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Guideline 3-8-4 Version 2

A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

The Use of Targeted Therapies in Patients with Inoperable Locally Advanced or Metastatic Renal Cell Cancer: Updated Guideline 2017

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Report Date: May 17, 2017

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PEBC Report Citation (Vancouver Style): Hotte S, Brown J, Canil C, Emmenegger U, Walker-Dilks C, and Winquist W. The use of targeted therapies in patients with inoperable locally advanced or metastatic renal cell cancer: updated guideline 2017. Toronto (ON): Cancer Care Ontario; *2017, May 16*. Program in Evidence-Based Care Evidence Summary No.: 3-8.4 Version 2, available on the CCO website.

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The Use of Targeted Therapies in Patients with Inoperable Locally Advanced or Metastatic Renal Cell Cancer: Updated Guideline 2017 Recommendations

This section is a quick reference guide and provides the guideline recommendations only. For key evidence associated with each recommendation, see full report.

GUIDELINE OBJECTIVES

The primary objective of this report is to determine the optimal targeted therapies for locally advanced or metastatic renal cell cancer (mRCC). The secondary objective is to determine whether a combination of targeted agents is better than any single targeted agent.

TARGET POPULATION

Adult patients with inoperable locally advanced or mRCC.

INTENDED USERS

Oncologists who treat patients with RCC.

RECOMMENDATIONS, KEY EVIDENCE, AND INTERPRETATION OF EVIDENCE - Question 1: What are the optimal targeted therapies for locally advanced or mRCC?

PREVIOUSLY UNTREATED PATIENTS

Recommendation 1

Either of the vascular endothelial growth factor receptor tyrosine kinase inhibitors (VEGF TKIs) sunitinib or pazopanib is recommended for previously untreated patients with locally advanced or mRCC.

Qualifying Statements for Recommendation 1

- Pazopanib and sunitinib have been shown to have similar survival benefits. However, sunitinib has been associated with more symptomatic side effects and pazopanib has been more frequently associated with hepatic toxicity.
- The dose used in the initial trial of sunitinib was 50 mg daily by mouth for four weeks, followed by two weeks off drug, in repeated six-week cycles. Alternative schedules of sunitinib (three-week cycles of two weeks on drug [50 mg] followed by one week off therapy) or continuous daily dosing [37.5 mg]) have been shown effective.

Recommendation 2

Although bevacizumab combined with interferon alpha (IFN-α) is superior to IFN-α alone, it is not recommended due to a high rate of side effects. Current data do not support the use of single-agent bevacizumab, and it is not recommended.

Recommendation 3

Temsirolimus is a treatment option for first-line therapy for the subset of patients with poor-risk disease.

Qualifying Statements for Recommendation 3

- The dose used in the trial of temsirolimus was 25 mg intravenously, once per week for patients with poor-risk disease.

- Based on comparative results with another mammalian target of rapamycin inhibitor similar to temsirolimus (everolimus), VEGF TKI therapy is preferred for first- and subsequent-line therapies for all patient types.

PREVIOUSLY TREATED PATIENTS

Recommendation 4
Nivolumab is recommended over everolimus as a treatment for patients with advanced RCC who have progressed on first- or second-line VEGF TKI.

Qualifying Statements for Recommendation

- Nivolumab has been associated with uncommon but severe immune-mediated adverse reactions, with the most common being enterocolitis, hepatitis, dermatitis (including toxic epidermal necrolysis), neuropathy, and endocrinopathy.
- Patients treated with nivolumab showed improved overall survival (OS), less toxicity, and better quality of life compared with everolimus.

Recommendation 5
Cabozantinib is recommended over everolimus as a treatment for patients with advanced or mRCC who have progressed on VEGF therapy.

Qualifying Statements for Recommendation

- Individuals treated with cabozantinib showed significantly improved OS, but with more toxicity, compared with everolimus.

Recommendation 6
Everolimus is a treatment option for locally advanced or mRCC patients previously treated with first- or second-line VEGF TKI.

Qualifying Statements for Recommendation

- The dose used in the trial of everolimus was 10 mg daily by mouth given in four-week cycles.
- Recent studies have found superiority of other agents (e.g., nivolumab, cabozantinib) over everolimus; however, for those who cannot tolerate these agents, everolimus is an option.

Recommendation 7
Axitinib is a treatment option for second-line therapies.

Qualifying Statements for Recommendation

- Two meta-analyses suggest axitinib's superiority over sorafenib and pazopanib for previously treated patients.
- One trial showed significantly improved progression-free survival and overall response rate with axitinib over sorafenib in previously treated patients.

Recommendation 8
Sorafenib is a treatment option in patients with favourable- to intermediate-risk RCC previously treated with cytokine therapies.

Qualifying Statements for Recommendation 8

- The dose used in the trial of sorafenib was 400 mg by mouth twice daily, continuously.

RECOMMENDATIONS, KEY EVIDENCE, AND INTERPRETATION OF EVIDENCE - Question 2: Is a combination of agents better than any single targeted agent?

Recommendation 9

Current evidence does not support the use of combinations of targeted agents outside of a clinical trial setting. Thus, there are no combinations of targeted therapies that can be recommended at this time.

Qualifying Statements for Recommendation 9

- LENEVE, a phase II randomized controlled trial comparing lenvatinib, everolimus, and a combination of the two, had promising efficacy results with the combination of lenvatinib and everolimus, and lenvatinib alone, over the single administration of everolimus; however, the sample size was small. A phase III randomized trial of the combination in mRCC is planned.