Stakeholder Input

Disclaimer: The views expressed in each submission are those of the submitting organization or individual; 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 view of CADTH. No endorsement by CADTH is intended or should be inferred.

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

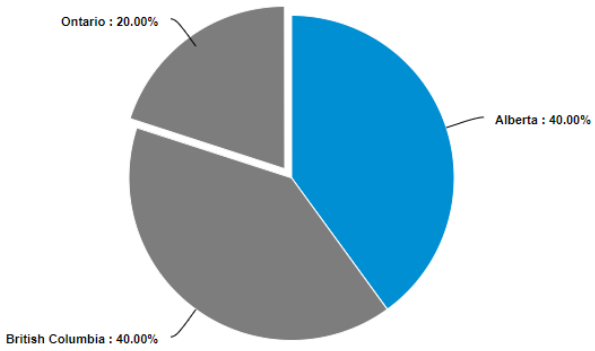
Information Gathering

The Canadian Cancer Society (CCS) gathered perspectives through interview responses. In total, four individuals agreed to participate in an interview. All participants reside in Canada, living in British Columbia, Alberta, and Ontario. All four patients are living with metastatic castration-sensitive prostate cancer. Three of four patients tried the drug abiraterone through a special access program. The fourth patient has not tried the drug.

Demographic Information

Perspectives from three provinces were captured.

Figure 1 – Geographic Location



For the remainder of this submission, respondents will be described as Patient A, Patient B, Patient C and Patient D.

Patient A
Patient A described himself as a retired man from British Columbia. He tried the drug abiraterone through a special access program and does not incur any expenses as a result. Patient A is currently taking Lupron and Prednisone in in combination with Abiraterone.

Patient B
Patient B described himself as a retired 70-year old man from Alberta. He tried abiraterone in May of 2018, in combination with Eligard and prednisone. He believes he was provided abiraterone through a special access program.

Patient C
Patient C described himself as a 77-year old man from Alberta. He is currently using abiraterone four tablets each night, in

combination with Eligard every four months, Zometa every three months, and prednisone twice a day. He was provided abiraterone through a special access program.

Patient D
Patient D described himself as a 69-year old man residing in British Columbia. He has not tried abiraterone but opted to participate in the survey to share barriers he experienced as someone with metastatic castration sensitive prostate cancer.

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?**

Patient A
When interviewed, Patient A stated that most of the impacts on his quality of life are due to the medications and not the cancer at this stage. That said, the patient expanded on the impact of a cancer diagnosis by stating:

> "Diagnosis was not a happy moment. I had just retired and got this diagnosis the same month. I experienced depression for 3 weeks after. I have been through bouts of depression since then. I have had to accept it [the diagnosis] and have to deal with it. I have my wife, who's very supportive" Patient A

Patient B
When interviewed, Patient B stated that he suffered from diminished sexual function due to the prostatectomy. He also experienced the common side effects of ADT therapy such as hot flashes and reduced muscle mass.

Patient C
Most of patient C's quality of life issues were expressed as a result of treatments. That said, he spoke about the impact of his cancer diagnosis on his loved ones and lack of available supports. He noted that he looks after his wife, who has mobility issues, fearing that if something happened to him she would be moved to a long-term care home. He desired support so he can live as long as his wife and look after her. He defined himself as having a high pain threshold and health conscious. While he still walks and rides his bike, he hired someone to do additional chores (snow removal etc.), and in the future would consider a house cleaner.

Patient D
Most of the quality of life issues expressed by patient D were related to treatments and are expanded on below. Overall, patient D has serious concerns about his treatment pathway and his overall experience with the health care system following his cancer diagnosis. The patient expressed that he suffers occasional depression and a significant amount of anxiety, with virtually no support.

Experiences With Currently Available Treatments

Patient A
Patient A is currently taking Lupron and Prednisone in combination with abiraterone—he has tried no other treatments.

Patient A stated there were no barriers to receiving medications. He stated that Prednisone is only $13 a month and all other drugs have been covered. He only needs to go to the clinic "once in a while," for Lupron injections which he described as "not bothersome". He stated that the clinic is approx. two hours away by public transit. He stated that wait times have not been an issue. He indicated this might be because his prostate cancer clinic is known for its exceptional prostate cancer care and services as well as research. He believes if he attended a different clinic, he would not be getting such quality care

Patient B
After his diagnosis of prostate cancer, Patient B received a prostatectomy and radiation therapy in 2010. The cancer later metastasized and further treatment was needed. He began taking Eligard as a monotherapy and used that drug alone until it was no longer effective.

In May 2018, Patient B began taking Eligard, abiraterone and prednisone together. His PSA score dropped from 30 to 20 from May 2018 to November 2018. At this point, his medical oncologist switched his steroid from prednisone to dexamethasone. Patient B states that this made a significant improvement with his PSA going from 20 to hardly detectable.

Patient B stated that this combination therapy was effective until October 2021 when his PSA began to rise again, however, his doctor said the abiraterone controlled his cancer for a good amount of time-based on what is expected. Once the abiraterone was no longer effective, he went off abiraterone and dexamethasone and remained on Eligard. He then received one round of docetaxel chemotherapy in 2022 and continues to take Eligard. His PSA is now 2.5.

Before trying abiraterone, he suffered from diminished sexual function due to the prostatectomy and the common side effects of ADT therapy such as hot flashes and reduced muscle mass.

The patient stated that many of the side effects he experiences today were caused by the initial prostatectomy. Radiation therapy was clinically intensive as he had many appointments. Overall, Patient B stated that the side effects of his past treatments were manageable.

Patient C
Patient C had his prostate removed in 2003 following his diagnosis of prostate cancer and then was cancer free for 6 years. The cancer returned and he received 32 doses of radiation. He then started taking Eligard after the radiation ended in 2008. At this time, his PSA is less than 0.1.

Prior to starting abiraterone, Patient C said he experienced hot flashes, constipation, incontinence, and sexual side effects, claiming that this was “mostly” caused by his prostatectomy.

Patient C started abiraterone in July 2018. Bone and CT scans were done which detected metastasis of his prostate growing. He was put on ABI, continued with Eligard, and received radiation in 2018 (concurrently)-Patient A indicated that there was no advancement since 2018.

When asked about barriers to accessing treatment, Patient C stated that he traveled two hours or longer in the winter, from Monday through Friday, making approx. 34 trips in total. Fuel and meals were recoverable through income tax. Since then, there was a cancer centre built closer to his home.

Patient D
Patient D was diagnosed with prostate cancer in 2014. Upon his diagnosis, he had a prostatectomy along with 33 rounds of radiation in 2015. The cancer returned around 2018/2019. In 2020 he was prescribed Degarelix. The patient indicated he was dissatisfied with his experience at the clinic as his Oncologist did not answer questions about this prescription and was adamant it was the right drug for him. Patient D states he was led to believe that the side effects caused by the drug are reversible and that there were few side effects.

Following three injections of this prescription, Patient D gained 30 -40 pounds within six weeks. He believes this weight gain caused a hernia in the abdominal muscles leading to severe pain. In addition, he experienced spinal stenosis which he also attributed to side effects related to the drug. Further, he described pain in his bone and ligaments, 90% loss of function in the right arm (in which he has regained most of the function in after stopping the medication), and wounds that never seem to heal on the back of his leg and buttocks. Patient D also indicated he has strange sensations on the right side of his head including a sense of warmth and blurry vision on that side.

Patient D stated that nearly all of these symptoms persisted for 20 months after discontinuing the drug. In addition, the patient believes he may be developing dementia as a result of this drug as his memory and concentration are declining. The patient expressed he regrets having done both the prostatectomy and the Degarelix. He believes he was not informed enough about the side effects for him to properly consent to Degarelix and has been unhappy overall with his entire healthcare experience. Patient D believes he had a negative reaction to this drug because he may have low androgen receptors. He indicated that elsewhere, they test for low androgen receptors before prescribing ADT, whereas in Canada this test is not available.

Currently, patient D eats only 1000 calories a day. Over the last 20 months, his only improvements have been after taking testosterone to eliminate some side effects but stated that this will encourage growth in prostate cancer. He believes the drug is still in his system and/or impacting him. He believes some of the medication didn’t properly absorb and is trapped in pockets in his abdomen, which he noted the doctor was going to remove.

Improved Outcomes & Experience With Drug Under Review

Patient A

Patient A stated that the Lupron and abiraterone had similar side effects. He lost 50% of his muscle mass, lost all hair on his body, experienced some fatigue, and lost of sexual function. He was very active prior to starting these drugs, but after taking them his stamina and strength have declined.

Patient A noted that abiraterone allows him to experience a generally good quality of life. He did not lose any abilities as a result of his treatment. He was a contractor before he retired and prior to his cancer. After starting abiraterone, he has built two houses (currently working on finishing the second). He has lost bone density due to his medications and experiences some hip pain but can't get a hip replacement because that's where cancer is. He has always eaten very well and stayed active, so he believes the side effects he is experiencing are all due to the medications he is taking.

Patient A has not received any scans since initial diagnosis aside from bone density. He stated that it pretty well stabilized. He went on to stated that his PSA is "practically nothing now" at .014 when it used to be 17." His cancer is now undetectable in scans, but still present.

Patient B
After his experience with abiraterone, Eligard and dexamethasone in combination, Patient B has noticed a reduction in stamina. He stated that, "Instead of long walks I go on shorter walks now. The other side effect was shortness of breath once in a while. It didn't seem to be related to physical exertion". Patient B then went on to state that knowing what it is like to take abiraterone and dexamethasone with Eligard, he would still take it and does not regret his choice. He stated abiraterone with dexamethasone and Eligard has been effective, allowing him to spend less time in the clinic than prior therapies (such as radiation). He noted it was easy to take one daily dose, and found abiraterone easy to take at home and less burdensome than prior therapies that needed to be taken in the clinic.

When asked if there was evidence in laboratory results that cancer growth has been impacted, as indicated by his physician, since starting abiraterone, Patient B stated:

> "Yes, my last CT scan was completely clear. I had a bone scan about a year ago and the bone scan prior to that one [before taking abiraterone] showed lesions on the spine and femur. During my course of abiraterone, my scans were clear."

Patient B indicated that he lives a "pretty good quality of life" at this point in time. He stated, "Loss of muscle mass is hard to live with at times. Sexual function has always been an issue but that was caused by surgery."

Patient C
When asked about his experience with abiraterone, Patient C said it was hard to differentiate between old age and drug effects. He also noted that while he was very active, he reduced his activity due to COVID-19, and concerns about contracting COVID-19.

Patient D
Patient D did not try abiraterone.

Anything Else?

Patient A
When asked about accessing any barriers in the past, Patient A stated that he had no barriers. As indicated above, patient A stated that Prednisone is only $13 a month and all other drugs have been covered. He only needs to go to the clinic once in a while for Lupron injections which is not bothersome. Door to door it takes two hours, and he needs to take a transit. Wait times have not been an issue.

When asked about the importance of more treatment options, Patient A stated:

> "It is very important to have more treatment options because at some point this medication will stop working so I need to have other options and hopefully something else will work later. You have to have multiple options. When one stops working, another might work for a while."

When asked if there was anything else he wanted to add, patient A stated that:

> “I don’t understand why they [people with mCSPC] can’t gain access to it [abiraterone] now. It seems ridiculous. It’s a lifesaving drug. I couldn’t afford $3500 a month. If my Lupron weren’t covered it would cost an extra$300 a month, so we’re up to almost $4000 a month. I’m on a fixed income, and that would be all of it…The alternative [not being able to access abiraterone] is not good. I get upset by the side effects, but I put up with it. The side effects are there but there not that bad, I can deal with it.” Patient A

Patient A ended by noting that extending his life is what’s most valuable to him and stating that his quality of life on this treatment combination is generally good.

Patient B
When asked about the importance of more treatment options, Patient B stated that, “ The more options the better, because every prostate cancer patient is different and the response to various treatments can vary from patient to patient.” He went on to say that if he had to pay for abiraterone that would put a significant “dent in the budget”. However, he would have no choice because “the alternative wouldn’t be good.”

At another point in the interview, he expanded on this and stated that he wants drugs or treatments that are highly effective and have less severe side effects, such as sexual side effects and hot flashes. While he found these side effects to be manageable, others in his prostate support were almost incapacitated by them. He also stated that impact on muscle mass is a big concern. When asked about why he participated in the interview process, Patient B stated that, “I think the financial and medical community benefits from as much input as they could get which includes patient input.”

Patient C
When asked about barriers to accessing treatment, Patient C stated that he traveled two hours or longer in the winter, Monday through Friday, making approx. 34 trips in total. Fuel and meals were recoverable through income tax. Since then, there was a cancer centre built closer to his home.

Patient D
Patient D lives with occasional depression and a significant amount of anxiety. He noted he has virtually no support. He underscored his concern that his doctor will not acknowledge his health issues and does not agree that Degarelix caused these problems. He filed a complaint about the clinician and indicated that many of the files related to his visits went missing and his doctor faced only mild repercussions for record keeping. As there was no evidence of his complaints on multiple visits, his complaint did not result in any repercussions for the clinician. He also noted the wait times to see other clinicians are long. He is hoping to see a neurologist, but he never received a call about his referral. He sees an endocrinologist who is agreeable to letting him try some hormone treatments to resolve some of his side effects. The patient does not feel supported by the healthcare system and has indicated he has applied for MAID as nothing has helped significantly with his side effects.

In addition, the patient indicated he has spoken to the FDA in the US to confirm his suspicions and research about Degrarelix and indicted the FDA confirmed with him that many of the side effects he was reading about and is experiencing can be associated with this drug.

Appendix: Patient Group Conflict of Interest Declaration

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.

   Prostate cancer treating clinicians who agreed to share our request for interviews with their patients

3. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

Table 1: Financial Disclosures

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
			X	

Industry Input

Janssen Inc.

Does the proposed project scope accurately reflect the treatment landscape?

The population outlined by CADTH is not sufficiently reflective of clinical data available to support the reimbursement of abiraterone acetate plus prednisone/dexamethasone (AAP) plus androgen deprivation therapy (ADT) plus docetaxel (herein AAP+ADT+docetaxel) in metastatic castration-sensitive prostate cancer (mCSPC). The scope of the proposed indication should be reflective of the PEACE-1 study inclusion criteria and clinical results;[1] suggested proposed language includes "for the treatment of de novo high volume mCSPC cancer in combination with ADT."

Additionally, we recommend the inclusion of the comparator darolutamide plus ADT plus docetaxel for the treatment of mCSPC, evidenced by the study ARASENS, which is currently under review by CADTH and pending Health Canada approval.[2]

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

PEACE-1 an open-label phase 3 study with a 2x2 factorial design evaluating the safety and efficacy of standard of care (SoC) (ADT alone or with docetaxel) and SoC plus radiotherapy compared to SoC plus AAP plus docetaxel or standard of care plus radiotherapy plus AAP for the treatment of de novo metastatic castration-sensitive prostate cancer (mCSPC).[1]

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

Janssen requests the proposed indication, medical need in mCSPC, PEACE-1 study design, interpretation of results, and comparative standard of care be thoroughly assessed:

Proposed Indication: As mentioned previously, the PEACE-1 study was not designed to assess the efficacy of the addition of docetaxel to AAP+ADT. However, considering the main inclusion criteria and baseline characteristics of the PEACE-1 population, mainly de novo high-volume metastases patients may benefit. As discussed in question #1, there is clinical uncertainty related to the proposed indication for AAP+ADT+docetaxel, which has not been reviewed by Health Canada. CADTH's recommendation regarding the indication should be clearly supported by evidence and aligned with inclusion criteria and results of the relevant clinical trial PEACE-1. The inclusion criteria for patients in the study were limited to:[1]

- De novo metastatic castration-sensitive prostate cancer
- ECOG performance status of 0-1 (or 2 due to bone pain)

Overall survival benefit was only seen in patients with high volume metastatic disease, which was defined as the presence of visceral metastases or at least four bone lesions with one beyond the vertebral bodies and pelvis.[1] Further, over 90% of patients had either bone and/or visceral metastases.[1] Additionally, patients also need to be willing and clinically fit to receive docetaxel, defined by respecting all inclusion and exclusion criteria, with no contraindications to docetaxel according to the SmPC of the drug and presenting all medical requirements to receive docetaxel according to the investigator's opinion. Therefore, the therapeutic benefit of adding docetaxel to AAP and ADT continues to be debated and consideration for reimbursement should be limited to chemo-fit patients with high volume mCSPC with bone and/or visceral metastases.

Medical Need in mCSPC: It is important to consider the lack of medical need in the mCSPC population. Overall, there exist several treatment options which provide significant and clinically meaningful improvement in both radiographic progression free survival and overall survival across a broad mCSPC population, including treatments such as apalutamide and enzalutamide. An area of unmet need in this population exists for those with aggressive phenotypes such as homologous recombinant repair mutations, for which there are currently no treatment options available in mCSPC. Ongoing studies such as AMPLITUDE and TALAPRO-3 aim to target the unmet need in this patient population.

Study Design: As per question #2, PEACE-1 is an open-label phase 3 study with a 2x2 factorial design.[1] It assessed the safety and efficacy of SoC (ADT alone or with docetaxel) and SoC plus radiotherapy compared to SoC plus AAP plus docetaxel or standard of care plus radiotherapy plus AAP for the treatment of de novo mCSPC.[1]

The PEACE-1 trial was not intended to evaluate the efficacy of docetaxel in addition to AAP+ADT as an experimental therapy; instead, it was intended to evaluate the efficacy of the addition of AAP to ADT with or without radiotherapy compared to ADT alone with or without radiotherapy. In 2015 midway through the trial, a protocol amendment was made which permitted the use of docetaxel in the SoC arm, and in 2017, docetaxel was made a mandatory addition to the treatment arms.[1] Thus, only a portion of patients in the trial received docetaxel as part of their treatment regimen (178/296 patients in the SoC arm, 177/293 patients in the SoC plus radiotherapy arm, 177/292 patients in the SoC plus AAP arm, and 178/291 patients in the SoC plus AAP plus radiotherapy arm).[1] This has still not changed the primary scope and purpose of the study. Given this and the introduction of docetaxel late in the study, based on PEACE-1 trial results, the question cannot be answered which patient specifically benefit from AAP+ADT+docetaxel.

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. Importantly, adverse event outcome reporting is much less robust than reporting conducted in a study designed for a regulatory body submission.

Interpretation of Results: Based on the data presented from PEACE-1, the overall survival benefit may primarily be derived from patients with high volume disease and the overall survival benefit seen in the entire patient population may more be related to the combination with AAP rather than the triple combination with docetaxel. The contribution of docetaxel to the benefit seen across all subgroups of patients is unclear and needs to be further evaluated. Therefore, the overall survival data may not sufficiently mirror activity of the PEACE-1 triplet regimen in a broader mCSPC population.

As mentioned above, the standard of care arm defined in PEACE-1 (ADT with or without docetaxel) was adjusted in 2015 to include docetaxel to align with current clinical practice.[1] Current treatment guidelines recommend the use of docetaxel only in a subset of patients with mCSPC.[3-5]

Further, triple therapy of AAP+ADT+docetaxel has not been established in CUA, American Urologic Association, or National Comprehensive Cancer Network guidelines.[3-5]

Importantly, as outlined by the PEACE-1 publication, authors concluded that “this study did not answer whether this triple combination yields clinical advantages over ADT plus a second-generation androgen receptor axis inhibitor (ARAT).”[1] To address the question of efficacy of use of AAP+ADT+docetaxel compared to ADT plus an ARAT, indirect treatment comparisons (ITCs) developed by independent bodies have evaluated the relative efficacy of treatments applied in PEACE-1 with current standard of care treatments.[6,7] Data from ITCs suggest that triplet therapy with docetaxel, AAP and ADT may not confer additional clinical benefit on disease progression and overall survival compared to an ARAT plus ADT or may only confer it in defined subsets of patients with mCSPC.[6,7] In addition, a regimen containing docetaxel confers additional toxicity such as febrile neutropenia and gastrointestinal disorder and may not be well tolerated, necessitating the careful balance with the uncertain clinical benefit.

In addition to the uncertain clinical benefit and potential harms associated with the AAP+ADT+docetaxel regimen, there may be additional costs which need to be considered compared to treatments comprised of oral agents only (e.g. an ARAT [AAP, enzalutamide, apalutamide] plus ADT). These costs include the cost of a third treatment (i.e. docetaxel) in the triplet regimen, chair time at an infusion clinic to receive docetaxel, and costs for management of additional AEs associated with docetaxel. Additional societal costs may include time to attend infusion treatment sessions and associated time off work.

This treatment regimen could also impact sequencing of later line treatment options as both AAP and docetaxel are options available for patients in metastatic castration-resistant prostate cancer.

Finally, given that the study was conducted only at European sites and predominantly France, 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.[1]

Comparative Standard of Care: The standard of care arm defined in PEACE-1 (ADT with or without docetaxel) is not considered current standard of care per current treatment guidelines or clinical practice for all patients with mCSPC irrespective of tumor volume. The Canadian Urologic Association guidelines recommend the use of docetaxel plus ADT in mCSPC patients with good performance status and high-volume metastatic disease, as defined by presence of visceral metastases, or four or more bone lesions with at least one beyond the vertebral bodies and pelvis; it is also recommended in "high-risk" patients and only weakly recommended for patients with low-volume disease.[3]

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