Canada's Drug and Health Technology Agency

# Abiraterone Acetate and Prednisone or Dexamethasone With Docetaxel

## FMEC Responses to Questions From the Drug Programs

### Table 1: Response Summary

| Drug program implementation questions | FMEC response |
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| **Relevant comparators** | |
| The comparators in the PEACE-1 trial were ADT (gonadotropin-releasing hormone agonist or antagonist, or bilateral orchiectomy) + docetaxel (SOC) ± RT.<br><br>Other publicly funded comparators for patients with mCSPC include 1of the ARTAs (apalutamide, enzalutamide, or abiraterone acetate-prednisone [or dexamethasone]) + ADT.<br>Patients receiving ARTA + ADT may have had prior treatment with docetaxel.<br><br>How does abiraterone acetate-prednisone (or dexamethasone) + ADT + docetaxel compare with other publicly funded alternatives? | FMEC agrees with the clinical expert that there is currently no direct clinical evidence evaluating the triplet therapy of abiraterone acetate-prednisone (or dexamethasone) + ADT + docetaxel versus publicly funded doublet therapies, other than docetaxel + ADT (the SOC arm in the PEACE-1 trial). Compared with docetaxel + ADT, there appears to be a modest survival benefit of the triplet therapy, but toxicity is increased, mainly as an increase in hypertension and aminotransferase increase.<br><br>Indirect treatment comparisons do not suggest an OS benefit of triplet therapy with abiraterone acetate-prednisone (or dexamethasone) + ADT + docetaxel over ARPI doublet therapies, including abiraterone acetate-prednisone (or dexamethasone) + ADT. PFS appears to be improved compared to abiraterone acetate-prednisone (or dexamethasone) + ADT (with associated uncertainty; refer to the Indirect Evidence section). There is currently a gap in both the direct and indirect evidence regarding the efficacy of triplet therapy with abiraterone acetate-prednisone (or dexamethasone) + ADT + docetaxel versus doublet therapy with apalutamide + ADT or enzalutamide + ADT. |
| There is a concurrent CADTH-sponsored Reimbursement Review (PC0294-000) for darolutamide in combination with docetaxel and ADT for the treatment of mCSPC in patients who are chemotherapy-eligible, in the same patient population based on the ARASENS study. | FMEC agrees with the clinical expert that there is currently no direct clinical evidence evaluating these 2 triplet regimens (abiraterone acetate-prednisone [or dexamethasone] + ADT + docetaxel versus darolutamide + docetaxel + ADT). However, indirect treatment comparisons have suggested that these regimens are potentially similar in efficacy and toxicity (refer to the Indirect Evidence section). |

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| How does abiraterone acetate-prednisone (or dexamethasone) + ADT + docetaxel compare with darolutamide + ADT + docetaxel? | |
| **Considerations for initiation of therapy** | |
| Patients with ECOG status scores of 0 to 1 or 2 if due to bone pain were eligible to participate in the PEACE-1 trial. Are the results of the trial generalizable to patients with worse performance statuses than those enrolled in the PEACE-1 trial? | FMEC agrees with the clinical expert that treatment may be given to patients with higher ECOG status scores at the discretion of the patient and clinician. Indirect comparisons suggest that triplet therapy is associated with greater severe toxicity than ARPI doublet therapy. Cautious use of ARPI + ADT is preferred for patients with a poor performance status. |
| Would patients with low-volume disease equally benefit from the abiraterone acetate-prednisone (or dexamethasone) + ADT + docetaxel triplet therapy compared to patients with high-volume disease? If there is a difference, what is the definition for low versus high volume disease? | FMEC agrees with the clinical expert that the PEACE-1 trial was not powered to assess differences in efficacy of this triplet therapy in patients with high-volume and low-volume disease, so this is currently unknown. The trial was stratified by metastatic site, but not high-volume or low-volume disease. Disease volume is an imprecise surrogate for cancer biology. Patients with low-volume disease may be at lower risk, and treatment with a triplet regimen versus the current SOC (ARPI + ADT doublet) should be considered clinically on an individual patient basis. As defined in the CHAARTED trial, high-volume disease is defined by the presence of visceral metastases, or 4 or more bone metastases, with at least 1 outside the spine and pelvis. |
| Should there be alignment with other triplet therapy being considered for mCSPC?<br><br>In the PEACE-1 trial, docetaxel had to be administered at least 6 weeks after ADT initiation. Abiraterone acetate-prednisone (or dexamethasone) was started within 6 weeks after ADT initiation. In the ARASENS trial, patients began ADT (± a first-generation antiandrogen), but not longer than 12 weeks before randomization, and the first cycle of docetaxel was administered within 6 weeks after the start of darolutamide. | FMEC agrees with the clinical expert regarding the inaccuracy of the clinical trial's figure describing the treatment flow in the PEACE-1 trial. The figure shows that docetaxel and abiraterone acetate had to be started simultaneously, but in the trial, docetaxel had to be started at least 6 weeks after ADT. However, randomization to abiraterone acetate or SOC was up to 3 months post–ADT initiation. Therefore, for example, one could have started docetaxel 8 weeks post–ADT initiation, and then been randomized at 12 weeks post–ADT initiation (i.e., abiraterone would have started after docetaxel in a subset of patients). In clinical practice, abiraterone acetate-prednisone (or dexamethasone) would likely be started prior to docetaxel.<br><br>Based on the PEACE-1 and ARASENS trials, docetaxel should start no sooner than 6 weeks and no later than 3 months after ADT initiation. Docetaxel and ARPIs should not be started simultaneously (to make accurate |

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| | assessments of drug-related toxicity). ARPIs should be started within 6 weeks before or after docetaxel. |
| **Considerations for discontinuation of therapy** | |
| For patients who were unable to complete 6 cycles of docetaxel, should they be eligible to continue with abiraterone acetate-prednisone (or dexamethasone) and ADT? | FMEC agrees with the clinical expert that patients who are unable to tolerate 6 cycles of docetaxel should still be continued on abiraterone acetate-prednisone (or dexamethasone) + ADT, which is one of the current SOC treatment options. |
| For patients who are unable to tolerate abiraterone acetate-prednisone (or dexamethasone), should they be eligible to switch to an alternative ARTA (such as darolutamide), provided all other criteria are met? | Patients who are unable to tolerate abiraterone acetate should be eligible to switch to another ARPI. |
| For patients who discontinued therapy (due to toxicities or the patient's choice), is there any evidence to support re-treatment with any component of the regimen when a patient progresses to mCRPC? | The available data on re-treatment with docetaxel for mCRPC after it has been used for mCSPC do not consistently demonstrate clinical benefit. If re-treatment with docetaxel is to be considered, it should be administered after a reasonable time has passed from previous treatment (e.g., 1 to 2 years). Re-treatment with abiraterone could also be considered if treatment were discontinued due to patient preference and not due to toxicity. Re-treatment decisions should be based on patient preference and clinician discretion. |
| **Considerations for prescribing of therapy** | |
| The protocol for the PEACE-1 trial was amended (January 22, 2018) to make G-CSF prophylaxis mandatory for patients who received docetaxel. Funding for prophylactic G-CSF may need to be considered, as some jurisdictions fund G-CSF with restricted eligibility. | Noted for inclusion in FMEC deliberations. |
| **Generalizability** | |
| Should patients who recently initiated docetaxel + ADT for mCSPC be eligible to add on abiraterone acetate-prednisone (or dexamethasone)? What would be an appropriate time frame to allow this addition? | FMEC agrees with the clinical expert that patients who recently initiated docetaxel + ADT prior to this recommendation being implemented should be eligible to add on abiraterone acetate-prednisone (or dexamethasone) within a period of approximately 6 months following treatment initiation to allow overlap with the policy change (i.e., if the triplet therapy is funded). However, after a reasonable time has elapsed from policy implementation, this time frame should align with the clinical trial (i.e., abiraterone acetate-prednisone (or dexamethasone) should be initiated within 3 months of starting treatment with docetaxel + ADT). |
| For patients with mCSPC who are currently receiving ATAR (apalutamide or enzalutamide or abiraterone | Patients who are currently receiving 1 of apalutamide or enzalutamide or abiraterone acetate + ADT should be |

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| acetate-prednisone) + ADT, should they be allowed to switch to abiraterone acetate-prednisone (or dexamethasone) + ADT + docetaxel when funding is implemented? | allowed to switch to the triplet therapy if funding is implemented. The clinical expert suggested this decision would be based on patient preference and clinician discretion, but should be made within a restricted time frame (e.g., approximately 4 to 6 months). |
| **Funding algorithm** | |
| PAG noted that this is a complex therapeutic space with multiple lines of therapy, subpopulations, and competing products. Therefore, the development of a provisional funding algorithm may be required. | FMEC is in favour of the development of a provisional funding algorithm. |

ADT = androgen deprivation therapy; ARPI = androgen receptor pathway inhibitor; ARTA = androgen receptor-targeted agent; ECOG = Eastern Cooperative Oncology Group; FMEC = Formulary Management Expert Committee; G-CSF = granulocyte-colony stimulating factor; mCSPC = metastatic castration-sensitive prostate cancer; PFS = progression-free survival; RT = radiotherapy; SOC = standard of care.