Drug Information Bulletin

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Volume: 07 ***Number: 35*** ***8th December 2013***

Content

Editorial

Millions of patients suffering from pain are eagerly waiting for the fate of the Narcotic Drugs and Psychotropic Substances (amendment) Bill-2011 expected to be placed before the ongoing session of Indian Parliament. The Bill has been introduced in the Lok Sabha earlier in 8th September 2011 and it was forwarded to the Parliamentary Standing Committee for examination and report on 13th September 2011. The Committee has consulted several stake holders like- Lawyers Collective, New Delhi; Amnesty International, London, U.K.; Indian Harm Reduction Network, New Delhi; Indian Chemical Council, New Delhi; Bulk Drug Manufacturers Association (India); Organization of Pharmaceutical Producers of India, Mumbai, Indian Drug Manufacturers' Association, Mumbai and so on. Thereafter they have finalized their recommendation and submitted their report, which was introduced before the both houses of the Parliament on 21st March 2012.

Initially there was diverse opinion on this Bill one hand regulators wanted stringent legislation to restrict misuse of Narcotic and Psychotropic Drugs, on the other hand health activists were in the opinion that this act should be amended to ensure this medicines for clinical purpose especially for pain management. The committee has made several recommendations and one of them are "The Bill proposes to add the term "management" after "identification, treatment" etc. of addicts at centres established by the government. The Committee is in agreement with this and recommends that the government should be more proactive in establishing, recognizing and approving more rehabilitation / management centres for persons with drug addiction".

Experts believe that the present form of the Bill is considered as a balanced legislation to ensure both the objectives and wanted the Bill should be cleared by both the houses of Parliament in the ongoing session in the interest of the millions of patients suffering from pain (especially terminal cancer and AIDS patients).

New Drug: Ruxolitinib

Approved indication in Australia: Myelofibrosis

5 mg, 15 mg and 20 mg tablets

Myelofibrosis can present as a primary disease or develop from polycythaemia vera or essential thrombocythaemia. It is characterised by fibrosis of the bone marrow, progressive anaemia and hepatosplenomegaly from overproduction of abnormal, immature blood cells. Survival of patients after diagnosis ranges from 2 to 11 years. Apart from stem cell transplant, current treatment is usually supportive and directed at symptoms.

Myelofibrosis is associated with overactivation of the Janus kinase pathway. In many patients, this is associated with a mutation in the Janus kinase 2 gene (V617F mutation). Overactivity of the pathway results in increased signalling of a number of cytokines and growth factors involved in haematopoiesis and immune functions.

Ruxolitinib is a selective inhibitor of Janus kinase 1 and 2. Its safety and efficacy has been assessed in two phase III trials – COMFORT-I and COMFORT-II.1,2 COMFORT-I compared ruxolitinib to placebo for 24 weeks whereas COMFORT-II compared it to best available therapy (usually hydroxyurea or glucocorticoids) for 48 weeks. Approximately half of the patients in the trials had primary myelofibrosis, a third had post-polycythaemia vera myelofibrosis and the rest had post-essential thrombocythaemia myelofibrosis.

In both studies, more patients receiving ruxolitinib (15–25 mg twice daily) had at least a 35% reduction in spleen size compared to patients receiving the control treatments (see Table). Spleen size increased in patients who did not receive ruxolitinib. In COMFORT-I, more patients taking ruxolitinib reported a 50% or more improvement in disease-associated symptoms (such as night sweats, itching and abdominal discomfort) than those taking placebo (45.9% vs 5.3%). Similarly in COMFORT-II, more patients taking ruxolitinib reported an improved quality of life and better functioning than those taking best available treatment. In both trials, patients with the V617F mutation seemed to have a better response to ruxolitinib than those without the mutation.

After a median follow-up of 12–14 months, there appeared to be a survival advantage for ruxolitinib over placebo in COMFORT-I (8.4% vs 15.6% of patients had died). However, this was not the case for ruxolitinib over best available treatment in COMFORT-II (7.6% vs 5.6% of patients had died).

Haematological effects with ruxolitinib are common. Anaemia (81.7%), thrombocytopenia (67.4%) and neutropenia (15.3%) were the most frequently reported in the trials. These were generally managed by dose interruption or adjustment but some patients required a blood or platelet transfusion. Three cases of bleeding were fatal in patients receiving ruxolitinib, but only one was attributed to the treatment. The dose should be reduced if platelets fall below 100 x 109/L and interrupted if they fall below 50 x 109/L.

Overall, infections were common with ruxolitinib and control treatments (38.1% vs 41.7% in COMFORT-I and 63.7% vs 42.5% in COMFORT-II) and were fatal in some cases. Urinary tract infections, herpes zoster, tuberculosis and progressive multifocal

leukoencephalopathy3 have been reported. Ruxolitinib should not be started until serious infections have resolved and patients should be monitored for signs and symptoms of infection. Diarrhoea1,2, headache, dizziness, fever and bruising frequently occurred with ruxolitinib, as did hypercholesterolaemia.

Elevations in alanine aminotransferase and aspartate aminotransferase were very common during treatment so monitoring of liver function should be considered.

Ruxolitinib is a pregnancy category C drug and is not recommended in pregnancy or lactation. Animal studies found that it crosses the placenta and is excreted in breast milk.

Following oral administration, ruxolitinib is rapidly absorbed with maximum plasma concentrations reached after an hour. The drug is mainly metabolised by cytochrome P450 (CYP) 3A4 and metabolites are excreted in the urine (74%) and faeces (22%). Its elimination half-life is approximately three hours.

Blood counts should be measured before starting ruxolitinib as the initial dose is determined by the patient's platelet count. Blood monitoring every 2–4 weeks is required to initially titrate the dose (maximum is 25 mg twice daily). A lower starting dose should be used in hepatic impairment, moderate to severe renal impairment (creatinine clearance <60 mL/minute) and in people taking concomitant strong CYP3A4 inhibitors (such as boceprevir, clarithromycin and ketoconazole).

After stopping treatment, myelofibrosis symptoms return to baseline after seven days. Serious withdrawal symptoms have been reported and tapering the dose has been recommended.4

Ruxolitinib reduces spleen volume and disease-associated symptoms in patients with myelofibrosis and offers another option for symptom control. However, its long-term efficacy and tolerability are still to be determined.

References * †

1. Vertovsek S, Mesa RA, Gotlib J, Levy RS, Gupta V, DiPersio JF, et al. A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis. N Engl J Med 2012;366:799-807.
2. Harrison C, Kiladjian JJ, Al-Ali HK, Gisslinger H, Waltzman R, Stalbovskaya V, et al. JAK inhibition with ruxolitinib versus best available therapy for myelofibrosis. N Engl J Med 2012;366:787-98.
3. Wathes R, Moule S, Milojkovic D. Progressive multifocal leukoencephalopathy associated with ruxolitinib [letter]. N Engl J Med 2013;369:197-8.
4. Tefferi A, Pardanani A. Serious adverse events during ruxolitinib treatment discontinuation in patients with myelofibrosis. Mayo Clin Proc 2011; 86:1188-91.

Source: Aust Prescr 2013;36:212-8

Nanosponge vaccine could fight drug-resistant staph infections

A nanosponge vaccine could help eliminate methicillin-resistant Staphylococcus aureus infections by targeting a toxic chemical released by the bacteria, according to a study in the journal Nature Nanotechnology. The vaccine is made of a biodegradable polymer core covered with red blood cells. "We anticipate that this study will open new possibilities in the preparation of anti-toxin vaccines against the many

virulence factors that threaten public health," researchers wrote.

India records major success in battling HIV/AIDS

India provides anti-retroviral therapy to more than 650,000 HIV-positive individuals, which represents a fourfold increase from 2007 and makes it the country with the second-highest number of people receiving such drugs. In addition, India manufactures most of the drugs used to treat HIV/AIDS around the world. In April, former President Bill Clinton praised India's contributions in supplying HIV/AIDS drugs to Africa.

Emerging countries to have a look at best drug facilities in India

In order to dismiss the idea that drugmakers in India don't carry out the highest standards of quality, the country is hosting health regulators from emerging countries -- including the Philippines, Egypt, Vietnam, South Africa, Ghana and Kenya -- to showcase its finest drug industry facilities. "The idea behind this programme is to promote Indian pharmaceutical exports, apart from improving confidence among the global community that India is a trusted source for quality generics at affordable prices," said P.V. Appaji, Pharmaceuticals Export Promotion Council director general.

As more payers demand outcome studies, drug development costs will rise

Drug makers increasingly must conduct expensive outcome and comparative effectiveness studies to win not only FDA approval but also to be included on payers' formularies, writes John LaMattina, former president of Pfizer Global Research and Development. "The greater need for outcome studies will strain even the biggest pharmaceutical company R&D budgets," LaMattina writes. Yet patients, physicians and payers will benefit from outcome studies, and showing the real value of new medicines will increase public confidence in their long-term health benefits, LaMattina writes.

Report finds drug prices in Australia much higher than in other Commonwealth nations

A report by the Grattan Institute found that wholesale drug prices in Australia were "orders of magnitude" higher than in the U.K., New Zealand and Canada, causing Australians to pay $1 billion more for their prescriptions last year. "There's a cancer drug Anastrozole, where in Australia it's $92 for a pack of 30 1-milligram tablets, but in the U.K. it's only $3.30," said Stephen Duckett, the institute's health program director. Duckett is calling for a new authority to manage the Pharmaceutical Benefits Scheme.

Overregulation of drugs leaves billions in "intolerable pain"

The overregulation of pain medication is causing "a pandemic of intolerable pain," according to the Global Opioid Policy Initiative in a study published in the journal Annals of Oncology. In the Caribbean, Africa, Asia, Latin America and the Middle East, researchers assessed the availability of drugs considered essential to treat cancer pain, finding that "more than four billion people live in countries where regulations leave cancer patients suffering excruciating pain," lead author Nathan Cherny said.

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