Drug Information Bulletin

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Content

Editorial

The attitude of the pharmaceutical company reflected by a statement by the CEO of a multinational company that the company didn't develop a cancer drug for the Indian market, but rather "for western patients who can afford". This statement has raised question about the investment of pharmaceutical companies on drug research of diseases of the rich like- Diabetes, High Blood Pressure, Cancer etc. instead of spending on R & D for development of diseases of the poor like-TB, Malaria etc. It has been supported by the statement of a multinational company that they are winding up research on Malaria, TB and neglected tropical diseases.

Recent policy change of some companies of investing on R & D of diseases other than antiinfectives is a worrying trend. It is the high time when more research requires to be done on antiinfectives due to development of some drug resistant strains like MDR/XRD-TB.

The lack investment on R&D for new drugs doesn't only affect developing/underdeveloped countries; developed countries are also faced with a huge gap in medical innovation. With the numbers of cases of antibiotic resistance on the rise in many parts of the world including in western part of the globe, worryingly, few new antibiotics being developed. A day will come when people will develop infections that are resistant to all existing antibiotics, and we'll have nothing effective with which to treat them.

The US priority review voucher scheme (PRV) was intended to encourage drug companies to invest in treatments for neglected diseases. But nearly seven years on, there is little demonstrated innovation and evidence that the benefits are not going where they were intended. It is felt that the PRV scheme should relooked and redesigned so that real benefit goes to them who actually require it.

Dr. Subhash C. Mandal
Editor

New Drug: Brentuximab vedotin

Approved indication: Hodgkin lymphoma, anaplastic large cell lymphoma
Adcetris (Takeda)
vials containing 50 mg powder for injection
Australian Medicines Handbook section 14.2.1

Brentuximab vedotin consists of an anti-CD30 antibody conjugated to a cytotoxic drug called monomethylauristatin E (MMAE). The cytotoxic part disrupts the microtubule network in cells and causes apoptosis. This drug is indicated for patients with relapsed or refractory classic Hodgkin lymphoma (including after autologous stem cell transplant) and systemic anaplastic large cell lymphoma. CD30 is selectively expressed on the surface of lymphoma cells in both of these diseases.

Maximum concentrations of the antibody–drug conjugate are reached at the end of a 30-minute intravenous infusion and its terminal half-life is 4–6 days. The antibody portion is thought to be catabolised and a fraction of the cytotoxic portion - MMAE - is metabolised and excreted in the urine and faeces. A lower starting dose should be considered in patients with hepatic impairment or severe renal impairment and close monitoring is recommended.

The anti-CD30 antibody on its own has minimal efficacy – in a trial of 72 people with relapsed or refractory CD30-positive lymphomas, only six responded.1 However, conjugating the antibody to a cytotoxic drug improved antitumour activity. In a single-arm, open-label phase II trial, 75% of patients with relapsed or refractory Hodgkin lymphoma responded to brentuximab vedotin.2 All of these patients had previously had an autologous transplant. In a similarly designed trial in relapsed or refractory systemic anaplastic large cell lymphoma, 86% of patients had a response to brentuximab vedotin.3 Just over a quarter of the participants had previously had an autologoustransplant.
Efficacy of brentuximab vedotin in two trials

Infection was the most common adverse event in the trials, occurring in 61% of people. In 16% of cases, infection was thought to be related to the study drug. Serious infections included pneumonia, staphylococcal bacteraemia, sepsis and herpes zoster. The opportunistic infections Pneumocystis jirovecii pneumonia and oral candidiasis also occurred.

The most common drug-related adverse effects included peripheral sensory neuropathy (44%), fatigue (42%), nausea (41%), diarrhoea (34%), neutropenia (21%) and vomiting (20%). Some of these were serious – neutropenia and peripheral sensory neuropathy resulted in delayed or reduced dosing. Other serious drug reactions included thrombocytopenia, constipation, diarrhoea, vomiting, fever, peripheral motor neuropathy, hyperglycaemia, demyelinating polyneuropathy, tumour lysis syndrome and Stevens-Johnson syndrome.

Some adverse events were fatal including sepsis, acute pancreatitis and progressive multifocal leukoencephalopathy. Treatment should be stopped if any of these are suspected.

Anaphylaxis has been reported to occur during and after the infusion. This was more common in people with antibodies to the study drug (approximately a third of patients).

Co-administration of strong inhibitors of cytochrome P450 (CYP) 3A4 and P-glycoprotein (e.g. ketoconazole) increases exposure to MMAE so may increase the risk of adverse effects such as neutropenia. The concomitant use of brentuximab vedotin with bleomycin causes pulmonary toxicity andis contraindicated.

Brentuximab vedotin has the potential to cause fetal harm and is not recommended during pregnancy. There are no data for its use during lactation. Animal toxicity studies indicated that this drug may affect reproductive function and fertility in males. Men are advised to have sperm frozen before

treatment and avoid fathering a child during and for six months aftertreatment.

Brentuximab vedotin seemed to be effective in advanced Hodgkin lymphoma and anaplastic large cell lymphoma, with 34−57% of patients achieving complete remission. However, the trials were small and there were no comparators. Adverse effects can be severe and sometimes fatal and are likely to limit treatment dose and duration. There are no safety data for this drug beyond 12 months of treatment.

References:

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2. Younes A, Gopal AK, Smith SE, Ansell SM, Rosenblatt JD, Savage KJ, et al. Results of a pivotal phase II study of brentuximab vedotin for patients with relapsed or refractory Hodgkin's lymphoma. J Clin Oncol 2012;30:2183-9.
3. Pro B, Advani R, Brice P, Bartlett NL, Rosenblatt JD, Illidge T, et al. Brentuximab vedotin (SGN-35) in patients with relapsed or refractory systemic anaplastic large-cell lymphoma: results of a phase II study. J Clin Oncol 2012;30:2190-6.

Source: Australian Prescriber

US incentive scheme for neglected diseases: a good idea gone wrong?

The US priority review voucher scheme was intended to encourage drug companies to invest in treatments for neglected diseases. But nearly seven years on, as Peter Doshi reports, there is little demonstrated innovation and evidence that the benefits are not going where they were intended.

Bill Gates believes or at least believed that government led market incentives could solve the fundamental conundrum in developing drugs for neglected diseases. For-profit companies see little economic justification to invest in treating diseases that affect the poor, but 'creative capitalism' as Gates put it, could lure companies into solving some of the world;'s most pressing problems by bringing to market new treatments for endemic tropical diseases.

For details: BMJ 2014; 349 doi: http://dx.doi.org/10.1136/bmj.g4665 (Published 21 July 2014)

Docs complain to CMS about 'Sunshine' data disclosures

A group of medical societies and pharmaceutical industry trade groups is pushing the government to flesh out data that will be published next month showing how much drug makers pay doctors.

They sent a letter today to the Centers for Medicare and Medicaid Services to ask the agency to explain what context will be provided to help the public understand the justification for payments, such as speaking fees and grants used to bankroll clinical research.

The letter is signed by more than 20 medical societies and organizations including the American Urological Association, as well as heavyweight industry trade groups Biotechnology Industry Organization and the Pharmaceutical Research & Manufacturers of America.

The missive was sent as CMS plans to post the payment data in an online, searchable database as required in the Sunshine Act provision of the Affordable Care Act. The provision was passed in response to concerns that medical practice may be unduly influenced by industry.

The law requires most drug and device makers to report to CMS detailed information about payments and gifts provided to U.S. doctors and teaching hospitals. The disclosures are being made in stages, but September marks the debut when payments will appear publicly.

Supporters of the Sunshine Act say the transparency will provide useful information to patients about the relationships their doctors may have with drug or device makers, and serve as a deterrent to the more

extreme examples of industry money unduly influencing medical care.

But some doctors and companies fear payment data will be misinterpreted by the public, or painted with a broad brush. They say there are legitimate interactions that serve to advance medicine, and that doctors should be compensated for services such as consulting for a company about the development of a new product.

Some medical societies teamed up with industry groups to form Partners for Healthy Dialogues, to defend such interactions between industry and doctors, and some of its members signed the letter sent to CMS.

The medical societies and industry trade group lament what they write in the letter is a dearth of context that accompanied CMS's milestone release of Medicare Part B payments to physicians earlier this year.

Some medical groups say the data did not include context to show which doctors may be abusing the system and which were receiving big payments because of high overhead costs.

"We do not believe this is an effective way to share data with the public and, in fact, can lead to confusion and misinterpretation," the groups wrote, adding that "we have heard nothing" about how CMS will present the data. And they want CMS to preview with doctors the proposed contextual information that will accompany the data.

Drug and device makers are required to report to CMS the payments made to individual physicians broken down by different categories including fees for speaking and consulting, food, research and gifts. But the letter says CMS has not explained how data will be publicly presented in order to distinguish between payments.

For instance, Robert Harbaugh, president of the American Association of Neurological Surgeons, one of the groups that signed the letter, notes that he is the recipient of a grant from a foundation affiliated with Integra Life Sciences, a device maker.

The company is funding a resident-physician exchange program between his institution, the Pennsylvania State University Milton S. Hersey Medical Center, and another in China. He fears the CMS data release will make it appear that he personally received the entire grant amount, which he estimated at about $250,000 for a five-year period.

"It would be nice to be able to put some context around the dollar figures," he says, although he acknowledges that he has not viewed his own data.

We asked CMS for comment and will update you accordingly.

The medical and trade groups also asked CMS to promote awareness among physicians that the payment data will be released soon, saying many doctors remain unaware.

CMS recently began letting doctors register online so they can view their payment data before it is made public, and dispute any amounts in hopes of resolving discrepancies with drug and device makers.

The groups complain the process, which runs through August 27, is cumbersome and creates the risk that doctors will not complete their registrations. After the deadline, physicians will lose the ability to easily challenge payment data, according to John Murphy, an assistant general counsel at the PhRMA trade group.

Source: The Wall Street Journal

Forthcoming Event

IPA Convention 2014

(IPAs Platinum Jubilee Celebration Launch Programme)

8th August 2014

Venue: NIMHANS Convention Centre, Bangalore

Registration:

Non Member: Rs.1500

Member: Rs. 1000

Student Member:Rs. 750

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