VOLUME 10 ISSUE 2

PSG NEWS DIGEST

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

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FROM THE PHARMACIST'S DESK

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ACRODERMATITIS ENTEROPATHICA

Acrodermatitis enteropathica (AE) is a rare inherited form of zinc deficiency, characterized by a triad of periorificial and acral dermatitis, alopecia, and diarrhea. It is the result of mutations in the SLC39A4 gene on chromosome 8q24.3. The SLC39A4 gene encodes a transmembrane protein that is part of the zinc/iron-regulated transporter–like protein (ZIP) family required for zinc uptake.

Zinc deficiency is an important problem in children and adolescents, particularly in resource-limited countries. AE usually manifests in infancy within days in cases of bottle-fed infants and days to weeks after weaning in breastfed infants.

The affected infants develop an erythematous and vesiculobullous dermatitis, alopecia, ophthalmic disorders, diarrhea, severe growth retardation, delayed sexual maturation, neuropsychiatric manifestations, and frequent infections.

Zinc is an essential trace nutrient required for the proper function of more than 100 enzymes including carbonic anhydrase, the alkaline phosphatases, dehydrogenases, and carboxypeptidases. It is involved in the regulation of nucleoproteins and the activity of various inflammatory cells and plays a role in growth, tissue repair and wound healing, carbohydrate tolerance, and synthesis of testicular hormones.

Zinc is involved in the immune response. Zinc deficiency is associated with impaired phagocytic function, lymphocyte depletion, decreased immunoglobulin production, a reduction in the T4+/T8+ ratio, and decreased interleukin (IL)-2 production.

Treatment of acrodermatitis enteropathica requires lifelong oral zinc supplementation with pharmacologic doses of zinc. Among different zinc salt forms that are available in the market (zinc acetate, zinc gluconate, zinc sulfate, zinc citrate, zinc oxide), both zinc citrate and gluconate salts are effective in the prevention of zinc deficiency and also in the treatment of diarrhea. Studies suggest that the absorption of zinc oxide is less when compared to other zinc compounds when given without food, and may be minimally absorbed by some individuals. Zinc acetate has been in use as an off-label drug in India for the treatment of AE.

Replacement doses of 3 mg/kg/day of elemental zinc (13.2 mg/kg/day of zinc sulfate) are recommended. Zinc levels are measured every three to six months and the dose is adjusted up or down as needed.

The parents or the care takers need to be counseled about the zinc deficiency and the importance of zinc supplementation to have a better quality of life.

References:

1)https://www.uptodate.com/contents/zinc-deficiency-and-supplementation-in-children-and-adolescents?search=Acrodermatitis%20enteropathica&sectionRank=1&usage_type=default&anchor=H8&source=machineLearning&selectedTitle=1~20&display_rank=1#H8
2) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3901420/
3) https://emedicine.medscape.com/article/1102575-overview

FDA APPROVED DRUGS FROM JANUARY TO JUNE 2019

S.NO	DRUG NAME	ACTIVE INGREDIENT	FDA APPROVED USE
1	Vyndaqel Vyndamax	Tafamidis meglumine Tafamidis	Treatment of the cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults.
2	Zolgensma	Onasemnogene abeparvovec-xioi	Pediatrics <2 years of age with spinal muscular atrophy with bi-allelic mutations in the SMN1 gene.
3	Duobrii	Halobetasol propionate and tazarotene	For the treatment of plaque psoriasis .
4	Tosymra nasal spray	Sumatriptan	For the treatment of acute migraine in adults.
5	Cablivi	Caplacizumab-yhdp	For the treatment of acquired thrombotic thrombocytopenic purpura.
6	Egaten	Triclabendazole	For the treatment of fascioliasis (liver fluke infestation).
7	Dengvaxia	Dengue Tetravalent Vaccine, Live	For the prevention of dengue disease.
8	Jakafi	Ruxolitinib	For the treatment of steroid-refractory acute graft-versus-host disease in adults and pediatrics >12 years.
9	Nayzilam	Midazolam	For the treatment of intermittent, stereotypic episodes of frequent seizure activity.
10	Ruzurgi	Amifampridine	For the treatment of Lambert-Eaton myasthenic syndrome in pediatrics.

11	Zulresso	Brexanolone	For the treatment of postpartum depression.
12	Jatenzo	Testosterone undecanoate	For the treatment of male conditions associated with a deficiency or absence of endogenous testosterone.
13	Cimzia	Certolizumab pegol	For the treatment of non-radiographic axial spondyloarthritis.
14	Sunosi	Solriamfetol	For the treatment of excessive daytime sleepiness due to narcolepsy or obstructive sleep apnea.

Ref - https://www.centerwatch.com/drug-information/fda-approved-drugs/ V.Amrutha Varshini, Vth-Pharm D

NEWS ROOM

CHALLENGES IN MONOCLONAL ANTIBODIES TRIAL

Monoclonal antibodies are used as treatment options particularly in oncology and immunology. In 2006 FIH trial, all subjects who received first dose of active drug TGN1412, a superagonist mAb against CD25, developed life threatening adverse reaction, due to uncontrollable cytokine release. The maximum recommended starting dose (MRSD) was determined from no-observed adverse effect level (NOAEL) (0.1mg/kg). When re-examining the dose, it was found that 0.1mg/kg would elicit greater than 90% receptor occupancy. Apart from the high PD effect, the increased receptor occupancy could have altered the PK, producing the cytokine storm. From the incident, it is understood that once receptor occupancy starts to increase, PK and PD response to further dose escalations become non-linear. As per revised EMA guidelines, FIH doses need to be calculated from both NOAEL and MABEL to reduce the risks of trial subjects being dosed with novel mAb for first time. Another challenge is determining the optimal route of administration as site reactions are common and can lead to termination of trials. Any prophylactic therapy may avoid reactions but may influence the further development of compound leading to termination of trials. Hence, it is recommended to observe the patients during the first few hours after the injection of new mAb. Another factor is the possible delayed PD effect related to duration of target inhibition or target mediated PF profile. Long follow-up of subjects should be foreseen to monitor possible delayed adverse reactions. Thus, while running mAb clinical trials, numerous PK & PD factors are to be considered.

References:

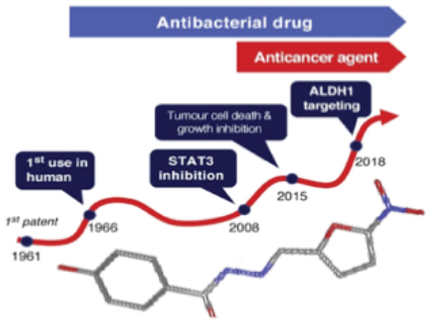
Narine Baririan, Pharm. D, 2018. Monoclonal Antibodies: Clinical Pharmacology Knowledge in Support of FIH and Early Development. Applied Clinical Trials. Available at :
http://www.appliedclinicaltrialsonline.com/monoclonal-antibodies-clinical-pharmacology-knowledge-support-fih-and-early-development

Suriya Dharsini, Vth Pharm D

BUDGE OF AN ANTIBACTERIAL TO AN ANTICANCEROUS DRUG

Nifuroxazide (NFX) is a broad-spectrum nitrofuran antibiotic used to treat gastrointestinal bacterial infections and associated diarrhoea for >50 years. In 2008, the discovery of potent inhibition of the transcription factor, signal transducer and activator of transcription STAT3 by NFX, provoked studies as a potential anticancer agent. Complementary biochemical studies revealed that NFX inhibits STAT3 phosphorylation through inhibition of the JAK family kinases JAK2 and Tyk2.

This kinase inhibitory activity accounts for the antiproliferative activity of NFX in myeloma cells with a constitutive activation of STAT3, with minimal effects on normal cells. Subsequently, in 2015, it was shown that NFX induces cancer cell apoptosis and inhibits tumour growth. Recently in 2018, NFX was identified as a potent inhibitor of aldehyde dehydrogenase (ALDH)1 that selectively kills ALDH high cancer-initiating cells. The 5-nitrofurans require bioactivation to exert their anticancer activity. NFX can be bioactivated by aldehyde dehydrogenase (ALDH) enzymes which are highly expressed in certain cancer-initiating cells (ALDH1 high stem cells). In sharp contrast, ALDH low cells were found to be resistant to NFX. This key discovery opens the door to the design of new melanoma treatment protocols with patient stratification based on the unique ALDH1 high-dependent activity of NFX. These two landmark discoveries – STAT3 and ALDH1 inhibition – strongly support the potential shift of NFX as a targeted anticancer agent.



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- https://www.nature.com/articles/cddis201563
- http://www.bloodjournal.org/content/108/11/3450?sso-checked=true
- https://www.sciencedirect.com/science/article/pii/S2451945618303003

Shuruthi Sankar, Pharm D, Vth Year,.

DEPARTMENT ACTIVITY

Community Services:

PSG College of Pharmacy, Department of Pharmacy Practice conducted World pharmacist day observed on September 25th at PSGIMS&R which highlights safe and effective medicines for all. Nearly I60 Public population attended and were benefited through this programme.

As a Part of social responsibility PSG College of Pharmacy, Department of Pharmacy Practice have conducted Dengue awareness programme at Coimbatore corporation School, Ramanathapuram,Coimbatore on 9th November 2019.

STUDENT'S ACHIEVEMENTS

• Saranya N., Pharm D Intern won the second place- for Oral presentation on Challenges and opportunities for Clinical Pharmacist- ICCO PHARMA held at Dayanand Sagar University, Bengaluru.

• Artificial Intelligence Workshop: Three of the interns, Joseph Noel Jacob, Dharani.A and Janani.P were selected for national level competition after a one week training programme organised by IIT at PSG College of Pharmacy.

• Sruthi K.Pharm D V year received First place in e-poster presentation held at the one day national level seminar on September 3rd 2019 "Current scenario of Patient safety Vigilance activities in India" conducted by KMCH College of Pharmacy for poster titled - Trigger tool based detection of ADE associated with high alert medication use under the guidance of Dr.G.Andhuvan.

• Total number of publications from the Department of Pharmacy Practice between the months of april to december 2019: 08

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