LE NUOVE FRONTIERE DELLA EDITORIA ELETTRONICA

Eugenio Santoro
Laboratorio di Informatica Medica
Istituto Mario Negri

Bologna, 23 Novembre 2001
Analysis of prevalence of HIV-1 drug resistance in primary infections in the United Kingdom

Editorial by Little


Correspondence to: D Filey, PHLS Antiretroviral Susceptibility Reference Unit, Division of Immunity and Infection, University of Birmingham Medical School, Edgbaston, Birmingham B15 2TT
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Abstract

Objectives: To identify changes since 1994 in the prevalence of resistance to anti-HIV drugs in primary HIV-1 infections in the United Kingdom.

Design: Retrospective and prospective assessment of viruses obtained from people recently infected with HIV.

Setting: Multiple centres (patients enrolled in the UK register of seroconverters) and a single large HIV clinic (active case ascertainment).


Main outcome measures: Prevalence of key mutations associated with drug resistance in the reverse transcriptase and protease genes of HIV-1, by...
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Dr Sarah Rider, Dr John Fraser, Lecturer in HIV, St Mary's Hospital, Paddington, London
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On line first
Modulation of Endothelial Cell Growth Arrest and Apoptosis by Vascular Endothelial Growth Inhibitor

Jingyi Yu, Song Tian, Linda Medenly-Barlow, Li-Jin Chew, Andrew J. Hayes, Hongguang Pan, Guo-Liang Yu, and Lu-Yuan Li*

From the Department of Oncology (J.Y., S.T., L.M.-B., L.J.C., A.J.H., H.P., L.-Y.L.), Georgetown University Medical Center, Washington, DC, and Mendel Biotechnology (G.-L.Y.), Hayward, Calif.

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Vascular endothelial growth inhibitor (VEGI), a new member of the tumor necrosis factor family, is an endothelial-specific gene and a potent inhibitor of endothelial cell proliferation, angiogenesis, and tumor growth. We report here that VEGI mediates the following two activities in endothelial cells: early G1 arrest in Q0/G1 cells responding to growth stimuli, and programmed death in proliferating cells. G1/G0-synchronized bovine aortic endothelial cells were treated with VEGI before and after the onset of the growth cycle. When the cells were stimulated with growth conditions but treated simultaneously with VEGI, a reversible, early-G1 growth arrest occurred, evidenced by the lack of late G1 markers such as hypophosphorylation of the retinoblastoma gene product and up-regulation of the c-myc gene. Additionally, VEGI treatment led to inhibition of the activities of cyclin-dependent kinases CDK2, CDK4, and CDK6. In contrast, VEGI treatment of cells that had entered the growth cycle resulted in apoptotic cell death, as evidenced by terminal deoxynucleotidyl transferase labeling of fragmented DNA, caspase 3 activation, and annexin V staining, all of which were lacking in nonproliferating cells treated with VEGI. Additionally, stress-signaling proteins p38 and JNK were not as fully activated by VEGI as were preinhibitor levels as compared with proliferating populations. These findings suggest a dual role for VEGI, the maintenance of growth arrest and induction of apoptosis, in the modulation of the endothelial cell cycle.
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Mathematical simulation of hemodynamical processes and medical technologies

Nadiya Tatsyura, Victor V. Novytskyy, Prof., Ph. D., Ulyana B. Lushchyk, MD.

Istyna Scientific Methodological Medical Ultrasound Center

Kiev, Ukraine

ABSTRACT

Vascular pathologies constitute a significant part of human’s diseases and their rate tends to increase. Numerous investigations of brain blood flow in a normal condition and in a pathological one has created a new branch of modern medicine - angiozonography. It combines the information on brain angiography and on blood supply in a normal condition and in a pathological one. Investigations of a disease’s development constitute an important problem of modern medicine.

Cerebral blood supply is regulated by arterial inflow and venous outflow, but, unfortunately, in the literature available arterial and venous beds are considered separately. This causes an one-sided interpretation of atherosclerosis and discomitant encephalopathies. As arterial inflow and venous outflow are interrelated, it seems to be expedient to perform a complex estimation of arteriovenous interactions, prove a correlation dependence connection between the beds and find a dependence in a form of mathematical formula. The results will be observed clearly in the graphs.

There were 139 patients aged from 2 up to 70 examined in the “Istyna” Scientific Medical Ultrasound Center by means of a Logipod 2 apparatus manufactured by Kranzli fir, Germany using a technique of cerebral arteries and veins ultrasound location (invented and patented by Ulyana Lushchyk, State Patent of Ukraine N10252 of 1990011993). A clinical interpretation of the results obtained was performed.

With the help of this technique and ultrasound Dopplerography the blood flow in major head and cervical arteries was investigated. While performing a visual graphic analysis we paid attention to the changes of carotid artery (CA), internal jugular veins (IV) and supratrochlear artery’s (STA) hemodynamical parameters. Generally accepted blood flow parameters: FS - maximal systolic frequency and FD -
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Some journals have made up their minds whether or not they will accept submissions of articles that have appeared on preprint servers, although most have yet to decide their policy. We invite editors of journals not appearing in either list below to contact us with their policy.

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BJU
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European Journal of Public Health
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Gastroenterology
Heart
Journal of Accident and Emergency Medicine
Journal of Biological Chemistry
Journal of Clinical Pathology
Journal of Cognitive Neuroscience
Journal of Epidemiology and Community Health
Journal of Medical Genetics
Journal of Medical Screening
Lancet
Molecular Biology of the Cell
Molecular Pathology
Nature Medicine
Nature
Neural Computation
Occupational and Environmental Medicine
Pre-Hospital Immediate Care
Proceedings of the National Academy of Sciences
Quality in Health Care
Thorax
Tobacco Control (12 month trial)
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- American Journal of Clinical Nutrition
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Interferon alfa with or without ribavirin for chronic hepatitis C: systematic review of randomised trials

Lise L Kjaergaard, research fellow\textsuperscript{a}, Kim Krogsgaard, research director\textsuperscript{b}, and Christian Chud, chief physician\textsuperscript{a}

\textsuperscript{a}Copenhagen Hepato-Biliary Group, Copenhagen Trial Unit, Centre for Clinical Intervention Research, H.S Rigshospitalet, DK-2100, Copenhagen, Denmark, \textsuperscript{b}Clinical Research Unit, H.S. Hvidovre Hospital, DE-2830, Hvidovre, Denmark

Correspondence to: L L Kjaergaard kjaerg@rsh.nh.dk

Accepted: 23 July 2001

Editorial by Davis

Abstract

Objective: To assess the efficacy and safety of interferon alfa with or without ribavirin for treatment of chronic hepatitis C.

Design: Systematic review of randomised trials on interferon alfa plus ribavirin combination therapy versus interferon alfa. Patients were naive (not previously treated with interferon), relapers (transient response to previous interferon therapy), or non-responders (no response to previous interferon therapy).

Studies reviewed: Of 1153 references identified, 48 trials with 6385 patients met the inclusion criteria. Patients were followed to the end of treatment in 20 trials and in 28 trials for 12-96 weeks after treatment.

Main outcome measures: Virological response and morbidity plus mortality
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Prenatal diagnosis of Down's syndrome

A selection from thelancet.com...

Global peer-review initiative. The Lancet is inviting comments on a meta-analysis of ibn/ila inhibitor therapy in acute coronary syndromes (click here for pdf file, 200K), and send comments by e-mail to correspondence@lancet.com.

Criminal deterrence as a medical intervention? Targeted policing and increased rates of conviction, together with pre-school education and family support, "should be integrated into strategies for injury prevention", concludes Prof Jonathan Shepherd from the Violence Research Group, UK. Click here to read more.

Painters and the American West. "Cowboys and Indians on horseback, pursued and pursuing, galloping across vast plains studded with mountains and framed by endless skies: this is the familiar scenario of America's Old West." Read more about this exhibition now showing at the Joslyn Art Museum, Omaha, USA.
I registri di sperimentazioni cliniche
Registri di sperimentazioni cliniche - Cosa sono

• Database liberamente accessibili su Internet
• Forniscono informazioni sui protocolli degli studi clinici (in corso e conclusi)
• Possono essere interrogati per patologia, tipo di farmaco, nome dello studio, tipo di studio, ecc
• Si contano circa 300 registri sul web
Registri di sperimentazioni cliniche - obiettivi

• Descrivere lo stato dell’arte
• Incoraggiare la collaborazione tra gruppi di ricerca
• Prevenire la duplicazione di sperimentazioni cliniche simili
• Pubblicare anche gli studi negativi
• Ridurre i bias di pubblicazione
Esempi di registri di sperimentazioni cliniche
Physician Data Query (PDQ)

- National Cancer Institute
- Sperimentazioni cliniche in ambito oncologico (2,000 ongoing 10,000 concluse)
- Interrogazione per tutti i dati raccolti (trattamento, acronimo, nome dello studio, fase, popolazione studiata,..)
- http://cancernet.nci.nih.gov/pdq.html
CardioSource

- ACC, ESC, Elsevier
- 500 sperimentazioni cliniche in ambito cardiovascolare
- Interrogazione per trattamento, acronimo, nome dello studio, stato pubblicazione
- http://www.cardiosource.com
Stroke Trials Directory

• American Stroke Association, NINDS
• Sperimentazioni cliniche sull’ictus
• Interrogazione per trattamento, acronimo, nome dello studio, tipologia dello studio
• Integrazione con database farmaci e procedure
• http://www.stroketrials.org
**Stroke Trials**

Multicentre Acute Stroke Trial-Italy
MAST-I

Contact: Prof Livia Candolisa, Istituto di Clinica Neurologica, Via F Sforza 36, 20122
Milano, Italy

**Status**
Results published 12/96.

**Intervention(s)**

- **Aspirin (acute stroke)**
  - Antithrombotic agent; inhibits thromboxane A2
- **Streptokinase (Streptase®)**
  - Thrombolytic agent

**Purpose**
To determine whether, separately or together, streptokinase and aspirin have clinical benefits in acute ischemic stroke similar to those in acute myocardial infarction.

**Design**  
Study Design: Randomized, controlled, multi-center, open trial of 622 patients.

Inclusion Criteria: Acute ischemic stroke presenting within 6 hours of symptom onset. No clear indication for or contraindication against streptokinase or aspirin.

Exclusion Criteria: Intracerebral hemorrhage, severe coma without any purposeful motor response, rapid resolution of neurological symptoms, and any medical condition that would increase the risk of hemorrhage.
Stroke Interventions

Streptokinase
Streptase®, Kabikinase®

Phase
No clinical development in stroke

Action
Thrombolytic agent

Company
Streptase®: Hoechst Marion Roussel, distributed by Astra USA; Kabikinase®: Pharmacia & Upjohn AB

Status
US FDA approved for acute evolving transmural myocardial infarction, pulmonary embolism, deep vein thrombosis, arterial thrombosis or embolism, occlusion of arteriovenous cannulae. In stroke clinical trials, intravenous streptokinase increased stroke mortality or morbidity in several studies. No further development in stroke.

Source
Published reports.

Trials
Completed
Australian Streptokinase Trial (ASK)
Multicenter Acute Stroke Trial-Europe (MAST-E)
Multicentre Acute Stroke Trial-Italy (MAST-I)

Publications
Thrombolytic Agents, Systemic Patient Information (MEDLINEplus)
ClinicalTrials.gov

- National Institutes of Health, National Library of Medicine
- 5.000 sperimentazioni per qualunque area medica, finanziate da NIH
- Interrogazione per area medica, per malattia, per parole chiave, trattamento, fase, tipo di popolazione
- Integrazione con MedlinePlus
- http://www.clinicaltrials.gov
Observational Aspirin Use and CVD in the Physicians' Health Study

This study is completed.

Sponsored by

National Heart, Lung, and Blood Institute (NHLBI)

Purpose

To analyze existing data from the Physicians Health Study (FHS), a randomized primary prevention trial of low-dose aspirin and beta carotene conducted among 22,071 U.S. male physicians, to address questions concerning aspirin and cardiovascular (CV) disease that could not adequately be addressed during the randomized aspirin period.

Condition

Cardiovascular Diseases
Coronary Disease
Heart Disease
Myocardial Infarction
Cerebrovascular accident

MEDLINEplus related topics: Coronary Disease, Heart Attack, Heart Diseases (General), Stroke

Study Type: Epidemiology

Location and Contact Information

Cook, Nancy R. Boston, Massachusetts, United States

Study chairs or principal investigators
Study chair or principal investigator

Cook, Nancy R., Study Chair
Brigham and Women's Hospital, Boston, Massachusetts, United States

More Information

Results

The randomized aspirin component of the Physicians' Health Study (PHS) was terminated early, after 3 years, primarily because of the emergence of a statistically extreme 44 percent reduction of first myocardial infarction (MI) among those assigned to aspirin. As a result, there were insufficient numbers of strokes or cardiovascular disease (CVD)-related deaths to evaluate these end points definitively. The analysis collected data on self-selected aspirin use until the beta carotene component ended as scheduled after 12 years. Posttrial use of aspirin was assessed at the 7-year follow-up among 18,495 participants with no previous reported CVD. Randomized and posttrial observational results in the PHS were compared, and differences between these self-selecting aspirin and those not were examined. At 7 years, 59.5 percent of participants without CVD reported self-selected aspirin use for at least 180 days per year, and 20.3 percent for 0 to 13 days per year. Use was significantly associated with family history of MI, hypertension, elevated cholesterol levels, body mass index, alcohol consumption, exercise, and use of vitamin E supplements. In multivariate analyses, self-selected aspirin use for at least 130 vs 0 to 13 days per year was associated with lower risk for subsequent MI, no relation with stroke, and significant reductions in CVD-related and total mortality. The authors concluded that these associations between self-selected aspirin use and CVD risk factors increase the likelihood of residual confounding and emphasize the need for large-scale randomized trials, such as the ongoing Women's Health Study, to detect reliably the most plausible small to moderate effects of aspirin in the primary prevention of stroke and CVD-related death.

Publications that report on this study


Study ID Numbers 2010
NLM Identifier NCT00005403
Date study started April 1, 1982; Date Study Completed March 31, 2001
Last Updated September 21, 2000

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I meta-registri
meta-Randomized Clinical Trials (mRCT)

• Current Controlled Trials
• 11,000 sperimentazioni cliniche
• 21 registri internazionali
• Raccolta di un set minimo (comune) di informazioni da ogni registro
• http://controlled-trials.com
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☑ Alzheimer's Society
☑ British Heart Foundation
☑ Canadian HIV Trials Network (CTN)
☑ Cardiosource
☑ CTSU - trials being randomised by the Clinical Trial Service Unit, Oxford
☑ GlaxoSmithKline (access restricted to healthcare researchers & professionals only)
☑ HIVInSite Trials Search
☑ Hong Kong Health Services Research Fund
☑ Laxdale Limited
☑ Leukaemia Research Fund

Registers on other websites searchable via the mRCT
☑ CoP CURE (Association for the Cure of Cancer of the Prostate) - Temporarily Unavailable
☑ National Institutes of Health (NIH) - have allowed searches to include access to randomised trial records held within the NIH ClinicalTrials.gov website
Source of record: Cardiosource

Title of trial: Gruppo Italiano per lo Studio della Supravivenza nell'Infarto Miocardico - GISSI-3

Acronym: GISSI-3

Design/methodology: Randomized controlled trial.

Disease: Myocardial infarction (MI)

Purpose of trial: To evaluate the efficacy of a treatment with angiotensin converting enzyme (ACE) inhibitors and/or nitrates on 6-week mortality following acute MI; evaluation of the extent to which such a favourable effect on left ventricular (LV) function (measured at 6 weeks) if present, is maintained up to 6 months following the event; the evaluation is carried out on the combined endpoint of mortality and LV damage.

Status: published

Further information: The CardioSource trial records in the metaRegister were last updated on 21 February 2001. Click here to link to the CardioSource site where you can obtain full details of this trial. The registry of randomized cardiovascular clinical trials on CardioSource provides a unique resource containing more than 600 ongoing and recent trials, as well as a listing of major trials going back many years. The site requires registration; access to the clinical trials database (and several other services) is free.
INTERNATIONAL STANDARD RANDOMISED CONTROLLED TRIAL NUMBER (ISRCTN)

COMING SOON...

The International Standard Randomised Controlled Trial Number (ISRCTN) is a simple numeric system for the unique identification of trials worldwide. It will simplify the identification of trials and provide a unique number that can be used to track all publications and reports resulting from each trial.

Current Controlled Trials has offered to generate and record these numbers so that they are accessible via this website. Please contact us if you would like to receive further information about the ISRCTN scheme.

A brief introduction to the ISRCTN scheme has been prepared in French, German and Spanish, and other languages will be added.

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metaRegister of Controlled Trials

Introduzione a Current Controlled Trials e metaRegister of Controlled Trials

"La registrazione di tutte le sperimentazioni cliniche non può essere più messa in discussione" (BMJ e The Lancet, ottobre 1999).

A cosa può servire il metaRegister?

- Assistere nella pianificazione di nuovi trial
- Evitare l'inedito duplicazione della ricerca
- Favorire la collaborazione tra ricercatori
- Ottimizzare la distribuzione dei fondi per la ricerca
- Facilitare ai pazienti l'accesso all'informazione e favorire il loro reclutamento per la partecipazione alle sperimentazioni cliniche
- Migliorare le opportunità per la ricerca metodologica
- Ridurre le discrepanze tra protocolli originali dei trial e risultati successivamente pubblicati
- Redimensionare il bias di pubblicazione

A chi può essere utile il metaRegister?

Il sito Current Controlled Trials (http://controlled-trials.com) viene realizzato nell'ottobre del 1996 in risposta alla crescente domanda di maggiore trasparenza sulle sperimentazioni cliniche.

Il metaRegister of Controlled Trials (mRCT) aiuta a promuovere la disponibilità e lo scambio d'informazioni sui trial condotti in tutte le aree assistenziali affinché:

- Ricercatori e soggetti finanziatori evitino di duplicare la ricerca e sprecare ingenti quantità di risorse
- Le revisioni sistematiche e le meta-analisi identifichino eventuali bias di pubblicazione
- Pazienti e medici possano disporre di un'informazione dettagliata ed accurata sui trattamenti, così da informarne meglio le proprie decisioni.