BIOBUSINESS BRIEFS

DEAL WATCH

Amgen buys oncolytic virus company

In a deal worth up to a possible US$1 billion, Amgen has acquired the biotechnology company BioVex. BioVex's lead product OncoVEX^{GM-CSF} (herpes virus JS1/34.5-/47-/granulocyte–macrophage colony stimulating factor (GM-CSF)) is an oncolytic virus that caused tumour regression and increased survival in patients with metastatic melanoma in a Phase II trial, and is also being investigated in head and neck cancer.

Oncolytic viruses — either naturally occurring or genetically engineered — are particularly useful tools in anticancer therapy as they replicate selectively in tumour cells. John Bell from the Ottawa Hospital Research Institute, Ontario, Canada, explains how this is achieved: "Malignant tumour cells have acquired genetic mutations that predispose them to viral infection. They lack many of the defence mechanisms that normal cells use to block virus replication and spread: they have defective apoptotic programmes, unlimited proliferation potential and can avoid immune recognition. Consequently, oncolytic viruses can grow unimpeded in tumour cells."

OncoVEX^{GM-CSF} is an engineered herpes simplex virus type 1 in which the protein ICP34.5 is deleted. ICP34.5 is normally used by the virus to counteract the host effects of interferon-α and interferon-β, therefore its loss leads to virus destruction in normal cells. The protein ICP47 (which normally blocks antigen presentation) is also deleted, leading to upregulation of the US11 protein and causing enhanced virus growth and replication in tumour cells. Moreover, OncoVEX^{GM-CSF} expresses GM-CSF, which further boosts antitumour immunity through stimulation of dendritic cells.

Once the virus is inside the tumour cell, its anticancer effects continue. "Following initiation of infection within the tumour bed, the virus not only destroys tumour cells but also initiates a targeted inflammatory reaction that appears to stimulate the patient's immune system to recognize the previously stealth tumour," says Bell.

Oncolytic viruses could have several benefits over conventional therapies. "A major theoretical advantage of oncolytic viruses is that through viral replication, the therapy renews itself as long as there are tumour cells left to destroy," according to E. Antonio Chiocca from the viral oncology program of the James Cancer Hospital and Ohio State University Medical Center, USA. "By contrast, drugs and antibodies target one cell at a time and then disappear … you need to give enough to destroy every tumour cell." Another advantage lies in the possible lack of resistance to oncolytic viruses, as Bell notes: "Oncolytic viruses target pathways — rather than individual molecular targets — and attack the cancer in more than one way (such as direct cell destruction, stimulation of immunity and vascular attack), so it may be more difficult for tumours to develop resistance." However, he adds that it is still not clear how important antiviral immunity will be in limiting repeat dosing.

In a Phase II clinical trial, patients with unresectable metastatic melanoma who received OncoVEX^{GM-CSF} had an overall response rate of 26%. Moreover, regression of injected and distant lesions occurred and the overall survival was 58% at 1 year, compared to 25.5% based on historical data (*J. Clin. Oncol.* **27**, 5763–5771; 2009). Key to its success could lie in the fact that melanoma is well-known to be responsive to immune therapy. "The OncoVEX^{GM-CSF} approach puts a lot of emphasis on stimulation of antitumour immunity for its effectiveness, so perhaps it is not surprising that melanoma is where OncoVEX^{GM-CSF} has had initial success," highlights Bell. "For other less immunogenic cancers, it may be that different oncolytic platforms — perhaps in combination with small molecules and/or chemotherapeutics — that can be administered systemically will be required." However, oncolytic viruses in general could have broad potential. "There is no limit to which cancers oncolytic viruses could be used for, because the signalling pathways and factors needed for tumour growth and survival are common among different cancers," concludes Chiocca. Other oncolytic viruses in development include Oncolytics Biotech's Phase III head and neck cancer candidate Reolysin and Jennerex Biotherapeutic's Phase II liver cancer candidate JX-594.