NEWS IN BRIEF

Approving pre-surgery cancer drugs

The US Food and Drug Administration (FDA) granted accelerated approval to Roche and Genentech's pertuzumab for neoadjuvant breast cancer, a move towards earlier use of cancer drugs.

The lowdown: Oncologists are increasingly thinking about using anticancer agents earlier on, arguing that pre-surgery tumour debulking and early treatment can improve long-term outcomes. Roche and Genentech have now snagged a first regulatory approval to use their pertuzumab in just such a setting, in early-stage breast cancer before surgery.

"We are seeing a significant shift in the treatment paradigm for early-stage breast cancer," said Richard Pazdur, Director of the Office of Hematology and Oncology Products at the FDA in a statement.

Pertuzumab — a monoclonal antibody (mAb) that binds to HER2, preventing receptor dimerization — was first approved last year for use in combination with the HER2-targeted mAb trastuzumab and docetaxel chemotherapy in patients with HER2-positive metastatic breast cancer. The new accelerated approval is based on a 417-patient trial showing that neoadjuvant pertuzumab plus trastuzumab plus docetaxel induced a pathological complete response (pCR) in 39% of patients, whereas neoadjuvant trastuzumab plus docetaxel only induced a pCR in 21% of patients. Trastuzumab and docetaxel are used off-label in the neoadjuvant setting.

The approval was made possible in part by guidance the FDA issued last year on pCR, which is a fast surrogate end point that looks at the absence of invasive cancer in the breast and lymph nodes at surgery.

Trials are underway to identify other neoadjuvant breast cancer drugs. The adaptive I-SPY 2 trial, for example, is testing multiple agents in women with newly diagnosed locally advanced breast cancer.

Len Lichtenfeld, chief medical officer of the American Cancer Society, says that interest in neoadjuvant drug development extends to other cancer indications as well, including pancreatic cancer, liver cancer and ovarian cancer. "I don't think this drug approval is going to influence the further investigation of neoadjuvant treatments; it is the results of neoadjuvant use that are already influencing the community," he adds.

Malaria vaccine on track

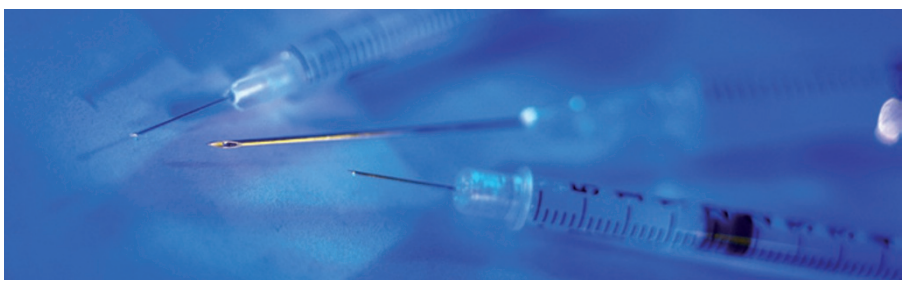
GlaxoSmithKline (GSK) presented 18-month safety and efficacy data for RTS,S and plans to submit the vaccine for regulatory review next year.

The lowdown: When GSK presented initial safety and efficacy data on its RTS,S malaria vaccine, it was met with a mix of muted enthusiasm and disappointment. The vaccine offered protection, but not to the degree to which researchers had hoped (50.4% efficacy in children aged 5 to 17 months, and 30.1% efficacy in infants aged 6 to 12 weeks).

While the new data don't change the less than perfect top-line results, they do start to address concerns that efficacy will wane over time. GSK reported at the 6th Multilateral Initiative on Malaria Pan-African Malaria Conference in Durban, South Africa, that at 18 months the vaccine offered efficacy in 46% of children, and in 27% of infants.

GSK and its non-profit partner PATH Malaria Vaccine Initiative (MVI) plan to submit the recombinant vaccine for regulatory review in the European Union next year, for a potential 2015 approval.

Around two dozen other vaccines are in various stages of clinical development for malaria. In September, Sanaria CEO Stephen Hoffman, who contributed to the development of RTS,S, reported in *Science* some preliminary clinical success with the PfSPZ vaccine, which is made by purifying attenuated sporozoites from the salivary glands of irradiated mosquitoes. None of six individuals given the highest dose of the vaccine was infected following experimental challenge with malaria, compared with three out of nine individuals who received a lower dose of vaccine and five out of six non-vaccinated individuals.



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First-in-class PI3K inhibitor advances

Gilead submitted its idelalisib for approval in indolent non-Hodgkin's lymphoma (iNHL), and stopped a pivotal trial in chronic lymphocytic leukaemia (CLL) after an interim analysis found early evidence of efficacy.

The lowdown: The phosphoinositide 3-kinase (PI3K) field has been fraught with false starts, but Gilead's submission of its PI3Kδ inhibitor idelalisib means that a first success for a large class of agents could be near.

The company is initially looking for approval in patients who are non-responsive to rituximab and alkylating-agent-containing chemotherapy. The new drug application (NDA) is based on a single-arm 125-patient Phase II trial in which patients treated with idelalisib achieved an overall response of 53.6% and a median duration of response of 11.9 months. Earlier this year Gilead also initiated larger Phase III trials of the drug — in combination with rituximab and in combination with rituximab plus the alkylating agent bendamustine — in previously treated patients with iNHL.

The drug is also in three Phase III trials in which it is being tested in combination with approved therapies for CLL. In October the company stopped a pivotal trial in this setting early because idelalisib plus rituximab had already hit the primary end point compared with rituximab alone. Gilead is also testing idelalisib with GS-9973, the company's spleen tyrosine kinase inhibitor.

Other late-stage PI3K inhibitors in the pipeline include Novartis's pan-PI3K inhibitor buparlisib, which is in Phase III development for breast cancer, and Infinity and Takeda's dual PI3Kδ and PI3Kγ inhibitor IPI-145, which is due to enter Phase III development for CLL by the end of the year. Numerous agents are in Phase II trials.