

THE INDEPENDENT CLINICAL TRIALS OF AIFA



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CLINICAL TRIALS ARE THE CORNERSTONE OF EVIDENCE BASED MEDICINE

- PHASE 1 TOLERABILITY
- PHASE 2 EFFICACY
- PHASE 3 BENEFIT-RISK

OVER 80% OF THESE TRIALS ARE
SUPPORTED AND EXECUTED BY
PHARMACEUTICAL COMPANIES

HUGE COMMERCIAL INTEREST MAY
MANIPULATE CLINICAL TRIALS INTRODUCING
A BIAS THAT AFFECTS THEIR OUTCOME

Association between competing interests and authors' conclusions: epidemiological study of randomised clinical trials published in the *BMJ*

Lise L Kjaergard, Bodil Als-Nielsen

Conclusions Authors' conclusions in randomised clinical trials significantly favoured experimental interventions if financial competing interests were declared. Other competing interests were not significantly associated with authors' conclusions.

Outcome of Studies by Support of Research

Outcome of Study	Studies Supported by a Drug Company (<i>n</i> = 40)	Studies Not Supported by a Drug Company (<i>n</i> = 112)
	<hr/> <i>n</i> (%)	
Favorable	39 (98)	89 (79)
Not favorable	1 (2)	23 (21)

Cho and Bero, 1996

	Outcome		
	Favourable	Neutral	Unfavourable
<i>Sponsorship v. outcome favouring SSRIs over TCAs: industry v. non-industry studies</i>			
Industry sponsor	13	4	0
Non-industry sponsor	1	2	3
<i>Sponsorship v. outcome favouring newest antidepressant: industry v. non-industry studies</i>			
Industry sponsor	25	7	1
Non-industry sponsor	1	2	4
<i>Sponsorship v. outcome favouring newest antidepressant: industry v. non-industry modelling studies</i>			
Industry sponsor	18	0	1
Non-industry sponsor	1	1	3

Baker et al., 2003

The fund for independent research at AIFA

(Art. 48, law 326/2003)

- Promotion of independent research is among the missions of AIFA
- Pharmaceutical companies are obliged to devote 5% of their promotional expenditure to a fund for independent research

The research topics funded by AIFA

- Relevance for the NHS
- Chronic limitations of private funding:
 - rarity of diseases
 - patients generally excluded from RCTs
 - drugs whose patent is expired

Studies that will likely not to be supported by pharmaceutical companies

The call for proposals

AREA 1

Orphan drugs for rare diseases and drugs for non-responders

AREA 2

Comparison among drugs and therapeutic strategies

AREA 3

Strategies to improve the appropriateness of drug use and pharmacoepidemiology studies

Peer review process

Each study protocol is evaluated by :

- 2 independent members who wrote a comment
- 1 discussant
- Through a process of consensus seeking, the committee arrives at a numeric rating for each proposal

The scoring system

- Final score: 1.0-5.0
 - 1.0-2.9: insufficient
 - 3.0-3.9: sufficient / low priority
 - 4.0-5.0: excellent / high priority
- Final ranking by topic and area

	2006	2007	2008
LETTERS OF INTENT	402	454	360
SELECTED PROJECTS	101	99	-
FUNDED PROJECTS	54	51	-

	N. OF PROJECTS	
	2006	2007
ORPHAN DRUGS	20	24
HEAD TO HEAD COMPARISONS	13	16
OUTCOME AND PHARMACOVIGILANCE	21	11
TOTAL	54	51
SUPPORT M €	35	31

EXAMPLES OF APPROVED PROJECTS

A prospective study on long-term outcome and potential usefulness of an intervention aimed at reducing adverse effects in patients with refractory epilepsy.

Evaluation of prescribing pattern and safety profile of antidepressant and antipsychotic medications in Italian general practice.

Pharmacist's outreach visits and new information formats: cluster and single-doctor randomised controlled trials for evaluating their feasibility and impact on knowledge, attitudes and prescribing practices of general practitioners in three Italian regions.

EXAMPLES OF APPROVED PROJECTS

A randomized, placebo-controlled study of the efficacy of low-dose aspirin in the prevention of cardiovascular events in subjects with diabetes mellitus treated with statins.

A randomized prospective, multicenter trial to compare the effect on chronic allograft nephropathy of mycophenolate mofetil versus azathioprine as the sole immunosuppressive therapy for kidney transplant recipients.

A randomized, controlled trial to evaluate the efficacy of low-molecular-weight heparin on pregnancy outcome of women with previous pregnancy complications.

EXAMPLES OF APPROVED PROJECTS

First adjuvant trial on all aromates inhibitors in early breast cancer.
A phase 3 study comparing anastrozole, letrozole and exemestane, upfront or sequentially.

A randomized clinical trial of trastuzumab optimization in patients with locally advanced and/or metastatic breast cancer overexpressing her 2 after a first-line chemotherapy plus trastuzumab.

Multicenter randomized controlled study of azathioprine versus interferon beta in relapsing-remitting multiple sclerosis.

TO ESTABLISH THE TOPICS OF THE YEARLY
CALL HEARINGS OF SCIENTIFIC SOCIETIES
AND STOCKHOLDERS ARE MADE.

A WEBB SITE IS AVAILABLE TO COLLECT
SUGGESTIONS

SOME TOPICS AIFA RESEARCH 2007

- EVALUATION OF BENEFIT-RISK PROFILE IN THE USE OF DRUGS IN PREGNANT WOMEN
- STUDIES ON BENEFIT-RISK PROFILE OF LONG TERM USE OF ANTIVIRAL DRUGS
- EVALUATION OF PSYCHO DRUGS COMBINED WITH PSYCHOTHERAPIES

SOME TOPICS AIFA RESEARCH 2007

- PHARMACOLOGICAL TREATMENTS OF DEPENDENCE INDUCED BY DRUGS OF ABUSE
- LONG TERM BENEFIT-RISK OF TREATMENTS FOR HYPOTHYROID PATIENTS

SOME TOPICS AIFA RESEARCH 2007

- COMPARISON OF CARDIOVASCULAR, ANTIDIABETIC AND ANTIASMATHIC DRUGS IN CHILDREN
- OPTIMIZATION IN THE USE OF ANESTHETICS AND MYORELAXANTS IN SURGERY
- STRATEGIES TO REDUCE FRACTURES IN ELDERLY

SOME TOPICS AIFA RESEARCH 2007

- EFFICACY OF CARDIOVASCULAR DRUGS
IN THE FEMALE POPULATION
- COMPARISON OF DRUGS IN THE TREATMENT
OF AUTOIMMUNE DISEASES
- OPTIMIZATION OF PAIN THERAPY IN NEOPLASTIC PATIENTS

SOME TOPICS AIFA RESEARCH 2007

- PREVENTION AND TREATMENT OF SEPSIS
- COMPARISON OF GASTROPROTECTIVE AGENTS IN ELDERLY
- COMPARISON OF THERAPEUTIC STRATEGIES IN PARKINSON