

THE PRESCRIBE AWARDS FOR 2019

The three annual *Prescrire* Awards, for Drugs, Packaging and Information, are granted in total independence by the *Prescrire* Editorial Staff. The rules governing the three *Prescrire* Awards are available online (in French) at english.prescrire.org > Topics > Annual *Prescrire* Awards > The *Prescrire* Drug Awards



2019 *Prescrire* Drug Awards

Each month, the *Prescrire* Editorial Staff publish systematic analyses of the data available on the evaluation of: new drugs, existing drugs authorised for different clinical situations, and new forms or new dose strengths of existing drugs. Occasionally, when the latest data on a drug we have already analysed justify reassessing its harm-benefit balance, we repeat our analysis “with more follow-up”. The goal is to help readers distinguish, among the plethora of new products, those worth adding to their list of useful therapies or worth using instead of other products, and also to point out which medicines are best avoided.

Our analyses are based on rigorous procedures, described in detail at English.prescrire.org. The *Prescrire* Editorial Staff conduct these analyses free from influence by the health industry or institutions. We ensure our independence by being wholly funded by *Prescrire*'s subscribers, carrying no paid advertising in either the French or the English edition, and receiving no grants or subsidies of any kind.

The 2019 *Prescrire* Drug Awards are based on the analyses published in our French edition in 2019. These awards recognise products that represent a therapeutic advance, in that they offer better efficacy than existing treatments, provoke less frequent or less severe adverse effects (provided they also have similar efficacy), or enable a drug with a favourable harm-benefit balance to be used more safely or easily.

Six *Prescrire* Drug Awards for 2019, but no Pilule d'Or

For the fifth year running, none of the drugs examined in 2019 represented a major therapeutic advance worthy of a Pilule d'Or (Golden Pill Award). Nevertheless, six received a *Prescrire* Drug Award.

Emicizumab for haemophilia A with “factor VIII inhibitors”: prevents bleeding episodes

Haemophilia A is a bleeding disorder due to a deficiency in clotting factor VIII. The standard treatment for preventing or treating bleeding episodes in patients with haemophilia A is to administer the factor VIII they lack. One major adverse effect of this treatment is the development of “factor VIII inhibitors”, which are antibodies produced by the patient's immune system against the administered factor VIII that render it ineffective. One option in this

situation is to administer a “bypassing” agent, so called because it bypasses the factor VIII-dependent step of the coagulation cascade.

Emicizumab is a monoclonal antibody that acts at the same step of the coagulation cascade as factor VIII but is not neutralised by “factor VIII inhibitors”. *Emicizumab* is effective in preventing bleeding episodes in patients with these inhibitors, even in those who have frequent bleeds while using bypassing agents. *Emicizumab* is administered by subcutaneous injection once a week (or once every 4 weeks), whereas preventive therapy with bypassing agents requires several intravenous infusions a week. Hemlibra® earned a place on the 2019 Honours List for these advantages.

These advantages must be weighed against the lack of evaluation in certain clinical situations, the risk of thrombotic events, the foreseeable allergic reactions, and many uncertainties over its adverse effects.

CAR T-cell therapies for haematological malignancies when other treatment options have been exhausted: probably prolong survival, but further evaluation required

In chimeric antigen receptor (CAR) T-cell therapy, the patient receives their own T cells that have been genetically modified to express a receptor at their surface designed to cause the T cells to bind to cancer cells so they can destroy them.

The 2019 Honours List features two CAR T-cell therapies: *tisagenlecleucel* (Kymriah®), authorised for the treatment of B-cell acute lymphoblastic leukaemia in children and young adults with no further treatment options, and *axicabtagene ciloleucel* (Yescarta®) for patients with certain types of large B-cell lymphoma and no further treatment options. The prognosis in both these clinical situations is poor, and patients often survive for no more than a few months. CAR T-cell therapy appears to prolong their survival: at least half of the patients in trials were still alive 1 to 2 years after receiving this treatment. It is difficult to quantify this advance because the trials were small and non-comparative. Further clinical evaluation of these therapies is required.

CAR T-cell therapies provoke a great many adverse effects that are often serious or even fatal, including cytokine release syndrome, neurological disorders, infections and haematological disorders.

Because CAR T cells are prepared specifically for one patient, special procedures are required to ensure they are given to the right person.

Ruxolitinib and trastuzumab emtansine: revealed to be advances by further evaluation

Two drugs were recognised as Noteworthy in 2019, several years after their market introduction. In both cases, it was not possible to determine their harm-benefit balance from their initial, inadequate clinical evaluation, but more recent data showed them to represent a therapeutic advance.

Further evaluation of the Janus kinase (JAK) inhibitor *ruxolitinib* (Jakavi®) in patients with symptomatic myelofibrosis showed that it reduces spleen volume in about half of patients, for as long as treatment continues. The spleen can be very large in this situation, impairing the patient's quality of life. *Ruxolitinib* has not been shown to affect other symptoms, but probably extends survival. These benefits must be weighed against its harms, in particular infections, worsening of the haematological disorders associated with myelofibrosis, and neurological disorders. Patients commonly discontinue treatment due to its adverse effects.

Two randomised trials have shown that, compared with other antineoplastic drugs, *trastuzumab emtansine* (Kadcyla®), an anti-HER2 monoclonal antibody conjugated to a cytotoxic drug, increases survival by 4 to 7 months in women with inoperable breast cancer overexpressing the protein HER2 who have already received a taxane and *trastuzumab*. This modest survival gain is tempered by its serious adverse effects, including heart failure, thrombocytopenia, haemorrhages and liver injury. Deaths have been caused by confusion between *trastuzumab emtansine* and *trastuzumab*.

Pembrolizumab as first-line therapy for certain types of lung cancer: alone or with other antineoplastic drugs, depending on PD-L1 expression

In four randomised clinical trials of first-line therapy for patients with metastatic non-small cell lung cancer, the immunostimulatory anti-PD-1 monoclonal antibody *pembrolizumab* (Keytruda®) extended median survival by several months. When most of the tumour cells express the PD-L1 protein, *pembrolizumab* is used alone. When fewer than half of the tumour cells express PD-L1, the benefit of *pembrolizumab* has mainly been demonstrated when added to platinum-based chemotherapy. Keytruda® was deemed Noteworthy in 2019 on the basis of these data.

Pembrolizumab's adverse effects are mainly of immunological origin and can affect multiple organs. They include pneumonitis, myocarditis, colitis, stomatitis, gastritis, pancreatitis, hepatitis and nephritis.

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2019 Pilule d'Or/Golden Pill

The Pilule d'Or (Golden Pill) is granted to drugs that represent a major therapeutic advance in a field in which no treatment was previously available.

2019

NOT AWARDED

2019 Honours List

Drugs included on the Honours List constitute a clear advance for some patients compared with existing therapeutic options, albeit with limitations. Those on this year's list, in alphabetical order, are:

- **HEMLIBRA® (*emicizumab*)**
Roche
Prophylaxis of bleeding episodes in patients with haemophilia A and "factor VIII inhibitors" (Prescrire Int n° 210)
- **KYMRIAH® (*tisagenlecleucel*)**
Novartis
B-cell acute lymphoblastic leukaemia in children and young adults when other treatment options have been exhausted (Prescrire Int n° 208)
- **YESCARTA® (*axicabtagene ciloleucel*)**
Kite Pharma (a Gilead company)
Certain types of large B-cell lymphomas when other treatment options have been exhausted (Prescrire Int n° 208)

Noteworthy in 2019

Drugs deemed "Noteworthy" provide a modest improvement in patient care. This year's Noteworthy drugs are, in alphabetical order:

- **JAKAVI® (*ruxolitinib*)**
Novartis
Symptomatic myelofibrosis (Prescrire Int n° 137 and Prescrire Int n° 205, with more follow-up)
- **KADCYLA® (*trastuzumab emtansine*)**
Roche
HER2-positive inoperable breast cancer in women who previously received *trastuzumab* and a taxane (Prescrire Int n° 155 and Prescrire Int n° 207, with more follow-up)
- **KEYTRUDA® (*pembrolizumab*)**
MSD
Metastatic non-small cell lung cancer, as first-line treatment (Prescrire Int n° 210 and Prescrire Int n° 212)