

SHORT COMMUNICATION ΒΡΑΧΕΙΑ ΔΗΜΟΣΙΕΥΣΗ

Clinical trial activity in Greece A case of missed opportunities?

K. Athanasakis,¹ M. Detsis,¹ B. Baroutsou,²
J. Kyriopoulos¹

¹Department of Health Economics, National School of
Public Health, Athens

²Hellenic Association of Pharmaceutical Companies
(SFEE), Athens, Greece

Η δραστηριότητα στο πεδίο των κλινικών
δοκιμών στην Ελλάδα: Μια ιστορία χαμένων
ευκαιριών

Περίληψη στο τέλος του άρθρου

Key words: Clinical trial, Human capital, Research and development

INTRODUCTION

Clinical trials (CTs) constitute the principal medium through which clinical research can be “translated” into innovative forms of treatment. Randomized CTs, the “gold standard” for clinical research, make a paramount contribution to evidence-based medicine and decision making, primarily in the clinical setting, leading to approval of new medications, extension of indications for use of medications, and formulation of clinical guidelines, but also supporting decisions on resource allocation, through the linkage of CTs with parallel economic evaluation.¹

CT research is a research and development (R&D) activity characterized by significant “positive externalities”, i.e., benefits that extend beyond the parties strictly involved in the conduct of the trial, and which apply to a wider societal perspective. Clinical research can positively influence economic growth² by contributing to a healthier workforce,³ enhancing the knowledge capital of the economy⁴ and

through commercial development.⁵ In a pragmatic context, CTs represent substantial capital inflow and investment, and utilization of a highly specialized workforce.

Bearing in mind the above, a survey was performed to document the volume and basic characteristics of CT activity in Greece in the year 2010. A further goal was to discuss the findings of the survey with respect to the country’s position in a globalized setting of clinical research.

METHOD

Primary research in the pharmaceutical setting is mainly undertaken by companies aiming to introduce prototype drugs to the healthcare market. These companies are represented in Greece by the Hellenic Association of Pharmaceutical Companies (SFEE). Thus, to obtain the necessary data for the analysis, a questionnaire-based survey was conducted among all the members of SFEE in the four months, December 2010 to March 2011. Each company was requested to return via a web-based platform one questionnaire per each interventional CT approved by the National Ethics Committee of Greece between 1st January and 31st December 2010. The questionnaire items focused on the phase of the trial, the planned duration (measured from the approval date until the final visit of the last patient), the number of patients to be recruited, the number and affiliation of recruiting sites, the therapeutic area of the agent under survey and the study budget. The first five questionnaires submitted served as a pilot for the final instrument; no major changes were deemed necessary following the pilot phase.

RESULTS

Fifty of the 65 SFEE members (77%) responded. Overall, the companies that participated in the survey had a total of 79 interventional CTs approved during 2010. The basic characteristics of these trials were as follows:

Phase of trial

The majority of CTs were phase-III (n=54, 68.3%), and of the remaining 25, 2 were phase-I (2.5%), 11 (14%) were phase-II and 12 (15.2%) were phase-IV trials.

Therapeutic area

The approved studies focused mainly on oncology (26.5%), endocrine disorders (16.4%), cardiovascular diseases (13.9%), diseases of the blood (10.3%), respiratory diseases (6.3%) and musculoskeletal disorders (6.3%).

Duration

The mean duration per trial was 36.9 ± 27.7 months, varying with the phase. Phase-III trials had a mean duration of 37.9 ± 26.7 months, while phase-II and -IV trials had a mean duration of 43.8 ± 38.3 and 20.5 ± 10.4 months, respectively.

Number and affiliation of recruiting sites

On average 4.75 ± 2.8 recruiting sites participated in each study. The participating sites were mainly affiliated with university (teaching) hospitals (46%) or National Health Service (NHS) hospitals (46%).

Each site recruited 6.3 ± 3.3 patients on average. The highest mean numbers of patients recruited per CT, according to the therapeutic area of the agent under investigation, were reported for circulatory diseases (53.2 patients per trial), respiratory diseases (52.2), central nervous system disorders (37.5) and endocrine disorders (25.8 patients).

Budget

The average budget per CT was 296,602 € (s.d. 389,948 €). Phase-II trials had the highest budget, 367,563.6 € (s.d. 688,885 €), followed by phase-III, 306,567.5 € (s.d. 365,845.5 €) and phase-IV, 234,515.5 € (s.d. 252,811.6 €).

DISCUSSION

The results of the analysis indicate fully developed CT activity in Greece, in terms of the qualitative characteristics of interventional trials, such as the phase, therapeutic area, numbers of recruiting sites and average budget per trial. What falls significantly short of the corresponding activity in other countries that are comparable from a population point of view is the absolute number of interventional CTs conducted in Greece. A simple search for open interventional trials in clinicaltrials.gov⁶ shows that the number of CTs conducted in Belgium or the Netherlands is three times higher than in Greece, in Austria and Switzerland more than twice as high, and in Hungary and the Czech Republic the number is over 175% higher. Similar findings have been reported by the European Medicines Agency for pivotal trials.⁷

This is strange, considering that there are no obvious obstacles in the country in terms of infrastructure or capacity; Greece's population (>11 million) provides a sufficient pool of patients, there is a fully developed and technologically equipped health care system with 136 public hospitals, 23 of which are tertiary, there are 7 medical schools with corresponding facilities and the country has the highest number of physicians per capital among OECD members.⁸

It is apparent that the reasons for this lag should be sought elsewhere, and specifically in the regulatory framework and the administrative procedures that outline the conduct of CTs. Major hurdles to the organization of CTs appear to be "bureaucracy" and the complexity of the approval process, mainly within the NHS, lack of acknowledgement of CTs as a key priority for research investment and the absence of a strong framework for health technology assessment (HTA).

If stakeholders wish to take advantage of the capacity and scientific expertise of the Greek system and benefit from the significant inflow of R&D capital that accompany CTs (an urgent necessity in view of the current economic crisis), rapid changes will be necessary to cover the distance lost. Definitive steps towards the acceleration of local administrative procedures are essential, specifically the adoption of one approval per trial, on a central level, fast-track approval of interventional CTs with already approved medicines in their registered indications and dosages, the pursuit of European harmonization on the principle of mutual recognition of approvals of CT applications to national pharmaceutical organizations, leading to the essential enhancement of HTA in Greece.

ΠΕΡΙΛΗΨΗ

Η δραστηριότητα στο πεδίο των κλινικών δοκιμών στην Ελλάδα: Μια ιστορία χαμένων ευκαιριών

Κ. ΑΘΑΝΑΣΑΚΗΣ,¹ Μ. ΔΕΤΣΗΣ,¹ Β. ΜΠΑΡΟΥΤΣΟΥ,² Γ. ΚΥΡΙΟΠΟΥΛΟΣ¹

¹Τομέας Οικονομικών της Υγείας, Εθνική Σχολή Δημόσιας Υγείας, Αθήνα, ²Σύνδεσμος Φαρμακευτικών Επιχειρήσεων Ελλάδας, Αθήνα

Αρχεία Ελληνικής Ιατρικής 2012, 29(6):734–736

Η παρούσα μελέτη στόχευσε στην αποτύπωση της δραστηριότητας στο πεδίο των κλινικών δοκιμών (ΚΔ) στην Ελλάδα με πληθυσμό αναφοράς το σύνολο των ΚΔ που εγκρίθηκαν από την Εθνική Επιτροπή Δεοντολογίας κατά το έτος 2010. Από την έρευνα συλλέχθηκαν στοιχεία για 79 ΚΔ, η πλειο-

νότητα από τις οποίες ήταν δοκιμές φάσης-III (68,3%), κυρίως στην Ογκολογία (26,5%), Ενδοκρινολογία (16,4%) και Καρδιολογία (13,9%), με μέσο προϋπολογισμό ανά εγκεκριμένη μελέτη τα 296.602 €. Με βάση διεθνή δεδομένα, ο αριθμός των ΚΔ που διεξάγονται στην Ελλάδα είναι σημαντικά χαμηλός. Το γεγονός αυτό στοιχειοθετεί ένα μείζον πρόβλημα χαμένων ερευνητικών ευκαιριών και μη αξιοποίησης του υγειονομικού προσωπικού της χώρας, το οποίο όμως μπορεί να αναιρεθεί με την άρση των «γραφειοκρατικών» εμποδίων έγκρισης, κυρίως σε επίπεδο νοσοκομείων, και την αναγνώριση της υψηλής σημασίας των ΚΔ ως ευκαιριών έρευνας και ανάπτυξης, ιδιαίτερα στη σημερινή οικονομική συγκυρία.

.....

Λέξεις ευρητηρίου: Ανθρώπινο κεφάλαιο, Έρευνα και ανάπτυξη, Κλινική δοκιμή

References

1. REED SD, ANSTROM KJ, BAKHAI A, BRIGGS AH, CALIFF RM, COHEN DJ ET AL. Conducting economic evaluations alongside multinational clinical trials: Toward a research consensus. *Am Heart J* 2005, 149:434–443
2. MURPHY K, TOPEL R. *Measuring the gains from medical research. An economic approach*. The University of Chicago Press, Chicago, 2003:41–74
3. ROSENBERG LE. Exceptional economic returns on investments in medical research. *Med J Aust* 2002, 177:368–371
4. SILVERSTEIN SC, GARRISON HH, HEINIG SJ. A few basic economic facts about research in the medical and related life sciences. *FASEB J* 1995, 9:833–840
5. SALTER AJ, MARTIN BR. The economic benefits of publicly funded basic research: A critical review. *Research Policy* 2001, 30:509–532
6. US NATIONAL INSTITUTE OF HEALTH. Clinical trials. Available at <http://clinicaltrials.gov> (accessed on 14.5.2012)
7. EUROPEAN MEDICINES AGENCY. *Clinical trials submitted in marketing authorisation applications to the EMEA: Overview of patient recruitment and the geographical location of investigator site*. Doc. ref.: EMEA/INS/GCP/58632/2009. EMEA, London, UK, 2009
8. ORGANIZATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT. OECD health data 2011 [CD ROM]. OECD, Paris, 2011

Corresponding author:

K. Athanasakis, National School of Public Health, 196 Alexandras Ave., GR-115 21 Athens, Greece
e-mail: kathanasakis@esdy.edu.gr

.....