News in brief

General market analysis

Datamonitor has reported an 8% growth in drug sales through retail pharmacies in 12 key markets over the period of September 1998 to August 1999, closing at $199 billion. IMS Health, the global healthcare information company, has reported that the world market continues to be pushed by strong sales in North America, where retail growth remained stable at 12% ($85.3 billion). Of the top five therapeutic groups in the USA, antiinfective and CNS agents are performing well at an above the market average of 15% and 14%, respectively.

In the top five European markets, sales sustained an 8% growth with the UK and Spain showing a 1% improvement. CNS agents have recently demonstrated the highest growth of 12% among the top five therapeutic areas, being worth $7.7 billion. The Japanese market, valued at $44 billion, demonstrated a general increase of 1% in the rate of growth to 6%. Respiratory, antiinfective and cardiovascular products are the major factors propelling the growth of this market. In stark contrast, the top Latin American markets continued to decline with a 6% decrease. In Brazil, an 18% sales drop was complemented by a continued decline in Argentina. Australia and New Zealand showed a continued growth and approached 12% to make the $2.7 billion mark. Global increase in alimentary/metabolism and musculoskeletal product sales has increased by 6% to $31.5 and $10.5 billion, respectively.

New promise for reducing cancer therapy-associated side effects

A new mechanism of controlling the p53 tumour suppressor protein has been discovered by Noriko Shikama (University of Glasgow, UK) and Nicholas La Thangue (Prolifix, Oxford, UK and University of Glasgow, UK)[1]. It is known that in normal cells, p53 restricts the impact of damaged cells, either by slowing down cell growth and division for long enough for the cells to be repaired, or by apoptosis (cell death). However, a unique factor has been discovered that mediates the apoptotic response and it is this response in normal cells that produces the main side effects observed with cancer therapy. This work might therefore lead to the discovery of new methods of controlling the severe side effects often associated with many of these therapies. For a detailed review of the cell cycle as a therapeutic target, see Ref. 2.

1 Shikama, N. *et al.* (1999) A novel cofactor for p300 that regulates the p53 response. *Mol. Cell* 4, 365–376

2 Brooks, G. and La Thangue, N.B. (1999) The cell cycle and drug discovery: The promise and the hope. *Drug Discovery Today* 4, 455–464

Locating disease-related genes: a new technique

A new method of identifying the location of genes involved in certain disease states has been adopted by GlaxoWellcome. This technique, called single nucleotide polymorphism (SNP) mapping, involves comparing the SNP map of patients with certain disease states with those without the diseases, and then focusing their research on the resulting different small portions of DNA that are likely to contain the relevant genes. So far, this technique has been used to identify some of the genes that might increase the susceptibility of patients to migraine, Type II diabetes and psoriasis. The results of these studies have suggested that it might not be necessary to have a very detailed SNP map to identify where some of these genes are located. The company is now using this technique to investigate the genetic basis of asthma, early-onset heart disease and generalized osteoarthritis.

Anti-vascular targeting: a new era in cancer therapy?

Anti-tumour vascular targeting agents are one of the latest novel drug classes to be added to the anticancer armory. The first drug of this novel class is Combretastatin A4 Prodrug (CA4P), (OXiGENE, Boston, MA, USA). This prodrug is converted into Combretastatin A4 (CA4) at the tumour vasculature, and binds to tubulin, which subsequently distorts the endothelial cells from being thin and flat to being large and round. This significantly reduces blood flow to the tumour, depriving it of vital oxygen and nutrients.

Preclinical studies have shown that this ischaemia leads to necrosis of the tumour[3]. When used in combination with either chemotherapy or radiation, the tumour reduces in size and is ultimately destroyed. A UK Phase I clinical study has recently suggested promising results. NMR imaging scans have shown that the drug significantly reduced the blood flow in all patients evaluated after doses of >52 mg m^{-2}. This is the first time that a drug has been shown to reduce blood flow to a tumour in humans. For a more detailed article, see Ref. 4.

3 Chaplin, D.J. *et al.* (1999) Anti-vascular approaches to solid tumour therapy: Evaluation of combretastatin A4 phosphate. *Anticancer Res.* 19, 189–195

4 Hillary, A. (2000) Anti-vascular targeting: A novel approach to cancer treatment. *Pharm. Sci. Technol. Today* 3, 4

HIV market information and analysis: a time to reflect and look forward

Over the next five years, the current leading HIV products are expected to rapidly lose their market share as the market becomes more competitive and new products are launched. This is the prediction heralded by Datamonitor's

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recent *Market Dynamics 1999 HIV Report**, released late in 1999, covering HIV market information and analysis from seven countries including the UK, the US and Japan. Epidemiological data gathered from all seven countries have been combined with national diagnosis and treatment trends in an attempt to identify the existing and future patient pool for HIV drug therapy. At present, the HIV market is growing rapidly and it appears that improvements in the effectiveness of HIV therapies are increasing the life expectancy of patients and, hence driving the growth of the market.

Key findings

Several key findings were highlighted in this report. Firstly, because of the success of combination therapies, the potential patient pool for HIV therapies is expanding. Secondly, an increase in life expectancy is producing an increase in the prevalence of HIV in all the significant pharmaceutical markets. In addition, the realm of the HIV combination therapy is likely to remain strongly supported by the nucleoside reverse transcriptase inhibitors, at least for the near future*. The global market in this area is increasing: it was valued at $4077 million in 1998 compared to $3217 million in 1997. As indicated earlier, the market is increasingly becoming more aggressive: Merck's protease inhibitor, Crixivan, was the leading HIV product globally in 1998 but this is now under much pressure from Agouron's Viracept, also a protease inhibitor. In fact, Viracept recently overtook Crixivan to become the leading HIV drug on the US market. The leading HIV company in every study country was GlaxoWellcome. The 1998 launch of Combivir (a combination of two antiretroviral drugs, lamivudine and zidovudine) in the EU helped to sustain the company's leading position in the global market.

The US market accounted for 54% of the global HIV market in 1998 and the performance of products in this market will continue to be the overriding factor in determining their success. The French and Spanish markets have recently reported the highest European HIV sales but the German market had the highest growth. The developing world is considered to have massive market potential for HIV therapies. Until recently, this was very underserved but this situation is now changing slowly and in 1998, Brazil was GlaxoWellcome's fifth largest market.

*Sales forecasts for all existing and future HIV drugs have been generated using Datamonitor's proprietary forecasting models.

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