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CADTH Reference List

Everolimus for Functional Neuroendocrine Tumours of Gastrointestinal or Lung Origin

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Reference List

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Authors: Camille Santos, Danielle MacDougall

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Questions or requests for information about this report can be directed to **requests@cadth.ca**

Key Messages

- No evidence was identified regarding the clinical effectiveness of everolimus for functional neuroendocrine tumours of lung origin.
- No evidence was identified regarding the clinical effectiveness of everolimus for functional neuroendocrine tumours of gastrointestinal origin.
- No evidence was identified regarding the cost effectiveness of everolimus for functional neuroendocrine tumours of lung origin.
- No evidence was identified regarding the cost effectiveness of everolimus for functional neuroendocrine tumours of gastrointestinal origin.
- One evidence-based guideline was found regarding the use of everolimus for functional neuroendocrine tumours of gastrointestinal or lung origin.

Research Questions

1. What is the clinical effectiveness of everolimus for functional neuroendocrine tumours of lung origin?
2. What is the clinical effectiveness of everolimus for functional neuroendocrine tumours of gastrointestinal origin?
3. What is the cost effectiveness of everolimus for functional neuroendocrine tumours of lung origin?
4. What is the cost effectiveness of everolimus for functional neuroendocrine tumours of gastrointestinal origin?
5. What are the evidence-based guidelines regarding the use of everolimus for functional neuroendocrine tumours of gastrointestinal or lung origin?

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, Embase, the Cochrane Database of Systematic Reviews, the International HTA Database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were everolimus and neuroendocrine tumours. CADTH-developed search filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, network meta-analyses, any types of clinical trials or observational studies, economic studies, or guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English-language documents published between January 01, 2012 and March 25, 2022. Internet links were provided, where available.

Table 1: Selection Criteria

Criteria	Description
Population	Q1, Q3, and Q5: Adults with functional neuroendocrine tumours of lung origin Q2, Q4, and Q5: Adults with functional neuroendocrine tumours of gastrointestinal origin
Intervention	Q1 to Q5: Everolimus
Comparator	Q1 to Q4: Sunitinib, somatostatin analogues (i.e., octreotide, lanreotide), chemotherapy, best supportive care Q5: NA
Outcomes	Q1 and Q2: Clinical effectiveness (i.e., efficacy measured using progression-free survival, overall survival, response rate, duration of response, quality of life) and safety (i.e., adverse events [≥ grade 3 and grade 4], serious adverse events, mortality) Q3 and Q4: Cost-effectiveness (e.g., QALY gained per unit of health benefit, ICER) Q5: Guidance, recommendations
Study designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies, economic evaluations, evidence-based guidelines

ICER = incremental cost-effectiveness ratio; NA = not applicable; Q = question; QALY = quality-adjusted life-year.

Selection Criteria

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed. Open access full-text versions of evidence-based guidelines were reviewed when available.

Results

One evidence-based guideline was found regarding the use of everolimus for functional neuroendocrine tumour of gastrointestinal or lung origin.[1] No health technology assessments, systematic reviews, randomized controlled trials, or non-randomized studies were identified regarding the clinical effectiveness of everolimus for functional neuroendocrine tumours of lung or gastrointestinal origin. No economic evaluations were identified regarding the cost-effectiveness of everolimus for functional neuroendocrine tumours of lung or gastrointestinal origin.

Additional references of potential interest that did not meet the inclusion criteria are provided in Appendix 1.

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References

Health Technology Assessments

No literature identified.

Systematic Reviews

No literature identified.

Randomized Controlled Trials

No literature identified.

Non-Randomized Studies

No literature identified.

Economic Evaluations

No literature identified.

Guidelines and Recommendations

1. Baudin E, Caplin M, Garcia-Carbonero R, et al. Lung and thymic carcinoids: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2021;32(4):439-451. PubMed
See: Recommendations (pg. 448)

Appendix 1: References of Potential Interest

Previous CADTH Reports

2. Drug Reimbursement Review: everolimus (Afinitor) for neuroendocrine tumors of gastrointestinal or lung origin. Ottawa (ON): CADTH; 2016: https://www.cadth.ca/afinitor-neuroendocrine-tumors-gastrointestinal-or-lung-origin-details. Accessed 2022 Mar 29.

Health Technology Assessments

Not Specific to Functional Neuroendocrine Tumours

3. Mujica-Mota R, Varley-Campbell J, Tikhonova I, et al. Everolimus, lutetium-177 DOTATATE and sunitinib for advanced, unresectable or metastatic neuroendocrine tumours with disease progression: a systematic review and cost-effectiveness analysis. *Health Technol Assessment*. 09 2018; 22(49): 1-326. PubMed

Systematic Reviews

Unclear Comparator

4. Wolin EM, Benson Iii AB. Systemic Treatment Options for Carcinoid Syndrome: A Systematic Review. *Oncology*. 2019; 96(6): 273-289. PubMed

Not Specific to Functional Gastrointestinal or Lung Neuroendocrine Tumours, Unclear Comparator

5. Gosain R, Gupta M, Roy AM, Strosberg J, Glaser KM, Iyer R. Health-Related Quality of Life (HRQoL) in Neuroendocrine Tumors: A Systematic Review. *Cancers (Basel)*. March-2 2022; 14(6). PubMed

6. Wu Q, Chen B, Yan G, Yang Z, Xiong L, He J. A systematic review and meta-analysis of gastrointestinal events associated with nonoperative therapies for neuroendocrine tumors. *Onco Targets Ther*. 2018; 11: 7655-7668. PubMed

Not Specific to Functional Gastrointestinal or Lung Neuroendocrine Tumours, Alternative Comparator - Placebo

7. Zhuo ZG, Zhu YK, Deng HY, et al. Role of everolimus in the treatment of advanced neuroendocrine tumor: a meta-analysis of randomized trials. *J BUON*. Jan-Feb 2019; 24(1): 368-373. PubMed

Not Specific to Functional Gastrointestinal Neuroendocrine Tumours, Unclear Methods

8. Pusceddu S, Facciorusso A, Giacomelli L, et al. Target therapies plus somatostatin analogs in NETs: a network meta-analysis. *Endocr Relat Cancer*. Jun 17 2021; 28(7): 467-479. PubMed

Not Specific to Functional Lung or Gastrointestinal Neuroendocrine Tumours

9. Ricci C, Lamberti G, Ingaldi C, et al. Treatment of Advanced Gastro-Entero-Pancreatic Neuro-Endocrine Tumors: A Systematic Review and Network Meta-Analysis of Phase III Randomized Controlled Trials. *Cancers (Basel)*. Jan 19 2021; 13(2): 358. PubMed

10. Liu T, Liao J, Dang J, Li G. Treatments for patients with advanced neuroendocrine tumors: a network meta-analysis. *Ther Adv Med Oncol*. 2019; 11: 1758835919853673. PubMed

Non-Randomized Studies

Not Specific to Functional Neuroendocrine Tumours

11. Yoo C, Cho H, Song MJ, et al. Efficacy and safety of everolimus and sunitinib in patients with gastroenteropancreatic neuroendocrine tumor. *Cancer Chemother Pharmacol*. Jan 2017; 79(1): 139-146. PubMed

Not Specific to Functional Lung or Gastrointestinal Neuroendocrine Tumours

12. Daskalakis K, Tsoli M, Angelousi A, et al. Anti-tumour activity of everolimus and sunitinib in neuroendocrine neoplasms. *Endocr Connect*. Jun 2019; 8(6): 641-653. PubMed

Not Specific to Functional Neuroendocrine Tumours, Alternative Comparator - Oxodotreotide

13. Khan MS, Stamp E, Sammon C, Brabander T, de Herder WW, Pavel ME. Matching-adjusted indirect treatment comparison of [177Lu]Lu-DOTA-TATE, everolimus and sunitinib in advanced, unresectable gastroenteropancreatic neuroendocrine tumours: Relative effectiveness of [177Lu]Lu-DOTA-TATE in gastroenteropancreatic neuroendocrine tumours. *EJC Suppl*. Nov 2021; 16: 5-13. PubMed

Economic Evaluations

Not Specific to Functional Gastrointestinal or Lung Neuroendocrine Tumours

14. White BE, Mujica-Mota R, Snowsill T, Gamper EM, Srirajaskanthan R, Ramage JK. Evaluating cost-effectiveness in the management of neuroendocrine neoplasms. *Rev Endocr Metab Disord*. 09 2021; 22(3): 647-663. PubMed

Not Specific to Functional Neuroendocrine Tumours, Alternative Comparator - Oxodotreotide

15. Glover M, Caplin M, Leeuwenkamp OR, Longworth L. Use of [177Lu]Lu-DOTA-TATE in the treatment of gastroenteropancreatic neuroendocrine tumours: Results of a UK cost-effectiveness modelling study. *EJC Suppl*. Nov 2021; 16: 14-23. PubMed

16. Smith-Palmer J, Leeuwenkamp OR, Virk J, Reed N. Lutetium oxodotreotide (177Lu-Dotatate) for the treatment of unresectable or metastatic progressive gastroenteropancreatic neuroendocrine tumors: a cost-effectiveness analysis for Scotland. *BMC Cancer*. Jan 05 2021; 21(1): 10. PubMed

17. Spada F, Campana D, Lamberti G, et al. [177 Lu]Lu-DOTA-TATE versus standard of care in adult patients with gastro-enteropancreatic neuroendocrine tumours (GEP-NETs): a cost-consequence analysis from an Italian hospital perspective. *Eur J Nucl Med Mol Imaging*. Dec 24 2021. PubMed

18. Palmer J, Leeuwenkamp OR. Cost-effectiveness of lutetium (177Lu) oxodotreotide vs everolimus in gastroenteropancreatic neuroendocrine tumors in Norway and Sweden. *World J Clin Cases*. Oct 26 2020; 8(20): 4793-4806. PubMed

Guidelines and Recommendations

Consensus Guidelines

19. Strosberg JR, Halfdanarson TR, Bellizzi AM, et al. The North American Neuroendocrine Tumor Society Consensus Guidelines for Surveillance and Medical Management of Midgut Neuroendocrine Tumors. *Pancreas*. 07 2017; 46(6): 707-714. PubMed
See: Question 10 (page 8)

Not Specific to Functional Neuroendocrine Tumours

20. Pavel M, Oberg K, Falconi M, et al. Gastroenteropancreatic neuroendocrine neoplasms: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2020;31(7):844-860. PubMed
See: Recommendations (pg. 855-856)

21. National Institute for Health and Care Excellence. Everolimus and sunitinib for treating unresectable or metastatic neuroendocrine tumours in people with progressive disease. *(Technology appraisal guidance TA449)* 2017; https://www.nice.org.uk/guidance/ta449. Accessed 2022 Mar 29.

22. Singh S, Asa SL, Dey C, et al. Diagnosis and management of gastrointestinal neuroendocrine tumors: An evidence-based Canadian consensus. *Cancer Treat Rev*. Jun 2016; 47: 32-45. PubMed

Not Specific to Functional Neuroendocrine Tumours, Consensus Guidelines

23. Kunz PL, Reidy-Lagunes D, Anthony LB, et al. Consensus guidelines for the management and treatment of neuroendocrine tumors. *Pancreas*. May 2013; 42(4): 557-77. PubMed

Not Specific to Functional Neuroendocrine Tumours, Unclear Methods

24. Bednarczuk T, Bolanowski M, Zemczak A, et al. Neuroendocrine neoplasms of the small intestine and appendix - management guidelines (recommended by the Polish Network of Neuroendocrine Tumours). *Endokrynol Pol*. 2017; 68(2): 223-236. PubMed

25. Bolanowski M, Bednarczuk T, Bobek-Billewicz B, et al. Neuroendocrine neoplasms of the small intestine and the appendix - management guidelines (recommended by the Polish Network of Neuroendocrine Tumours). *Endokrynol Pol*. 2013; 64(6): 480-93. PubMed