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Cabazitaxel Plus Prednisone for Patients With Metastatic Castration-resistant Prostate Cancer Previously Treated With a Docetaxel-containing Regimen − Interim Analysis Results From an Ongoing Compassionate-use Programme

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Background: The TROPIC trial (NCT00417079) demonstrated that cabazitaxel plus prednisone (CbzP) improves overall survival compared with mitoxantrone plus prednisone (MP) in patients with metastatic castration-resistant prostate cancer (mCRPC) who progressed during or after docetaxel (D)-based therapy (hazard ratio 0.70; $P < 0.0001$) (de Bono J, *et al. Lancet* 2010; 376:1147–1154). This survival benefit supported establishing a compassionate-use programme (CUP) to provide patients with mCRPC the opportunity to receive treatment with CbzP after therapy with a D-containing regimen in countries where cabazitaxel is not yet licensed.
Material and Methods: This single-arm CUP includes 13 countries and 71 centres, and enrolled patients with mCRPC who were previously treated with a D-containing regimen to receive treatment with CbzP (25 mg/m^2 every 3 weeks plus oral prednisone or prednisolone 10 mg daily given throughout the cycle).
Results: We report baseline characteristics and safety data from the first 123 patients who participated in this programme and received up to two cycles of CbzP in five active countries July 2010–February 2011. The median age (interquartile range [IQR]) was 67 years (63−71), 93% of patients had an ECOG PS 0−1 and 7% had a PS of 2. Patients had previously received a median cumulative dose (IQR) of D of 750 mg/m^2 (525–1200) and a median of 10 (6−15) cycles of D. During treatment with D, 46% of patients progressed. The median time from last dose of D to progression for those progressing after D was 1.4 months. The median time from last dose of D to inclusion was 3.2 months. A quarter of patients had measurable lesions and half had at least three metastatic sites, including bone 91%, regional lymph nodes 44%, distant lymph nodes 34%, pelvis 17%, liver 13% and lung 13%. Of patients included in the interim analysis, 94% received two cycles of CbzP. Adverse events associated with the first two cycles of CbzP occurred in 66% of patients. Rates of grade 3−4 haematological toxicities (adverse events) were: neutropenia 4%, febrile neutropenia 4% and leukopenia 2%. Prophylactic and therapeutic use of G-CSF was permitted in the CUP. All-grade non-haematological toxicities (in >10% patients) were: nausea 18%, diarrhoea 16% and fatigue 14%. Two treatment-related deaths were reported (one myelosuppression with complications and one sudden death).
Conclusion: The CUP interim analysis provides additional safety information about cabazitaxel for the treatment of mCRPC previously treated with a docetaxel-containing regimen in a more representative real-life patient population.

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Docetaxel and Curcuminoids Combination in Patients With Hormone Resistant Prostate Cancer − a Phase II Study

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Background: Prostate cancer is one of the major medical problems in the male population. Docetaxel, the first-line reference treatment in hormono-resistant prostate cancer (HRPC) induces a prostate-specific antigen (PSA) response in 45% of treated patients and an objective tumour response in 12%. Otherwise, some preclinical studies suggested that curcuminoids can inhibit tumour metastasis, invasion and angiogenesis and could reverse mechanisms involved in the acquisition of drug resistance. We wanted to potentiate docetaxel by curcuminoïds for HRPC in first line. Our previous phase I study showed the safety and the tolerability of curcuminoids in association with docetaxel for advanced breast cancers. For this reason, we have conducted a phase II study to assess the response of HRPC to docetaxel/curcuminoids combination.
Methods: Patients (n = 30) with progressing HRPC and rising PSA were enrolled to receive the experimental treatment. Docetaxel was given in standard conditions (75 mg/m^2 + prednisolone, 1h i.v infusion every 3 weeks for 6 cycles) in combination with curcuminoids orally at the dose of 6 g/day according to the schedule previously defined (7 days by cycle: d −4 to d +2). The primary endpoint was the response rate assessed by biological and paraclinical examinations. The secondary end points included safety, time to progression and compliance. Twenty nine patients were evaluable on PSA assessment and 15 on RECIST criteria.
Results: Twenty six patients received the treatment totality and 4 withdrew prematurely. No patient withdrew for toxicity (2 deaths and 2 PSA progression). A PSA response was observed in 17/29 patients (59%) (4 complete response and 13 partial response) observed rapidly (before the 3rd cycle) for 15 patients. The median time to subsequent PSA progression (TTP) was 6.0 months (n = 23/29). Six patients (40%) had a partial objective response and 9 (60%) a stable disease. The median TTP on targets was 6.87 months (n = 9/15). The regimen was well tolerated, with uncommon grade 3/4 toxicity; no adverse event was attributed to curcuminoids. Of 169 cycles, 150 (89%) were completed with perfect compliance.
Conclusions: These preliminary results are promising to improve the response rate of docetaxel in terms of both PSA decrease and objective response, with good tolerability and patient acceptability of curcuminoids. This justify the interest to conduct a randomized trial.

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Final Analysis of a Phase I/IIa Study With CV9103, an Intradermally Administered Prostate Cancer Immunotherapy Based on Self Adjuvanted mRNA

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Background: Safety and Efficacy Trial of a RNActive®-Derived Prostate Cancer Vaccine in Castrate-resistant Disease (CV-9103–001) sponsored by CureVac GmbH. A prostate cancer (PCA) vaccine containing the four antigens PSA, PSCA, PSMA and STEAP1 as self-adjuvanted full-length mRNAs (EudraCT No.: 2008–003967-37).
Material and Methods: 44 castrate resistant prostate cancer patients with metastatic disease and rising PSA were enrolled into a first-in-man phase I/II open, uncontrolled, multi-center, international, prospective, in-patient study. Study objectives in Phase I were determination of the recommended dose (RD) for exploration in the phase II part, assessment of safety of the trial regimen and evaluation of induction of immune response, in Phase II assessment of safety of the trial regimen, evaluation of induction of immune response and assessment of anti-tumour activity. Over a period of 23 weeks 5 vaccinations with CV9103 were administered.
Blood samples were taken before the first and two weeks after the 2nd to 4th vaccination. Immune response was assessed by ELISPOT (IFN-g), intracellular cytokine staining (IFN-g, TNFa), tetramer analysis (all ex vivo) or ELISA (PSA).
Recruitment is completed.
Results: In phase I, one dose limiting toxicity, urinary retention, was observed at the high dose level. A maximum tolerated dose was not defined. Overall, 389 AEs were reported, 282 were classified as related. Of these, most were injection site reactions or flu-like symptoms such as chills and fever. Of 21 serious adverse events, 7 were classified as related. In phase II, the high dose level was expanded by 32 patients. Immunomonitoring was possible in 33 of the 38 patients enrolled at the high dose level. Antigen-specific T-cells were detected in 79% patients. Importantly, 58% of the immunological responders reacted against multiple antigens. Immune responses were detected against all antigens regardless of cellular localization. The frequency of antigen-unspecific B-cells was