Adjuvant pembrolizumab following kidney cancer surgery

A novel patient decision aid to facilitate shared decision-making

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INTRODUCTION

In KEYNOTE-564, patients with clear-cell renal cell carcinoma (ccRCC) at increased risk of recurrence after surgery were randomized to adjuvant pembrolizumab or placebo.[1] The trial reported a statistically significant improvement in disease-free survival (DFS) (hazard ratio [HR] 0.72, 95% confidence interval [CI] 0.59–0.87) and overall survival (OS) (HR 0.62, 95% CI 0.44–0.87) in favor of adjuvant pembrolizumab;[1] however, there was an increased risk of grade 3–4 adverse events in patients receiving pembrolizumab (18.6% vs. 1.2%).[1] For this reason, patients may debate if adjuvant therapy is best for them.

For challenging healthcare decisions, patient decision aids (PtDA) can be used as clinical tools to facilitate shared decision-making between a patient and their clinician.[2] A critical component of a PtDA is the ability of the tool to help patients clarify and communicate their informed individual values and preferences.[2]

Following the report of KEYNOTE-564, Kidney Cancer Canada engaged with a team of kidney cancer and decision aid experts to develop a PtDA addressing the decision of whether or not to receive adjuvant pembrolizumab after kidney cancer surgery.

METHODS

The development of this PtDA followed the International Patient Decision Aids Standards (IPDAS) and the Ottawa Decision Support Framework.[3,4] A steering committee of stakeholders was assembled.

The PtDA was first drafted in 2023, after the 30-month followup publication of KEYNOTE-564.[5] The steering committee members were sent the PtDA draft. Multiple rounds of iterative feedback were required to make revisions until consensus was reached.

Once the PtDA draft was complete, alpha-testing was performed with additional representatives of the stakeholder groups using a validated online survey of 10 questions.[6] Alpha-testing is also known as acceptability testing, and is performed to assess whether the PtDA is acceptable to stakeholders. The results of the alpha-testing were reviewed and used to optimize the PtDA.

Prior to the release of the adjuvant pembrolizumab PtDA, a manuscript of KEYNOTE-564 results with updated OS, DFS, and adverse effects rates was published in April 2024.[1] Consequently, the PtDA was revised to include this data. The updated PtDA was then circulated to all steering committee members to obtain feedback and gain final consensus.

RESULTS

The steering committee consisted of members of the Kidney Cancer Research Network of Canada (KCRNC), including four urologists, three medical oncologists, two methodologic experts, and one patient advocate. Alpha-testing of the PtDA was completed with additional stakeholders not part of the steering committee, including nine patient advocates, three urologic oncologists, five medical oncologists, and two methodologic experts. The results of the alpha-testing survey were reviewed and the participants reported agreement with the content of the PtDA.

The language was felt to be easy to follow by 18 of 19 responders (94%). All responders felt that the PtDA would be a useful tool for a patient facing this decision (19/19, 100%). The majority of responders felt the information on the PtDA was well-balanced between the treatment options (15/19, 79%), with three responders reporting they felt the PtDA was biased towards receiving adjuvant pembrolizumab (3/19, 16%) and one responder reporting they felt the PtDA was biased towards not receiving adjuvant pembrolizumab (1/19, 5%).

Narrative feedback was reviewed and used to update the PtDA. This included addressing all comments and feedback from responders who felt the PtDA was biased to ensure the final tool was as balanced as possible. Additional information regarding the risks of overtreatment for patients receiving adjuvant pembrolizumab and the limitations of treatment options for patients who do recur when receiving adjuvant pembrolizumab were added to the PtDA.

The final adjuvant pembrolizumab PtDA was 19 pages and included the necessary elements of a high-quality PtDA, including: 1) explicit statement of the decision to be made; 2) presentation of the management options; 3) probabilities for harms and benefits of each management option; and 4) a values clarification exercise to help patients clarify and communicate their values and preferences.[2] The language used was at a seventh-grade reading level.

The adjuvant pembrolizumab PtDA is posted on the Kidney Cancer Canada website in English (*https://online.fliphtml5.com/fexz/risp/#p=1*) and French (*https://online.fliphtml5.com/fexz/wtdu/#p=1*) and a paper version is available to any requesting patients or clinicians. In addition, it is freely available on the Ottawa Hospital Research Institute's A-to-Z PtDA Inventory at *https://decisionaid.ohri.ca/docs/das/Adjuvant%20Pembrolizumab%20PtDA%20McAlpine%20202041008.pdf.*

DISCUSSION

A multidisciplinary team of KCRNC members created an evidence-based PtDA to support eligible patients who are deciding if they should receive adjuvant pembrolizumab after kidney cancer surgery. This PtDA development process followed a systematic approach and was deemed to be acceptable by stakeholders.[2,3]

The decision about receiving adjuvant pembrolizumab following kidney cancer surgery is complex. Following surgical resection of ccRCC, many patients are cured, and their cancer will never recur. For these patients, receiving adjuvant pembrolizumab is overtreatment, exposing them to potentially lifelong toxicities of systemic therapy with no benefits.[7]

Alternatively, for patients who were ultimately going to relapse, adjuvant pembrolizumab may delay or prevent recurrence and thus, prolong survival; however, at this time, it is not possible to accurately predict which patients will recur and which will not. Therefore, the choice to receive adjuvant therapy requires a personalized approach that considers the unique patient's values and preferences.

This PtDA was created and tested to facilitate shared decision-making for patients facing this challenging decision and is, to our knowledge, the only available PtDA available to facilitate the decision regarding adjuvant pembrolizumab. Specifically, the PtDA describes potential positive and negative patient outcomes, including rates of DFS and OS for each group, as well as serious and common adverse events, presented with patient-friendly diagrams and language.

The role of adjuvant therapy following surgery for ccRCC for patients at high risk of recurrence is still debated. Some clinicians remain understandably skeptical regarding the benefits of adjuvant pembrolizumab because the results of KEYNOTE-564 are not consistent with all other adjuvant immunotherapy trials for patients with RCC.[8] Also, a limitation of the KEYNOTE-564 trial is that the treatment received by patients who recurred in the control group may not have always been the standard of care based on current practices. As a result, clinicians postulate that treating patients who recur with standard-of-care therapies at the first sign of recurrence may lead to similar survival outcomes, while avoiding the toxicity of adjuvant therapy for many patients who were never going to recur.

An additional concern is that some patients will recur during or shortly after receiving adjuvant pembrolizumab and may no longer be eligible to receive therapies proven to be most effective in the metastatic setting because they received adjuvant pembrolizumab. Despite this controversy, urologists are responsible for educating and managing patients who are eligible to receive adjuvant therapy after surgery and need to ensure the best available data is presented to patients. Our PtDA aims to facilitate this complex discussion in an unbiased fashion to truly support shared decision-making.

Strength and limitations

The strength of this PtDA development and testing is the evidence-based approach by a team of individuals with experience creating high-quality PtDAs; however, this must be balanced with the limitations of this project.

First, the alpha-testing of this PtDA was done with urologic and medical oncologists involved with KCRNC, as well as patient advocates identified by Kidney Cancer Canada. At the time of the PtDA development and testing, there were very few patients who had faced the decision of whether to receive adjuvant pembrolizumab after kidney cancer surgery. As such, we relied on the feedback of patient advocates to elicit the patient's perspective on our PtDA content. It is possible that the opinions of these stakeholders are not representative of patients or stakeholders in other settings.

Second, although we used a well-tested PtDA template known to improve patient outcomes and completed acceptability testing of this PtDA, we did not evaluate this PtDA via beta-testing; this may be explored in a future study.[9] By not completing beta-testing, the real-world validity of the PtDA is not yet known.

CONCLUSIONS

We have created a novel, evidence-based PtDA to facilitate shared decision-making for patients choosing between adjuvant pembrolizumab or observation after kidney cancer surgery at increased risk of recurrence. This tool is freely accessible for use at *https://decisionaid.ohri.ca/docs/das/Adjuvant%20Pembrolizumab%20PtDA%20McAlpine%20202041008.pdf*.

COMPETING INTERESTS: Dr. McAlpine has participated in advisory boards for Bayer, Knight, and Tolmar; and has received honoraria from Bayer, Knight, TerSera, and Verity. Dr. Tanguay has participated in advisory boards for Ipsen, Merck, and TerSera. Dr. Lalani has received grants/research support from BMS (paid to his institution), BioCanRx (paid to his institution), EMD Serono (paid to his institution), Ipsen (paid to his institution), Novartis (paid to his institution), and Roche (paid to his institution); and has received honoraria from AbbVie, Astellas, AstraZeneca, Bayer, BMS, Eisai, EMD Serono, Ipsen, Janssen, McKesson, Merck, Novartis, Pfizer, Roche, and TerSera. Dr. Kollmannsberger has participated in advisory boards for Abbvie, Astellas, Bayer, BionTech, BMS, Eisai, Ipsen, Janssen, Merck, Novartis, and Pfizer; has received honoraria (for talks) from Abbvie, Astellas, Bayer, BMS, Eisai, Ipsen, Janssen, Merck, Novartis, and Pfizer; and has participated in clinical trials supported by Abbvie, Astellas, Bayer, BionTech, BMS, Eisai, Ipsen, Janssen, Merck, Novartis, Pfizer, and Roche. Dr. Bansal has received honoraria from Abbvie, Knight, and Merck. Dr. Lavallée has participated in advisory boards for Knight; and received an unrestricted research grant (paid to his institution) from Tolmar. The remaining authors do not report any competing personal or financial interests related to this work.

REFERENCES

1. Choueiri T, Tomczak P, Park S, et al. Overall survival with adjuvant pembrolizumab in renal-cell carcinoma. *N Engl J Med* 2024;390:1359-71. https://doi.org/10.1056/NEJMoa2312695
2. Stacey D, Légaré F, Lewis K, et al. Decision aids for people facing health treatment or screening decisions (Review). *Cochrane Database Syst Rev* 2017;4. https://doi.org/10.1002/14651858.CD001431.pub5
3. Elwyn G, O'Connor A, Stacey D, et al. International Patient Decision Aids Standards (IPDAS) Collaboration. Developing a quality criteria framework for patient decision aid: Online international Delphi consensus process. *Br Med J* 2006;333:417. https://doi.org/10.1136/bmj.38926.629329.AE
4. Legare F, O'Connor AM, Graham ID, et al. Impact of the Ottawa Decision Support Framework on the agreement and the difference between patients' and physicians' decisional conflict. *Med Decis Mak* 2006;26:373-90. https://doi.org/10.1177/0272989X06290492
5. Powles T, Tomczak P, Park S, et al. Pembrolizumab versus placebo as post-nephrectomy adjuvant therapy for clear cell renal cell carcinoma (KEYNOTE-564): 30-month followup analysis of a multicenter, randomized, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol* 2022;23:1133-44. https://doi.org/10.1016/S1470-2045(22)00487-9
6. O'Connor A, A C. Acceptability. *Ottawa Ottawa Hosp Res Inst* 1996; 2:5p
7. McAlpine K, Lavallée LT, Breau RH. Evidence-based urology: Surrogate endpoints – Con. *Eur Urol Focus* 2021;7:1219-21. https://doi.org/10.1016/j.euf.2021.10.008
8. Fitzgerald KN, Motzer R, Lee CH. Adjuvant therapy options in renal cell carcinoma – targeting the metastatic cascade. *Nat Rev Urol* 2023;20:179-93. https://doi.org/10.1038/s41585-022-00666-2
9. Hoefel L, Lewis KB, O'Connor A, et al. 20th Anniversary update of the Ottawa Decision Support Framework: Part 2 subanalysis of a systematic review of patient decision aids. *Med Decis Making* 2020;40:522-39. https://doi.org/10.1177/0272989X20924645

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