

## RARELY SEEN IN UNDERWRITING ARTICLE SERIES: WHILE YOU WERE SLEEPING...



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I started to write a single topic article on something we rarely see in underwriting, but I kept getting side tracked by interesting and compelling scientific advancements that I found in my reading. Our daily workloads, onslaught of emails, and information overload of all things underwriting make it hard for underwriters to keep abreast of what's new in medicine. New information comes out every day as knowledge expands, and it's practically a full-time job just to keep up. Here are some interesting tidbits to consider as you sip your morning coffee.

### **Bacteria like to sleep at night, too**

Scientists discovered within the last year how cyanobacteria, which help plants to grow through nitrogen conversion, use proteins to regulate genetic expression that control day and nighttime metabolic processes.<sup>13</sup> Isn't that amazing that these bacteria have circadian rhythms like humans do?

This is important to health since chronic desynchronization of human cellular clocks (hello, grave yard shift workers!) increases susceptibility to disease.<sup>13,14</sup> Research has led to the diagnosis of six circadian sleep-wake rhythm disorders, all of which can negatively impact neurobehavioral performance, mental and physical health, and social and occupational functioning.<sup>14</sup> Companies should consider the cost of shift work from an employee retention, productivity and healthcare cost standpoint: Is it really worth it to keep the workforce up at night?

### **Genetic therapy breakthrough for CF**

Cystic fibrosis (CF), which we don't often see in underwriting, is caused by mutations of the cystic fibrosis transmembrane conductance regulator (CFTR) gene located on chromosome 7.<sup>12</sup> Research discovered an entirely new class of drugs called CFTR modulators that improve production, intracellular processing,

**Executive Summary** *Big data isn't the only trend in technology having an impact on today's underwriting world. Every day brings new scientific discoveries and medical advancements. Underwriters must stay informed to remain relevant in today's fast paced, ever changing environment. Join us for a journey through a brief overview of today's hottest discoveries which are changing healthcare as we know it.*

and function of defective CFTR genes. Previously, the treatment of CF only targeted the symptoms of the disease, not the root cause.

In 2017, the FDA approved the first drug in this class, an oral drug named ivacaftor, to treat patients who have a particular genetic mutation (G551D) on the CFTR gene.<sup>4</sup> Approximately 4.4% of those with CF have this particular gene mutation. Multiple studies showed decreases in pulmonary symptoms, decreased hospitalizations and increase in body weight when ivacaftor was used.

Scientists are continuing work to develop other drugs that address other CF genetic mutations. This research was groundbreaking because it translated scientific knowledge into real-time treatment, which hopefully will lead to other treatments for a variety of genetic diseases.<sup>5</sup>

### **Score another win for the children...**

Continuing on the genetic trend, in August 2017 the FDA approved the first-ever treatment that genetically alters a patient's own cells to fight cancer.<sup>7</sup> This discovery is expected to transform cancer treatment as we know it. Doctors call it a "living drug" because it takes the patient's own T lymphocytes and transduces them with a gene that encodes a chimeric antigen

receptor (CAR) to direct the patient's T cells against the leukemic cells.<sup>9</sup> Thus, it is known as CAR-T cell therapy.

Pharmaceutical giant Novartis developed the CAR-T therapy, which is now known as Kymriah.<sup>7</sup> The patient's T cells are genetically modified *ex vivo* (meaning outside the body) and then expanded in a production facility. The genetically modified cells are then infused back into the patient.

It was specifically designed for children and young adults with B-cell acute lymphoblastic leukemia (ALL) that resisted standard treatment or had relapsed. There are two downsides to the treatment. The therapy can cause a severe systemic response to the T cells called cytokine release syndrome (CRS); thus, it is only available in the US as a risk evaluation and mitigation strategy (REMS). The treatment is also costly and has a lengthy preparation time.<sup>3</sup>

Risk Evaluation and Mitigation Strategies (REMS) are required risk management plans for prescription drug use beyond the US Food and Drug Administration's (US FDA) professional labeling. REMS ensure the benefits of the drug outweigh the risks of taking it. This law, which aims to ensure safe use of prescription medication, was enacted in 2007 by the US FDA.<sup>1</sup>

### **Precision shots**

Immunotherapy using cellular engineering, like the CAR-T cell therapy listed above, isn't the only treatment being studied since medical researchers widely believe that understanding the human immune system is the answer to curing cancer. Developing these type of tailored treatments using the immune system to fight cancer is an example of precision medicine. At Stanford University in California, precision medicine researchers recently discovered that activating T cells in tumors eliminated even distant metastases in mice.<sup>3,11</sup>

The name for this approach is cancer in-situ vaccination. Two different immune-stimulating drugs were injected directly into solid tumors in mice, and through reactivation of the body's own T cells, the cancer cells in the tumor were destroyed. Research found that some of these tumor-specific, activated T cells then leave the original, injected tumor to find and destroy other identical tumors in the body. This is how the metastatic tumors were destroyed in 87 of the 90 mice studied.<sup>3,11</sup> In the three mice who had tumor recurrence, the tumors regressed after a second injection of the two drugs.

One of the drugs is already approved for use in humans, and the other has been tested for human use

in several unrelated clinical trials.<sup>2</sup> Human trials are now beginning on patients suffering from low grade lymphoma. Can you imagine a cure for lymphoma?

### Forget the wig...

Cancer affects most of us in one way or another, whether or not you are a cancer survivor yourself or know someone who has been diagnosed with cancer. Every day 1,670 people die from cancer, and cancer is second only to heart disease as the leading cause of death.<sup>2</sup> Undergoing cancer treatment is a stressful process for everyone involved, and chemotherapy-induced alopecia can cause added emotional stress.

Use of scalp cooling to prevent hair loss during chemotherapy has been documented outside the US since the 1970s, but the US was slow to catch on.<sup>8</sup> The FDA finally approved the first scalp cooling system, Digni-Cap, to be marketed in 2015. It took until July 2017 for wider use to gain approval.<sup>6</sup> Scalp cooling before, during and after chemotherapy is highly effective in preventing hair loss. It is thought to work through local vasoconstriction which reduces delivery of chemotherapy to the scalp and reduces drug uptake.<sup>10</sup>

### Underwriting bottom line

The world of underwriting is ever changing as the world of science and medicine advances. As underwriters, we need to keep abreast of the latest trends and advancements to keep our skills sharp and relevant. To do that, keep reading *ON THE RISK*.

### Notes

1. A Brief Overview of Risk Evaluation & Mitigation Strategies. United States Food & Drug Administration. [www.fda.gov/downloads/AboutFDA/Transparency/Basics/UCM328784.pdf](http://www.fda.gov/downloads/AboutFDA/Transparency/Basics/UCM328784.pdf) (Accessed on April 6, 2018).
2. Cancer Facts & Figures 2018. American Cancer Society. [www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2018/cancer-facts-and-figures-2018.pdf](http://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2018/cancer-facts-and-figures-2018.pdf) (Accessed on March 14, 2018).
3. Conger, K. Cancer “vaccine” eliminates tumors in mice. <https://med.stanford.edu/news/all-news/2018/01/cancer-vaccine-eliminates-tumors-in-mice.html> (Accessed on January 31, 2018).
4. FDA Approves Ivacaftor for 23 Additional CFTR Mutations. Cystic Fibrosis Foundation. 17 May 2017. [www.cff.org/News/News-Archive/2017/FDA-Approves-Ivacaftor-for-23-Additional-CFTR-Mutations/](http://www.cff.org/News/News-Archive/2017/FDA-Approves-Ivacaftor-for-23-Additional-CFTR-Mutations/) (Accessed on March 14, 2018).
5. FDA Approves New Cystic Fibrosis Treatment for 4% of Patients. The Tech Museum of Innovation. [http://genetics.thetech.org/original\\_news/news150](http://genetics.thetech.org/original_news/news150) (Accessed on March 14, 2018).
6. FDA Clears Wider Use of Cooling Cap to Reduce Hair Loss During Chemotherapy. National Cancer Institute. 21 July 2017. [www.cancer.gov/news-events/cancer-currents-blog/2017/fda-cooling-cap-chemotherapy](http://www.cancer.gov/news-events/cancer-currents-blog/2017/fda-cooling-cap-chemotherapy) (Accessed on March 14, 2018).
7. Grady, D. FDA Approves First Gene-Altering Leukemia Treatment, Costing \$457,000. *New York Times*. 30 August 2017. [www.nytimes.com/2017/08/30/health/gene-therapy-cancer.html](http://www.nytimes.com/2017/08/30/health/gene-therapy-cancer.html) (Accessed on March 14, 2018).
8. Komen, MM et al. Factors Influencing the Effectiveness of Scalp Cooling in the Prevention of Chemotherapy-Induced Alopecia. *Oncologist* 18.7(2013): 885-891.
9. Larson, RA. Treatment of relapsed or refractory acute lymphoblastic leukemia in adults. Lowenberg, B & Rosmarin, AG, ed. UpToDate. Waltham, MA: UpToDate Inc. [www.uptodate.com](http://www.uptodate.com) (Accessed on March 14, 2018).
10. Rugo, MD et al. Chemotherapy-induced alopecia. Drews, RE et al. ed. UpToDate. Waltham, MA: UpToDate Inc. [www.uptodate.com](http://www.uptodate.com) (Accessed on March 14, 2018).
11. Sagiv-Barfi, I., et al. Eradication of spontaneous malignancy by local immunotherapy. *Science Translational Medicine* 10.426 (31 January 2018).
12. Simon, RH. Cystic fibrosis: Overview of the treatment of lung disease. Mallory GB & Hoppin AG, ed. UpToDate. Waltham, MA: UpToDate Inc. [www.uptodate.com](http://www.uptodate.com) (Accessed on March 14, 2018).
13. Tseng, R, et al. Structural basis of the day-night transition in a bacterial circadian clock. *Science* 355.6330 (2017): 1174-1180.
14. Wyatt, JK. Overview of circadian sleep-wake rhythm disorders. Goldstein, CA & Eichler, AF, ed. UpToDate. Waltham, MA: UpToDate Inc. [www.uptodate.com](http://www.uptodate.com) (Accessed on March 14, 2018).