

SCT 30th Annual Meeting
Atlanta, GA, May 3-6, 2009

Are large, simple trials still feasible in 2009?

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Chalmers TC (1977)
Randomize the first patient.
N Engl J Med; **296**:107.

THOMAS C. CHALMERS
1917 - 1995



SIR RICHARD PETO

Peto, R (1995)

Large-scale randomized evidence: large, simple trials and overviews of trials.

J Clin Epidemiol; **48**: 23-40.

American Society of Clinical Oncology (ASCO), June 2005

- Three major trials showed the benefit, in terms of disease-free survival, of 1 year of Herceptin[®] for the adjuvant treatment of women with breast cancer
 - HERA (N = 5,081) : **HR = 0.54**
 - NSABP / NCCTG (N = 3,351): **HR = 0.48**

San Antonio Breast Cancer Symposium (SABCS), December 2005

- Another major trial confirmed the benefit of 1 year of Herceptin[®]
 - BCIRG (N = 3,222): **HR = 0.49**

San Antonio Breast Cancer Symposium (SABCS), December 2005

- Another major trial confirmed the benefit of 1 year of Herceptin[®]
 - BCIRG (N = 3,222): **HR = 0.49**
- A smaller trial showed a similar benefit with only 9 weeks of Herceptin[®]...
 - FinHer (N = 232): **HR = 0.42**

Congestive heart failures (CHF) when Herceptin[®] given after anthracyclines

In trials using anthracyclins and prolonged Herceptin[®]

- HERA : 1 vs. 29 CHF
- NSABP / NCCTG : 5 vs. 51 CHF
- BCIRG : 1 vs. 18 CHF

Agence Française de Sécurité Sanitaire des Produits de Santé (AFFSAPS), October 2005

The Agency allows French patients to receive adjuvant Herceptin[®] through a **Temporary Treatment Protocol** which « *does not replace regulatory approval, but provides patients with fast and controlled access to an innovative therapy until a full evaluation of this therapy by the health authorities is completed.* »



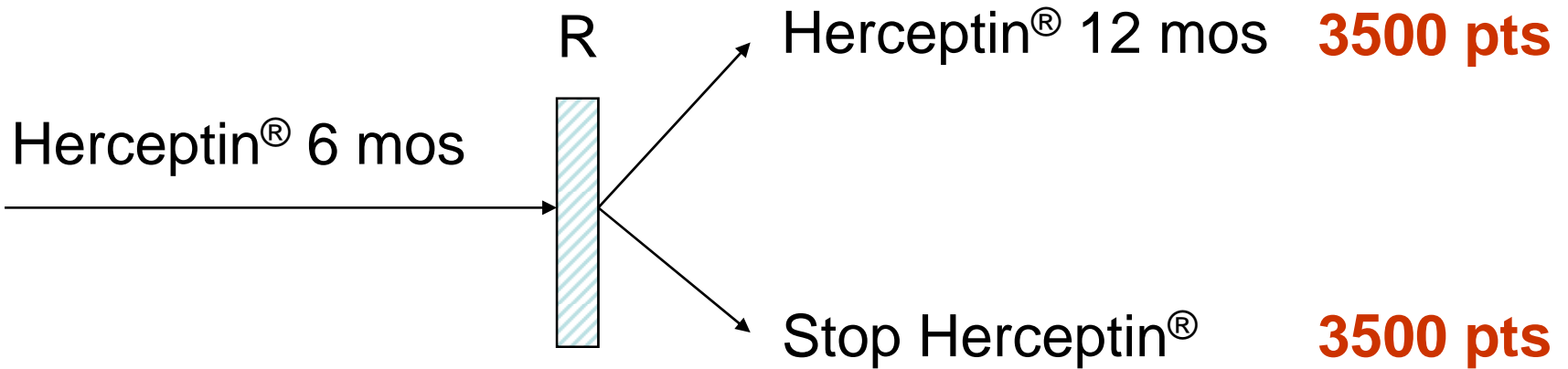
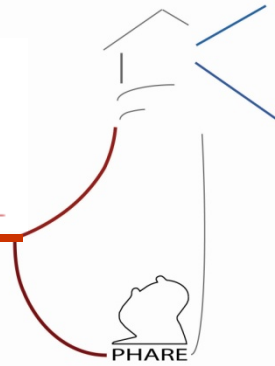
PHARE (*lighthouse*):

**Protocol for
Herceptin[®]
Adjuvant therapy with
Reduced
Exposure**

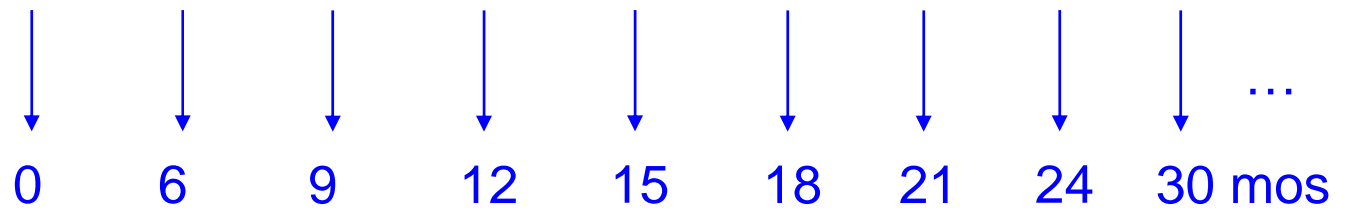
Design of PHARE



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Clinical exam
FEV-G
CA15-3



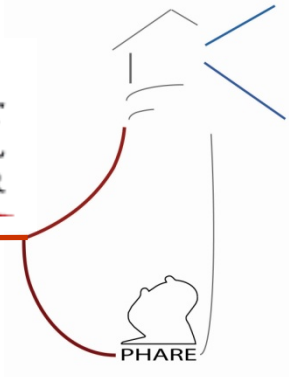
Mammography



Key features of PHARE

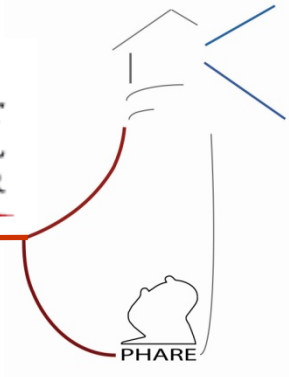


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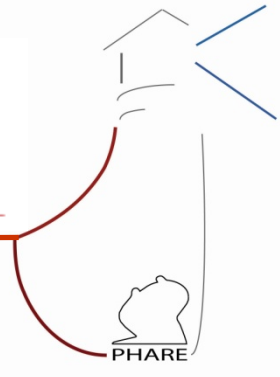
- All patients eligible

Key features of PHARE



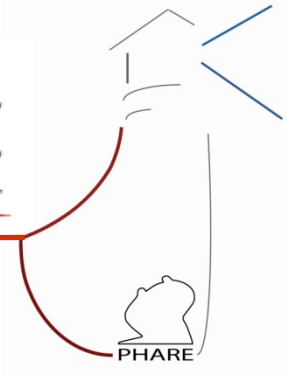
- All patients eligible
- Simple web-based randomisation

Key features of PHARE



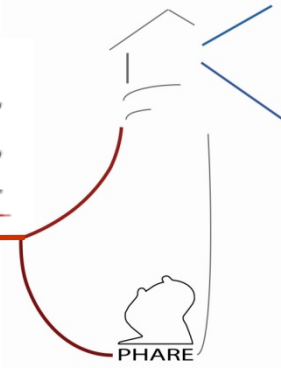
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- Simple web-based randomisation
- Simple follow-up (as in clinical practice)

Key features of PHARE



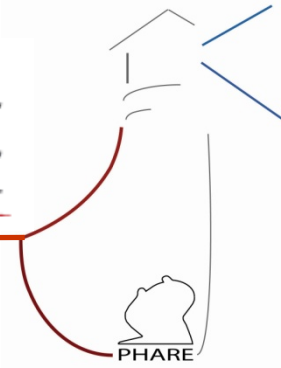
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Key features of PHARE



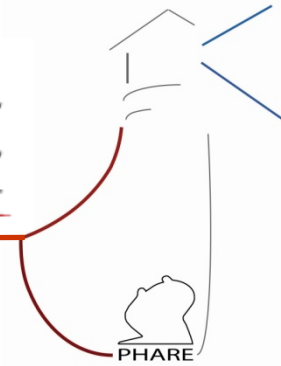
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Key features of PHARE



- All patients eligible
- Simple web-based randomisation
- Simple follow-up (as in clinical practice)
- Simple protocol (16 pages !)
- Simple Case Report Form (15 pages over 5 years!)
- All documents freely available from INCa's website

My main regret for PHARE...



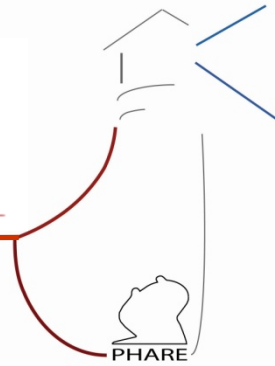
Inclusion in the PHARE trial was left to the discretion of treating oncologists. Today, about 25% of all potentially eligible patients in France are being randomized.

Prior to the approval of Herceptin[®] for marketing authorization, the French Ministry of Health could and should have granted full reimbursement of Herceptin[®] only for patients entering a clinical trial.

Acknowledgments for PHARE



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Operational Team:

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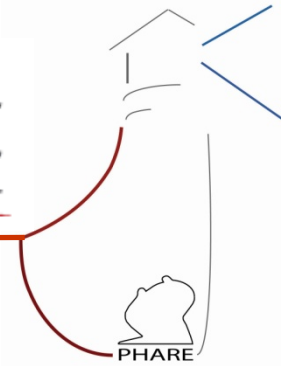
Principal Investigator: Xavier Pivot

Statisticians:

Xavier Paoletti

Marc Buyse (2005-2006)

A closing thought...



Human institutions are so imperfect by their nature that in order to destroy them it is almost always enough to extend their underlying ideas to the extreme.

Alexis de Tocqueville (1805 – 1859)

And so it goes for on-site monitoring, data checking, central review panels, QA, SDV, IRBs, IDMCs, SAPs, SOPs, etc, etc.