NEWS IN BRIEF

Trio of recent anticancer drug approvals

The FDA has approved pazopanib (Votrient; GlaxoSmithKline) for renal cell carcinoma (RCC), ofatumumab (Arzerra; Genmab/GlaxoSmithKline) for chronic lymphocytic leukaemia (CLL) and romidepsin (Istodax; Gloucester Pharmaceuticals) for cutaneous T cell lymphoma (CTCL).

The lowdown: Pazopanib, a small molecule that inhibits several receptor tyrosine kinases (RTKs), was approved for the treatment of advanced RCC on 19 October 2009. In common with the two small-molecule RTK inhibitors approved for the same indication around 4 years ago — sunitinib (Sutent; Pfizer) and sorafenib (Nexavar; Bayer/Onyx) — it targets receptors for vascular endothelial growth factor, which is thought to have an important pathogenic role in most patients with clear-cell RCC.

Ofatumumab, a human monoclonal antibody (mAb) that targets CD20 on the surface of B cells, was granted accelerated approval for the treatment of CLL on 26 October 2009. Although rituximab (Rituxan/MabThera; Genentech/Roche/Biogen Idec) is well established as the first CD20-targeting mAb, having been approved for the treatment of non-Hodgkin's lymphoma in 1997, ofatumumab is the first such agent to be approved for CLL. In May 2009, Genentech and Biogen Idec submitted two supplementary biologic licence applications for the use of rituximab in combination with standard chemotherapy in treatment-naive and pretreated patients with CLL. The FDA was expected to make a decision regarding approval of rituximab for these indications on 17 November 2009.

Romidepsin, a histone deacetylase (HDAC) inhibitor, was approved for the treatment of CTCL on 6 November 2009. It is the second HDAC inhibitor to be approved for the treatment of CTCL, following the approval of vorinostat (Zolinza; Merck) by the FDA in October 2006.

Protease inhibitors continue to show promise against HCV

Data presented at the 2009 meeting of the American Association for the Study of Liver Diseases (AASLD) provide further support for the efficacy of protease inhibitors against the hepatitis C virus (HCV).

The lowdown: There are currently eight small-molecule inhibitors of the NS3–4 HCV protease in mid-to-late stage clinical development: six in Phase II trials and two in Phase III trials. The product that is expected to be first to market is telaprevir (developed by Vertex Pharmaceuticals, Johnson & Johnson, Lilly and Mitsubishi Tanabe Pharma), for which interim data from the first three Phase III trials are expected in the first half of 2010. At the AASLD meeting, Vertex announced data from a Phase II study, C208, which was designed to explore the safety, efficacy, tolerability and pharmacokinetics of telaprevir administered twice or three times daily in combination with either polyethylene glycol (PEG)–interferon-α2a (Pegasys; Roche) or PEG-interferon-α2b (PEG-Intron; Merck) and ribavirin. Data from the trial showed comparable efficacy between the two dosing schedules studied, with sustained virological response (SVR) rates achieved in 81–85% of treated patients. The demonstration that a twice-daily dose of telaprevir has comparable effectiveness to a thrice-daily dose is important, because the six small-molecule inhibitors that are in Phase II trials are being developed for either once- or twice-daily dosing, and less frequent dosing might increase patient compliance to therapy and therefore improve treatment response.

Boceprevir (developed by Schering–Plough, which was recently acquired by Merck), the other small-molecule inhibitor in Phase III development, is also administered thrice daily. However, Schering–Plough had already started to develop narlaprevir, which is in Phase II clinical trials at a once- or twice-daily dose. To achieve the required pharmacokinetics, narlaprevir is combined with ritonavir — an HIV protease inhibitor that acts as a pharmacokinetic enhancer of drugs metabolized by the cytochrome P450 3A metabolic enzymes. Data presented at the AASLD meeting showed that 85–87% of patients receiving narlaprevir at a once-daily dose — in addition to interferon and ribavirin, which had been administered for the previous 4 weeks — achieved an SVR. In addition, results presented from a Phase II trial of BI-201355, an HCV protease inhibitor being developed by Boehringer Ingelheim, showed that 62–90% of patients receiving this inhibitor once daily achieved rapid virological responses within 4 weeks of treatment.

Dendreon finalizes BLA for Provenge

Dendreon has announced that it has completed the submission of its amended biologics licence application (BLA) for sipuleucel-T (Provenge) for men with metastatic castration-resistant prostate cancer.

The lowdown: When Dendreon submitted its original BLA for sipuleucel-T in January 2007, it was widely anticipated that sipuleucel-T would become the first approved therapeutic cancer vaccine (*Nature Rev. Drug Discov.* **6**, 333–334; 2007). It received a 17–0 vote in support of its safety and a 13–4 vote in favour of its efficacy from the FDA's Office of Cellular, Tissue and Gene Therapies Advisory Committee in March 2007. Despite this, Dendreon received an approvable letter from the FDA in May 2007 requesting additional clinical data, as well as chemistry, manufacturing and controls information. Earlier this year, Dendreon announced that it had completed the IMPACT (Immunotherapy for Prostate Adenocarcinoma Treatment) trial, and sipuleucel-T met the primary end point by extending median survival by 4.1 months compared with placebo and improving 3-year survival by 38%, which could provide the additional evidence required by the FDA to support the efficacy of the vaccine (*Nature Rev. Drug Discov.* **8**, 685–686; 2009).