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VISION

To emerge as one of the premier pharmacy colleges in the country and produce pharmacy professional of global Standards.

MISSION

- To deliver quality academic programs in Pharmacy and empower the students to meet industrial standards.
- To build student community with high ethical standards to undertake R&D in thrust areas of national and international standards.
- To extend viable outreach programs for the health care need of the society.
- To develop industry institute interaction and foster entrepreneurial spirit among the graduates

A Retrospective Study On Prescription Patterns Of Antiplatelets-Anticoagulants And Role Of Risk Factors In The Treatment Of Deep Vein Thrombosis

P Sai Tejasswni, Pharm D Internee

Background Information:

Peripheral venous insufficiency or disease occurs when the veins in the legs don't allow blood to flow back up to the heart because the leg veins don't shut properly during blood's return to the heart. Normally, in the valves of veins the blood flows toward the heart. If any structural changes occur in these valves blood flow will be restricted to one direction that can cause blood pooling and formation of blood clot in the vein results in varicose vein and Deep Vein Thrombosis (DVT). It is associated with multiple risk factors. Treatment includes lifestyle changes to control risk factors, along with antiplatelet and anticoagulation therapy.

Methodology:

This is a hospital-based Retrospective observational study, conducted in the medical records department of Cardiothoracic and vascular surgery, SVIMS, SPMC(W) – Tirupati. Carried out for a period of 6 months and collected a total of 75 DVT cases. A structured data collection form was used to record the prescription patterns and risk factors of the patient.

Results:

Out of 75 DVT subjects, antiplatelets were received by 2(2.7%), anticoagulants received by 18(24%), and combination therapy received by 55(73%). The commonly prescribed combination pattern was dual therapy 34(45%). According to patient medical records among 6smokers, 3 were involved in smoking cessation and disease regressed to 60%. Out of 18 diabetics, 12 subjects had controlled blood sugar levels and the disease regressed to 65%. Overall, 17 hypertensives, 10 subjects had controlled blood pressure and had improved their disease stat to 53%.

PRESCRIPTION PATTERN IN DVT

SL. NO	TREATMENT	NO. OF PATIENTS(n=75)	PERCENTAGE OF SUBJECTS
1.	Antiplatelet therapy	2	2.7%
2.	Anticoagulation therapy	18	24%
3.	Combination therapy	55	73.3%

COMBINATION OF ANTIPLATELETS AND ANTICOAGULATION THERAPY IN DVT

SL.NO	THERAPY	NUMBER OF SUBJECT	PERCENTAGE OF SUBJECTS
I.	Dual therapy	42	56%
	1. Acenocoumarol, clopidogrel	34	45.3%
	2. Clopidogrel, heparin	1	1.3%
	3. Clopidogrel, warfarin	2	2.7%
	4. Aspirin, acenocoumarol	5	6.7%
II.	Triple therapy	13	17.3%
	1. Aspirin, clopidogrel, acenocoumarol	4	5.3%
	2. Clopidogrel, aspirin, warfarin	1	1.3%
	3. Clopidogrel, cilostazole, acenocoumarol	3	4%
	4. Clopidogrel, acenocoumarol, heparin	4	5.3%
	5. Clopidogrel, acenocoumarol, fondaparinux	1	1.3%

Conclusion:

This retrospective observational study concluded that the majority of subjects with deep vein thrombosis were received combination therapy and risk factors play a major role in the management of the disease.

Review on p53 and Nutlins

T Shamitha, Pharm D III Yr

Introduction:

Nutlins are cis-imidazoline analogs recently developed as anticancer agents. Nutlins restoring p53 activity by inhibiting the interaction between p53 and MDM2 represents an attractive approach for cancer therapy.

Function of p53:

P53 is a tumor suppressor that is induced and activated by a variety of potentially tumorigenic stresses, including inappropriate oncogene signaling and DNA damage. The induction of p53 occurs through post-transcriptionalmechanisms. Upon activation, p53 primarily functions as a transcription factor, recruited to binding sites in chromatin and regulating the expression of genes that control a diverse group of biological activities, including apoptosis, cell cycle regulation, senescence, DNA metabolism, energy metabolism, angiogenesis, immune responses, cell differentiation, motility and migration, and cell–cell communication.

Due to its potent tumor suppressor role, the function of p53 is almost always compromised in tumor cells. Inactivating mutations in p53 are found in approximately 50% of all human cancers.

Mutation of p53:

The vast majority of tumor-associated p53 mutations are missense mutations within p53's DNA binding domain and inhibit the ability of p53 to bind DNA and activate transcription [5]. In the remaining cancers in which the p53 gene is not mutated, the function of the p53 pathway is often inhibited through other mechanisms, including increased expression of MDM2 or MDMX (both negative regulators of p53) or inactivation of the tumor suppressor protein p14/ARF.

Regulation of p53:

The transformed phenotype of tumor cells is especially responsive to restoration of p53 activity, which leads to either apoptotic death or senescence growth arrest followed by immune system-assisted tumor clearance.an E3 ubiquitin-ligase enzyme responsible for p53 ubiquitination,p53 and MDM2 form an auto-regulatory feedback loop.

- *P53 binds to the P2 promoter of the MDM2 gene and promotes MDM2 gene expression.*In turn, MDM2 protein binds to the N-terminal transactivation domain of p53 and inhibits p53, primarily by promoting its ubiquitination and subsequent degradation by the proteasome.
- MDM2 can also inhibit p53 by promoting its ubiquitin-dependent exclusion from the nucleus

- The increase in p53 levels following stress results, in large part, from stabilization of the p53 protein. P53 stabilization following DNA damaging stress is believed to result from stress-induced modifications in p53 or MDM2 that disrupt p53-MDM2 binding. In contrast, p53 stabilization in response to other stresses (e.g. oncogenic or ribosomal stress) can result from an *inhibition of the E3-ligase activity of MDM2* that results from stress-induced interactions of MDM2 with other proteins

Nutlins:

Nutlins, a group of cis-diphenyl substituted imidazoline-containing compounds (nutlin-1,-2,and-3), are the first small molecules developed to specifically target p53-MDM2 interaction.

Mechanism of action of nutlins:

Nutlins fit into the hydrophobic binding pocket between MDM2 and p53, mimicking the α-helical p53 peptide structure in its binding to MDM2 and sterically disrupting p53-MDM2 interaction

Nutlin 3a:

One of the most potent compoundswhich binds to MDM2 protein. It acts as a p53 nongenotoxic activator to study p53 function, and its inhibitory effect on the growth of cancer cells was tested in a variety of cell model systems alone or in combination with cytostatic drug. It exhibit synergistic effect with a number of cytostatic drugs.

Example, nutlin-3 synergizes with the genotoxic drugs doxorubicin, chlorambucil, and fludarabine in B-cell chronic lymphocytic leukemia cells. nutlin-3 potentiates antitumor activity of doxorubicin, methotrexate, or cisplatin in sarcoma cell lines

MDM2 inhibitors:

1.**RG7112**: first MDM2 inhibitor that advanced into clinical trialsshows enhanced MDM2-binding affinity.Selectively inhibits cell growth in cancer cell lines with wild-type p53, and robustly activates wild-type p53 in vitro and in vivo

Treatment with RG7112 showed signs of antitumor activity in patients, but late hematological toxicity, particularly thrombocytopenia was found to correlate with RG7112 exposure.

2.RG7388: Based on the structures of RG7112 and MI-219,designed and synthesized a novel nutlin, RG7388.It binds to MDM2 and displays > 100-fold selectivity in cancer cell lines containing wild-type p53 over those containing mutated p53Currently it is in three phase-I clinical trials for treatment of patients with solid tumors, acute myelogenous leukemia, or advanced malignancies as a single agent and in combination with chemotherapeutics.

Conclusion:

Racemic Nutlin-3 (30; 200 mg/kg, twice daily [BD], 20 days) showed in vivo efficacy in an SJSA-1 osteosarcoma xenograft, giving 90% inhibition of tumor growth, with no significant toxicity or weight loss. Similarly, the active Nutlin-3a enantiomer (30a) showed substantial activity in a 3-week antitumor efficacy study with SJSA xenografts (30a; 200 mg/kg, BD, 21 days), giving eight partial and one full tumor regression, without significant weight loss or toxicity. Antitumor activity was also seen. The MDM2 amplified tumors showed similar sensitivity to the inhibitor. These results confirmed Nutlin-3a (30a) as a potent and selective MDM2–p53 inhibitor

ADCETRIS (BRENTUXIMAB VEDOTIN) – A NEWLY APPROVED DRUG FOR HODGKIN LYMPHOMA

P Humera Khanam, Pharm D V yr

Brand Name: ADCETRIS

Generic Name: Brentuximab vedotin **Mwt:**149.2-151.8 Kg/mol

Molecular Formula: C6476 H9930 O2030 S40 (C68 H105 N11 O15) 3 – 5

Manufacturing Company: Seattle genetics (U.S licens

PHARMACOKINETICS:

Absorption:

- Steady state concentration was achieved within 21 days with every 3 weeks dosing of ADCETRIS.
- Minimal to no accumulation of ADC was observed with multiple doses at the every 3-week schedule.
- Maximum concentration for MMAE was approximately 1 – 3days.

Distribution:

- Plasma protein binding ranging from 68 – 82%.
- Volume of distribution was approximately 6 – 10 liters.

Metabolism:

- The MMAE metabolism that occurs primarily in oxidation by CYP3A4/5.

Elimination:

- Approximately 24% of total MMAE administered as part of the ADC during an ADCETRIS infusion was recovered mostly in urine and feces over a period of time (1 week time)
- In this recovery 74% was recovered unchanged in feces.

Indication:

ADCETRIS is indicated for the treatment of patients with Hodgkin's Lymphoma after the failure of ASCT or after the failure of at least two prior multi-agent chemotherapy regimens in a patient who is not an ASCT candidate.

Dosage Form , Route Of Administration And Dose:

Normal renal and hepatic function: The recommended dose is 1.8mg/kg up to 180mg.

For mild hepatic impairment: 1.2 mg/kg up to 120mg.

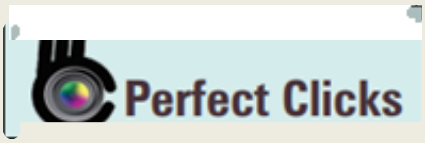
Adverse Effects: Peripheral neuropathy

Anaphylaxis and infusion reaction

Tumor lysis syndrome

Departmental Activities February-2022:

No of Patients Screened	Drug Information Queries	Adverse Drug Reactions	Medication Errors	No of Prescriptions Audited
769	24	32	06	851



Fresher's Orientation Programme-2022