EudraCT Clinical Trial Results: Secondary Endpoint (endocrine impact of abiraterone acetate)

EudraCT number	2007-003240-30
Protocol number	CR9304-21
Protocol title	A Cancer Research UK Phase I/II Open Label Study to Evaluate the Safety, Endocrine Effects and Anti-tumour Activity of Abiraterone Acetate (CB7630) in Patients with Oestrogen (ER) or Androgen Receptor (AR) Positive Advanced or Metastatic Breast Carcinoma.
Sponsor	Cancer Research UK 407 St John Street, London, United Kingdom, EC1V 4AD
End of Trial date	04 June 2016

For the purpose of posting clinical trial results for the Cancer Research UK clinical trial CR9304-21 to the European Clinical Trials Database (EudraCT), the following text summarising the endocrine impact of abiraterone acetate from the trial has been extracted from the approved Clinical Study Report (Version 1.0, dated 30 September 2016):

Secondary endpoint: endocrine impact of abiraterone acetate

Blood samples were collected pre-treatment and during the trial for all patients who received abiraterone acetate in the Phase I and Phase II parts of the trial, for the analysis of the endocrine impact of abiraterone acetate. The endocrine impact was assessed by measuring the levels of oestradiol [oestradiol-17 beta, E2], androstenedione, testosterone, DHEA-S and corticosterone for patients in the Phase I and II parts of the trial; oestrone, 17 OH progesterone, SHBG and DHEA for patients in the Phase I part of the trial only and oestrone sulphate for patients in the Phase II part of the trial.

Phase I

In the Phase I part of the trial, all 25 patients (100%) treated with abiraterone acetate provided samples for the quantification of the nine separate analytes described above. Overall, all analytes apart from SHBG demonstrated consistent time dependent changes. Progesterone showed a clear dose dependent increase with a variable time to peak across the four doses tested. Corticosterone also produced an increase with a variable time to peak post-abiraterone acetate administration. Oestradiol, oestrone, testosterone, androstenedione, DHEA and DHEA-S all produced a consistent and marked reduction in levels of analyte, post drug administration on Cycle 1 Day 1 and remained at low levels when the last measurement was taken during the Off-Study assessment.

Abiraterone acetate demonstrated dose dependent efficacy that correlated with the suppression of hormone levels. Additionally, at the highest dose investigated (2000 mg abiraterone acetate), oestradiol, testosterone, DHEA and DHEA-S were all suppressed to below the lower limit of the analytical procedure used for quantification in five out of five patients.

Phase II

In the Phase II part of the trial, 44 (88%) of the 50 patients treated with abiraterone acetate provided samples for the quantification of the six separate analytes described above. Testosterone and DHEA-S levels were suppressed below (or close to) the limit of detection in all patients. Levels of oestradiol, oestrone sulphate and androstenedione were also suppressed on treatment with the Phase II dose of abiraterone acetate (1000 mg); however levels of oestradiol were not completely suppressed in five patients from the ER+ (any AR status) cohort. Endocrine treatment with steroidal agents immediately prior to trial entry may be an explanation for the apparent incomplete suppression of oestrogens in some patients due to interferences in the immunoassay caused by molecules of a similar molecular structure. Corticosterone levels rose, as expected, in response to treatment with abiraterone acetate, except in three patients.

Blood samples were also analysed for cortisol, LH and FSH to determine the endocrine impact of abiraterone acetate on the pituitary-adrenal-gonad endocrine axis. There was no consistent evidence for either a time or dose dependent effect of abiraterone acetate on cortisol, LH or FSH.