Statistics 1B Interludes

7. Clinical trials

Neyman-Pearson hypothesis testing

- 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.

Abiraterone 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
- Abiraterone 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.

\[ P-value = 0.0033 \]
\[ Estimate of HR = 0.81 \] [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.

Revised patient access scheme and more information allow NICE to recommend abiraterone for prostate cancer

5. The Committee concluded that the ICER (cost per quality-adjusted life year) for the one prior chemotherapy subgroup would be more than the manufacturer’s estimate of £46,800 per QALY gained, but less than £50,000 after taking into account the discount agreed between the manufacturer and the Department of Health.

6. The list price of abiraterone is £2,930 for a 30-day supply of 120 tablets. It is taken as a single dose of 1 g per day, taken as four 250-mg tablets. The manufacturer of abiraterone (Janssen) has agreed a revised patient access scheme with the Department of Health which makes abiraterone available at a discounted price. The size of the discount is commercial in confidence at the request of the manufacturer.