Drug Information Bulletin

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Regulatory Affairs Division (RAD), IPA

CDSCO approved EUA for single dose Covid-19 Vaccine of J & J on 7.8.2021

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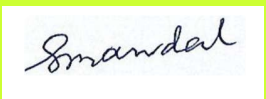
Content

Editorial

Independence Day Greetings from DIB!

India has approved Emergency Use Authorization (EUA) to the 5th candidate Covid Vaccine on 7th August 2021-single dose Jansen Ad26.CoV2.S vaccine developed by Jansen (sister organization of John & Johnson). It is a viral vector vaccine indicted for above 18 years. It is found that 28 days after inoculation of Janssen Ad26.CoV2. have an efficacy of 85.4% against severe disease and 93.1 % against hospitalization. A single dose of Janssen Ad26.COV2.S was found in clinical trials to have an efficacy of 66.9% against symptomatic moderate and severe SARS-CoV-2 infection. This vaccine has undergone review by the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) and found to be safe for use. The Janssen/Ad26.COV 2.S developed by Johnson & Johnson, was listed for EUL on 12 March 2021by WHO.

It is expected that this single dose vaccines will help quick vaccination of major portion of the population.



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New Drug: Trabectedin for soft tissue sarcoma

Approved indication: soft tissue sarcoma
vials containing 0.25 mg or 1 mg powder
for reconstitution

Soft tissue sarcomas are rare cancers that have a poor prognosis with up to 50% of patients developing metastases. Chemotherapy is not very effective, so the median survival with metastatic disease is about one year. The search for new treatments has led to the study of trabectedin. This is an alkaloid that was originally extracted from a sea squirt (*Ecteinascidia turbinata*). The molecule can now be synthesised.

Trabectedin is thought to act by binding to DNA. This distorts the DNA, which affects transcription and DNA repair mechanisms. These changes lead to multiple effects including cytotoxic, antiproliferative and antiangiogenic actions.

The drug has to be infused over 24 hours every three weeks. Trabectedin is widely distributed after infusion. It is metabolized by cytochrome P450 3A4 so plasma concentrations are likely to be altered by inducers and inhibitors of this enzyme system. Trabectedin is also a substrate of P-glycoprotein, so it may interact with drugs such as verapamil. Most of the metabolites are excreted in the faeces. The terminal half-life is about 180 hours. Liver impairment will increase concentrations of trabectedin. Renal impairment is unlikely to have much effect as little drug is excreted in the urine, but there have been no studies in patients with severe impairment.

The main clinical trial of trabectedin enrolled patients with unresectable, locally advanced or metastatic leiomyosarcoma or liposarcoma. These patients had previously been treated with at least an anthracycline regimen. A group of 345 patients was randomised to receive trabectedin and 173 were randomised to receive dacarbazine. They were treated every 21 days until the disease progressed or toxicity became unacceptable. An interim analysis took place after 188 patients had died. This found that there had been an objective response in 9.9% of the patients given trabectedin and 6.9% of those given dacarbazine. Progression-free survival was 4.2 months with trabectedin and 1.5 months with dacarbazine, but there was little difference in median overall survival (12.4 vs 12.9 months).[1]

The trial continued with eventually 384 patients in the trabectedin group and 193 in the dacarbazine group. In the final analysis 67% of the trabectedin group had died compared with 64% of the dacarbazine group. The median overall survival was 13.7 months with trabectedin and 13.1 months with dacarbazine.[2]

Trabectedin is a very toxic drug. Nearly all patients will experience adverse effects and in 63% of cases these will be serious. Approximately 4% of the patients had a fatal adverse reaction to trabectedin. In the clinical trial, dose reductions were required in 42% of the patients and 63% required a delay in treatment. The corresponding figures for dacarbazine were 12% and 42%.[2] Reasons for revising the trabectedin regimen include neutropenia, thrombocytopenia and increases in bilirubin or liver enzymes. Treatment must stop if the patient develops rhabdomyolysis, cardiomyopathy, or capillary leak syndrome. There can be severe injection-site reactions with tissue necrosis if there is extravasation of trabectedin. It is therefore strongly recommended that the drug is infused through a central venous line. Patients should be given intravenous dexamethasone half an hour before the infusion. This may provide some protection for the liver as well as reducing the nausea and vomiting associated with trabectedin.

Despite the significant hepatic and haematological toxicity, patients were able to endure trabectedin for longer than dacarbazine. The median number of treatment cycles was four versus two for dacarbazine.[2] There was no difference in overall survival between the drugs, but switching patients from dacarbazine to other drugs may have affected this result. The median time to starting another therapy was 3.5 months in the dacarbazine group and 6.8 months with trabectedin. However, a post hoc analysis taking these factors into account did not show a great advantage for trabectedin.[2] In Australia its use will be limited to patients with unresectable or metastatic liposarcoma or leiomyosarcoma who have already been treated with a regimen containing an anthracycline.

References

1. Demetri GD, von Mehren M, Jones RL, Hensley ML, Schuetze SM, Staddon A, et al. Efficacy and safety of trabectedin or dacarbazine for metastatic liposarcoma or leiomyosarcoma after failure of conventional chemotherapy: results of a phase III randomized multicenter clinical trial. J Clin Oncol 2016;34:786-93.
2. Patel S, von Mehren M, Reed DR, Kaiser P, Charlson J, Ryan CW, et al. Overall survival and histology-specific subgroup analyses from a phase 3, randomized controlled study of trabectedin or dacarbazine in patients with advanced liposarcoma or leiomyosarcoma. Cancer 2019;125:2610-20.

Status in India:

Trabectedin powder for concentrate for solution for infusion 1 mg/ vial for the treatment of patients with advanced soft tissue sarcoma, after failure of anthracyclines and ifosfamide, or who are unsuited to recieve these agents approved by CDSCO on 30.03.09. Subsequently Trabectedin powder for Conc. solution for infusion in combination with pegylated liposomal doxorubicin, it is indicated for the treatment of patients with relapsed platinum sensitive ovarian cancer approved by CDSCO on 20.03.2010. Presently it is manufactured in India and available in Indian market.

Covid Jabs May Not Provide Absolute Protection but Reduces Risk of Death, Complications: Soumya Swaminathan

Emphasising the importance of mass Covid vaccination through easy availability and accessibility, WHO's chief scientist Soumya Swaminathan on 12th August said even though vaccines may not be able to provide absolute protection against different variants of SARS-CoV2, it can certainly reduce the risk of death and complications.

The World Health Organisation's chief scientist said there will be a need to be on guard in the months to come as well.

She called on Science and Technology minister Jitendra Singh and discussed various aspects of the current COVID-19 pandemic as well as a wide range of other issues.

"Even though the vaccine may not be able to provide absolute protection against different variants of virus, it can certainly reduce the risk of death and complications," a statement quoting Swaminathan said.

In a country as diverse and heterogeneous as India, with multiple beliefs and faiths, it could not have been easy to embark on such a massive vaccination drive, Singh said.

"What is important to note is that India under Prime minister Narendra Modi showed a remarkable capacity to rise to the occasion and despite the constraints of resources, within one year, we are in a position to dispense more than one vaccine and other countries of the world are also looking up to us," the statement quoting Singh said.

Source: The New Indian Express

WHO to Test 3 Pre-Existing Drugs for Use against Covid-19

The World Health Organization says it will soon test three drugs used for other diseases to see if they might help patients sickened by the coronavirus.

In a statement on 11th August, the UN health agency says the three drugs would be adopted into the next phase of its ongoing global research into identifying potential treatments for Covid-19.

The drugs were chosen by an independent panel based on the likelihood they could prevent deaths in people hospitalised for coronavirus.

They include artesunate, a malaria drug, the cancer drug imatinib, and infliximab, currently used in people with diseases of the immune system.

“Finding more effective and accessible therapeutics for Covid-19 patients remains a critical need,” says WHO director-general Tedros Adhanom Ghebreyesus.

Source: India Today

Parliamentary Panel Recommends Implementation of Track & Trace Mechanism for Pharmaceutical Products

Expressing its concern on the rising incidences of spurious and adulterated drugs in India, the Department related Parliamentary Standing Committee on Commerce has recommended to the government to roll out a track and trace mechanism at the earliest for the detection of

authenticity and genuineness of medicines and medical devices from manufacturers to end users in supply chain.

The surge in spurious drugs in the country is not only a potential threat to the lives of its citizens but also dents its image as being one of the largest suppliers of drugs and pharmaceuticals in the world, stated the committee in its report presented to Rajya Sabha and Lok Sabha on July 23, 2021.

There has been a rise in the number of drug samples declared spurious or adulterated over the last four years. A total of 74586 drug samples were tested in 2015-16. Of them, 3703 drug samples were declared not of standard quality which is 4.96 per cent of the total drug samples while 234 drug samples were declared spurious or adulterated which is 0.31 per cent of the total drug samples.

In 2016-17 about 76721 drug samples were tested. Of them, 2780 drug samples (3.6 per cent) were declared NSQ and 123 drug samples (10.16 per cent) were declared spurious or adulterated.

In 2017-18 around 82599 drug samples were tested. Of them, 2783 drug samples (3.36 per cent) were declared NSQ while 236 drug samples (10.28) were declared spurious or adulterated.

In 2018-19 over 76101 drug samples were tested. Of them, 2549 drug samples (3.35 per cent) were declared NSQ while 205 drug samples (10.27 per cent) were found spurious or adulterated.

The committee raised its concern on the rise in manufacturing of spurious and adulterated drugs in the country.

In this regard, the Department of Pharmaceuticals (DoP) informed that various measures are being undertaken by the Central Drugs Standard Control Organisation (CDSCO) to address the issue of spurious drugs and ensure the quality of drugs in the country.

The CDSCO is responsible for approval of drugs, conduct of clinical trials and in laying down the standards of drugs in the country.

Since five years, the reforms are being initiated by CDSCO in the drugs regulatory system which include strengthening of testing capacities of Central Drugs Testing Laboratories under CDSCO and amendments in the Drugs and Cosmetics Rules, 1945 to bring in stricter rules pertaining to manufacturing of pharmaceuticals such as submission of bioequivalence study when applying for license of oral dosage form of certain drugs, joint inspection of manufacturing establishment by drugs inspectors of both central and state government, etc.

Besides the committee's recommendations, the implementation of bar coding/QR coding as part of trace and track mechanism for pharmaceutical products has been under discussion for quite some time now.

The Drugs Technical Advisory Board (DTAB), the highest decision-making body under the Union health ministry on technical matters, deliberated the issue of bar coding or QR coding on packaging of drugs in its meeting a couple of months back and deferred for examining it separately in its next meeting.

Earlier, the DTAB in its 79th meeting held on May 16, 2018 agreed for introduction of a trace and track mechanism for major 300 pharmaceutical brands on a voluntary basis. The Board informed that an order may be issued by Drugs Controller General of India (DCGI) to all the concerned to this effect.

Subsequently, the Union Health Ministry has published draft notification vide GSR. 567 (E) on August 8, 2019 mandating QR code for active pharmaceutical ingredients (APIs) only based on the recommendations of 82nd DTAB meeting. A number of objections have been received from the industry, which are being examined.

Source: Pharmabiz