Rollout of high-priced cell and gene therapies forces payer rethink

The high prices of pioneering gene therapies are forcing urgent discussions around value, affordability and payment methods. The Boston-based Institute for Clinical and Economic Review (ICER) has recently had its say on the cost-effectiveness of the first two chimeric antigen receptor T-cell (CAR-T) drugs for aggressive blood cancers: Basel, Switzerland–based Novartis' Kymriah (tisagenlecleucel), priced at $475,000, and Foster City, California–based Gilead's Yescarta (axicabtagene ciloleucel), at $373,000. Its headline verdict: the CAR-T drugs are, broadly, cost-effective. But Philadelphia-based Spark Therapeutics' gene therapy Luxturna (voretigene neparvovec), which treats an inherited form of blindness (*Nat. Biotechnol.* **36**, 6, 2018), is at least twice as expensive as it should be given its clinical benefits.

The reality is far more complex than these headlines suggest. Both treatment categories are designed as one-time therapies, whose benefits may endure over years or even a lifetime. Both provide patients with options where none currently exist. These therapies are a triumph of science, and their prices should reflect that. But the lack of evidence supporting their long-term effects is putting clinicians and payers on guard. These single-use treatments also challenge current drug payment systems, designed around small molecules or biologics treatments administered every few weeks or months.

For now, cell and gene therapies' budgetary impact is limited, given the tiny populations to benefit. Kymriah is indicated for relapsed or refractory pediatric B-cell precursor acute lymphoblastic leukemia, which affects fewer than 3,000 patients in the US annually. Yescarta is approved for the estimated 6,000 US adults with relapsed or refractory diffuse large B-cell lymphoma. Luxturna, approved by the US Food and Drug Administration (FDA) in December 2017 to treat retinal dystrophy, may help restore vision for fewer than 2,000 US patients with the biallelic *RPE65* genetic mutation.

But this is just the first of a wave of similar therapies likely to reach the market over the next few years. Kymriah and Yescarta are being studied in further cancer types including solid tumors, and many other gene therapies are in the pipeline. The class will ultimately have a huge impact on health systems, which is why ICER got involved.

This independent, not-for-profit organization cannot mandate what drugs payers should fund, but has become increasingly influential in driving the drug pricing debate. On March 2, ICER convened payers, clinicians and patients to discuss its CAR-T pricing report, and how new drugs might be covered. A similar policy meeting for Luxturna was held on January 25.

Methods for determining the cost-effectiveness of drug treatments are imperfect at

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Creative new therapies need equally creative payment systems.

New drug for multidrug-resistant HIV

The US Food and Drug Administration has approved a new drug to treat patients with multidrug-resistant HIV-1, the first therapy in more than a decade with a new mechanism of action. Developed by Taipei, Taiwan–based TaiMed Biologics, Trogarzo (ibalizumab-uiyk) is a humanized monoclonal antibody that binds to the second extracellular domain of CD4 and prevents entry of HIV-1 into $CD4^+$ immune cells. Wuxi Biologics of China, its manufacturer, said that this is also the first FDA approval for a biological drug produced by a Chinese company. Trogarzo is to be used with other HIV medicines as part of an antiretroviral therapy. In August 2017, WuXi Biologics announced that the FDA had completed its pre-license inspection of its facilities in the city of Wuxi, China. Theratechnologies of Canada acquired US rights to market and distribute the drug from TaiMed. In phase 3 trials, Trogarzo used in combination with other antiretrovirals achieved a 70% viral load reduction in a week in over 80% of treatment-experienced, multidrug-resistant patients with HIV-1, and after a 24-week period the viral load of 43% of patients was undetectable. TaiMed Biologics obtained the monoclonal antibody from Genentech in 2007 (*Nat. Biotechnol.* **32**, 508–510, 2014). According to the US Centers for Disease Control and Prevention, approximately 1.1 million people in the US were living with HIV at the end of 2015. Theratechnologies says that 20,000 to 25,000 US citizens with HIV-1 are currently resistant to at least one antiretroviral therapy. Luc Tanguay, president and CEO of Theratechnologies, said in an early March press release that they hope to bring the therapy to patients in the US within 6 weeks at an annual wholesale acquisition cost of $118,000 per year.

"We need to stop investing in the third Fitbit for the 50-year-old upper-class person and start innovating for people who have common diseases and conditions, but live in communities with low access to care." Andy Slavitt, former head of the Centers for Medicare and Medicaid Services, comments on why he is investing in companies that will bring healthcare to those most in need, the oldest and sickest Americans. (*CNBC*, 4 March 2018)

"The insurers don't want to end up on the front page of the newspaper saying Little Timmy bled to death because his drug wasn't covered." Jerry Avorn, health economist at Harvard, speculates on the reasons that keep hemophilia treatment costs at an average $270,000 per year despite there being 28 drugs on the market. (*NPR*, 5 March 2018)