NEWS IN BRIEF

Regulatory decision suggests high bar for obesity drugs

The US FDA's Endocrinologic and Metabolic Drugs Advisory Committee voted 10–6 against the use of Vivus' investigational product Qnexa for the treatment of obesity.

The lowdown: The FDA's advisory committee's negative vote against Qnexa — a product that combines two previously approved drugs, phentermine and topiramate — surprised investors. Phentermine is an amphetamine that was originally approved as an appetite suppressant, and works by causing noradrenaline release in the hypothalamus. Topiramate is an anticonvulsant thought to act as a GABA (γ-aminobutyric acid) agonist that increases satiety. However, the precise mechanism of action of these agents in patients with obesity is unclear.

Although Qnexa met both of the FDA's efficacy benchmarks — producing a mean weight loss at least 5% greater than placebo, and at least 35% of subjects losing at least 5% of baseline body weight in the treatment group compared with the placebo group — concerns were raised about treatment-associated adverse events, including teratogenicity, and adverse psychiatric, cognitive and cardiovascular events. The main reasons why the committee voted against the use of Qnexa were concerns that the safety data were not long-term enough, given that a proportion of patients could be receiving the therapy for many years, as well as concerns about the risk of birth defects, given that some users would be women of child-bearing age.

Around the same time that Qnexa received a negative vote, positive Phase III trial data were released for another novel anti-obesity therapy, lorcaserin (developed by Arena Pharmaceuticals). The trial showed that 47.5% of patients taking lorcaserin lost at least 5% of their body weight compared to only around 20% of subjects taking the placebo (*N. Engl. J. Med.* **363**, 245–256; 2010). Lorcaserin is designed to specifically target the 5-hydroxytryptamine 2C (5-HT_{2C}) receptor, which has been strongly linked to the control of appetite, without targeting the 5-HT_{2A} or 5-HT_{2B} receptors, which are associated with heart valve defects or hallucinogenic effects, respectively. No adverse effects on heart valves or pulmonary arterial pressure were observed with lorcaserin treatment in the recent trial. This was important to demonstrate because a weight-loss treatment known as Fen–Phen, a combination of fenfluramine (which targets several 5-HT receptors) and phentermine, was withdrawn from the market in 1997 after it was linked to abnormalities in heart valves.

Genomics of drug sensitivity project releases first data

US–UK collaboration has described the responses of 350 cancer samples to 18 anticancer therapeutics.

The lowdown: In December 2008, the Massachusetts General Hospital Cancer Center and the Wellcome Trust Sanger Institute launched the 'Genomics of drug sensitivity in cancer' project aiming to test the sensitivity of 1,000 cancer cell samples to 400 targeted anticancer treatments — both approved and investigational agents. The goal was to correlate the sensitivity patterns of the cell lines to the treatments with genomic data to identify genetic features that are predictive of the observed sensitivity. In July 2010, the first data from this study were released and are freely available to academic and medical communities (http://www.sanger.ac.uk/genetics/CGP/translation). The drugs that have been tested so far include the launched products erlotinib (Tarceva; Roche), sunitinib (Sutent; Pfizer) and imatinib (Gleevec; Novartis), as well as the investigational compounds TAE684 (Novartis) and AZ628 (AstraZeneca). There is a growing body of evidence showing the considerable heterogeneity between cancers, even of the same tumour type, and this study will therefore help inform the optimal clinical use of such targeted therapies, as well as help reduce toxicity and increase efficacy (*Nature Rev. Drug Discov.* **9**, 363–366; 2010). Such data may also help inform the design of clinical trials for the investigational compounds.

US agencies agree to share drug information

The FDA and the Centers for Medicare & Medicaid Services (CMS) have signed a memorandum of understanding to share information that includes the review and use of FDA-regulated drugs and biologics.

The lowdown: The purpose of the agreement between the FDA and the CMS is to "promote collaboration and enhance knowledge and efficiency by providing for the sharing of information and expertise between the Federal partners." More specifically, the federal agencies want to "promote efficient utilization of tools and expertise for product analysis, validation and risk identification" and to "build infrastructure and processes that meet the common needs for evaluating the safety, efficacy, utilization, coverage, payment, and clinical benefit of drugs, biologics and medical devices." Importantly, this represents the first time that the FDA has agreed to share information about new drug or biologic applications that are being reviewed with the CMS, the agency that will decide whether or not to reimburse the relevant products after they have been approved by the FDA.

Similar discussions are also ongoing between the European Medicines Agency (EMA) and the European network for Health Technology Assessment (EUnetHTA), which represents 24 health technology agencies (HTAs) in Europe. It has been recognized that European public assessment reports (EPARs) can contribute to the evaluations of relative effectiveness conducted by HTAs in Europe (*Nature Rev. Drug Discov.* **9**, 277–291; 2010). The EPAR is a summary of the examination process that the EMA's Committee for Medicinal Products for Human Use completes when it assesses a marketing authorization application for a new product. It includes all clinical trial data in support of a product's efficacy and safety, and is published at the end of the evaluation process. The EMA and the EUnetHTA are in discussions to assess how the EPARs can be formally shared with European HTAs.