UMIN-Clinical Trials Registry (UMIN-CTR)

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New York State Official Sues Drug Maker Over Test Data
Glaxo Challenged in the Use of Paxil for Children

By GARDINER HARRIS

In a novel claim testing the way that the $400 billion worldwide pharmaceutical industry is regulated, the New York State attorney general, Eliot Spitzer, sued the British-based drug giant GlaxoSmithKline yesterday, accusing the company of fraud in concealing negative information about its popular antidepressant medicine Paxil.

The civil lawsuit, filed in State Supreme Court in Manhattan, contends that GlaxoSmithKline engaged in persistent fraud by failing to tell doctors that some studies of Paxil showed that the drug did not work in adolescents and might even lead to suicidal thoughts. Far from warning doctors, the suit contends, the company encouraged them to prescribe the drug for youngsters.

"The point of the lawsuit is to ensure that there is complete information to doctors for making decisions in prescribing," Mr. Spitzer said in an interview. "The record with Paxil, we believe, is a powerful one that shows that GSK was making selective disclosures and was not giving doctors the entirety of the evidence."

GlaxoSmithKline officials issued a statement yesterday saying in part that the company "has acted responsibly in conducting clinical studies in pediatric patients and disseminating data from those studies."

On Wall Street yesterday, the American depository receipts of GlaxoSmithKline fell $1.38, or 3.2 percent, to $41.35.

Mr. Spitzer filed his suit at a time that the tendency of many drug companies to publicize only studies with positive results has come under increasing criticism. [Page C1.]

As he has done in actions involving the financial services and mutual fund industries, Mr. Spitzer is entering regulatory terrain that has been largely the preserve of the federal government, in this case the Food and Drug Administration. This time, though, he maintains that his suit is not a criticism of federal drug regulators.

"This isn't Harvey Pitt and the S.E.C.,” he said, referring to the former chief of the SEC.

Democrats Seek Rigor Aid Rice
Prehistory and History of CTR

(1976) Meta-analysis in education research
1993 The Cochrane Collaboration
2000.10 Declaration of Helsinki (Edinburgh)
2004.6 GSK Paxil (paroxetine) scandal
2004.9 ICMJE statement
2004.10 Ottawa statement
2004.10 WHO Int’l CT Registry Platform Meeting, NY
2004.11 Ministerial Summit on Health Research, Mexico
2005.1 IFPMA Statement
2005.4 WHO Technical Consultation on CT Registration Standards Meeting
2005.6 UMIN-CTR established
2008.10 Declaration of Helsinki (Seoul)
WHO Trial Registration Data Set
(Version 1.2.1)

1. Primary Registry and Trial Identifying Number
2. Date of Registration in Primary Registry
3. Secondary Identifying Numbers
4. Source(s) of Monetary or Material Support
5. Primary Sponsor
6. Secondary Sponsor(s)
7. Contact for Public Queries
8. Contact for Scientific Queries
9. Public Title
10. Scientific Title
11. Countries of Recruitment
12. Health Condition(s) or Problem(s) Studied
13. Intervention(s)
14. Key Inclusion and Exclusion Criteria
15. Study Type
16. Date of First Enrollment
17. Target Sample Size
18. Recruitment Status
19. Primary Outcome(s)
20. Key Secondary Outcomes
Symposium on clinical trial registration. At 25th Annual Conference of Japanese Society of Clinical Pharmacology and Therapeutics. 18 September 2004, Hamamatsu, Japan

The ICMJE statement effectively alerted Japanese investigators.
The Japanese perspective on registries and a review of clinical trial process in Japan

Hisako Matsuba¹, Takahiro Kiuchi², Kiichiro Tsutani³, Eiji Uchida⁴ and Yasuo Ohashi⁵

¹EPS Co., Ltd., Shinjuku-ku, Tokyo, Japan; ²University Hospital Medical Information Network, The University of Tokyo, Tokyo, Japan; ³Graduate School of Pharmaceutical Sciences, The University of Tokyo, Tokyo, Japan; ⁴Second Department of Pharmacology, School of Medicine, Showa University, Tokyo, Japan; ⁵School of Health Sciences and Nursing, The University of Tokyo, Tokyo, Japan

Introduction

The University Hospital Medical Information Network (UMIN) has been operating as Japan’s first clinical trial registry [1], known as UMIN-CTR, since June 2005 [2]. UMIN is a public information network for medical professionals, established within the national university system. Besides operating

- Domestic clinical trial information will be scattered to overseas’ clinical registries if Japan does not establish its own registry.

- Information should be provided in Japanese for Japanese people for easier understanding.
シンポジウムの内容は、VOD及びビデオファイルとして、インターネットでご覧いただけます。

UMIN臨床試験登録システムシンポジウム

概要：平成17年7月以降に開始された臨床試験については、臨床試験概要を公的な組織に事前登録しておかないと主要な有力医学雑誌が受理してくれなくなるなど、本シンポジウムでは、このような決定がなされた背景、臨床試験の登録の意義・役割、登録時の記載法に関する講演を行うとともに、UMINで平成17年4月よりサービス開始予定の臨床試験登録システム(CTR)の説明を行います。

日時：平成17年2月2日（水）15：00～18：00
会場：東京大学医学部附属病院旧中央診療棟3階 MINCS室
（地図等：東大病院/MNCS室）

●プログラム●

司会：木内貴弘（東京大学医学部附属病院UMINセンター）

1. 臨床試験登録について
Dr. A. Metin Gulmezoglu（Department of Reproductive Health and Research, WHO）（テレビ会議による中継）

2. 臨床試験登録の意義と役割について
津谷喜一郎（東京大学大学院薬学系研究科医薬経済学）

3. 臨床試験のデザインと論文への記載法 — 臨床研究登録を念頭において
大橋靖雄（東京大学大学院医学系研究科生物統計学）

4. UMIN臨床試験登録システムの概要
松葉尚子（東京大学医学部附属病院UMINセンター）

http://www.umin.ac.jp/ctr/symposium20050202.htm
What is UMIN?

• Established in 1989 as a cooperative organization for national university hospitals in Japan.

• It is sponsored by the Ministry of Education, Culture, Sports, Science and Technology (MEXT).
Cumulative number of registrations in JPRN
(Jun 2005 - Dec 2012)

Registration number

Date

Cumulative number of registrations in JPRN (Jun 2005 - Dec 2012)

UMIN-CTR

9,617 (82.1%)

Japic-CTI

1,993 (17.0%)

JMACCT

108 (0.9%)
Three Clinical Trial Registries in Japan

Jun 2005   UMIN-CTR
The University Hospital Medical Information Network-Clinical Trials Registry

Jul 2005   Japic-CTI
The Japan Pharmaceutical Information Center-Clinical Trials Information

Dec 2005   JMACCT
The Japan Medical Association Center for Clinical Trials

According to the policy, only one primary registry from each country is permitted.

To join the ICTRP network, a study group was granted by Ministry of Health, Labour and Welfare (MHLW) to establish an overall search portal for the three Japanese registries.

This was established in the National Institute of Public Health (NIPH) in October 2007.

After amendment of a part of registry systems in Japan to satisfy the requirements of ICTRP, the three registries and the search portal cooperate as a whole system and became a WHO-ICTRP Primary Registry (Japan Primary Registries Network, JPRN) in October 2008.
Japan Primary Registries Network (JPRN) search portal
http://rctportal.niph.go.jp/

Percentage in ICTRP (total number=206,877 as of 28 Jul 2013)

JPRN : 5.8% (11,917)
ClinicalTrials.gov: 68.3%(141,197)
UMIN-CTR is the main information source of clinical studies registered in JPRN, especially for academic (non-industry funded) studies.
UMIN臨床試験登録システム
UMIN Clinical Trials Registry (UMIN-CTR)

重要: 臨床試験登録システムご利用者様へ

URL変更のお知らせ

centerサーバへのDos攻撃対策と致しまして、平成22年5月1日より、centerサーバからuploadサーバに全面的に移行致しました。これにより、UMIN臨床試験登録システムのURLが以下に変更になりました。URLについても以下とおり変更の上、ご利用ください。

- URL変更前: https://center.umin.ac.jp/xxxx/xxxx/～
- URL変更後: https://upload.umin.ac.jp/xxxx/xxxx/～

重要: UMIN-CTR臨床試験登録番号のフォーマット変更について

2006年4月1日より、UMIN-CTRの臨床試験登録番号が、「Ｃ＋9桁の数字」(例: C0000013422)から、「UMIN＋9桁の数字」(例: UMIN0000013422)に変更になりました。なお、2006年7月31日までに出された番号はそのままご利用いただけます。

おしらせ
・UMIN-CTRがICMJEの基準を満たす登録サイトとして正式に認められました。
・厚生労働科学研究費における臨床試験登録の義務化について
・システム仕様の不具合等の修正に伴う登録データの修正について

UMIN臨床試験登録システム（UMIN-CTR）を利用する

Homepage of UMIN-CTR in Japanese
http://www.umin.ac.jp/ctr/index-j.htm
UMIN-CTR

UMIN Clinical Trials Registry (UMIN-CTR)

Searching trial information

- Search clinical trials
  - Search for disclosed clinical trials
- List of all clinical trials currently registered and disclosed.

Registering and updating trial information

- Entering (registering) your trial information for the first time.
- Incomplete registration
  - You can suspend your registration procedure in mid course and resume it by clicking here.
- Updating your registered trial information

Test use

- Test system – Practice registering and updating trial information

Homepage of UMIN-CTR in English
http://www.umin.ac.jp/ctr/index.htm
Registration policies in UMIN-CTR

• Objective of registration system
  
  (1) Preventing publication bias
  
  (2) Fulfilling ethical obligations
  
  (3) Providing registration and information in the Japanese language

• What can be registered in UMIN-CTR?
  
  All clinical studies (observational studies included)
  
  UMIN-CTR accepts registration of studies which are conducted outside Japan or registered in foreign registries.
Registration policies in UMIN-CTR 2

• Language
  Japanese site included : English & Japanese
  Japanese site not included: only English is required

• Registration items
  Based on WHO’s 20-item dataset and ICMJE requirements, UMIN-CTR adopts a set of 85 registration items according to the local needs of information.

• Approximately, 53 items are mandatory items while 32 items are optional items.
Clinical Trial Registration at ClinicalTrials.gov (May-Oct 2005)

Figure 2. New Trials Registered in ClinicalTrials.gov, According to Week.

The figure shows the number of new registrations per week (beginning on the date indicated) from mid-May through early October 2005. The “Industry” category includes all commercial data providers; the “Federal” category includes the National Institutes of Health and other U.S. federal data providers; and the “University” category includes universities, foundations, and other providers.

Zarin AZ, et.al. NEJM 2005; 353: 2779-87
Review of clinical trials registration in UMIN-CTR
(1 Jun 2005 - 18 Jan 2011, 4,774 registrations)
Review of clinical trials registration in UMIN-CTR (1 Jun 2005~ 18 Jan 2011, 4,774 registrations)

Country of recruitment
- Japan domestic: 4,688 (98.2%)
- Global (Japan included): 37 (0.8%)
- Foreign studies: 49 (1.0%)

Clinical trial/observational study
- Clinical trial: 4,045 (84.7%)
- Observation study: 729 (15.3%)
Review of clinical trials registration in UMIN-CTR
(1 Jun 2005-18 Jan 2011, 4,774 registrations)

Sponsor

- University (University hospital included) 2,764 (57.9%)
- Other hospitals 568 (11.9%)
- Research institute 51 (1.1%)
- Others (research group, etc.) 1,341 (28.1%)
- Pharmaceutical company 50 (1.0%)

Funder

- Self funding 2,360 (49.4%)
- Government 1,142 (23.9%)
- Non-profit foundation 464 (9.7%)
- Profit company 352 (7.4%)
- Outside Japan 24 (0.5%)
- Others (university department, etc.) 432 (9.0%)
## Source of funding

### Category of Organization (select one)

<table>
<thead>
<tr>
<th>Organization</th>
<th>Translation</th>
</tr>
</thead>
<tbody>
<tr>
<td>厚生労働省</td>
<td>MHLW(JAPAN)</td>
</tr>
<tr>
<td>文部科学省</td>
<td>MEXT(JAPAN)</td>
</tr>
<tr>
<td>農林水産省</td>
<td>MAFF(JAPAN)</td>
</tr>
<tr>
<td>経済産業省</td>
<td>METI(JAPAN)</td>
</tr>
<tr>
<td>その他の国の官庁</td>
<td>Other Japanese Government offices</td>
</tr>
<tr>
<td>地方自治体</td>
<td>Local Government</td>
</tr>
<tr>
<td>財団</td>
<td>Non profit foundation</td>
</tr>
<tr>
<td>営利団体</td>
<td>Profit organization</td>
</tr>
<tr>
<td>海外</td>
<td>Outside Japan</td>
</tr>
<tr>
<td>自己調達</td>
<td>Self funding</td>
</tr>
<tr>
<td>その他</td>
<td>Other</td>
</tr>
</tbody>
</table>

For a clinical study conducted without any financial support, categorize the funding source as “self funding” and register “none” in the funding source field (text item).
### “Sponsor” and “Funder”

<table>
<thead>
<tr>
<th>Sponsor (takes the responsibility for the initiation, management, and/or financing)</th>
<th>UMIN-CTR</th>
<th>Japic-CTI</th>
<th>JMACCT</th>
<th>Clinical Trials.gov</th>
</tr>
</thead>
<tbody>
<tr>
<td>實施責任組織 (Required)</td>
<td>実施者 (Required)</td>
<td>主要な実施責任組織 (Required)</td>
<td>Sponsor (Lead) (Required)</td>
<td></td>
</tr>
<tr>
<td>Co-sponsor (provides support for a clinical study with sponsor)</td>
<td>共同実施組織</td>
<td>共同開発者</td>
<td>共同実施組織 (Required)</td>
<td>Collaborator</td>
</tr>
<tr>
<td>Funder (provides funding for the clinical study)</td>
<td>研究費提供組織 (Required)</td>
<td>出資の出所 (研究費の名称)</td>
<td>研究費提供元 (Required)</td>
<td>Only “Funder type”</td>
</tr>
</tbody>
</table>
Review of clinical trials registration in UMIN-CTR
(1 Jun 2005-18 Jan 2011, 4,774 registrations)

Prospective/retrospective registration

- Recruitment first
  4,213 (88.2%)
- Registration first
  561 (11.8%)

Results publication

- Published
  183 (3.8%)
- Partially published
  244 (5.1%)
- Unpublished
  4,347 (91.1%)

Partially published (only interim analysis results)

Takahisa Sawada¹, Hiroyuki Yamada¹, Björn Dahlöf², Hiroaki Matsubara¹, for the KYOTO HEART Study Group¹

This article has been retracted by the journal. Critical problems existed with some of the data reported in the above paper. The editors of the European Heart Journal hereby retract this paper and discourage citations of it.
Effects of valsartan on morbidity and mortality in uncontrolled hypertensive patients with high cardiovascular risks: KYOTO HEART Study

Takahisa Sawada\textsuperscript{1*}, Hiroyuki Yamada\textsuperscript{1}, Björn Dahlöf\textsuperscript{2}, and Hiroaki Matsubara\textsuperscript{1} for the KYOTO HEART Study Group

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Received 4 August 2009; accepted 13 August 2009; online publish-ahead-of-print 31 August 2009

See page \textsuperscript{2427} for the commentary on this article (doi:10.1093/eurheartj/ehp364)

\begin{tabular}{|p{0.5\textwidth}|p{0.4\textwidth}|}
\hline
\textbf{Aims} & The objective was to assess the add-on effect of valsartan on top of the conventional treatment for high-risk hypertension in terms of the morbidity and mortality. \\
\hline
\textbf{Methods and results} & The KYOTO HEART Study was of a multicentre, Prospective Randomised Open Blind endpoint (PROBE) design, and the primary endpoint was a composite of fatal and non-fatal cardiovascular events (clinicaltrials.gov\textsuperscript{NCT00149227}). A total of 3031 Japanese patients (43\% female, mean 66 years) with uncontrolled hypertension were randomized to either valsartan add-on or non-ARB treatment. Median follow-up period was 2.7 years. In both groups, blood pressure at baseline was 157/88 and 133/76 mmHg at the end of study. Compared with non-ARB arm, valsartan add-on arm had fewer primary endpoints \textsuperscript{(83 vs. 155; HR 0.53, 95\% CI 0.42–0.72, \textit{P} = 0.00001)}. \\
\hline
\textbf{Conclusion} & Valsartan add-on treatment to improve blood pressure control prevented more cardiovascular events than conventional non-ARB treatment in high-risk hypertensive patients in Japan. These benefits cannot be entirely explained by a difference in blood pressure control. \\
\hline
\end{tabular}
Kyoto Heart Study was only registered in ClinicalTrials.gov in English. It is not registered in Japanese registries to be accessible in Japanese.
Retraction Watch

Does anesthesiology have a problem? Final version of report suggests Fujii will take retraction record, with 172

with 7 comments

Japanese investigators have concluded that Yoshitaka Fujii, an expert in postoperative nausea and vomiting whose findings drew scrutiny in 2000 but who continued to publish prolifically for a decade after, fabricated his results in at least 172 published studies.

That number nearly doubles that of the current unofficial retraction record holder, Joachim Boldt.

An inquiry by the Japanese Society of Anesthesiologists (JSA) has determined that Fujii, who was fired in February from his post at Toho University, falsified data in 172 of 212 papers published between 1993 and 2011. Investigators said they found no evidence of fraud in three of the papers, but could not determine whether the results reported in the remaining 37 were reliable.

Of the 172 bogus studies, 126 involved randomized controlled trials. Investigators believe this was not a coincidence:
Challenges posted for UMIN-CTR

• Clarification of funding source in registration

• Countermeasure against retrospective registration

• Establishment of a system for reporting study results in UMIN-CTR

• Accessibility of Japanese clinical studies in the Japanese language
Acknowledgements

• Dept. of Drug Policy & Management, Graduate School of Pharmaceutical Sciences, The University of Tokyo
  Fukuzawa Manabu 福澤 学
  Tang Wentao 唐 文濤
Thank you