Trial watch

PROGRESS FOR PROSTATE CANCER?

Three papers published in the *Journal of Clinical Oncology* indicate that a new treatment might be on the way for castration-resistant prostate cancer. Abiraterone acetate is a prodrug of abiraterone, which is an irreversible inhibitor of CYP17 (an enzyme required for androgen biosynthesis). Inhibition of CYP17 blocks androgen production in all tissues, including the prostate and adrenal glands, and as such might be more effective than drugs such as ketoconazole, which is an antifungal agent that at high doses blocks prostate and adrenal gland production of androgens.

In a Phase I study aimed at assessing safety, pharmacokinetics, and effects on steroidogenesis and prostate-specific antigen (PSA) levels, 33 men with progressive, castration-resistant prostate cancer who had not previously been treated with chemotherapy were recruited. Of these, 58% of patients had previously been treated with ketoconazole. Fasted or fed cohorts were given 250, 500, 750 or 1,000 mg per day. No dose-limiting toxicities were encountered, and hypertension grade 3 (12% of patients) and low concentrations of potassium in the blood (hypokalaemia; grade 3 in 6% and grade 4 in 3% of patients) were the most frequent serious toxicities. At week 12, 55% of patients had a >50% reduction in PSA levels. These data further support the move to Phase II trials: data from these trials have also been published.

To try and reduce the incidence of hypokalaemia and hypertension one Phase II study assessed the effect of giving abiraterone acetate with low-dose prednisone. Fifty-eight men with progressive, castration-resistant disease in which treatment with docetaxel-based chemotherapy had failed were treated with 1,000 mg of abiraterone acetate daily and 5 mg of prednisone twice daily. Twenty-seven patients had also been previously treated with ketoconazole. A >50% decline in circulating PSA levels was observed in 36% of all patients, and partial responses according to response evaluation criteria in solid tumours (RECIST) were seen in 4 of 22 patients with evaluable lesions. No grade 4 toxicity events were evident in the cohort, and the incidence of hypertension and hypokalaemia was reduced. Therefore, adding prednisone to Phase III trials of abiraterone acetate is recommended.

A further Phase II trial that was aimed at assessing the effect of abiraterone acetate in docetaxel-treated patients with castration-resistant prostate cancer has also reported positive findings. Of 47 patients treated with 1,000 mg per day of abiraterone acetate, 68% showed a >30% decline in PSA levels, 51% a >50% and 15% a >90% decline. Partial responses according to RECIST were seen in 8 of 27 patients with disease that could be assessed.

ORIGINAL RESEARCH PAPERS Ryan, C. J. *et al.* Phase I clinical trial of the CYP17 inhibitor abiraterone acetate demonstrating clinical activity in patients with castration-resistant prostate cancer who received prior ketoconazole therapy. *J. Clin. Oncol.* **28**, 1481–1488 (2010) | Reid, A. H. M. *et al.* Significant and sustained antitumour activity in post-docetaxel, castration-resistant prostate cancer with the CYP17 inhibitor abiraterone acetate. *J. Clin. Oncol.* **28**, 1489–1495 (2010) | Danila, D. C. *et al.* Phase II multicenter study of abiraterone acetate plus prednisone therapy in patients with docetaxel-treated, castration-resistant prostate cancer. *J. Clin. Oncol.* **28**, 1496–1501 (2010)