Département d'oncologie
Plateformes du DO
Bâtiment Maternité PAV1
Avenue Pierre Decker 2
CH-1011 Lausanne

Indication	**Prostate**, métastatique hormonorésistant
Title	Orteronel maintenance therapy in patients with metastatic castration resistant prostate cancer and nonprogressive disease after first-line docetaxel therapy: A multicenter randomized double-blind placebo-controlled phase III trial
Protocol ID	**SAKK 08/11**
Phase	Phase III
Sponsor	SAKK (Swiss Group for Clinical Cancer Research)
Local Principal Investigator	Dr Dominik Berthold
Primary Objective	The main objective of this trial is to assess the impact of maintenance orteronel on disease progression and hence on quality of life (QL) in patients with metastatic castration-resistant prostate cancer (mCRPC) who have achieved at least disease stabilization after first line chemotherapy with docetaxel.
Inclusion/exclusion criteria	**Inclusion Criteria include the following :** • Patient has given voluntary written informed consent before performance of any study related procedure not part of normal medical care • Male patient 18 years or older • WHO performance status of ≤2 • Adenocarcinoma of the prostate, histologically or cytologically confirmed • Castration resistance: tumor progression after orchiectomy or during treatment with GnRH analogues (agonists or antagonists) • Metastatic disease, radiographically documented (CT/MRI, bone scan) • Total testosterone ≤ 50 ng/dL (≤ 1.7 nmol/L) • Non-progressive disease after docetaxel first-line treatment with a cumulative dose ≥ 300mg/m_2 o No evidence of progression on imaging according to PCWG2 and modified RECIST 1.1 criteria o PSA levels not elevated ≥ 25% AND at least 2 ng/mL above the nadir since start of docetaxel treatment • Non-surgically castrated patient agrees on ongoing use of GnRH analogues (agonists or antagonists) during the trial • Laboratory values as specified below o PSA ≥ 2 ng/mL o Potassium ≥ 3.5 mmol/L o Absolute neutrophil count (ANC) ≥ 1.5 x 10_9/L and

platelet count ≥ 100 x 10^9/L
- Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤ 2.5 x ULN
- Total bilirubin ≤ 1.5 × ULN (except for patient with Gilbert's disease)
- Estimated creatinine clearance using the Cockcroft-Gault formula > 40 mL/minute

- Planned start of trial treatment 3 to 6 weeks after last docetaxel administration
- Screening calculated ejection fraction of ≥ 50% or normal according to local standard by echocardiogram or by multiple gated acquisition (MUGA) scan.
- Baseline QL questionnaire completed
- Patient is able and willing to swallow study drug as whole tablet
- Patient compliance and geographic proximity allow proper staging and follow-up
- Patient, even if surgically sterilized (i.e., status post vasectomy)
  - Agrees to practice effective barrier contraception during the entire study treatment period and for 4 months after the last dose of study drug,
  - or Agrees to completely abstain from intercourse

Exclusion Criteria include the following:

- Prior therapy with aminoglutethimide, ketoconazole, orteronel, abiraterone or other modern CYP17 inhibitors
- Prior chemotherapy for prostate cancer within 12 months before enrollment except from docetaxel
- Retreatment with docetaxel after interruption of > 5 weeks
- Concurrent disease requiring higher doses of corticosteroid than the equivalent of 10 mg prednisone per day
- Known hypersensitivity to trial drug or hypersensitivity to any of its components
- Patient has received other investigational drugs within 30 days before enrollment
- Presence of a small cell component in histological specimen
- Radiotherapy within the last 2 weeks before expected start of the trial treatment
- Known history of central nervous system (CNS) or spinal cord metastases
- Current spinal cord compression
- Diagnosed or treated for another malignancy within 2 years of registration, with the exception of complete resection of basal cell carcinoma or squamous cell carcinoma of the skin, or any in situ malignancies

	• History of myocardial infarction, unstable symptomatic ischemic heart disease, ongoing arrhythmias of Grade ≥ 3 (NCI CTCAE version 4.0) or thromboembolic events (e.g., deep vein thrombosis, pulmonary embolism, or symptomatic cerebrovascular events) within 6 months prior to first dose of study drug. Chronic stable atrial fibrillation on stable anticoagulant therapy is allowed • New York Heart Association Class III or IV heart failure • ECG abnormalities of: o Q-wave infarction, unless identified ≥ 6 months prior to registration o QTc interval > 460 msec • Uncontrolled hypertension despite appropriate medical therapy (blood pressure (BP) of greater than 160 mmHg systolic **AND** 90 mmHg diastolic at 2 separate measurements no more than 60 minutes apart during the pretreatment evaluation). Note: patients may be rescreened after adjustment of antihypertensive medications. • Likely inability (e.g. due to a psychiatric disorder) to understand information on trial related topics, to give informed consent, to comply with the protocol, to fill in QL forms and to cooperate fully with the investigator and site personnel • Known gastrointestinal (GI) disease or GI procedure that could interfere with the GI absorption or tolerance of orteronel • Known active chronic hepatitis B or C, life-threatening illness unrelated to cancer, or any serious medical or psychiatric illness that could, in the investigator's opinion, potentially interfere with participation in this study