Molecules of the Millennium

Mycograb®: Human recombinant antibody to HSP90

Systemic infection by Candida species in the United States still tags with it a significant 35-40% mortality rate and data does not look better in any other part of the world either.\[1,2\] This high rate despite the advances in antifungal treatment can be attributed to non-Candida albicans Candida species and their growing resistance to commonly used antifungal drugs.\[3,4\]

This has resulted in a thrust to produce newer and more powerful drugs and drug delivery systems giving birth to variconazole, pneumocandin-B like caspofungin acetate, ABCL (Amphotericin-B Lipid Complex), ABCD (Amphotericin-B Colloid Dispersion), AmBisome (Unilamellar vesicle formulation of amphotericin-B), and lyophilized powders.

In fungal infections, and especially deep-seated systemic infections, heat shock protein 90 (HSP90) plays a crucial role and is essential for the viability of the yeast.\[5\] Considering this, a new molecule is developed called Mycograb® (Neu Tec Pharma plc).\[6\] Mycograb® is a polyhistidine tagged purified human recombinant antibody to HSP90. It is the first human recombinant antibody fragment to be used in fungal infections.\[7\] In the pre-clinical studies it was found to be highly effective when used in combination with amphotericin-B and showed significant antifungal activity against all five species of Candida, namely C. albicans, C. krusei, C. tropicalis, C. parapsilosis, and C. glabrata. However, when combined with fluconazole, it did not increase the response rate in fluconazole-resistant species but increased the clearance of fluconazole-sensitive species of Candida.\[8\]

Phase I clinical trials began in December 2000 with five patients of systemic candidiasis. The drug was given intravenously and safety assessment, kinetic, and dynamic parameters were studied. Results of these data were first presented at the American Society of Microbiologists Annual Conference, 2001. After confirming the favorable side-effect profile in July 2001, the drug entered Phase II trials. It was a double-blind randomized controlled trial involving 60 patients with culture-confirmed systemic candidiasis. The results were so encouraging that the company was hopeful of getting Phase III waiver from the United States Food and Drug Administration (US FDA) and directly marketing the drug. In January 2003, the Multi Research Ethical Committee (MREC) approved the drug to be tested in the UK and in February of the same year, the company filed the Investigational New Drug (IND) application with FDA. Mycograb® has been granted the status of orphan drug in Europe and the US by the European Medicine Evaluation Agency (EMEA) and the US FDA respectively.

The time has come to look beyond the physical molecules for the treatment of various infections and to search for some ways to produce biological agent which can take care of biology itself. Mycograb® is a major leap ahead in this field and like all other drugs it brings with it two hopes: first, it will be useful for the prophylaxis and treatment of systemic candidiasis, and second, that it could be of immense help in overcoming the growing resistance against antifungal agents.

A. Garg, P. V. Rataboli
Dept. of Pharmacology and Therapeutics, Goa Medical College, Bambolim, Goa - 403202, India
E-mail: drag_dragon@yahoo.com

References