7. Clinical trials

Main current application of NP is in clinical trials of new drugs. Designed on the basis of size ($\alpha$) and power (1-$\beta$). Typically $\alpha = 0.05$ (two-sided test), and 1-$\beta = 0.80$. Regulators check this before approving a trial design.

Abiratone acetate plus prednisone versus placebo plus prednisone in chemotherapy-naive men with metastatic castration-resistant prostate cancer (COU-AA-302): final overall survival analysis of a randomised, double-blind, placebo-controlled phase 3 study

- Aim: improve survival in men with advanced prostate cancer who have not had chemotherapy
- Abiratone acetate (Zytiga) is a hormone treatment
- Patients randomly allocated to have drug or not

‘Power calculations’ carried out before trial started

- OS = overall survival
- ‘hazard ratio’ (HR) is ratio of monthly risks of death between those with and without drug
- Null hypothesis: HR=1
- Alternative hypothesis: HR=0.8 (20% risk reduction)
  - “Significance level= 0.04” : Type 1 error rate = 4%
  - "Power = 0.85" : Type 2 error rate of 15%.
Results (January 2015)

- 1088 patients randomised in 2009-2010
- After median follow-up of 49 months, 741 deaths observed
- 354 (65%) deaths in 546 patients in the abiraterone acetate group
- 387 (71%) deaths in 542 in the placebo group.

- Four months extra survival after 2.5 years treatment
  P-value = 0.0033
  Estimate of HR = 0.81 (bang on initial alternative hypothesis)
  95% confidence interval for HR is 0.70 to 0.93

"The list price of abiraterone is £2,930 for a 30-day supply of 120 tablets"