Drugs that made headlines in 2017

In 2017, cancer drugs once again dominated the news, with many of these medications making headlines for being the first of their kind to gain approval. Beyond cancer, drugs for inflammatory diseases also received attention, for both their successes and their failures.

Green light

Dupixent

In March, the US Food and Drug Administration (FDA) approved a drug for adults with a moderate-to-severe form of eczema. Dupixent (dupilumab) is being developed jointly by Regeneron Pharmaceuticals and Sanofi, and is administered by injection. The dupilumab antibody binds to the receptor for a protein called IL-4, thereby inhibiting the inflammation underlying eczema. Although Dupixent provides a new option to those who have not had relief from topical eczema treatments such as creams, the drug comes at a hefty price of $37,000 a year.

Ocrevus

The FDA approved Ocrevus (ocrelizumab) in March for severe and relapsing forms of multiple sclerosis, making it the first drug to treat the severe form of the disease, known as primary progressive multiple sclerosis (PPMS). The US Centers for Disease Control and Prevention (CDC) estimates that roughly 15% of the people with multiple sclerosis in the US have PPMS. In a phase 3 trial evaluating Ocrevus in those with PPMS, the proportion of participants who had not relapsed or experienced disease progression after 96 weeks of treatment was 82% greater than for participants who were given another standard multiple sclerosis treatment. Ocrevus is being produced by Genentech.

Kymriah

In August, Kymriah (tisagenlecleucel) became the first gene therapy approved in the US when the FDA granted approval for use of the drug to treat a form of acute lymphoblastic leukemia (ALL) in patients 25 years of age or younger. Kymriah uses a patient's own T cells that have been genetically modified to include a gene encoding a chimeric antigen receptor (CAR). The modified T cells are injected into the patient, at which point the CAR protein directs the T cells to find and kill cancerous cells that have the CD19 antigen on their surface. In a clinical trial of 63 patients with relapsed or refractory B cell ALL, Kymriah, which is made by Novartis, achieved a remission rate of 83% within three months of treatment.

Radicava

New Jersey–based Mitsubishi Tanabe Pharma America won approval from the FDA for its amyotrophic lateral sclerosis (ALS) drug Radicava (edaravone) in May. The drug, which has been approved in Japan since 2015, is administered as an injection and could help the approximately 12,000 Americans, according to the CDC, who suffer from ALS. FDA officials approved Radicava based on data from a trial of 137 participants conducted in Japan. Those being treated with Radicava demonstrated a 33% reduction in the rate of decline in their physical function when compared to those treated with placebo. The approval of Radicava is the first of an ALS drug in the US in more than two decades.

Ilaris

Two new studies funded by Novartis found signs that Ilaris (canakinumab), a drug that is already being marketed by the company to treat a form of systemic juvenile idiopathic arthritis, could also reduce the risk of heart attack, stroke and even lung cancer in those who have already had a heart attack and are at risk for another. For every 100 patients followed for a year, 4.5 in the placebo group had a heart attack, stroke or died from a heart attack (*N. Engl. J. Med.* **377**, 1119–1131, 2017). That figure for those treated with the optimal dose of Ilaris was around 3.9. In a second study, researchers found that the highest dose of Ilaris also seemed to reduce the incidence of lung cancer by 67% and deaths by 77% (*Lancet* **390**, 1833–1842, 2017).

Idhifa

Those who have acute myeloid leukemia (AML) with isocitrate dehydrogenase-2 (*IDH2*) mutations have a new therapeutic option in Idhifa (enasidenib), which received FDA approval in August. Idhifa is produced by Celgene and is approved for use with the companion diagnostic assay produced by Abbott Laboratories that detects mutations in the *IDH2* gene. Idhifa works by blocking the activity of an enzyme that promotes cell growth. All participants in a 199-person trial received Idhifa, and 19% of participants experienced remission for roughly eight months following at least six months of treatment. One-third of the participants who previously needed blood or platelet transfusions because of their AML no longer required transfusions for at least one 56-day cycle after receiving Idhifa.

Imfinzi (durvalumab)

The immunotherapy agent Imfinzi (durvalumab), when compared with placebo, improved the overall length of time during which disease did not worsen in patients with locally advanced, unresectable stage 3 non-small-cell lung cancer (NSCLC). According to results from the Pacific trial, which is evaluating Imfinzi, the 473 patients treated with the drug had a median progression-free survival time of almost 17 months, as compared to an average survival time of less than 6 months in the 236 placebo-treated patients (*N. Engl. J. Med.* http://dx.doi.org/10.1056/NEJMoa1709937, 2017). Imfinzi is being developed by AstraZeneca, which received breakthrough designation for Imfinzi for the treatment of stage 3 unresectable NSCLC from the FDA in July of this year.

Heplisav-B

An FDA advisory panel voted 12–1 in favor of approving the hepatitis B virus vaccine from Dynavax Technologies, Heplisav-B, in July of this year. But in August the agency delayed its decision on whether to approve the vaccine, pending information from Dynavax about its plans for post-market studies. As far back as 2008, the FDA placed a clinical hold on trials testing the vaccine because of an adverse autoimmune event in a clinical trial. In 2013, the FDA rejected Dynavax's application, requesting more clinical trial data, and again rejected it in 2016, citing concerns over cardiac events in a different trial. Finally, on 9 November, the company announced that the FDA had approved Heplisav-B.

Yellow light

UCART123

Paris-headquartered Cellectis faced a setback to its CAR-T program when the FDA placed a clinical hold in September on two of its phase 1 trials evaluating the company's candidate therapy UCART123. The two trials were testing UCART123 in AML and in blastic plasmacytoid dendritic cell neoplasm (BPDCN), a rare and aggressive form of blood cancer. The clinical hold was placed after a patient in the BPCDN trial died after experiencing a lung infection and cytokine release syndrome. A patient in the AML arm also experienced cytokine release syndrome, after which an advisory committee recommended reducing the dose of UCART123. The FDA removed the clinical hold on Cellectis' phase 1 trials on 6 November.

Keytruda

Merck faced both ups and downs this year with its anti-PD-1 drug Keytruda (pembrolizumab). On the positive side, the FDA approved Keytruda for use in patients with solid tumors—usually colorectal, endometrial or gastrointestinal—with a biomarker of high microsatellite instability or deficiency for DNA mismatch repair. This marks the first time the FDA has granted approval to a drug that will be administered based not on tumor location but on the genetic qualities of the tumor. In a disappointment, however, Keytruda failed to improve the overall survival of clinical trial participants with head and neck cancers. The drug is still being evaluated in two other trials in individuals with head and neck cancers, and so Keytruda's ability to treat this type of cancer remains to be seen.

Fitusiran

Alnylam and Sanofi's collaborative study of the RNA interference drug fitusiran was halted after a patient died of a blood clot in a phase 2 trial. The drug is being evaluated in patients with the A and B types of hemophilia and works by targeting defective RNA code with small interfering RNA molecules, thereby suppressing the synthesis of a defective protein that fails to produce coagulation. The death of the study participant led to Alnylam pausing other clinical trials of fitusiran. As *Nature Medicine* went to press, Alnylam and the FDA had agreed upon new safety measures when it came to dosing fitusiran, and the FDA was considering removing the clinical hold on the phase 2 trial.

Red light

Lampalizumab

Roche's Genentech announced in September that one of its two phase 3 trials to evaluate lampalizumab had failed to meet its primary endpoint. Lampalizumab is a monoclonal antibody for the treatment of geographic atrophy, an advanced form of age-related macular degeneration. When compared to placebo, lampalizumab fared no better when it came to reducing the average size of geographic atrophy lesions in patients, and the company stopped further treatment of study participants. On 10 November, Genentech announced that its other phase 3 trial evaluating lampalizumab had also failed to meet its primary endpoint. As a result of the two trials' results, Genentech announced that it would not be pursuing marketing approval for lampalizumab for the treatment of geographic atrophy.

Imfinzi, again

Despite success in the Pacific trial, AstraZeneca's Imfinzi (durvalumab) failed to meet a primary endpoint when combined with tremelimumab (anti-CTLA-4) in patients with metastatic NSCLC in a trial known as Mystic. Although not formally tested, a secondary endpoint evaluating Imfinzi on its own as a therapy to block disease progression in study participants also would have failed when comparing the drug with the current standard of chemotherapy. The trial will continue to evaluate Imfinzi's effect, both as a standalone therapy and in combination with tremelimumab, on the overall survival of patients with metastatic NSCLC, with results from those endpoints expected in the first half of 2018.

Verubecestat

Merck announced in February that it was suspending its Epoch study, which was evaluating verubecestat for treating mild-to-moderate Alzheimer's disease. Verubecestat is an inhibitor of beta-site amyloid precursor protein–cleaving enzyme 1 (BACE1) that would have helped prevent the buildup of amyloid-β and, according to some theories surrounding Alzheimer's disease, stop progression or prevent onset of the disease. The drug was being evaluated in two phase 3 studies, but an external data-monitoring committee said that there was "virtually no chance of finding a positive clinical effect," adding to the string of phase 3 disappointments in the Alzheimer's disease field. Merck is evaluating the drug in another trial in those with a very early form of Alzheimer's disease, and results of that trial are expected in early 2019.

Plivensia

Janssen Biotech in Horsham, Pennsylvania, announced in early August that the FDA did not recommend approval of its rheumatoid arthritis drug Plivensia (sirukumab). The drug is an antibody that works to block inflammation caused by the cytokine IL-6. An FDA panel voted 12–1 against approving the drug, saying that its safety profile did not justify putting the drug on the market, especially when two similar drugs without the same safety issues are already available commercially.

Baricitinib

In April of this year, Eli Lilly and Incyte failed to receive FDA approval for their rheumatoid arthritis drug baricitinib. The FDA cited concerns that the clinical trial data presented in the application were not sufficient to determine the most appropriate dosages for the drug. In response, the two companies announced plans in August to resubmit an application with new efficacy data by January 2018. Baricitinib works by inhibiting enzymes in the Janus kinase (JAK) family, which are known to enhance cytokine signaling and, in turn, inflammatory responses.

NSI-189

Maryland–based biopharmaceutical company Neuralstem announced in July that the lead candidate in its pipeline, an antidepressant known as NSI-189, failed to meet its primary endpoint of a statistically significant reduction in depression symptoms. The company was evaluating NSI-189 in a phase 2 trial of 220 patients with major depressive disorder and measuring changes in scoring on the Montgomery–Åsberg Depression Rating Scale, a questionnaire used to determine the severity of depression. Neuralstem is also evaluating NSI-189 for the treatment of other conditions, including diabetic neuropathy and ischemic stroke.

Shraddha Chakradha