

### Borstkliniek Voorkempen



# Are patients better treated in clinical trials?



YES - NO

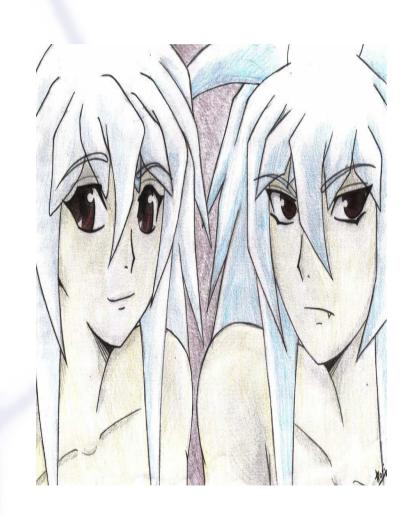
D. VERHOEVEN





# not the same as...,similar but so different!

- Are patients treated well in clinical trials?
- Must we include patients in clinical trials?



### **ASCO**

- "Treatment in a clinical trial is often cancer patient's best option"
- Political statement to increase accrual and third party payment



# US National Comprehensive Cancer Network

- Position with patients and doctors :
  - "the best management for any patient with cancer is in a clinical trial"
  - <u>www.nccn.org/patients</u>guidelines/breast/index.html#/40/

### Definition of a clinical trial

Clinical trials are experiments with as purpose:

- determine the value of a treatment
- 2. key components
  - Results
  - Answers to questions
  - Society and company driven





### Right of the patients

- Good medicine everywhere
- To have a superior physician
- Clinical trials not available everywhere
  - No trials
    - 95% patients
    - 40% children
- Fear to become a guinea pig
- Informed consent



### Phase I trials

- Clinical benefit minimal (perhaps growing?)
- Competition for patients and inclusion between centres
- Independent ethical considerations
- Much examinations and hospital visits
- Knowledge of palliative care can be critical



# Selection criteria for phase 1 trial

- AIM: toxicity and dose finding of a new drug
- Challenging criteria
  - 90 day mortality: 14%
  - 0,5% toxic death



### Phase 3 study

- AIM: to answer questions
  - Conventional versus new, promising treatment

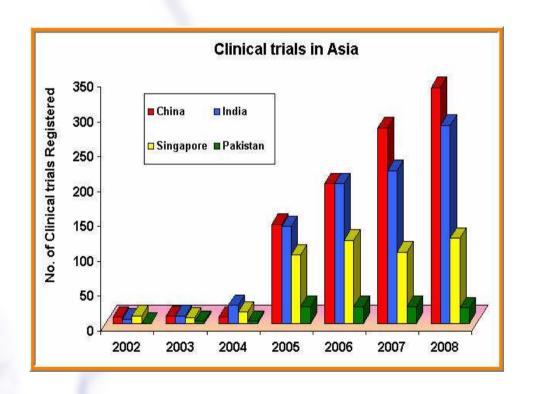


- Promising treatment can be inferior, more toxic (or more costly)
  - Herceptin studies
  - ALTO study
  - Beth study



## Clinical Trials in developing countries

- Growing market
- Rules and ethics less restrictive
- Lower cost and method to obtain new drugs



### Regulations of clinical trials

- Bureaucracy
- Stopping rules
- Clear endpoints
- GCP <u>NOT</u> in function of a company!
- Value of informed consent
  - Research biopsies in Clinical Trials
- Benefit patient comes first





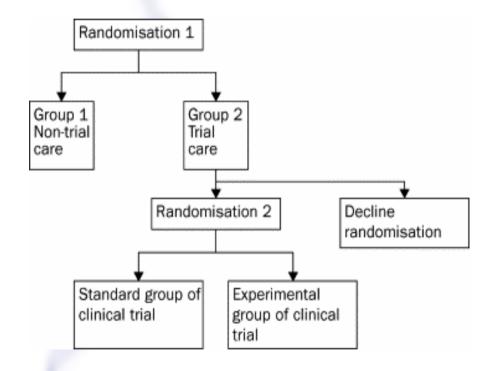
#### Less Burdens... More time for you and your business





## Comparison of outcomes in cancer patients treated within and outside clinical trials: conceptual framework and structured review, Peppercorn et al ,2004,Lancet

- Large retrospective study (only ethical way)
- Conceptual framework for comparison of trial and non trial patients
- Search of the medline
- 26 comparisons from 24 published trials



## Possible reasons for improved outcome?

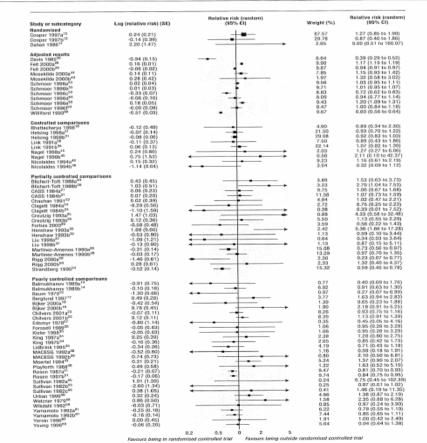
- Experimental treatment effect
- Participation effect
- Prognostic favourable subset
- Method of data gathering
- Publication bias
- => Very little unbiased evidence of outcome improvement is available

## Systematic review to determine whether participation in a trial influences outcome, Vist G, 2005, BMJ

Pape

Results of dichotomous main outcomes: trial versus non-trial participation

Comparison of mortality :trial versus non-trial participation



Relative risk (random) Relative risk (random) Weight (%) (95% CI) Log (relative risk) (SE) (95% CI) Study or subcategory Adjusted mortality 0.39 (0.29 to 0.52) Davis 1985<sup>26</sup> 13.00 0.94 (0.91 to 0.97) Felt 2000x<sup>20</sup> 1.17 (1.15 to 1.19) Felt 2000b<sup>26</sup> 0.16 (0.01) 13.16 11.95 1.00 (0.90 to 1.11 Schmoor 1996a<sup>51</sup> 0.00 (0.05) 1.18 (1.10 to 1.27 Schmoor 1996b<sup>50</sup> 0.17 (0.04) 12.57 Schmoor 1996c<sup>89</sup> -0.13 (0.09) 10:13 0.88 (0.74 to 1.05) 1.54 (1.28 to 1.85) Schmoor 1996d<sup>St</sup> 0.43 (0.09) 1.29 (1.17 to 1.43) Schmoor 1996e<sup>69</sup> 0.26(0.05)1.10 (0.93 to 1.31) Schmoor 1996/53 0.10 (0.09) Unadjusted mortality 6.87 CASS 1984a<sup>2</sup> 8.53 1.07 (0.73 to 1.59) CASS 1984b<sup>21</sup> 0.07 (0.20) 12.20 0.93 (0.70 to 1.22) -0.07 (0.14) Helsing 1998a<sup>3</sup> 0.92 /0.83 to 1.03 19.32 -0.08 (0.06) Helsing 1998b 0.95 (0.28 to 3.29) -0.05 (0.63) 1,31 Kieler 1998<sup>33</sup> King 1997a<sup>34</sup> 0.25 (0.39) 1.28 (0.60 to 2.75) 0.85 (0.42 to 1.73) King 1997b<sup>3</sup> -0.16 (0.37 0.71 (0.43 to 1.18 Lidbrink 1995<sup>35</sup> -0.34(0.26)3.28 (0.22 to 49.81) 1.19 (1.39) Link 1991a<sup>36</sup> Link 1991b36 0.00 (1.97) 7.88 1.37 (0.90 to 2.07) Moentel 1984<sup>©</sup> 0.31(0.21)0.84 1.27 (0.27 to 6.06) Nagel 1998a<sup>45</sup> 0.24 (0.80) 0.23 2.11 (0.10 to 42.37) Nagel 1998b<sup>45</sup> 0.75 (1.53) 1.16 (0.61 to 2.19) 0.15 (0.32) 4.24 Nicolaides 1994a<sup>48</sup> 1.27 0.32 (0.09 to 1.12) -1.14 (0.64) Nicolaides 1994b45 1.63 (0.52 to 5.10) 0.49 (0.58) Playforth 1988<sup>4</sup> -1.46 (0.61) 0.23 (0.07 to 0.77 Rigg 2000a<sup>6</sup> 1.32 (0.40 to 4.37) Rigg 2000b<sup>90</sup> 0.28 (0.61) 0.59 (0.45 to 0.78) -0.52(0.14)Strandberg 1995<sup>51</sup> 1.16 (0.06 to 22.10) 0.15 (1.50) Sullivan 1982a55 -0.90 (1.48) Sulfivan 1982b<sup>50</sup> 0.90 (0.04 to 20.82) Sullivan 1982c<sup>6</sup> 0.32 (0.24) 0.5 Favours being in randomised controlled trial Favours being outside randomised controlled trial

Fig 2 Results of dichotomous main outcomes in participants of randomised controlled trials and comparable non-participants who received the same or similar treatment.

## Patients do better at hospitals with clinical trials

- Clinical trials are performed in bigger hospitals
- Bigger hospitals have better teams
  - Physician leadership
  - Shared team goals
  - Administrative support
  - Credible feedback



### Conclusions



#### PRO

- Chance that new treatment will improve outcome
- Participation will improve medical care and follow-up

#### CONTRA

- Change that new treatment will NOT improve outcome
- More toxicity
- Feel like research subject
- More time spent in the study, administrative burden!
- Less attention to palliative care

# OH, Christoph...patients are treated well in clinical trials, TOO..., but...

- Do not use one-liners!
- Insufficient data to claim trial effect
- Enrol on the basis of improving treatment for future patients!



### Acknowledgement

• Steve Joffe, Professor Global Health, Dana-Farber Cancer Institute, Boston

