Table 1. Lipid formulations of polyenes: in development and marketed

Polyene	Formulation	Name	Company	Status
Amphotericin B	Liposomal	AmBisome	NeXstar	Marketed in UK
Amphotericin B	Lipid complex (ABLC)	Abelcet	The Liposome Company	Marketed in UK and USA[a]
Amphotericin B	Colloidal dispersion (ABCD)	Amphotec	Sequus in USA	Phase 4
		Amphocil	Zeneca in UK	Marketed
Nystatin	Liposomal	Nyotran	Aronex	Phase 2/3

[a]Marketed in February 1996

Status of antifungal chemotherapy

A familiar theme when discussing antifungal chemotherapy is to contrast the paucity of drugs available to treat deep-seated serious mycoses with the plethora of agents available for bacterial infections. Dr Donald Armstrong (Sloan-Kettering Cancer Center, New York, USA) pointed out the sobering fact that 40 years after its launch, the poorly tolerated, toxic, polyene amphotericin B (Fungizone, Bristol-Myers Squibb) is still regarded as the drug of choice for many fungal infections. Fluconazole (Diflucan, Pfizer) and itraconazole (Sporanox, Janssen) have replaced it for some, mostly indolent, infections, and have great utility for follow-up and maintenance therapy. However, in life-threatening situations, most of the clinicians present opted for amphotericin B. There is still a great need for drugs with greater efficacy against Zygomycoses, *Fusarium*, *Penicillium marneffii*, Phaeohyphomycoses and *Aspergillus*. The azoles are poor or ineffective, and amphotericin B is not always fully effective. As the spectrum of fungal pathogens increases, it is probable that more inadequacies of current treatments will become evident.

It is difficult to assess the value of some pipeline compounds from available literature; but some major presentations are expected at the *Interscience Congress on Antimicrobial Agents and Chemotherapy* (*ICAAC*), which is also to be held in New Orleans (15–18 September, 1996). Three azoles in Phase 3/4 development (UK 109496, Pfizer; DO 870, Zeneca; SCH 56592, Schering Plough) are claimed to have improved activity against *Aspergillus* infections, and β-glucan-synthase inhibitors from Merck and Eli Lilly are in Phase 2/3 development.

A surprising feature in this field, given that the market is far less than for a new antibacterial, and given the dominance (in sales at least) of fluconazole and itraconazole, is the competition for a less toxic replacement for amphotericin B. At least five companies have lipid preparations of polyenes (see table), and the competition is quite intense.

The newest entry into the field is a liposomal preparation of nystatin (Nyotran, Aronex Pharmaceuticals Inc.). Aronex claim that Nyotran has now entered Phase 3, although results of Phase 2 studies have not been published. The preparation is a true liposome, as is one of the amphotericin formulations, AmBisome (NeXstar). Other amphotericin preparations are ABLC, a lipid complex (Abelcet, The Liposome Company) and ABCD, a colloidal dispersion in sodium cholesterol sulphate (Amphotec, Sequus [USA]; Amphocil, Zeneca [UK]).

Amphotericin preparations have now been used quite widely, and seem to offer advantages in seriously ill patients, because it is possible to give higher doses while still avoiding the nephrotoxicity that is so often seen with amphotericin B. A point of concern however, is the high cost of these agents. Amphotericin B is an expensive drug to use; the bulk of the cost lies not in the drug itself but in the time needed to give the slow infusion, and the aftercare for the patient. Although lipid preparations are easily given (rapid bolus injection) and less toxic (requiring less patient care), they are still more expensive overall than amphotericin B. Dr Ben De Pauw (University Hospital, Nijmegen, The Netherlands) estimated that AmBisome, for example, is 25–60 times more expensive for a course of treatment. Although acknowledg-ing its therapeutic superiority, he believes that the cost could be justified only in areas like bone marrow transplants. Some insurance companies in the USA refuse to pay the cost of treatment if the use is 'off label'. Most of such agents are for use where the patient has failed on, or cannot tolerate, amphotericin B – they cannot therefore be used as first-line agents.

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Novartis who? An update

In the May issue of *Drug Discovery Today* (*Novartis who?* p. 176), David Jack explained the rationale behind the monicker of the giant formed by the Ciba/Sandoz merger (Latin: *nova* meaning new, *artis* meaning skill). In the *Wall Street Journal* (11 March, 1996) the relevance of the new logo is revealed. Malcolm Parkinson, Managing Director of Siegel & Gale (London), the company hired to come up with the name, has now identified the thinking behind the bowl shape encircling a vertical arrow. The bowl suggests "the flower of life, or a mortar as in mortar and pestle," while the arrow indicates precision. So now you know.

David Hughes