Drug Information Bulletin

Drug Information Centre (DIC)
Indian Pharmaceutical Association
Bengal Branch
Tele fax: 033 24612776, E-mail: ipabengal.dic@gmail.com
Web Site: http://www.ipabengal.org
Contact: 09830136291
&
Regulatory Affairs Division (RAD), IPA

Volume: 08 **Number: 18** **7th December 2014**

Content

Editorial

Pharmacoeconomics and outcome Research is a new branch of science in India involving Medical, Pharmaceutical, Social science. Though it has long history in some other countries but its application is not so popular in the past. Though this science is in its infancy in India, a few groups are trying to promote this branch of science in our country. Pharmacoeconomics refers to the scientific discipline that compares the value of one pharmaceutical drug or drug therapy to another. It is a sub-discipline of health economics. A pharmacoeconomic study evaluates the cost (expressed in monetary terms) and effects (expressed in terms of monetary value, efficacy or enhanced quality of life) of a pharmaceutical product. There are several types of pharmacoeconomic evaluation: cost minimization analysis, cost-benefit analysis, cost-effectiveness analysis and cost-utility analysis. Pharmacoeconomic studies serve to guide optimal healthcare resource allocation, in a standardized and scientifically grounded manner. Pharmacoeconomic evaluation is an analytical tool used with increasing frequency to assist decision making in the financing and management of pharmaceutical products in the health care system or national health insurance programs of an individual country. Pharmacoeconomic (PE) guidelines can be used as a standard for preparation of studies to be included in application for reimbursement, a guide for designing and conducting a study, or a template for evaluating the economic study reports. In India it has tremendous scope in price control mechanism, new drug approval and reimbursement mechanism. He also suggested to introduce this subject in the course curriculum of Medical, Pharmacy and other health care specialties.

Dr. Subhash C. Mandal
Editor

New Drug: Trametinib

Approved indication: melanoma
Mekinist (GlaxoSmithKline)
0.5 mg and 2 mg tablets
Australian Medicines Handbook section 14.2.4

In 40–60% of melanomas there is a genetic mutation which results in an abnormal serine-threonine protein kinase (BRAF). This kinase is involved in the activation of mitogen-activated extracellular signal regulated kinases (MEK1 and 2) which are part of a pathway which regulates cell proliferation. Trametinib is a kinase inhibitor which reversibly blocks MEK1 and MEK2 in melanoma cells with the BRAF mutation. It therefore acts at a different point in the pathway from the BRAF inhibitors – vemurafenib (Aust Prescr 2012;35:128-35) and dabrafenib (Aust Prescr 2014;37:32-5).

A phase II trial studied trametinib in patients with metastatic melanoma. There were 40 patients who had previously been treated with a BRAF inhibitor (cohort A) and 57 who had received chemotherapy or immunotherapy (cohort B). Cohort A took 2 mg trametinib daily for a median of 56 days while cohort B took the drug for a median of 120 days. None of the patients in cohort A had a clinical response, but 25% of cohort B responded to treatment. The median progression-free survival was 1.8 months in cohort A and 4 months in cohort B.1

An open-label phase III trial compared trametinib against chemotherapy with dacarbazine or paclitaxel. The 326 patients in the trial had metastatic or stage IIIc melanomas containing BRAF mutations. Only 11 patients had a history of brain metastases and they were excluded from the primary efficacy analysis. There was a response to treatment in 47 of the 214 (22%) patients given trametinib and 9 of the 108 (8%) of those given chemotherapy. Progression-free survival was 4.8 months with trametinib and 1.5 months with chemotherapy. By the end of the study 16% of the trametinib group and 27% of the chemotherapy group had died. 2
Comparison of trametinib and chemotherapy for BRAF–mutated advanced melanoma

The results for cohort A in the phase II trial suggested that patients who have been previously treated with a BRAF inhibitor develop a resistance to treatment with trametinib.1 This led to another study which combined trametinib and dabrafenib for metastatic melanoma. After the pharmacokinetics of the combination had been assessed, 162 patients were randomised to take dabrafenib 150 mg twice daily as monotherapy, or in combination with trametinib 1 mg or 2 mg. After a median follow-up of 14.1 months, monotherapy had produced a response in 54% of patients while 50% of the trametinib 1 mg group and 76% of the trametinib 2 mg group responded. Progression-free survival was a median of 5.8 months with monotherapy, 9.2 months with the 1 mg combination and 9.4 months with the 2 mg combination. After one year 41% of the patients taking the 2 mg combination were alive and free of progression compared to just 9% of the monotherapy group.3

Adverse reactions to trametinib are common and may require the dose to be reduced or stopped. In the comparative study with chemotherapy 27% of patients had to reduce the dose of trametinib and 35% had to interrupt their treatment.2 Adverse effects which require dose interruptions include rashes, reduced left ventricular function and retinal pigment epithelial detachment. Interstitial lung disease, congestive heart failure and retinal vein occlusion are indications for stopping trametinib. The most common adverse effects, which are more frequent with trametinib than with chemotherapy, are rashes (57% of patients), diarrhoea (43%) and peripheral oedema (26%).2

Patients taking trametinib in combination with dabrafenib will experience adverse effects from both drugs. Among the patients who took trametinib 2 mg with dabrafenib, common adverse events were fever (71%), chills (58%), fatigue (53%), nausea (44%) and vomiting (40%). Squamous cell carcinoma developed in 7% of these patients, but this was less than the 19% of patients affected by dabrafenib monotherapy.3 The combination increases the risk of bleeding and fatal haemorrhages have occurred.

Trametinib is embryotoxic. If a woman of childbearing age is treated with this drug, pregnancy must be avoided.

Although trametinib is mainly metabolised there have been no studies of patients with moderate or severe hepatic impairment. As less than 20% of the dose is excreted in the urine, mild or moderate renal impairment is unlikely to affect the pharmacokinetics of trametinib. There are no studies in severe renal impairment. As the absorption of trametinib is reduced by food, it should not be taken with meals.

The overall five-year survival of patients with metastatic melanoma is 7–19%. While trametinib can increase progression-free survival, its effects on long-term survival are currently uncertain. The six-month overall survival rate was 81% with trametinib and 67% with chemotherapy.2 Trametinib monotherapy is not effective if the melanoma has progressed despite treatment with a BRAF inhibitor.

References:

1. Kim KB, Kefford R, Pavlick AC, Infante JR, Ribas A, Sosman JA, et al. Phase II study of the MEK1/MEK2 inhibitor trametinib in patients with metastatic BRAF-mutant cutaneous melanoma previously treated with or without a BRAF inhibitor. J Clin Oncol 2013; 31:482-9.
2. Flaherty KT, Robert C, Hersey P, Nathan P, Garbe C, Milhem M, et al. Improved survival with MEK inhibition in BRAF-mutated melanoma. N Engl J Med 2012; 367:107-14.
3. Flaherty KT, Infante JR, Daud A, Gonzalez R, Kefford RF, Sosman J, et al. Combined BRAF and MEK inhibition in melanoma with BRAF V600 mutations. N Engl J Med 2012; 367:1694-703.

Ref. Aust Prescr 2014; 37:214-21

Draft Schedule M-III published for comments

Good Manufacturing Practices and requirements of premises, plant and equipment for medical devices and in – vitro diagnostic kits & reagents has been published on 1st December 2014 published by CDSCO on 1st December 2014. Document is available at : http://www.cdsco.nic.in/writereaddata/SCHEDULE_M_III

Comments and suggestions should be submitted within 15 days of publication to CDSCO (HQ), FDA Bhavan, Kotla Road, New Delhi-110002.

Announcements

ANNUAL PICNIC
Of
IPA Bengal Branch

4th January 2015
All members are requested to join with family
Venue: Samrat Gardens
Joinpur, South 24 Pgs.

Please Contact:
Mr. Pradip Kumar Mallik:
Dr. Sambhu Nath Dey:
Mr. Ashok Kumar Maity:
Mr. Sovon Bagchi:

Health Camp

at Ganga Sagar Mela
10th – 15th January 2015
Contact:
Dr. Jayanta K. Chaudhury, Hony. Secretary, IPA, Bengal Branch

National seminar on “"Control of Viral Menace using Delivery Design" at B. C. Roy College of Pharmacy & Allied Health Sciences, Durgapur.

From L –R:
Dr. S. Chakraborty, Dr. Srirup Chatterjee, Dr. G. P. Srivastava, Dr. Subhash C. Mandal

Mr. P.K.Mallik and Dr. Goutam Bagchi in poster session

SOCIETY FOR ETHNOPHARMACOLOGY (SFE-INDIA)

23/3 Saktigarh, Kolkata 700032, India

Affiliated to: International Society for Ethnopharmacology, UK

email:sfeindian@gmail.com; ***website:***www.ethnopharmacology.in

ANNUAL AWARDS: SOCIETY FOR ETHNOPHARMACOLOGY, INDIA

Society for Ethnopharmacology, India (SFE-INDIA)would like to recognize the outstanding contributions made by the scientists or researchers in the field of medicinal plant research and Ethnopharmacology.

Nominations are invited for the following Awards of SFE-INDIA with in January 20, 2015.

SFE - Lifetime Achievement Award - 2015 *“BisheswarSaha Memorial Award”*	SFE - Outstanding National Ethnopharmacologist Award – 2015 *“Harihar Mukherjee Memorial Award”*
SFE – Outstanding International Ethnopharmacologist Award –2015 *“PranabBanerji Memorial Award”*	SFE - Best Poster & Paper Presentation Award -2015 *“Manujusree Pal Memorial Award”*
SFE - ZANDU Award - 2015 *“Best Research on Plant Drug”*	SFE Herbal Industry Leader Award - 2015
SFE- Outstanding Service Award - 2015	SFE- Travel Grant Award – 2015

For details of Nomination procedure please go through the website: www.ethnopharmacology.in

For further details please contact:
Dr. Pulok K Mukherjee, Secretary, Society for Ethnopharmacology (SFE-INDIA), Kolkata, India
email: sfeindian@gmail.com; *website:* www.ethnopharmacology.in