New drugs, old drugs – dear drugs, cheap drugs

Bernard Hirschel, Jorge Garbino
Division des Maladies infectieuses, Hôpital cantonal universitaire, Genève, Switzerland

The current issue of SMW contains two articles dealing with anti-fungal drugs. K. Furrer et al. present data from a particularly difficult group of patients, i.e., those with bone marrow transplants needing cyclosporine at the same time as amphotericin B. Both of these drugs are nephrotoxic and impaired renal function was indeed observed: Mean serum creatinine concentration at discharge was 132 μmols/L in the group with both drugs, as compared to 96 μmols/L in the group receiving cyclosporine A only. However, that there was a difference is perhaps less remarkable than the fact that this difference was quite small, with no cases of end-stage renal failure and no case requiring dialysis in the combined-therapy group. The authors believe that this relatively favourable outcome was due to their method of administering amphotericin B deoxycholate by continuous 24 hour infusion (continuous ampho B).

Lipid formulations of amphotericin B are among the new antifungal drugs discussed by Groll et al. Echinocandin (Cancidas® – MSD) and voriconazole (Vfend® – Pfizer) are two others which have recently become available in the United States and parts of Western Europe. They are efficacious, have excellent pharmacokinetics and few side effects. However, their costs, however, are a problem. We currently have a patient with chronic granulomatous disease with a voriconazole-resistant aspergillus infection of the chest wall, being treated with liposomal amphotericin B (Ambisome® – Fresenius Kabi) and echinocandin (Cancidas®). These drugs cost approximately 20,000 Swiss francs per week. This is admittedly an extreme example – but most patients with systemic fungal infections are somewhat extreme.

Prices are easiest to compare between old and new preparations of amphotericin. 1 mg of amphotericin B (Fungizone® – BMS) deoxycholate costs 0.9 Swiss francs, or about 60 c. 1 mg of Ambisome® costs 10 times more, i.e., 9 Swiss francs per mg. Unfortunately, this is not all there is to the cost increase. Because of doubts about the bio-equivalence of traditional and liposomal amphotericin B, and because of the life-threatening nature of fungal infections in neutropenic patients, there is a tendency to give higher doses of Ambisome® (up to 5 mg/kg/d, compared to 0.5 to 1 mg/kg/d for amphotericin B deoxycholate). In addition, treatment of suspected infection is often empirical. Most patients with prolonged neutropenia have fever at some time and receive antibiotics. Why not antifungals in addition? The one thing which held back prescribers was the toxicity of amphotericin B deoxycholate. Ambisome® is less toxic [1], so that the tendency will be towards earlier administration in cases where fungal infection is possible, albeit neither likely nor proven. Higher price per mg times higher doses times more patients means that expenses for lipid formulations of amphotericin can easily multiply expenses for amphotericin B deoxycholate by a factor of 50.

I hear you say: “Why didn’t Furrer et al. do such a study?” The answer is money. Equivalence studies are notoriously difficult to do because for statistical reasons the number of patients enrolled has to be very high [3]. Costs for clinical studies vary, but a reasonable estimate for an equivalence study enrolling 500 to 1000 patients would be 5 to 10 million US$. Who provides the money for clinical research? In the vast majority of cases, it is the drug companies. They invest in studies which establish the value of new drugs and recoup their investment.
through sales during the lifetime of the patent. But who would invest in a study comparing liposomal with continuous amphotericin? Certainly not the manufacturers of Ambisome® or Abelcet®; they have all to lose and nothing to gain. And certainly not the manufacturers of amphotericin B, a cheap substance without patent protection; the costs of the study could never be recovered.

“But”, you object, “how about the public interest? The sickness funds and the Federal Social Insurance Office have most to gain from cheaper treatment; don’t they invest in cost-effective medicine?” The answer is No.

Let’s look at the sickness funds first. They have no tradition of furthering any research. By law, they must use the funds they receive for paying medical bills and for nothing else. They could spend money on research from what they receive for complementary (private, semiprivate) insurance. However if they wanted to do that, they would face another problem: Their investment in research is not patentable. Sickness fund A, if it paid for Furrer’s hypothetical equivalence study, might save some money, but so would sickness fund B who paid nothing. Here is a quote from a letter signed by E. David, the president of Helsana and a member of the Swiss parliament1: “This (financing research) is not the task of a medical insurance company, which has to compete in the market with other insurers.”

The Federal Social Insurance Office claims that they have no legal mandate nor any money for research into cost-saving measures, and recommends the Swiss Foundation for Health Promotion and the parent organisation of the sickness funds, Santé Suisse. However, the Foundation’s mission does not include financial health, and specifically excludes medical research, whereas Santé suisse claims they can only do something if the Federal Office provides the legal mandate – at which time even the most persistent researcher will be slightly discouraged. The more so because his sense of urgency is not shared by the officials he has approached; on the contrary, they consider his request a bother to be disposed of, not a mission to be accomplished. Why should he persist? Much easier to accept the offer to study some promising new antifungal drug, complete with invitations to symposia in nice places, and consultancy contracts of 2000 US$ per day.

Mind you, I am not criticising the drug companies here. They are doing their job: developing new drugs and selling them at a profit. What I am criticising are those people in health politics and health insurance who do not recognise their enlightened self-interest, do not realise that research into cost effectiveness will not occur without investment and continue the refrain: “that’s not my business”.

There are faint stirrings of what the French call a “prise de conscience”. The Swiss Council of Science and Technology has recently published a position paper on the state of clinical research in Switzerland, calling for action to increase education and career possibilities at university medical schools. The Swiss National Research Fund, so far almost exclusively involved in basic biomedical research, is planning to add a division of clinical research for its next budget period starting in 2004. It will be interesting to see how this proposal fares when resources are allocated. Don’t bet on it.

References


The many reasons why you should choose SMW to publish your research

**What Swiss Medical Weekly has to offer:**

- SMW’s impact factor has been steadily rising, to the current 1.537
- Open access to the publication via the Internet, therefore wide audience and impact
- Rapid listing in Medline
- LinkOut-button from PubMed with link to the full text website http://www.smw.ch (direct link from each SMW record in PubMed)
- No-nonsense submission – you submit a single copy of your manuscript by e-mail attachment
- Peer review based on a broad spectrum of international academic referees
- Assistance of our professional statistician for every article with statistical analyses
- Fast peer review, by e-mail exchange with the referees
- Prompt decisions based on weekly conferences of the Editorial Board
- Prompt notification on the status of your manuscript by e-mail
- Professional English copy editing
- No page charges and attractive colour offprints at no extra cost

**Editorial Board**

- Prof. Jean-Michel Dayer, Geneva
- Prof. Peter Gehr, Berne
- Prof. André P. Perruchoud, Basel
- Prof. Andreas Schaffner, Zurich (Editor in chief)
- Prof. Werner Straub, Berne
- Prof. Ludwig von Segesser, Lausanne

**International Advisory Committee**

- Prof. K. E. Juhan Airaksinen, Turku, Finland
- Prof. Anthony Bayes de Luna, Barcelona, Spain
- Prof. Hubert E. Blum, Freiburg, Germany
- Prof. Walter E. Haefeli, Heidelberg, Germany
- Prof. Nino Kuenzli, Los Angeles, USA
- Prof. René Lutter, Amsterdam, The Netherlands
- Prof. Claude Martin, Marseille, France
- Prof. Josef Patsch, Innsbruck, Austria
- Prof. Luigi Tavazzi, Pavia, Italy

We evaluate manuscripts of broad clinical interest from all specialities, including experimental medicine and clinical investigation.

We look forward to receiving your paper!

**Guidelines for authors:**

http://www.smw.ch/set_authors.html

**ALL manuscripts should be sent in electronic form, to:**

EMH Swiss Medical Publishers Ltd.
SMW Editorial Secretariat
Farnburgerstrasse 8
CH-4132 Muttenz

Manuscripts: submission@smw.ch
Letters to the editor: letters@smw.ch
Editorial Board: red@smw.ch
Internet: http://www.smw.ch