VOLUME 11 ISSUE 1

PSG NEWS DIGEST

A news letter from PSG College of Pharmacy, Department of Pharmacy Practice,

Pulse of the Issue | Pharmacist's Desk | Drugs Approved | News Room | Department Activities

FROM THE PHARMACIST'S DESK

Dr.Sheryl Elizabeth Jess
Assistant Professor/Clinical Pharmacist,
Department of Pharmacy Practice,
PSG College of Pharmacy.

HEPCIDIN AND IRON HOMEOSTASIS- AN OVERVIE

Iron is a vital mineral that is involved in the distribution of oxygen from the lungs to various parts of the body, in the form of haemoglobin. The level of iron in the body is maintained in homeostasis through a complex interplay of many proteins such as tranferrin, ferritin, ceruloplasmin, haemojuvilin and bone morphogenetic protein.Hepcidin is one such protein that is produced primarily in the liver and contributes to the negative regulation of iron. It has two isoforms: hepcidin-25 and hepcidin 20. The role of hepcidin-20 is yet to be elucidated. Hepcidin 25 is a peptide hormone that blocks the entry of iron into the blood stream from major sources (i.e. it inhibits absorption from the duodenum, stops the macrophages from releasing the recycled iron and blocks the release of stored iron from the hepatocytes).It is postulated that Alpha-2 macroglobulin acts as the hepcidin transporter in the blood. When iron is found in abundance, the hepatocytes produce more hepcidin thereby limiting intestinal iron absorption and release of iron from its stores by interacting with the iron export protein ,ferroportin. It is excreted through the kidney, but reabsorbed from the proximal convoluted tubule. Hence there is an increased level of hepcidin in Chronic Kidney Disease patients, which inturn contributes to CKD induced anaemia .Defects in the signaling to hepcidin can produce an array of disorders from hereditary hemochromatosis to iron- refractory iron deficiency anaemia. Studies are still going on for the standardization of hepcidin.

Many studies are being conducted to identify hepcidin inducers and are still in the invitro and pre-clinical phases. One potential antisense oligonucleotide targeted against Matriptase 2 enzyme is in the Phase 1 Clinical trial.Martiptase 2 enzyme is produced in the liver and negatively regulates the production of hepcidin. Two Hepcidin antagonists that are targeted against ferroportin are in the Phase 2 of the clinical trials. Studies are also being done to identify inhibitors of hepcidin expression.Tocilizumab and Siltuximab, which have been approved for use in patients with Castleman's syndrome, are found to inhibit hepcidin expression. Tocilizumab was primarily approved as an immunosuppressant in patients with Rheumatoid Arthritis.

According to some clinical studiesTocilizumab caused an improvement in Rheumatoid Arthritis patients who had anaemia, since there was a reduction in serum hepcidin. The use of monoclonal antibodies may be limited as they are expensive. Testosterone and 17-β Estradiol are also under study, but it needs more clarity in the mechanism of hepcidin regulation. There are several ongoing clinical trials on the effect of Vitamin D in hepcidin regulation, as RCT's done previously show controversial results.

The recent advances in science have helped us in our understanding on iron regulation; we are yet to find answers for many queries regarding the pathobiology which provides important avenues for further studies.

References:

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NEWS ROOM

BLUE IS THE CALMEST COLOUR

The colour blue has long been considered to invoke feelings of calmness, slowing down, serenity and was theorized to lower pulse rate in colour psychology. New research now shows that the colour blue does in fact have a calming effect by reducing blood pressure!

Researchers in London found that upon consumption of equivalent of 200 grams of whole wild blueberries decreased systolic blood pressure to an extent rivaling the effect of anti-hypertensive agents such as ACE-inhibitors. This effect was attributed to the presence of anthocyanins in blueberries.

Anthocyanins are a type of polyphenol flavanoids that form the pigments responsible for giving the rich red, purple and blue colors to many grains, fruits and vegetables. The cardiovascular effects of blueberries were not as well established in earlier studies as their cognitive benefits but now the anthocyanins in blueberries are credited with improving endothelial function ultimately providing beneficial effects on the vascular system.

Researchers at King's College in London, randomnly assigned 40 men into two arms who were administered with a drink of 11 g of freeze dried wild blue berry powder in water and a control drink matched for color and flavor. The Flow mediated dilation, 24 hour ambulatory BP, blood levels of plasma blueberry polyphenols and their metabolites were measured along with other routine lab parameters.

The systolic BP dropped by an average of 5.6 mm Hg at the end of 24 hours in subjects who took the blueberry drink while flow mediated dilation, which is a measure of endothelial function, improved by 1.5 % within 2 hours of consuming blueberry drink and the increase was sustained at 2.3% after 28 days of daily consumption.

The increase in FMD by 2% is clinically significant as it reflects a 20 % decrease in CVD risk. Though the researchers comment that these findings are too early to be translated into Physician recommendations, the results are causing a stir in the medical community and further research is already underway to translate the findings to kids and the elderly.

References:

• Blueberries may help lower Blood pressure – Harvard health
• "Blue" in blueberries tied to BP lowering that rivals medications – Medscape medical news
• SruthiKrishnamoorthi, Pharm D Intern.

A SELECTIVE ORAL KINASE INHIBITOR GRANTED APPROVAL FOR GIST HARBOURING A PDGFRA EXON 18 MUTATION

Avapritinib (AYVAKIT), a potent selective tyrosine kinase inhibitor was approved by food and drug administration on 9th January, 2020 for adults with unresectable or metastatic gastrointestinal stromal tumor (GIST).

GIST is a sarcoma, or tumor of bone or connective tissue of the GI tract. Tumors arise from cells in the wall of the GI tract and occur most often in the stomach or small intestine. Most patients are diagnosed between the ages of 50 to 80.

In unresectable or metastatic GIST, clinical benefits from existing treatments can vary by mutation type. Most GIST cases are caused by mutations in KIT(Proto-Oncogene, Receptor Tyrosine Kinase is a Protein Coding gene) or PDGFRA (Platelet-derived growth factor receptors) that force protein kinases into an increasingly active state.
Although Imatinib [Gleevec] is an effective first-line treatment for patients with advanced gastrointestinal stromal tumors, most patients inevitably relapse or progress.

Sunitinib and Regorafenib are approved second and third-line agents, but they have shown limited activity and tolerability, defining an unmet need for patients with imatinib-resistant GIST.

There were no approved therapies for patients with KIT-driven GIST whose disease progresses beyond the above mentioned therapies.Because, they primarily bind to the inactive protein conformations and certain primary and secondary mutations typically result in treatment resistance and lead to disease progression.
Secondary mutation in KIT or PDGFRA is likely the most important event leading to TKI (Tyrosine kinase inhibitors) resistance. These mutations can occur in KIT exon 13 and 14, encoding the ATP-binding pocket of the receptor, or in exon 17 and 18, in the kinase activation loop. The latter stabilize the receptor in its active conformation, and the majority of these mutations are known to cause resistance to both imatinib and Sunitinib. Although Regorafenib is active against some of these mutated forms, a typical patient receiving this third-line treatment progresses after a median period of only 4–5 months. Apart from the unsatisfactory efficacy of second- and third-line agents, their broader activity against multiple molecular targets leads to offtarget toxicity, and many patients do not tolerate Sunitinib and Regorafenib as well as the first-line standard of care.
Avapritinib is the first therapy approved for patients with GIST harboring a PDGFRA exon 18 mutation. Avapritinib (BLU-285, Blueprint Medicines) is an oral, highly selective, and is a known driver mutation in systemic mastocytosis. In vitro, Avapritinib disrupts KIT signaling as assessed by inhibition of both KIT phosphorylation and activation of downstream proteins such as AKT and STAT3 in human mast cell and leukemia cell lines. In vivo, Avapritinib achieves dose-dependent tumor growth inhibition in a mouse model of systemic mastocytosis. Moreover, Avapritinib also inhibits PDGFRA D842V, the mutation responsible for one out of five primary gastric GISTS, for which there is no effective treatment available.

References:

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•https://www.drugs.com/newdrugs/fda-approves-ayvakit-avapritinib-adults-unresectable-metastatic-pdgfra-exon-18-mutant-5138.html

Susreetha.P.Nair, PharmD Intern

DEPARTMENT ACTIVITY

Community services:

The following are the community services provided by the Department of Pharmacy Practice for the general public

DATE	PROGRAMME	PLACE	SERVICE PROVIDED
08.01.2020	Awareness camp on Dengue, menstruation, and government health scheme and free medicine supply	Sundapalayam Village	Counselling, distribution of pamphlets, free medicine supply

10.01.2020	Awareness camp on Dengue, menstruation, and government health scheme and Anaemia check up	Attukal Village	Door - door visit. Counselling, distribution of pamphlets
27.02.2020	Awareness on immunization and OTC medication use	Vedapatti Village	Door - door visit. Counselling, distribution of pamphlets
08.03.2020	Medical camp - PSG Hospital	Hassanur	Counselling

CPE (Continuing Pharmacy Education)

DATE	TITTLE	RESOURCE PERSON
21.01.2020	Ethics in Research	Mrs. Y.Ashruf, Associate Professor, PSG COP Mrs. M.Nirmala, Professor, PSG CON
08.01.2020	Chirality in clinical practice	Dr.G.Umaa, Professor, Department of Chemistry, PSG CP
	Anti - platelets and anti - coagulants	Dr.Giphy susan Varghese, Clinical Pharmacist, Intensive Care Unit, PSGH.
	Career opportunities for Pharm D	Dr.C.Jaikanth, Associate Professor, Department of Pharmacology, PSG CP.

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