |
| 1c. Is the focus on effectiveness or comparative effectiveness? | Yes. |
| 1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic? | Yes. |
| 2. Importance | |
| 2a. Represents a significant disease burden; large proportion of the population | Yes. The estimated number of new cases and deaths in the United States in 2022 is 43,800 and 2,230, respectively. ² |
| 2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the United States population or for a vulnerable population | Yes. The financial burden of thyroid cancer in the United States is higher than for other cancers, with estimated out-of-pocket cost of initial thyroid cancer diagnosis and treatment ranging from \$1,425-\$17,000. ³ |
| 2c. Incorporates issues around both clinical benefits and potential clinical harms | Yes. |
| 2d. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers | Yes. The financial burden of thyroid cancer in the United States is higher than for other cancers, with estimated out-of-pocket cost of initial thyroid cancer diagnosis and treatment ranging from \$1,425-\$17,000. ³ |
| 3. Desirability of a New Evidence Review/Absence of Duplication | |
| 3. A recent high-quality systematic review or other evidence review is not available on this topic | We found a systematic review and meta-analysis that covers KQ 1 examining the efficacy and safety of multi-kinase inhibitors in patients with radioiodine-refractory differentiated thyroid cancer. ⁶ |
| 4. Impact of a New Evidence Review | |
| 4a. Is the standard of care unclear (guidelines not available or guidelines inconsistent, indicating an information gap that may be addressed by a new evidence review)? | Yes. There is a paucity of guidance. |
| 4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)? | Yes. With recent changes in the therapeutic landscape of radio-iodine refractory thyroid cancers and the approval of multiple TKIs in the first line, second line as well as molecularly targeted agents, the therapeutic landscape for this disease has been transformed in a relatively short period of time. This fact, coupled with the lack of guidelines to medical oncologists as far as the utilization of TKIs and the appropriate indications and sequence of use, makes the establishment of such guidelines a very high priority. |
| 5. Primary Research | |
| 5. Effectively utilizes existing research and knowledge by considering: | For KQ 2, we found one study, and we found no studies for KQ 3. |

| | |
|---|---|
| <ul style="list-style-type: none">- Adequacy (type and volume) of research for conducting a systematic review- Newly available evidence (particularly for updates or new technologies) | We estimate the size of a new review to be limited. |
|---|---|

Abbreviations: AHRQ=Agency for Healthcare Research and Quality; KQ=key question; TKIs=tyrosine kinase inhibitors.