DOCETAXEL ADDITION IN METASTATIC CASTRATE-SENSITIVE PROSTATE CANCER (ASPIRE)

Eligibility Criteria (see Section 3.0)

- All high volume or de novo low volume mCSPC
- ADT+/-ARSI ≤120 days prior to registration is allowed.
- ECOG PS 0 -2
- Candidate for docetaxel
- NGS results available

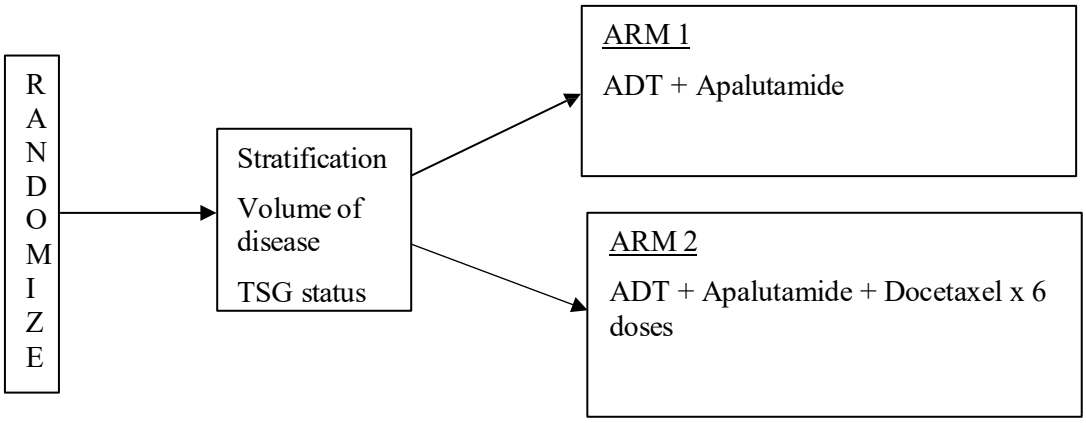
Required Initial Laboratory Values (See Section 3.2.9)

ANC	≥ 1500/mm^3
Hemoglobin	≥ 9.0 g/dL
Platelet count:	≥ 100,000/mm^3
Total Bilirubin:	≤ 1 x ULN
AST (SGOT)/ALT (SGT):	≤ 1.5 x ULN
Calc. Creatinine Clearance	> 30 mL/min

Schema

1 cycle =12 weeks

Treatment is to continue until disease progression or withdrawal. Patients will be followed until consent withdrawal or death.



mCSPC: metastatic castrate sensitive prostate cancer; ARSI: androgen receptor signaling inhibitor; TSG: tumor suppressor gene; ADT: androgen deprivation therapy; PS: performance status; NGS: next generation sequencing; ULN: upper limit of normal.

Please refer to the full protocol text for a complete description of the eligibility criteria and treatment plan.

3.2 Eligibility Criteria

Use the spaces provided to confirm a patient's eligibility by indicating Yes or No as appropriate. It is not required to complete or submit the following page(s). Please note that an optional signature line has been provided for use by institutions wishing to use the eligibility checklist as source documentation.

When calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test were done on a Monday, the Monday one week later would be considered Day 7.

___ **3.2.1 Documentation of Disease:**

Histologically or cytologically confirmed adenocarcinoma of the prostate without small cell histology**.**

___ **3.2.2 Must have had evidence of metastatic disease (AJCC M1 disease) based on conventional CT/MRI and/or bone scan. This will be defined as:**

- Bone metastases detected by CT, radionuclide ^{99}Tc- methylene bisphosphonate bone scan, or MRI as defined by PCWG3 criteria; OR
- Non-pelvic lymph node metastases (measurable lymph nodes above the aortic bifurcation; lymph nodes are measurable if the short axis diameter is ≥15 mm) detected on CT or MRI as defined by RECIST version 1.1. Subjects with regional lymph node metastases only (N1, below the aortic bifurcation) will not be eligible for the study; OR
- Visceral or soft tissue metastases detected on CT or MRI as defined by RECIST version 1.1. Soft tissue/visceral lesions are measurable if the long axis diameter is ≥10 mm
- Evidence of metastatic disease by PSMA-PET only and not visible by CT, radionuclide bone scan, or MRI will not satisfy eligibility criteria.

___ **3.2.3 No metachronous low-volume disease** (defined as recurrent metastatic disease after definitive treatment of prostate primary) and with ≤ 4 bone metastasis and no visceral metastasis on conventional imaging by CT, radionuclide ^{99}Tc-biphosphonate bone scan, or MRI).

___ **3.2.4 Next generation sequencing (NGS) results from any tissue based CLIA test must be available at the time of registration.** NGS from soft tissue or visceral lesion if available is preferred. NGS from bone or primary prostate will be accepted. Patients with failed NGS testing are not eligible.

___ **3.2.5 Prior Treatment**

- ADT (LHRH agonist/antagonist or orchiectomy) with or without first generation anti-androgen, or second-generation ARSI within 120 days of registration is permitted. No washout period will be needed for the first generation- androgen or ARSI prior to registration. Anti-androgen treatment is only permitted if used within 120 days of registration.
- **No prior chemotherapy for prostate cancer.**

___ **3.2.6 Age ≥ 18 years**

___ **3.2.7 ECOG Performance Status ≤ 2**

___ **3.2.8 Required Initial Laboratory Values:**

Absolute Neutrophil Count (ANC)	≥ 1,500/mm3
Hemoglobin	≥ 9.0 g/dL
Platelet Count	≥ 100,000/mm3
Total Bilirubin	≤ 1 x upper limit of normal (ULN) (Note: In subjects with Gilbert's syndrome, if total bilirubin is >1 × ULN, measure direct and indirect bilirubin and if direct bilirubin is ≤1 × ULN, subject may be eligible)
AST (SGOT)/ALT (SGT)	≤ 1.5 x upper limit of normal (ULN)
Calc. Creatinine Clearance	> 30 mL/min

___ **3.2.9 Comorbid Conditions**

- Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial.
- **Leptomeningeal metastases:** Patients with treated leptomeningeal metastases are eligible if follow-up brain imaging 30 days after CNS-directed therapy shows no evidence of progression.
- **HIV:** Patients with known HIV infection on effective anti-retroviral therapy with undetectable viral load within 6 months prior to registration are eligible for this trial.
- **Hepatitis B:** For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated.
- **Hepatitis C:** Patients with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are currently on treatment, they are eligible if they have an undetectable HCV viral load.
- No seizure or known condition that may pre-dispose to seizure (e.g. prior stroke within 1 year to randomization, brain arteriovenous malformation or condition requiring CNS surgery or radiation therapy).
- Patients with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification. To be eligible for this trial, patients should be lass II or better. Any condition that in the opinion of the investigator, would preclude participation in this study. Patients

with stable asymptomatic deep venous thromboembolism on stable anti-coagulation will be eligible.

- **Hypertension:** Subjects with uncontrolled hypertension as indicated by a resting systolic BP ≥160 mmHg or diastolic BP ≥100 mmHg despite medical management are not permitted to register.
- **Allergies:** Subjects with known hypersensitivity to any of the study drugs, or excipients in the formulation of the study drugs are not permitted to register.

___ **3.2.10 Concomitant Medications**

Chronic concomitant treatment with strong inhibitors of CYP3A4 is not allowed on this study. Patients on strong CYP3A4 inhibitors must discontinue the drug prior to registration on the study. See Section 8.1.9 for more information.

Chronic concomitant treatment with strong CYP3A4 inducers is not allowed. Patients must discontinue the drug 14 days prior to the start of study treatment. See section 8. 1.9 for more information.

Medications known to lower the seizure threshold (see list under prohibited meds) must be discontinued or substituted prior to study entry.

___ **3.2.11 Patient agrees to use a condom (even men with vasectomies) and another effective method of birth control if having sex with a woman of childbearing potential** or agrees to use a condom if having sex with a woman who is pregnant while on study drug and for 3 months following the last dose of study drug. Must also agree not to donate sperm during the study and for 3 months after receiving the last dose of study drug.

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