AFT 19 - A Phase 3 Study of Androgen Annihilation in High-Risk Biochemically Relapsed Prostate Cancer

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**Rationale/ Objective**

Randomized, open-label, three-arm, phase 3 study in men with biochemically recurrent prostate cancer and PSA doubling time ≤ 9 months at the time of study entry. Patients will be stratified by PSA doubling time (< 3 months vs. 3-9 months) and randomized in 1:1:1 fashion to one of three treatment arms:

1. Control arm consisting of degarelix monotherapy,
2. Experimental arm consisting of apalutamide in combination with degarelix, and
3. Experimental arm consisting of apalutamide, abiraterone acetate + prednisone, and degarelix.

Patients will be treated for a maximum duration of 52 weeks and then enter follow up phase until the time of PSA progression. Patients with PSA progression will be followed long term for development of castration resistance, first metastasis, and death.

**Primary**

- To compare PSA progression-free survival in each of the experimental arms versus the control arm of degarelix monotherapy.

**Secondary**

- To compare PSA progression-free survival in testosterone-evaluable population in each experimental arm versus the control arm. Testosterone-evaluable population includes all patients who achieve serum testosterone recovery to > 50 ng/dL with subsequent PSA measurements sufficient for evaluation.
- To compare the 36-month PSA progression-free survival rate in each experimental arm versus the control arm.
- To compare the time to recovery of serum testosterone to greater than 50 ng/dL in each experimental arm versus the control arm.
- To compare the time to castration resistance in each experimental arm versus the control arm.
- To compare the metastasis-free survival in each experimental arm versus the control arm.
- To compare the overall survival in each experimental arm versus the control arm.
- To characterize the safety profile in each treatment arm.
- To compare short-term and long-term health-related quality of life (HRQOL) in each experimental arm versus the control arm.
- To compare the quality-adjusted PSA progression- survival (PSA progression-free survival multiplied by utility score) of patients in each experimental arm versus the control arm.
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N = 504 patients

- Prior radical prostatectomy
- Biochemically relapsed disease with PSAADT <= 9 months
- No metastases (abdominal/pelvic nodes < 2 cm allowed)
- No prior ADT for biochemical relapse
- No ADT within 9 months of study entry

Randomize 1:1:1

Arm A: Degarelix

Arm B: Degarelix + Apalutamide

Arm C: Degarelix + Apalutamide + Abiraterone + Prednisone

Follow up for PSA Progression

Follow up for time to CRPC, metastasis-free survival and overall survival

Stratified by:
PSA doubling time (< 3 mos vs 3-9 mos)

12 months
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- Histologically confirmed prostate adenocarcinoma
- Prior radical prostatectomy
- Biochemically recurrent prostate cancer with PSA doubling time ≤ 9 months at the time of study entry
- Prior adjuvant or salvage radiation or not a candidate for radiation based upon clinical assessment of disease characteristics and patient co-morbidities
- Screening PSA > 0.5 ng/mL
- No definitive evidence of metastases on screening CT or MRI of abdomen/ pelvis and radionuclide whole body bone scan per the judgment of the investigator.
- Abdominal and/or pelvic lymph nodes measuring 2 cm or less in short axis diameter are allowed.
- Lesions identified on other imaging modalities (e.g. PSMA or choline PET) that are not visualized on CT and/or MRI or radionuclide bone scan are allowed.
- Equivocal lesions on bone scan should be followed up with additional imaging as clinically indicated.
- Screening serum testosterone > 150 ng/dL
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Study Number: AFT 19
Study Phase: Interventional Phase III
Clinical Indication: Biochemically recurrent prostate cancer after prior radical prostatectomy
ClinicalTrials.gov Identifier: NCT03009981
Number of Trial Patients: 504
Estimated Trial Duration: 6 years

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