Propositions

to uphold the thesis

Prostate Cancer: Prognostic Factors, Markers of Outcome and Design of Clinical Trials

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1. PSA progression is a sensitive prognostic factor for overall survival in advanced prostate cancer. It is however not extremely specific. Competing causes of death might in part explain part of the low specificity (*This Thesis*)

2. Time to PSA progression is not statistically validated as a surrogate for overall survival in metastatic prostate cancer patients treated with Casodex. *(This Thesis)*

3. To shorten the duration of clinical trials in advanced prostate cancer, time to PSA progression could efficiently be used as an intermediate, though not definitive endpoint, to take interim decisions regarding the future conduct of a phase III trial. (*This Thesis*)

4. In patients presenting with pT2-3 N0 prostate cancer and pathological risk factors, adjuvant radiation therapy significantly prolongs biochemical progression-free survival in all subgroups, however the benefit is less for patients with negative surgical margins. Whether treatment will delay long term clinical relapse in all groups is at present unknown. *(This Thesis)*

5. Quality of life at baseline affects overall survival in patients with metastatic hormone refractory prostate cancer. We would not recommend the use of quality of life items in the routine baseline assessment of a patient's prognosis. (*This Thesis*)

6. PSA response should not be used as an endpoint for phase II trials in hormone refractory prostate cancer in absence of pre-clinical or clinical evidence elucidating the relationship between the impact of the studied drug on the PSA expression level and its impact at the tumor level.

7. To statistically demonstrate the validity of PSA endpoints as surrogate for long term endpoints is likely to remain an extremely difficult undertaking, even using modern statistical techniques.

8. The failure of some clinical trials is due to their design: just select the wrong endpoint. The so called "success" of some clinical trials is due to their design: just pick the wrong endpoint.

9. How to lie with statistics? If you did not find significant differences, look again.

10. Statistics are a modern and rationale type of soothsaying.

11. There are domains in life where gender equality is inappropriate and even some level of machismo may be appropriate.

Rotterdam, 25 January 2006
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