NEWS IN BRIEF

Regulators approve the first cancer-killing virus

Regulators in the United States and Europe have approved Amgen's talimogene laherparepvec, a genetically modified live oncolytic herpesvirus therapy that replicates inside cancer cells and causes them to rupture and die.

Both the FDA and the European Medicines Agency (EMA) approved the first-in-class therapy for treatment of melanoma lesions that cannot be removed completely by surgery. In a 436-patient pivotal trial, tumours shrank for at least 6 months in 16% of virus-treated participants and in only 2% of patients in the comparator arm (*J. Clin. Oncol.* **33**, 2780–2788; 2015). Treated patients trended towards a 4.4-month longer median overall survival than control patients, but the FDA noted that treatment "has not been shown to improve overall survival". The most common side effects were fatigue, chills, pyrexia, nausea, influenza-like illness and injection site pain.

Amgen is now testing the oncolytic virus in colorectal, head and neck, and breast cancer.

At least seven other oncolytic viruses are in development, with companies tapping into genetic engineering approaches and the innate tumour-killing properties of viruses to treat a range of cancers (*Nat. Rev. Drug Discov.* **14**, 369–371; 2015). Companies are also optimistic that oncolytic viruses will benefit from being paired with checkpoint-blocking antibodies that prime the immune system to take down cancer cells. Amgen, for example, is testing its talimogene laherparepvec in combination with Bristol-Myers Squibb's anti-CTLA4 (cytotoxic T lymphocyte-associated antigen 4) antibody ipilimumab and with Merck & Co.'s anti-PD1 (programmed cell death protein 1) antibody pembrolizumab.

Analysts forecast annual global sales of nearly US$400 million for talimogene laherparepvec by 2020, shows the Thomson Reuters Cortellis database. Analysts at BCC Research have estimated that the global market for oncolytic viruses will reach $6.4 billion by 2023.

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Priority review voucher pitfalls

Last month, the FDA granted its eighth priority review voucher (see TABLE 1). These transferable vouchers can be sold or used at the FDA to secure a priority review of a drug, and are intended to encourage drug developers to work on neglected tropical diseases and rare paediatric indications. An analysis of the first six vouchers found little evidence that the vouchers were achieving their public health aims.

Aaron Kesselheim, of Harvard Medical School, and his colleagues found that the vouchers were awarded to drugs that had been shown to be effective in the clinic and sometimes approved outside the United States years before they were filed with the FDA (*JAMA* **314**, 1687–1688; 2015). In some cases drug development had depended on significant public sector investment, raising the question of whether the right group was being rewarded. "One way to potentially prevent such windfalls would be to redesign the voucher system so that drug companies would have to show some level of investment," the authors write.

The FDA's Office of New Drugs Director John Jenkins recently told *Pharma&MedTech Business Intelligence* that the agency has concerns about these vouchers and noted that a voucher-triggered review can be "very challenging and has the adverse impact of requiring managers and reviewers to refocus time and resources away from other important public health work".

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Table 1 | **Priority review vouchers to date**

Drug	Sponsor	Indication	Sold (US$)
Neglected tropical diseases			
Artemether-lumefantrine	Novartis	Malaria	-
Bedaquiline	Johnson & Johnson	Multidrug-resistant tuberculosis	-
Miltefosine	Knight Therapeutics	Leishmaniasis	$125 million
Rare paediatric diseases			
Elosulfase alfa	BioMarin	Morquio A syndrome	$67.5 million
Cholic acid	Retrophin	Bile acid synthesis disorders	$245 million
Dinutuximab	United Therapeutics	High-risk neuroblastoma	$350 million
Uridine triacetate	Wellstat	Hereditary orotic aciduria	Undisclosed
Asfotase alfa	Alexion	Hypophosphatasia	-

FDA approves anticoagulant antidote

Since 2010, the FDA has approved four novel oral anticoagulants. These drugs offer key benefits over the 60-year-old standard of care warfarin — including easier dosing regimens — but uptake of the newcomer drugs has been hampered by the inability to reverse their effects when clotting is needed; for example, after an accident or during emergency surgery. The FDA has now granted accelerated approval to Boehringer Ingelheim's idarucizumab, which acts as an antidote to the company's blood-thinning direct thrombin inhibitor dabigatran.

Idarucizumab is an antibody fragment that binds to dabigatran. In a 283-patient pivotal trial in healthy volunteers, it provided an immediate reduction in the amount of dabigatran in participants' blood that lasted for at least 24 hours. In another trial in 123 patients on dabigatran who needed to reverse its effects owing to uncontrolled bleeding or for emergency surgery, the anticoagulant effect of dabigatran was fully reversed in 89% of patients within 4 hours of administration of the antidote.

Other companies are working in this space as well. Portola Pharmaceuticals' Phase III andexanet alfa is a recombinant modified factor Xa molecule that acts as a decoy to clear factor Xa inhibitors such as Pfizer and Bristol-Myers Squibb's apixaban, Bayer's rivaroxaban and Daiichi Sankyo's edoxaban. Perosphere's small molecule aripazine is in Phase II trials to reverse the effects of factor Xa inhibitors and dabigatran.

These reversal agents could allay lingering concerns from patients and clinicians over the novel anticoagulants, providing a boost to the multibillion-dollar drugs (*Nat. Rev. Drug Discov.* **14**, 5–6; 2015).

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