Stakeholder Input

Disclaimer: The views expressed in each submission are those of the submitting organization or individual and not necessarily the views of CADTH or of other organizations. As such, they are independent of CADTH and do not necessarily represent or reflect the views of CADTH. No endorsement by CADTH is intended or should be inferred.

By filing with CADTH, the submitting organization or individual agrees to the full disclosure of the information. CADTH does not edit the content of the submissions.

CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no identifying personal information or personal health information is included in the submission. The name of the submitting organization or individual and all conflict of interest information are included in the submission; however, the name of the author, including the name of an individual patient or caregiver submitting the patient input, are not posted.

CADTH is committed to treating people with disabilities in a way that respects their dignity and independence, supports them in accessing material in a timely manner, and provides a robust feedback process to support continuous improvement. All materials prepared by CADTH are available in an accessible format. If materials provided to CADTH by a submitting organization or individual are not available in an accessible format, CADTH will provide a summary document upon request. More details can be found within CADTH's accessibility policies.

Patient Input

Canadian Cancer Society

About the Canadian Cancer Society

Our purpose: To unite and inspire all Canadians to take control of cancer.

Our mission: In trusted partnership with donors and volunteers, we improve the lives of all those affected by cancer through world-class research, transformative advocacy and compassionate support.

We set ourselves apart from other cancer charities by taking a comprehensive approach against cancer. We are also the only national charity that supports all Canadians living with all cancers across the country.

We shared our survey and interview opportunity with patients and their caregivers through our Cancer Connection forums, social media, through various support groups and prostate cancer treating clinicians who agreed to share it with their patients.

Information Gathering

The Canadian Cancer Society (CCS) gathered perspectives through survey and interview responses. Ten survey responses were collected from patients with high-risk non-metastatic prostate cancer and one from a patient previously diagnosed with metastatic castration-sensitive prostate cancer (mCSPC) that is now in remission (cancer is undetectable in scans). However, he is still at risk of detectable cancer re-occurring. Of the 11 patients who engaged with us, two had direct experience with abiraterone acetate and completed both the survey and an interview. One of these patients had high-risk non-metastatic prostate cancer, and one was the patient described above who was previously diagnosed with mCSPC and is now in remission. CCS gathered this data within the time frame of July 19, 2022 – August 2, 2022.

To maintain anonymity, the individuals that engaged in an interview will be referred to as Patient A (patient with high risk non-metastatic prostate cancer) and Patient B (patient in remission from mCSPC) throughout this report.

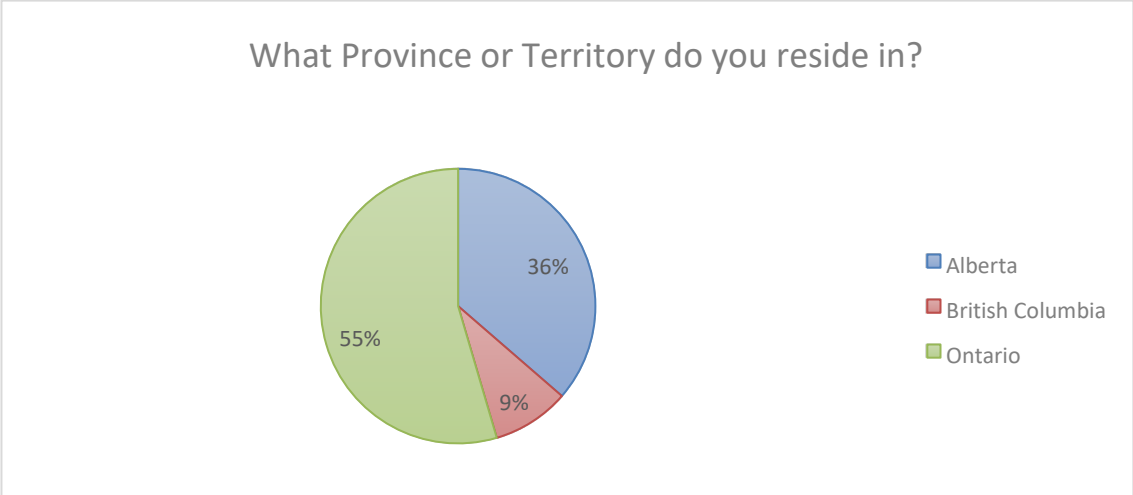
Demographic Information

Demographic information collected from the survey is displayed below. Percentages represented in the Figures are rounded up to the nearest whole number. Please note that not all offered survey options are shown within the Figures as they are limited to the options respondents selected.

1) What Province or Territory do you reside in?

Perspectives from three provinces were captured. The majority of responders resided in Ontario (55%) and Alberta (36%). The remaining 9% resided in British Columbia. The patients that went on to complete an interview resided in Alberta (Patient A) and Ontario (Patient B).

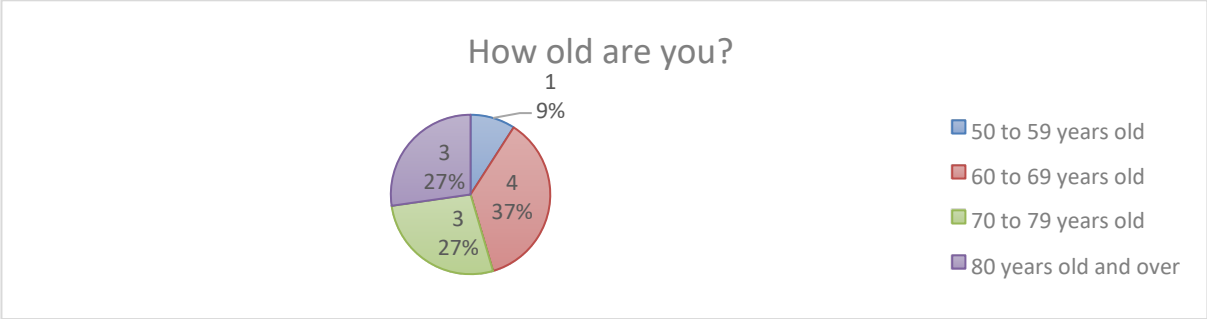
Figure 1 – Geographic Location



2) How old are you?

The majority of responders were between the ages of 60 – 69 years of age (37%), 27% were between 70 – 79, 27% were 80 years old or older and 9% were between 50 – 59. Patient A was between 70 – 79 and Patient B was between 60 – 69.

Figure 2 - Age



3) What gender do you identify with?

For inclusivity, survey respondents had six options available to identify their gender: man, women, nonbinary or third gender, two-spirit, prefer not to say and prefer to self-describe with an open field—all 11 patients identified as a man.

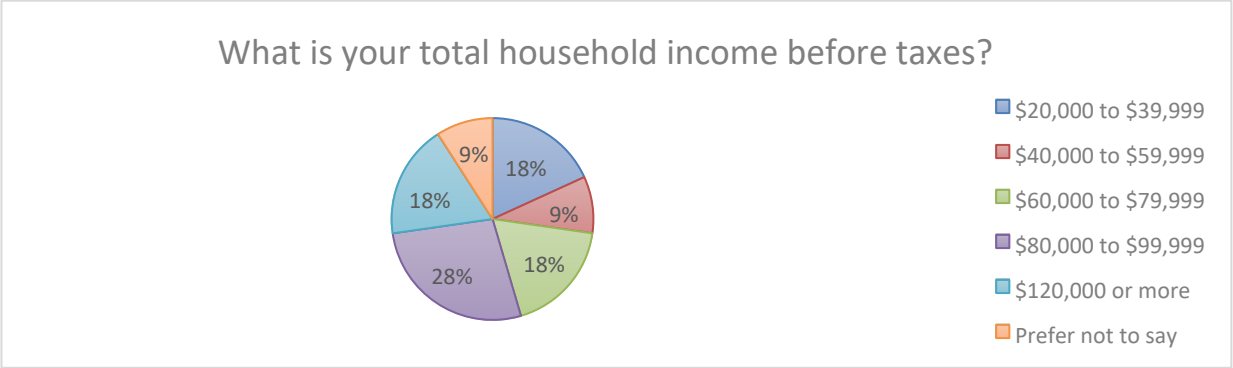
4) What is your racial or ethnic background?

For inclusivity, responders had 16 options including a self identify option and could select all racial or ethnic backgrounds that applied to them. All eleven respondents identified as white.

5) What is your total household income before taxes?

Ten out of eleven patients provided their annual household income before taxes. The majority (28%) indicated their household income before taxes was $80,000 – $90,999 per year. Eighteen percent of patients indicated their household income was $20,000 - $39,999, $60,000 – $70,000 or $120,000 or more. The remainder of respondents indicated they made between $40,000 – $59,999 (9%). Patient A did not indicate their household income and Patient B indicated they made $120,000 per year or more.

Figure 3 – Socioeconomical Status



Disease Experience

1) How much of an impact do symptoms associated with high-risk non-metastatic prostate cancer have on your day-to-day activities and quality of life?

Survey respondents were presented with a list of day-to-day activities their cancer diagnosis may impact. Patients were asked to rate each activity on how their cancer impacted that area of their life.

The ability to engage in sexual activity scored highest as a negatively impacted activity affecting their quality of life, with ten responses (91%) falling into the moderate to significant impact range. The second greatest impact was seen in the ability to work with six responses (55%) landing in the moderate to significant impact range. The ability to travel and the ability to concentrate were the next most impacted activities, with four responses each falling in the moderate to significant impact range (36%). Other impacted activities of note include the ability to exercise, spend time with family and friends and maintain mental health, each with 27% of responses falling in the moderate to significant impact range. For further detail, please refer to Table 1 and Figure 3.

There were 36 responses which fell in the moderate to significant impact range across the 11 participants. Thirty-three percent of the total responses landed in the moderate to significant impact range, indicating some significant impacts on patients' quality of life due to symptoms associated with cancer and treatments.

One patient provided additional comments and stated, "It is a source of continuous low-level anxiety and depression which distracts from living life in a carefree manner. I have made changes in diet, discontinued alcohol consumption, and exercise more. Perhaps in some strange way it has encouraged me to live a more healthy lifestyle." Another patient indicated, " [I experienced] some physical issues following clean up radiation after surgery that were not explained or mentioned prior to having it. Radiation burn affecting bowels and some slight urinary issues."

<u>Patient A and B</u>

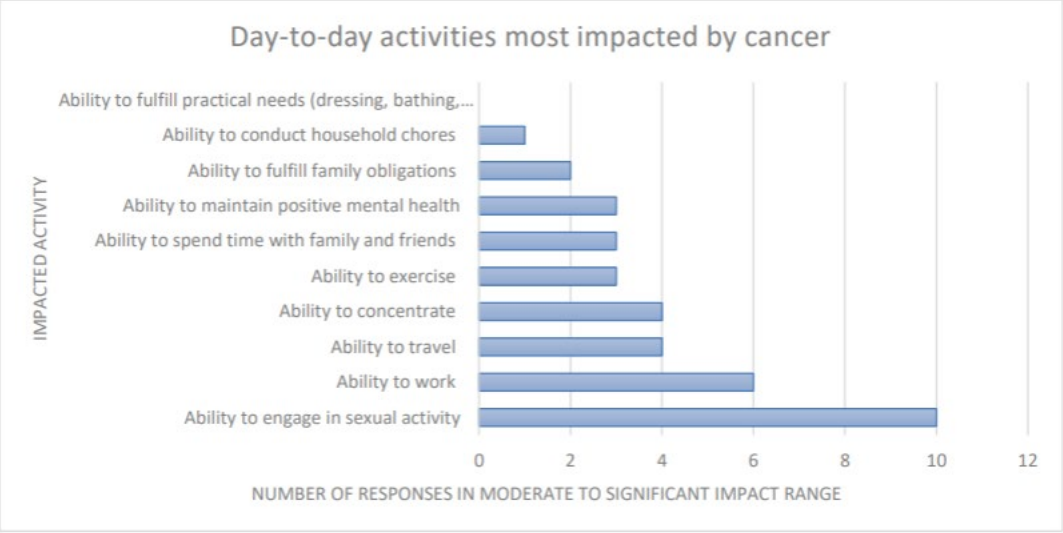
In the survey, Patient A indicated he did not experience an impact in any of the tasks listed in Table 1 except sexual activity, which he indicated was significantly impacted. Patient B indicated he experiences significant impacts on his ability to work and engage in sexual activity. He also experienced moderate impacts to his concentration and mental health. He reported small impacts on his ability to exercise, conduct household chores, fulfill family obligations and spend time with family and friends. Both patients provided further details during their interview, described in the section titled "Experiences with Currently Available Treatments" section.

Table 1 – Quality of life

Task	Small impact	Moderate impact	Significant impact	I'm not sure	Not applicable/No Impact
Ability to work	1 (9%)	3 (27%)	3 (27%)	0 (0%)	4 (36%)
Ability to travel	3 (27%)	2 (18%)	2 (18%)	0 (0%)	4 (36%)
Ability to exercise	4 (36%)	1 (9%)	2 (18%)	0 (0%)	4 (36%)
Ability to conduct household chores	7 (63%)	1 (9%)	0 (0%)	0 (0%)	3 (27%)
Ability to fulfill family obligations	5 (45%)	2 (18%)	0 (0%)	(0%)	4 (36%)
Ability to spend time with family and friends	4 (36%)	3 (27%)	0 (0%)	0 (0%)	4 (36%)
Ability to concentrate	4 (36%)	4 (36%)	0 (0%)	0 (0%)	3 (27%)
Ability to fulfill practical needs (dressing, bathing, preparing meals)	5 (45%)	0 (0%)	(0%)	1 (9%)	5 (45%)
Ability to maintain positive mental health	5 (45%)	2 (18%)	1 (9%)	0 (0%)	3 (27%)
Ability to engage in sexual activity	0 (0%)	3 (27%)	7 (64%)	0 (0%)	1 (9%)

***Note**: Percentages have been rounded to the nearest whole number and therefore rows may not add up to exactly 100%.*

Figure 3 - Day-to-day activities with the most moderate or significant impact scores



Experiences With Currently Available Treatments

1) Which of the following barriers have you faced related to receiving treatment(s) for your cancer?

Respondents had 15 potential barriers to choose from, along with an “other” and “not applicable” option. Patients could select all the barriers from the list they experienced.

There were a total of 20 responses across the 11 patients. Nine of the 11 patients experienced one or more barriers in receiving care (82%). The most common barriers experienced (36% of the group each) were long wait times to receive tests or treatments and costs associated with complementary medicines that were recommended by their healthcare team. The next most common barriers (27% of the group each) were a lack of familiarity with navigating the healthcare system and transportation costs to attend appointments (gas, parking, public transit etc.). Other barriers that patients experienced include costs associated with take-home cancer drugs, costs related to lodging and accommodations when receiving treatment, loss of income due to absence from work and difficulty attending appointments due to disability or mobility issues. Refer to Figure 4 for a visual depiction of the results.

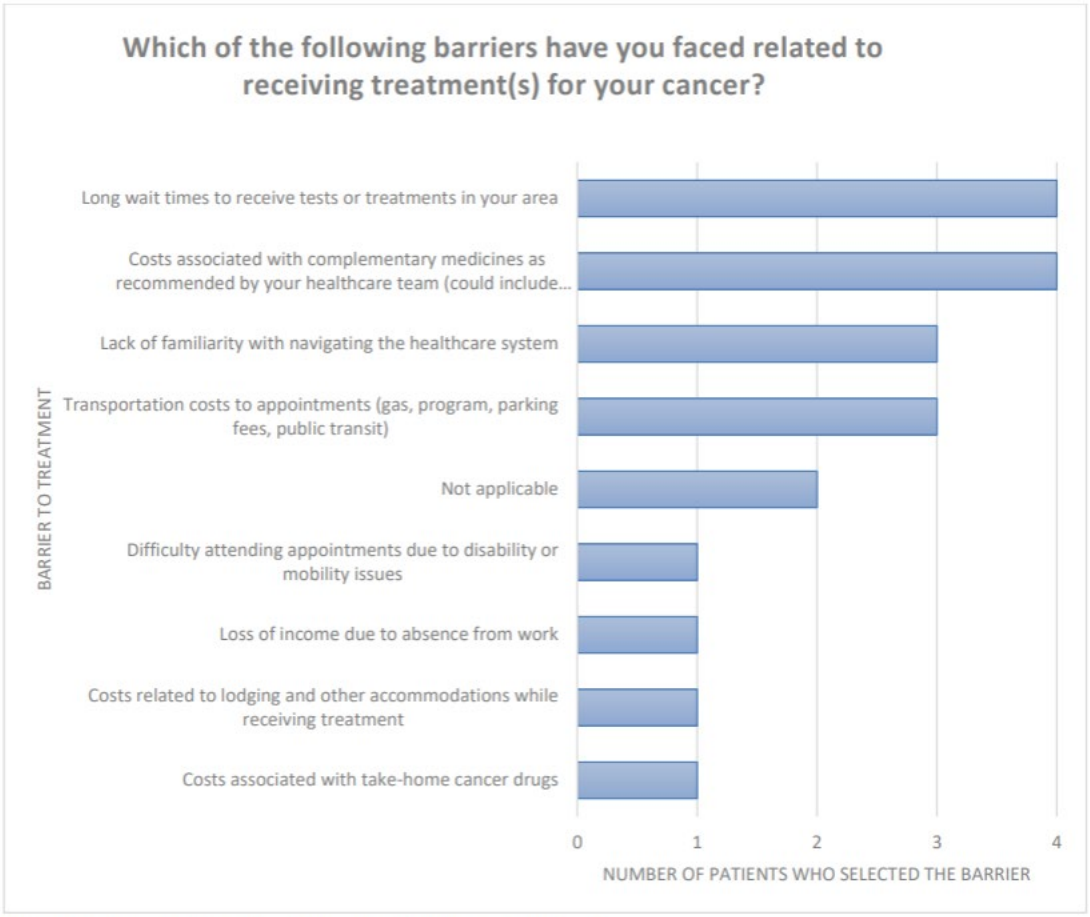
Patient A and B

Patient A did not identify any barriers in the survey but provided further detail about his current situation regarding treatment access in his interview. Patient A is a 30-minute drive from his oncologist’s office and attends his appointments every couple of months; therefore, transportation does not contribute as a financial barrier. Patient A indicated his oncologist is often quite busy, and sometimes he has had to wait over an hour to receive his Eligard treatment. Moving forward, he is now receiving this medication from his family physician.

Patient B identified costs associated with take-home cancer drugs and costs related to complementary medicines as recommended by his healthcare team in the survey as barriers he experienced. Patient B provided further details in his interview. Patient B indicated that Janssen supplied him with 2-3 months of abiraterone acetate; once that time period was over, he would need to find a new way of accessing it.

Patient B indicated the cost of abiraterone acetate would be approximately $4000 a month. He stated, “how can anyone afford it without some kind of coverage? There’s no way. Not many people have that kind of spare change rolling around”. Patient B and his wife began researching other avenues to access abiraterone acetate and discovered that Sunlife had a program for people with special requirements. He applied with assistance from his doctor and was approved for Sunlife to cover the drug in six-month intervals. Every six months, he would need to re-apply. Patient B stated, “if Sunlife no longer wishes to cover me, I would need to find a replacement for abiraterone. In Ontario, it’s still expensive to access the generic version. The place to turn would be web pharmacies. I found one that operates out of Winnipeg where I can get generic abiraterone for them for $1200 a month.” He further went on to state “I would like to see that there be some kind of compensation to make it more affordable so it takes away the strain on the family and the patient from managing cancer to dramatically improve quality of life. If you’re looking at a staggering price, it doesn’t help your quality of life”.

Figure 4 - Barriers to treatment

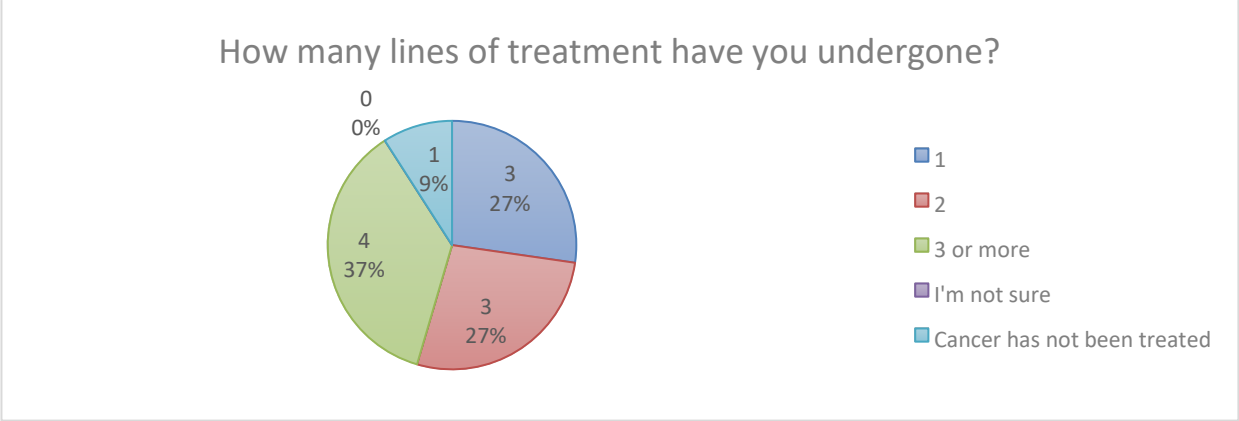


Note: *Only the options that were selected are shown in this figure.*

2) How many lines of treatment have you undergone?

A description of what a line of treatment entails was provided. The majority of patients indicated they had undergone 3 or more lines of therapy (36%). The next most common response was one or two lines of therapy (27% each). One patient indicated their cancer had not been treated. Patient A and B had undergone 3 lines of therapy.

Figure 5 – Number of lines of treatment undergone



3) Since your diagnosis of prostate cancer, which treatments have you tried?

Respondents could select from 11 treatment types, indicate if their cancer has not been treated, if they have engaged in watchful waiting, are unsure or provide additional information through an open field. Respondents were able to select all treatments that applied to them.

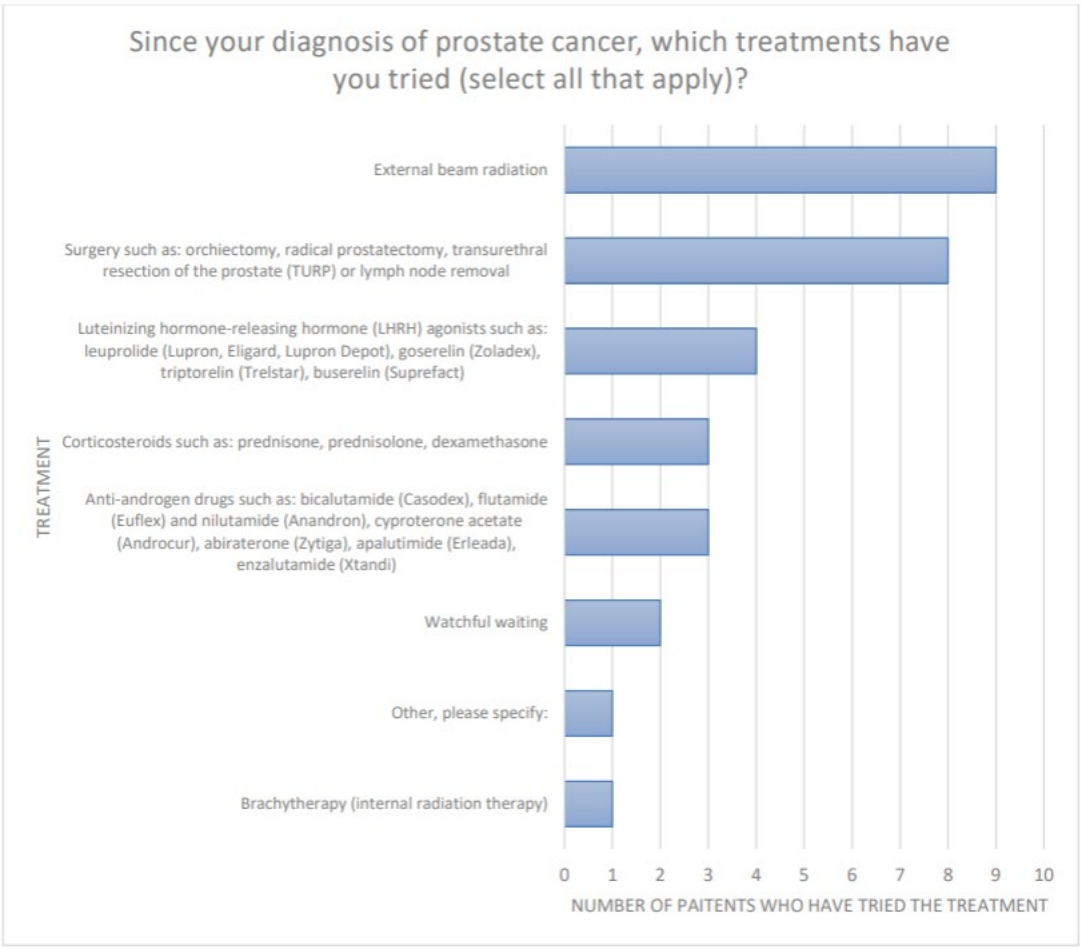
The majority of patients (82%) had tried external beam radiation at some point in their treatment journey. The next most common treatments tried were surgery (73%) and LHRH agonists (36%). Twenty-seven percent of survey patients tried a corticosteroid or anti-androgen drug. For a complete depiction of the results, refer to Figure 6.

Patient A and B

Patient A (diagnosed with high-risk non-metastatic prostate cancer) takes abiraterone acetate, dexamethasone and Eligard. He was previously taking prednisone, but it was ineffective. Patient A was previously on Eligard alone for two years, however, it stopped working which prompted the decision to switch take abiraterone.

Patient B was initially diagnosed with stage three N1 prostate cancer in fall 2014. He had a radical prostatectomy after his diagnosis. In the spring of 2015, he began radiation and Lupron. He engaged in watchful waiting for two years. Patient B then entered a clinical trial and had a PSMA PET scan which showed five areas of his abdomen where the cancer was present but inoperable. His radiation oncologist recommended abiraterone acetate. He is currently taking abiraterone, Eligard every four months and prednisone. His cancer is now in remission and cancer is undetectable with traditional scanning tools.

Figure 6 – Treatments tried by survey respondents



Note: *Only the options that were selected are shown in this figure.*

4) How much of an impact do the following cancer treatment side effects have on your daily life?

CCS asked about treatment side effects to identify which had the most significant negative impacts on patients and, therefore, indicate what side effects would be the most ideal to avoid or prevent worsening in new treatments and current treatments. For context, refer to Figure 6 to review what treatments patients have tried that may have contributed to these side effects.

The most significant impacts on patients' day-to-day lives were due to changes in libido and sexual function, with nine respondents (82%) rating it as having a severe impact and one respondent rating it as having a moderate impact. The second most impactful side effect in this group was fatigue, with 64% of participants indicating it was either moderately or severely impacting their lives. Hot flushes were rated as either moderate or severe for nearly 55% of patients. Appetite changes, anemia and loss of muscle mass each impacted 45% of this group in either a moderate or severe way. Refer to Figure 7 to view all the side effects that received scores in the moderate to significant impact range.

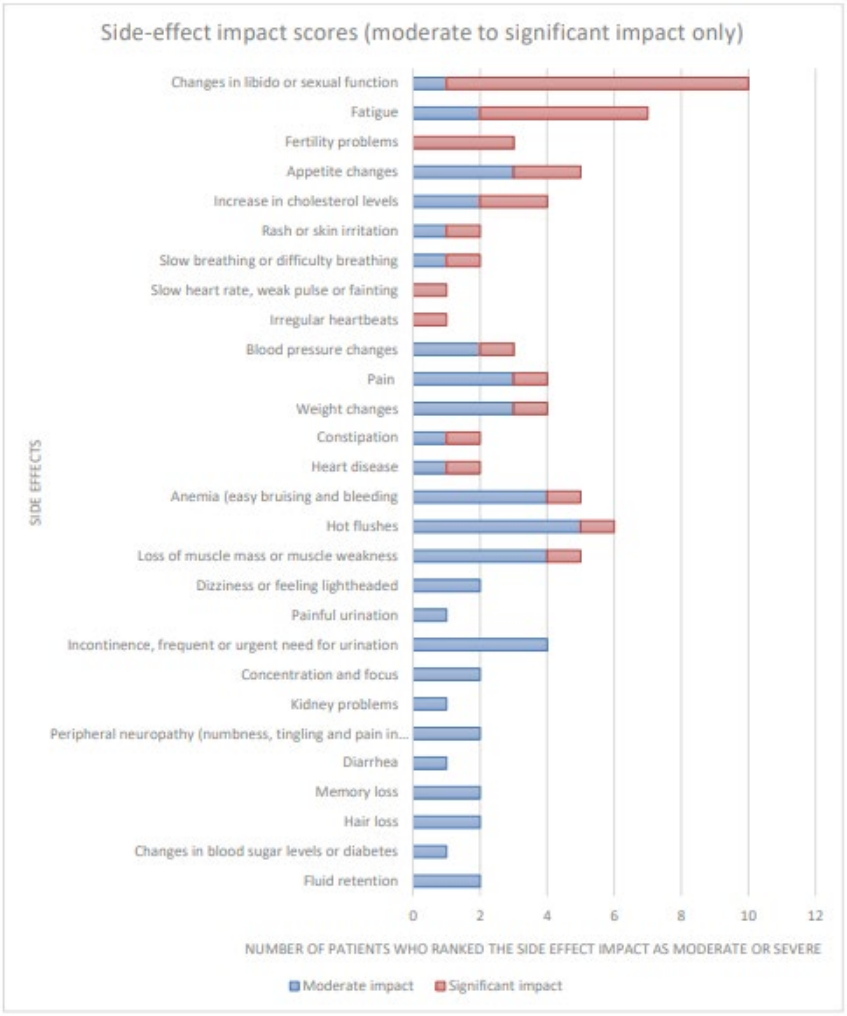
Of the 407 responses across the 11 patients, 95 landed in the small impact category (23%), 53 fell into the moderate impact category (13%), and 33 landed in the severe category (8%). In addition, 29 responses fell into the "I'm not sure" category (7%), and 197 fell into the not applicable/no impact category (48%). For a figure containing detailed data on all levels of severity, please view Figure 1 in Appendix 1.

Patient A and B

Patient A expressed in the survey that loss of muscle mass, anemia, appetite changes, weight changes, changes in sexual function and rash or skin irritation impacted him significantly. He further shared in his interview that when he was initially diagnosed with prostate cancer, he had just completed an Iron Man race and was in excellent physical condition. Once he began taking Eligard and abiraterone in combination, he noticed his stamina and muscle tone were declining. However, he continued to run and swim despite his dip in performance. He later ran a half marathon and a full marathon while taking Eligard and abiraterone acetate. While training for a marathon, he got pneumonia. Since then, he has reduced his physical activity to daily walks and a 30-minute bike, culminating in one to two hours of physical activity per day. In addition, he golfs twice a week and attends the Alberta cancer exercise program twice a week. He indicated there are some days when he feels a lack of energy and sometimes feels the need to take a nap in the afternoon. He stated he was doing better before having pneumonia. Patient A further commented on side effects, highlighting that Eligard caused severe hot flashes when he first started taking it, but he no longer experiences this. When he began taking abiraterone, he experienced severe cramping in the legs; however, this has also resolved. At this point, he expressed his side effects are manageable.

Patient B expressed in the survey that he experiences severe impacts on his sexual function and libido. He also experiences moderate peripheral neuropathy, memory loss, hot flushes, anemia and hair loss. Several other side effects impact him; however, the impact is small. These include loss of bone density, loss of muscle mass, low blood potassium levels, fluid retention, fatigue, nausea, appetite changes, constipation, changes in concentration and focus, pain, blood pressure changes, incontinence or urgency, headaches or pounding in the neck, blurred vision and dizziness or light-headedness. Patient B provided further details in his interview about the impact of side effects. Patient B indicated the “hot flashes are brutal, but they aren’t as severe as when I was taking Lupron.” He also indicated he believes his body hair loss is related to abiraterone acetate as he didn’t experience this to the same extent when he was only taking Eligard. Patient B went on to express he no longer has the stamina he once possessed; however, this could also be related to his rheumatoid arthritis (RA). He is currently taking methotrexate for his RA.

Figure 7 – Moderate to severely ranked side effect related impacts on patients' day-to-day life



5) What improvements would you like to see in new treatments that are not achieved in currently available treatments? For example: effectiveness for relieving certain symptoms or side effects, affordability, ease of use etc.

Several comments were made regarding what improvements this group of patients would like to see in future treatments.

- "*1. Costs of PDE5 inhibitors for nerve reconstruction needs to be covered by provincial health care plans and/or insurance plans. 2. ADT increases the risk of developing diabetes by up to 60% and the risk of heart disease, sudden death and stroke by 30%. The Canadian Association of Urologists and drug manufacturers recommend regular medical monitoring of patients on ADT (lipids, cardiovascular, etc.) but it is not happening. […] Regular medical monitoring of those on ADT should be the norm and not the exception. 3. ADT is chemical castration and has been in use for over 80 years to treat cancer. By now, somebody should have come up with something better. CCS needs to advocate for alternatives to ADT as they do for chemotherapy. The effect on QOL caused by ADT is awful.*"
- *"Better communication from health professionals on a personal level, (maybe due to too many patients or only a need to know basis thinking)."*

- *"Improved methods to maintain sexual functioning. Reduction of hot flashes."*
- *[Access to] MRI to keep watch on growth or spreading of cancer. [My] doctor says no."*
- Patient B also submitted a comment through the survey and stated *"Affordability especially for Zytiga! Having to source generic equivalents to prevent financial ruin."*

Improved Outcomes & Experience With Drug Under Review

This section of this report will be focused on Patient A and B. Patient A and B answered a series of questions about their experience with abiraterone acetate in the form of a survey and provided further detail in their interviews.

Patient A

At the time of the interview, Patient A had been taking abiraterone acetate, dexamethasone and Eligard. As noted in section four of this report, he was previously on prednisone, but discontinued its use as it was ineffective for him. Patient A was initially on Eligard exclusively for two years, however, it stopped working and he switched oncologists. His new oncologist prescribed him abiraterone acetate once his PSA began to rise. Patient A does not need to pay for his abiraterone; however, he was unclear how his oncologist got him covered access.

Patient A indicated that after beginning his treatment with abiraterone acetate, his tumour has shown no signs of growth according to scans. He stated, "it's been working very well to control my cancer. It's really controlled my PSA." He further went on to state that there is no need for further treatment since his current treatment regimen is effective. He has not taken docetaxel at this point.

As stated in section four of this report, Patient A continues to be very active and has indicated the side effects related to his treatments are manageable. He continues to golf, swim, bike and attends an exercise program on these medications. In addition, he stated he would still be running marathons if not for a diagnosis of pneumonia which further reduced his performance. In addition, Patient A feels the number of appointments he must attend at his clinic is manageable. He appreciates the ability to take abiraterone at home and does not find it difficult to take. Patient A stressed that lengthening of life is the most important facet of treatment for him and that he is willing to undergo temporary side effects to reach that end.

Patient B

As stated in section four, at the time of the interview, Patient B had been on abiraterone acetate and prednisone for two years in combination with Eligard. Patient B had a PSA of .9 after his radical prostatectomy and radiation, which initiated the need for Lupron. His PSA was then undetectable for three years and he was not on any medication for one to two years. His PSA slowly began to rise after that. Due to his rising PSA, his doctor assisted him with entering a clinical trial for the PSMA PET. They found five areas in the abdomen where cancer was present but inoperable and inappropriate for radiation therapy. These areas did not appear in traditional scans. The radiation oncology suggested abiraterone acetate. His PSA is now below .006. Patient B stated, "Without abiraterone, with the likelihood of hormone suppression stopping the progression of cancer in other areas, I don't think that I would be around." He further stated he would not consider docetaxel unless his current effective treatment regimen stops working. Due to this treatment regimen (abiraterone, prednisone and Eligard) his cancer is no longer detectable on traditional scans, and his oncologist considers him in remission. Patient B has some concerns about the cost of getting another PSMA PET scan if his current treatment stops working.

Due to the access issues described in Section 4, Patient B has concerns about his ability to access abiraterone acetate in the future. Patient B stated, "In some countries, abiraterone is the standard of care for men with prostate cancer. The combination of Eligard and abiraterone is the treatment of choice."

Patient B noted he only missed one dose of abiraterone acetate since his initial prescription and that he finds it easy to take. He doesn't mind waiting one hour after taking the drug to eat breakfast and uses the hour as an opportunity to take care of morning tasks. In addition, Patient B stated, "To have access and be able to be treated and enjoy life, drugs like Zytiga are critical."

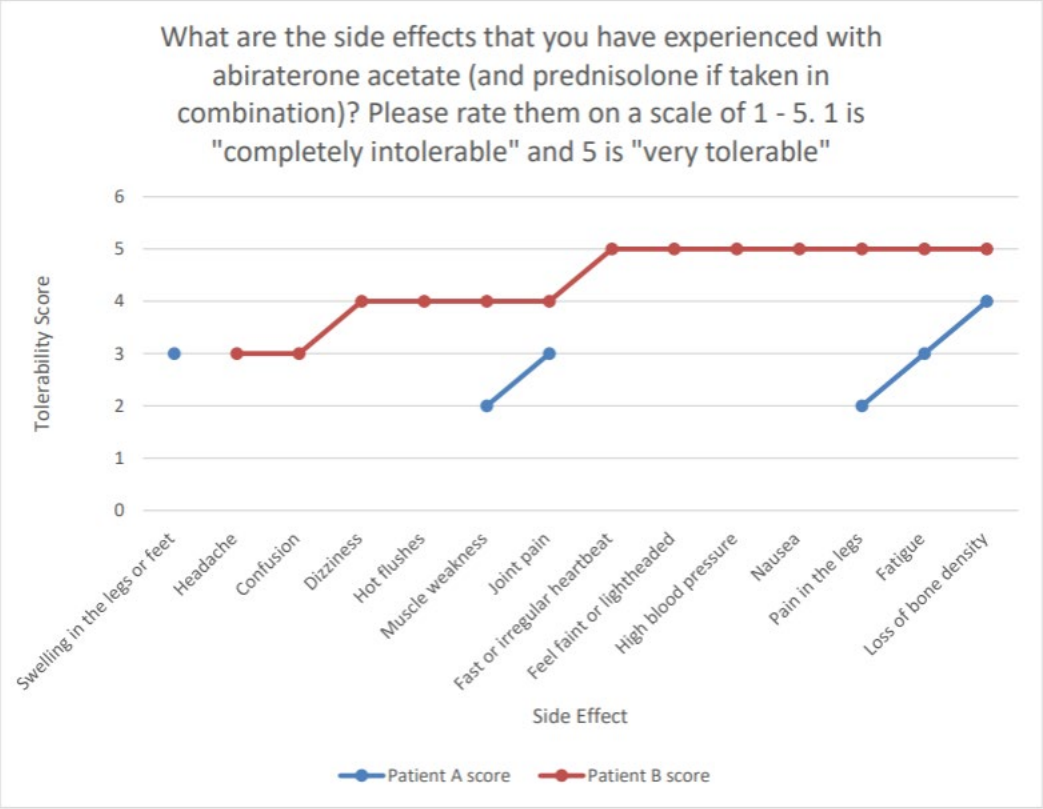
1) What are the side effects that you have experienced with abiraterone acetate (and prednisolone if taken in combination)? Please rate them on a scale of 1 - 5. 1 is "completely intolerable" and 5 is "very tolerable".

CCS explored effect tolerability to determine if abiraterone acetate allowed patients to live an acceptable quality of life. Patients were provided with a list of 22 side effects associated with abiraterone acetate and prednisone/prednisolone.

Patient A indicated he experiences loss of bone density but ranked it as tolerable. He provided neutral scores to fatigue, joint pain and swelling in the hands and feet. He ranked muscle weakness and pain in the legs as less tolerable.

The majority of side effects experienced by patient B were tolerable or very tolerable. Patient B provided a neutral score for his symptoms of headache and confusion. There were no side effects experienced by either Patient A or Patient B ranked as intolerable or very intolerable. Both patients were provided with an opportunity to express any additional side effects they may be experiencing; however, neither patient had anything further to share.

Figure 8 – Tolerability of side effects associated with abiraterone acetate



Note: *Only the options that were experienced by at least one of the patients are displayed.*

2) How much do you agree or disagree with the following statements about abiraterone acetate?

Patient A and B were asked to rate statements about abiraterone acetate on a scale of strongly disagree to strongly agree.

Patients A and B strongly agreed that abiraterone acetate has been effective at controlling their cancer, that it was easy to use, and that they would recommend it for high-risk non-metastatic prostate cancer patients. Patient A agreed that it was tolerable and that he would still choose to take it considering the side effects and wasn't sure if it allowed him to spend less time in the clinic. Patient B strongly agreed with all of the remaining statements including strongly agreeing the side

effects were tolerable, that considering the side effects he would still choose to take it, and that it allowed him to spend less time in the clinic.

Table 2 – Patients level of agreement on statements related to abiraterone acetate

Statements	Patient A Response	Patient B Response
Overall the side effects of abiraterone acetate were tolerable	Agree	Strongly agree
Considering the side effects I experienced so far, I would still choose to take abiraterone acetate	Agree	Strongly agree
Abiraterone acetate has been effective at controlling my cancer	Strongly agree	Strongly agree
Abiraterone acetate allowed me to spend less time in the clinic receiving treatment compared to other treatments I've tried in the past	I'm not sure	Strongly agree
Abiraterone acetate was easy to use	Strongly agree	Strongly agree
I would recommend this treatment to others with high-risk nonmetastatic prostate cancer	Strongly agree	Strongly agree

Anything Else?

1) Please provide any further comments you would like CADTH to consider when they are deciding if they should recommend if abiraterone acetate in combination with prednisolone should be covered by provincial drug plans for people with high-risk non-metastatic prostate cancer in Canada:

Patient A did not have further comments to share.

Patient B: "For me the combination has been very effective. PSA remains below 0.006 after 2 years and testosterone undetectable as well. If it wasn't for the fact that Zytiga is stunningly expensive, it would be the BEST drug to manage high-risk non-metastatic and mCSPC. Government support for Zytiga or generics would dramatically reduce the stress that patients and their families are under. The financial burden means the patient may have to stop or not even start treatment, meaning a reduced life span."

2) How important is it to you to have more treatment options, including new therapies?

Patient A: "Very important, I listen all the time to keep up to date as much as I can."

Patient B: "It is extremely important especially for the potential that I have with regard to metastatic cancer right now. Without affordable and available treatments, my life span is threatened, my QOL is threatened and my future is threatened and none of those are attractive alternatives. When the track record for drugs like abiraterone is substantial and overwhelmingly positive , it is really counterintuitive why the government would not be in support of funding the drug to ensure I can be a contributing member of society for a longer time without being a burden on the healthcare system."

Overall, the sentiments expressed across responses to the survey and interviews include:

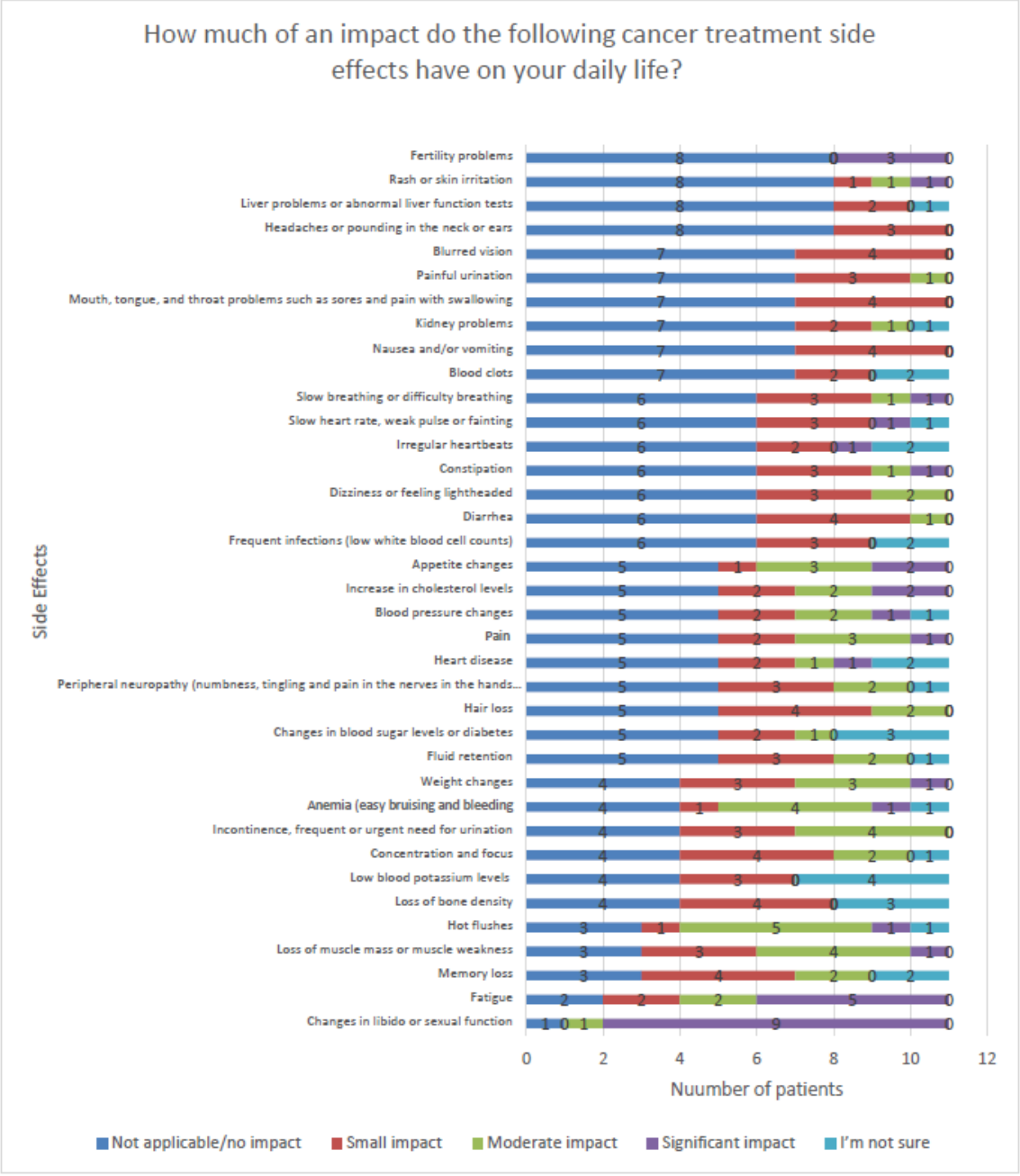
- Patients with high-risk non-metastatic prostate cancer (and one patient with mCSPC in remission) stated their cancer most impacted their day-to-day life through their ability to engage in sexual activity, work, travel and concentrate.
- Eighty-two percent of patients (9 of 11) experienced at least one barrier in accessing treatment. The most common barrier was long wait times to receive treatment and costs associated with complementary medicines as recommended by their healthcare professionals. Patient B, as the only patient surveyed taking abiraterone

gaining coverage through private insurance that may not choose to cover him indefinitely, underscored the need for more affordable take-home cancer drugs.

- The most significant treatment side-effects impacting patients' day-to-day lives were changes in libido and sexual function, fatigue and hot flashes, among others. Across the 11 patients, 28 side effects were identified, indicating that current treatments can inflict a wide range of life-impacting symptoms.
- Patients would like to see improvements in future prostate cancer treatments to reduce side effect profiles, improve take-home cancer drug affordability, achieve more holistic care, better communication among healthcare workers and patients, and better access to imaging.
- Patient A and B both indicated they agreed or strongly agreed the side effects of abiraterone acetate have been tolerable, that considering the side effects they would still choose to take it, that it has been effective at controlling their cancer, that it was easy to use and that they would recommend this drug to others.

Appendix: Additional figures

Figure 1 – Impacts of cancer treatment side effects on day-to-day life: All responses



Patient Group Conflict of Interest Declaration - Canadian Cancer Society

To maintain the objectivity and credibility of the CADTH reimbursement review process, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

   No

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   No

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Janssen				X

Clinician Input

Ontario Health (CCO) Genitourinary Cancer Drug Advisory Committee

About the Canadian Cancer Society

OH-CCO's Drug Advisory Committees provide timely evidence-based clinical and health system guidance on drug-related issues in support of CCO's mandate, including the Provincial Drug Reimbursement Programs (PDRP) and the Systemic Treatment Program.

Information Gathering

Jointly discussed via email.

Current Treatments and Treatment Goals

Treatments goals for this drug would be to delay disease recurrence and/or prolong life.

Treatment Gaps (unmet needs)

Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.
Better treatment options are needed beyond ADT alone, as there are no systemic therapies approved in this indication. The drug under review would provide a new option.

Place in Therapy

How would the drug under review fit into the current treatment paradigm?
Abiraterone with prednisone would be a first systemic therapy option, in addition to ADT, in this indication for men with high-risk non metastatic prostate cancer.

Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?
This regimen would benefit men with high-risk non metastatic prostate cancer who are clinically suitable for abiraterone/prednisone, in addition to ADT.

What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?
As per standard of care assessment including clinical assessment and/or lab tests.

What factors should be considered when deciding to discontinue treatment with the drug under review?
Clinical progression or intolerability of abiraterone/prednisone.

What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?
Hospital (outpatient clinic) for abiraterone/prednisone. A specialist with expertise in prostate cancer is required.

Additional Information

The DAC would like to mention radiation to the primary tumour. However, they would advocate for language such as "In qualifying cases, ADT/pred with ADT would be optimally combined with radiation therapy to the prostate. Exceptions are allowed for qualifying patients who have a medical contraindication to prostate radiation therapy or refuse radiation therapy."

Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the Procedures for CADTH Drug Reimbursement Reviews (section 6.3) for further details.

Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

Ontario Health provided secretariat function to the DAC.

Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

No.

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Girish Kulkarni,
Position: Ontario Health (CCO) GU Cancer Drug Advisory Committee Lead
Date: 28-07-2022

Table 1: Conflict of Interest Declaration for Clinician 1

Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
No COI	-	-	-	-

Declaration for Clinician 2

Name: Dr. Chris Morash,
Position: Ontario Health (CCO) GU Cancer Drug Advisory Committee Member
Date: 28-07-2022

Table 2: Conflict of Interest Declaration for Clinician 2

Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
No COI	-	-	-	-

Declaration for Clinician 3

Name: Dr. Eric Winquist,
Position: Ontario Health (CCO) GU Cancer Drug Advisory Committee Member
Date: 28-07-2022

Table 3: Conflict of Interest Declaration for Clinician 3

Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
No COI	-	-	-	-

Declaration for Clinician 4

Name: Dr. Aly-Khan Lalani
Position: Ontario Health (CCO) GU Cancer Drug Advisory Committee Member
Date: 28-07-2022

Table 4: Conflict of Interest Declaration for Clinician 4

Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
No COI	-	-	-	-

Industry Input

Janssen Inc.

Does the proposed project scope accurately reflect the treatment landscape?

The population outlined by CADTH is not sufficiently defined. Although the STAMPEDE trial references a “high-risk non-metastatic prostate cancer” as the patient population evaluated, this term is broad in nature and is not reflective of the entire STAMPEDE patient population as per inclusion criteria.[1] Suggested language to define the population is “very high-risk localized prostate cancer”, which is aligned with language used to describe the majority of STAMPEDE patients per the National Comprehensive Cancer Network (NCCN) guideline definition.[2] The Canadian Urologic Association guidelines also uses the language “very high-risk localized prostate cancer,”[3] although its definition is not outlined.

Are you aware of relevant published studies that you would like considered in the clinical review?

STAMPEDE is a multi-arm multi-stage (MAMS) platform trial protocol that in arm G assessed the efficacy of adding abiraterone acetate plus prednisolone (AAP) alone or with enzalutamide to androgen-deprivation therapy (ADT) for patients with “high-risk non-metastatic prostate cancer.”[1]

Do you have additional comments that you feel are pertinent to this review?

Janssen requests the proposed indication, STAMPEDE study design and generalizability to the Canadian population be thoroughly assessed:

Indication: As discussed in question 1, there is clinical uncertainty related to the proposed indication for AAP, which has not been reviewed by Health Canada. CADTH’s recommendation regarding the indication should be clearly supported by evidence. Although the STAMPEDE trial references a “high-risk non-metastatic prostate cancer” as the patient population evaluated, this term is broad in nature and is not reflective of the entire STAMPEDE patient population as per inclusion criteria.[1] The definition of high-risk disease in the study is limited to:[1]

- Node positive or, if node negative, having at least two of the following: tumour stage T3 or T4, Gleason sum score of 8-10, and prostate-specific antigen [PSA] concentration ≥40 ng/mL),
- Or relapsing with high-risk features (≤12 months of total ADT with an interval of ≥12 months without treatment and prostate-specific antigen (PSA) concentration ≥4 ng/mL with a doubling time of <6 months, or a PSA concentration ≥20 ng/mL, or nodal relapse) non-metastatic prostate cancer,
- And a World Health Organization performance status of 0-2.

Per the NCCN prostate cancer guideline definition of “very high-risk” disease, the majority of patients in the STAMPEDE trial met this criterion.[2] In the STAMPEDE trial, 90-94% of patients had stage T3-T4 disease and 79% of patients had a Gleason score of 8-10 at baseline.[1] As per the STAMPEDE protocol publication, “the conclusions of the study should be restricted to patients who meet the protocol’s definition for disease at high risk of relapse.”[1]

Further, radiotherapy was mandated (unless contraindicated) for patients with node-negative disease and encouraged for node-positive disease in the study, leading to 81% of all study participants receiving radiotherapy.[1] Thus, this additional treatment should be taken into consideration when assessing benefit for all patients.

NCCN guidelines recommend the use of AAP with ADT and external beam radiation therapy only in patients with very high-risk localized prostate cancer.[2] Similarly, recent European Association of Urology guidelines recommend AAP in the high-risk localized setting only when used in conjunction with radiotherapy.[2] The guideline recommendation is aligned with the STAMPEDE protocol, for “2 years of abiraterone when offering intense-modulated radiation therapy (IMRT)/volumetric modulated arc therapy (VMAT) plus image-guided radiation therapy (IGRT) to the prostate plus pelvis (for cN1) in combination with long-term ADT, for M0 patients with cN1 or >2 high-risk factors (cT3–4, Gleason >8 or PSA >40 ng/mL).”[4] Overall, there is insufficient evidence to make an informed recommendation on the use of AAP in patients with high-risk features other than those defined in the STAMPEDE protocol.

Furthermore, the uncertainty around the magnitude of benefit in specific high-risk subgroups should be taken into consideration. There is significant uncertainty on the clinical benefit for non-metastatic patients relapsing after previous local therapy given this

group is under-represented in the STAMPEDE study.[1] It is plausible that the final recommendation may be difficult to implement for decision-makers as recommendations may differ across high-risk subgroups.

Finally, ongoing studies in the prostate cancer therapeutic area should be taken into account when assessing the broadness of the indication given the new evidence may disrupt the proposed treatment algorithm. Of note, the recent ATLAS study encompasses a broader group of high-risk patients with localized or locally advanced prostate cancer, and as such the STAMPEDE population represents a subset of the ATLAS study.

Study Design: As per question #2, STAMPEDE is a MAMS platform trial protocol. Trial arm G in the study protocol assessed the efficacy of adding AAP alone or with enzalutamide to ADT for patients with "high-risk non-metastatic prostate cancer."

It should be noted that the study was not designed with regulatory rigor for filing, has not yet been reviewed nor approved by Health Canada and as such the certainty in the evidence is limited. The study design has been previously assessed by CADTH,[5] and limitations regarding the introduction of detection bias and adverse event outcome reporting were briefly discussed. Importantly, adverse event outcome reporting is much less robust than reporting conducted in a study designed for a regulatory body submission such as the types of adverse events evaluated and extensive details of patient deaths. Thus, it is important to consider the potential harms versus benefits that may not be captured in the trial, particularly for the use of AAP in a new disease stage where patients are generally younger and healthier, and that has not been reviewed by Health Canada in this population.

Given that the strength of the recommendation and broadness of the indication should be tied to the certainty in the evidence, results of the study should be interpreted with caution if they are to be used for decision-making purposes.

Generalizability: Given that the study was conducted only at sites in the United Kingdom and Switzerland,[1] further clarity as to the relevance to the intended population in Canada and the generalizability of treatment patterns to the Canadian clinical practice is needed.

Of note, STAMPEDE is an open-label study where there is a "1 novel therapy" rule in place meaning patients can only ever receive 1 NHT in their treatment pathway. Moreover, many of these patients would have progressed within the study before NHTs were reimbursed in the UK for non-metastatic castration-resistant prostate cancer, metastatic castration-sensitive prostate cancer and even metastatic castration-resistant prostate cancer (mCRPC). An assessment on whether the subsequent treatments received by patients in the study represent the current Canadian SoC should be undertaken, taking jurisdictional differences in implementation into account. As per CADTH's clinical assessment of a recent mCRPC treatment, "there is a limited number of available therapies for prostate cancer and sequencing of prior agents is variable in Canadian clinical practice"[6] which will need to be taken in consideration when generalizing the STAMPEDE results to a Canadian setting.

References:

1. Attard G, Murphy L, Clarke NW, Cross W, Jones RJ, Parker CC, *et al.* Abiraterone acetate and prednisolone with or without enzalutamide for high-risk non-metastatic prostate cancer: a meta-analysis of primary results from two randomised controlled phase 3 trials of the STAMPEDE platform protocol. *Lancet.* 2022 Jan 29;399(10323):447-460. doi: 10.1016/S0140-6736(21)02437-5.
2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer. 2022 May 10. Accessed 2022 Jul 4. https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf.
3. Kokorovic A, So AI, Hotte SJ, Black PC, Danielson B, Emmenegger U, *et al.* A Canadian framework for managing prostate cancer during the COVID-19 pandemic: Recommendations from the Canadian Urologic Oncology Group and the Canadian Urological Association. *Can Urol Assoc J.* 2020 Jun;14(6):163-168. doi: 10.5489/cuaj.6667.
4. Mottet N, Cornford P, van den Bergh RCN, Briers E, De Santis M, Gillessen S, et al. EAU – EANM – ESTRO – ESUR – ISUP – SIOG Guidelines on Prostate Cancer. EAU. 2022 Mar. Accessed 2022 Jul 4. https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-EANM-ESTRO-ESUR-ISUP_SIOG-Guidelines-on-Prostate-Cancer-2022_2022-04-25-063938_yfos.pdf.
5. Shane A, Walter M. Abiraterone Acetate for Metastatic Castration-Sensitive Prostate Cancer. *Cad J Health Tech.* 2021 May. Accessed 2022 Jul 4. https://www.cadth.ca/sites/default/files/pdf/htis/2021/RD0060%20Abiraterone%20for%20Prostate%20Cancer%20Final.pdf.
6. CADTH. Clinical Report – Olaparib (Lynparza). CADTH. 2021 Apr 1. Accessed 2022 Jul 4. https://www.cadth.ca/sites/default/files/pcodr/Reviews2021/10223OlaparibmCRPC_inCGR_REDACT_Post01Apr2021_final.pdf.