ODM-201, is a novel, oral androgen receptor (AR) inhibitor that has high antitumor activity in nonclinical models (Molaren et al. 2013) and in metastatic CRPC (mCRPC) patients (Fizazi et al. 2013).

Objectives and Methods

The ARADES trial was an open, multicentre, phase II/III trial with inter-subject dose escalation part and dose expansion part (Fizazi et al. 2013). Patients in the ARADES phase II expansion part were enrolled into three daily dose levels 200mg, 400mg and 1400mg (e.g. 200mg=100mg b.i.d.). The trial was undertaken in 23 centers in Europe and USA. We report here the long-term data in chemotherapy/CYP17i-naïve and post-chemotherapy/CYP17i-naïve mCRPC pts in the ARADES phase II/III trial (Figure 1, data cut-off Oct 4th 2013).

![Figure 1. Distribution of patients](image1)

Radiographic progression was evaluated either according to RECIST 1.1 for soft tissue or defined by at least 2 new lesions on bone scan compared to a prior scan. Serum PSA concentrations were measured at baseline, on day 28, at weeks 8 and 12, monthly from week 12 until month 9 and every 3 months thereafter, and at the end of the study. Changes in serum PSA were assessed as percentage change in PSA at 12 weeks from baseline. ITT population was used in all analyses.

![Figure 2. Percentage change in serum PSA at week 12 from baseline: (A) chemotherapy/CYP17i-naïve, (B) post-chemotherapy/CYP17i-naïve.](image2)

For CYP17i-naïve population a total of 77 pts were enrolled and used in safety and efficacy analyses: 42 pts were chemotherapy-naïve and 35 were chemotherapy-pretreated. The median age was 69 yrs (53-83 yrs) at baseline. At baseline 63 pts (82%) had bone lesions, 47 pts (61%) had soft tissue lesions and 12 (16%) had visceral lesions. The median PSA was 94 ng/mL (3-1294) and the CTC count was 5 or more per 7.5ml in 45% of the pts. Of these, 53 (69%) pts continued drug over 12 weeks (wks). The median time on study drug was 59 (95% CI: 38-110) wks.

The median time to PSA progression by PCWG2 was 72.3 (95% CI: 24.3–not reached) wks for chemotherapy-naïve pts, and 20.3 (95% CI: 16.9–26.1) wks for chemotherapy-pretreated pts. The median time to radiographic progression was not reached for chemotherapy-naïve (95% CI: 35.4–not reached), and was 20.4 (95% CI: 12.1–not reached) wks for chemotherapy-pretreated pts.

Treatment-emergent AEs occurred in 26/77 (34%) pts. Most commonly reported treatment-emergent AEs in the trial were asthenia/fatigue 8 (10%), decreased appetite 4 (5%), diarrhea 4 (5%), hot flushes 3 (4%), arthralgia 2 (3%), back pain 2 (3%), flatulence 2 (3%), gynaecomastia 2 (3%), headache 2 (3%), nausea 2 (3%), and myalgia 2 (3%), of which only 1 asthenia/fatigue event was grade 3, and none of the events were grade 4.

![Figure 3. PSA progression.](image3)

![Figure 4. Time to radiological progression.](image4)

Conclusions

This phase II/III trial demonstrates that ODM-201 exhibits encouraging antitumour activity in both chemotherapy-/CYP17i-naïve and post-chemotherapy/CYP17i-naïve men with mCRPC. ODM-201 had a favorable safety profile with no seizures being reported. These results support further investigation of ODM-201 in a large phase III trial in men with CRPC – a phase III trial in non-metastatic CRPC pts is currently under preparation.