Clinical Pharmacy

A Newsletter of Drug and Prescribing Information

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ADVERSE DRUG REACTION REPORTS: MAY - AUG 2015

A total of 754 Adverse Drug Reactions (ADRs) were reported or detected by the Department of Clinical Pharmacy during May to August 2015. The following are some of the suspected ADRs that were either reported to or detected by the Department of Clinical Pharmacy. In most of the cases there was a change in drug therapy e.g. cessation of suspected drug or reduction in dose, and/or either specific or symptomatic treatment for the suspected ADR.

Betamethasone	Myopathy
Bupropion	Tremors
Cefixime	Leucoctoclastic Vasculitis
Clindamycin	Pseudomembraneous Colitis
Colistin	Nephrotoxicity
Cyclophosphamide	Amenorrhea
Enoxaparin	Seborrhoeic Dermatitis
Ifosfamide	Haematuria
Olanzapine	Tardive Oculogyric Crisis
Phenytoin	DRESS Syndrome
Pirfenidone	Dizziness
Prednisolone	Psychosis
Silodosin	Diarrhoea
Sorafenib	Hand Foot Syndrome
Ticagrelor	Gynaecomastia

Phenytoin Induced DRESS Syndrome

Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome is an uncommon but serious hypersensitivity drug reaction most frequently associated with antiepileptics. Clinical manifestations include rash, fever, and visceral organ involvement, most commonly hepatitis. DRESS has a later onset and longer duration than other drug reactions, with a latent period of 2 to 6 weeks. It may have significant multisystem involvement, including hematologic, hepatic, renal, pulmonary, cardiac, neurologic, gastrointestinal, and endocrine abnormalities. The mortality rate associated with DRESS syndrome is approximately 10%, the majority due to fulminant liver failure. Early diagnosis and prompt treatment with corticosteroids is imperative in managing the drug Induced DRESS Syndrome.

Olanzapine Induced Tardive Oculogyric Crisis

Tardive syndromes are much lower in prevalence in second generation antipsychotics (SGA) than in the typical antipsychotics. Although, olanzapine, which is an SGA, has a high risk of causing weight gain, metabolic syndrome, raised blood sugar, and dyslipidemias; it is widely used as the risk of developing extrapyramidal syndromes (EPS) is low. Among the various forms of EPS, tardive syndromes are the most feared, tardive dyskinesia, tardive akathisia, and tardive dystonia are the commonest tardive syndromes, the others being less common. Tardive Oculogyric crisis (TOC) are a rare form of tardive dystonia.

Sorafenib Induced Hand-Foot Syndrome

Sorafenib, a multikinase inhibitor, is approved for treatment of renal cell cancer and hepatocellular cancer. It is a small molecule multikinase inhibitor (tyrosine kinase, Raf serine/threonine kinases) and also inhibits vascular endothelial growth factor (VEGF), platelet-derived growth factor β (PDGF β), and tumour progression. Hand-foot syndrome (HFS) is a condition where erythema, scaling, and bullous lesion affect the hand and feet. HFS caused by multikinase inhibitors are distinct from that caused by the traditional chemotherapeutic agents. Prevention of HFS can be made by reducing the exposure of hands and feet to hot water, avoiding constrictive clothing, excessive rubbing, exercises that place undue stress on hands and feet, applying alcohol-free moisturizing creams, and exfoliating hyperkeratosed areas of palms and soles.

We encourage you to report all suspected adverse drug reactions to Department of Clinical Pharmacy. Adverse drug reaction reporting forms are available at all nursing stations. Alternatively you may call Department of Clinical Pharmacy on 2335577 or 2335555; Extn. 5577 or SMS to 07411137840. (Format: ADR/IP or OP Number/ Name of the patient/ Ward)

DRUGS APPROVED BY US FDA: MAY - AUG 2015

DRUG	BRAND	INDICATION
Cardiology/Vascular Diseases		
Sacubitril and Valsartan	Entresto	Chronic Heart Failure
Cangrelor	Kengreal	Reducing Periprocedural Thrombotic Events
Alirocumab	Praluent	Heterozygous Familial Hypercholesterolemia or Atherosclerotic Cardiovascular Disease
Evolocumab	Repatha	High Cholesterol
Endocrinology		
Flibanserin	Addyi	Generalized Hypoactive Sexual Desire Disorder
Empagliflozin and metformin Hydrochloride	Synjardy	Type 2 Diabetes
Gastroenterology		
Eluxadoline	Viberzi	Irritable Bowel Syndrome with Diarrhoea
Rifaximin	Xifaxan	Irritable Bowel Syndrome with Diarrhea
Hepatology (Liver, Pancreatic, Gall Bladder)		
Daclatasvir	Daklinza	Chronic HCV Genotype 3
Ombitasvir, Paritaprevir and Ritonavir	Technivie	Chronic HCV Genotype 4
Immunology		
Tacrolimus Extended-Release	Envarsus XR	Prophylaxis of Organ Rejection in Kidney Transplant Patients
Oncology		
Sonnidegib	**Odomzo**	Locally Advanced Basal Cell Carcinoma
Psychiatry/Psychology		
Brexpiprazole	Rexulti	Depression and Schizophrenia
Pulmonary/Respiratory Diseases		
Lumacaftor and Ivacaftor	Orkambi	Cystic Fibrosis
Tiotropium Bromide and Olodaterol	Stioltorespimat	Chronic obstructive pulmonary disease

DRUGS APPROVED BY CDSCO, INDIA: MAY - AUG 2015

DRUG	STRENGTH	INDICATION
Emphagliflozin	Tablet 10 mg	As an adjunct to diet and exercise to improve glycemic control in adults with Type 2 Diabetes Mellitus.
Gadobutrol	Solution for injection	In adult, adolescence and children aged 2 years and older for: 1. Contrast enhancement in cranial and spinal magnetic resonance imaging (MRI). 2. Contrast enhancement MRI of other body regions: liver, kidneys 3. Contrast Enhancement in Magnetic Resonance Angiograpy (CE-MRA) 4. For MRI of the breast to assess the presence and extent of malignant breast
Teneligliptin	Tablet 20 mg	For the treatment of Type 2 Diabetes Mellitus as a monotherapy adjunct to diet and exercise

DPP-4 Inhibitors for Type 2 Diabetes: Drug Safety Communication

Clinicians use dipeptidyl peptidase-4 (DPP-4) inhibitors in conjunction with diet and exercise to reduce blood sugar levels in patients with type 2 diabetes. They are either combined with other diabetes drugs such as metformin or dispensed as stand-alone products.

DPP-4 inhibitors for type 2 diabetes may cause joint pain so intense it is disabling, the US Food and Drug Administration (FDA) warned recently. Fortunately, the pain goes away, usually in less than a month, once patients stop taking the medicine.

The agency said that it identified 33 cases of severe arthralgia associated with DPP-4 inhibitors from October 16, 2006, through December 31, 2013, in its FDA Adverse Event Reporting System database. Twenty-eight of the cases involved sitagliptin (Januvia, Merck & Co, Inc). Saxagliptin (Onglyza, AstraZeneca), linagliptin (Tradjenta, Boehringer Ingelheim Pharmaceuticals), alogliptin (Nesina, Takeda Pharmaceutical Company), and vildagliptin, accounted for the rest of the 33 cases.

Patients began experiencing joint pain anywhere from 1 day to years after they started taking the drugs. For 10 patients, disabling pain required hospitalization.

Reference : http://www.fda.gov/Drugs/DrugSafety/ucm459579.htm

AVOID Oxygen in STEMI Evidence of Harm

Results of a new trial suggest supplemental oxygen therapy in patients with ST-Elevation MI (STEMI) may actually be harmful for patients who are not hypoxic. The Air Versus Oxygen in ST-Elevation Myocardial Infarction (AVOID) trial compared supplemental oxygen (8 L/min) vs no oxygen (unless O2 fell below 94%) in patients with STEMI diagnosed on paramedic 12-lead electrocardiogram.

Mean peak troponin was similar in the oxygen and no oxygen groups (57.4 mcg/L vs. 48.0 mcg/L; ratio, 1.20; 95% confidence interval [CI], 0.92 to 1.56; P=0.18). There was a significant increase in mean peak creatine kinase in the oxygen group compared to the no oxygen group (1948 U/L vs. 1543 U/L; means ratio, 1.27; 95% CI, 1.04 to 1.52; P=0.01). There was an increase in the rate of recurrent myocardial infarction in the oxygen group compared to the no oxygen group (5.5% vs. 0.9%, P=0.006) and an increase in frequency of cardiac arrhythmia (40.4% vs. 31.4%; P=0.05).

At 6-months the oxygen group had an increase in myocardial infarct size on cardiac magnetic resonance (n=139; 20.3 grams vs. 13.1 grams; P=0.04).

"The AVOID study found that in patients with STEMI who were not hypoxic, there was this suggestion that, potentially, oxygen is increasing myocardial injury, recurrent myocardial infarction, and major cardiac arrhythmia and may be associated with greater infarct size at 6 months".

"These findings certainly need to be confirmed in larger randomized trials that are powered for hard clinical end points, but the AVOID study investigators would really question the current practice of giving oxygen to all patients and certainly to those who have normal oxygen levels to begin with".

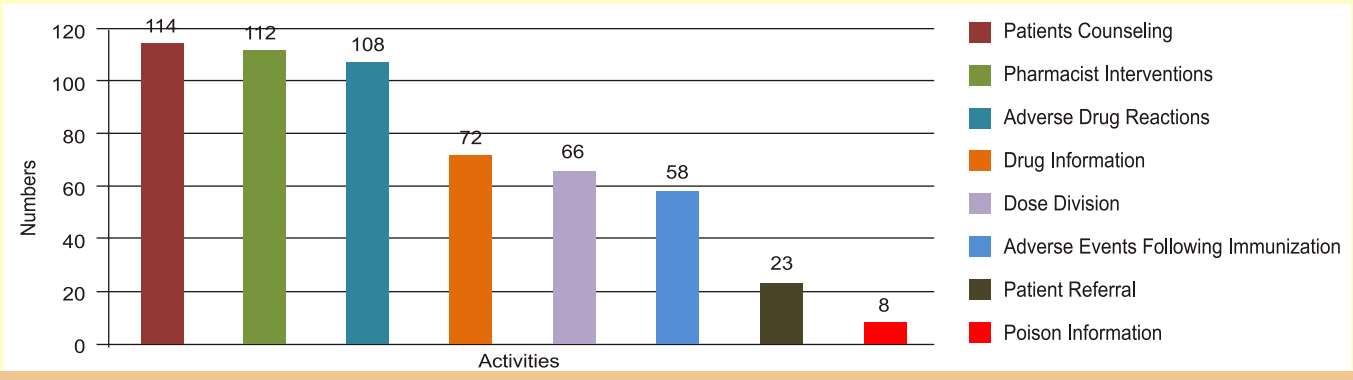
Reference: Stub D et al. Air Versus Oxygen in ST-Segment-Elevation Myocardial Infarction. Circulation 2015;131(24):2143-50.

DEPARTMENT ACTIVITIES

Monthly Cum Cumulative Statistics of Clinical Pharmacy Services for the Academic Year 2014-15

Activity	July	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	March	April	May	June	Cumulative
DI	175	160	233	120	135	134	127	117	122	101	116	72	**1612**
PI	40	24	11	13	16	11	04	18	23	06	06	08	**180**
ADR	193	289	311	203	229	210	131	189	190	122	136	108	**2311**
Ph.I	97	196	212	169	173	142	155	237	142	106	144	112	**1885**
PC	315	377	379	120	303	313	274	343	372	171	125	114	**3206**
PR	43	38	43	84	29	32	30	27	40	32	37	23	**458**
AEFI	50	75	46	37	35	24	99	76	101	66	116	58	**783**
DD	40	40	40	29	24	41	51	53	73	64	59	66	**580**
Total	**953**	**1199**	**1275**	**775**	**944**	**907**	**871**	**1060**	**1063**	**668**	**739**	**561**	**11015**

(**DI-** Drug Information, **PI-**Poison Information, **ADR-**Adverse Drug Reaction, **Ph.I-**Pharmacist Intervention, **PC-** Patient Counseling, **PR-**Patient Referral, **AEFI-**Adverse Events Following Immunization, **DD-**Dose Division)



Department Activities

Guest Lecture by Dr. Ralph J Altiere

Dr. Ralph J Altiere, Professor and Dean of University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences visited Department of Clinical Pharmacy located at JSS Hospital, Mysuru and interacted with the Staff and Students (PhD Research Scholars and Pharm.D Interns). During his visit, Dr. Ralph delivered a guest lecture on 'Overview of Pharmacy Education in Colorado University Skaggs School of Pharmacy and Pharmaceutical Sciences' for the Pharm.D students in the seminar hall of JSS College of Pharmacy, Mysuru. The first part of his talk was about the historical context of the his Pharmacy School, where he talked about the transition of the pharmacy education program from a 3-year baccalaureate degree program to a 4-year Doctor of Pharmacy (Pharm.D) degree program to meet accreditation standards. He mentioned that, during this transition, experiential education was expanded greatly from a 1-Semester program to a 4-year comprehensive experiential education program that created numerous innovative models of experiential education and practice under the capable leadership of the experiential program director. The second part of the talk was about the Pharm.D Curriculum and he stated that the major goal of the curriculum is to prepare pharmacist to provide patient care services through the evidence-based practice. He explained about the competencies of the Pharm.D graduates and the development of Entrustable Professional Activities (EPA) from the competencies. He also discussed about the Pharm.D interns Advanced Pharmacy Practice Experience (APPE) and their different rotations. About 70 seventy students attended the lecture and students had actively interacted with the speaker after the lecture.

Dr. Ralph was active on various committees within the American Association of Colleges of Pharmacy and currently serves the International Pharmaceutical Federation (FIP) in numerous capacities. Ralph is President of the Academic Pharmacy Section and a member of the FIPEd Internal Reference Group, the Board of Pharmacy Practice, the Congress Program Committee and the Academic Institutional Membership (AIM) Deans Forum Advisory Group.

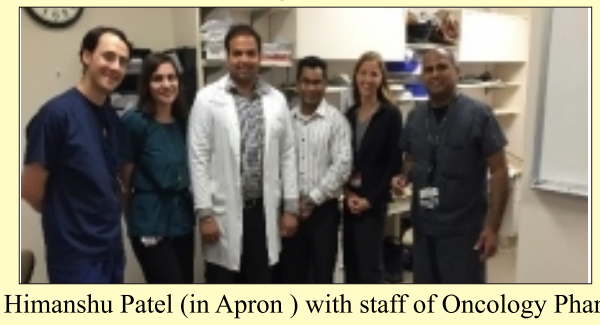
Dr. Ralph addressing the gathering

Faculty Attended to International Training Course in Oncology

Mr. Himanshu Patel, Lecturer, Department of Pharmacy Practice, JSS College of Pharmacy, JSS University, Mysuru had undergone three months comprehensive research scholarship program in oncology pharmacy practice at Rutgers Cancer Institute of New Jersey (CINJ), USA from 17th April to 16th July 2015. Rutgers Cancer Institute of New Jersey is the state's first and only National Cancer Institute-designated Comprehensive Cancer Center. The Cancer Institute of New Jersey Network is comprised of hospitals throughout the state and provides the highest quality cancer care and rapid dissemination of important discoveries into the community. Research scholarship program in oncology pharmacy practice was designed to learn and strengthen the clinical skills to provide various clinical pharmacy services in cancer care setting. The main objective of this training was to strengthen the understanding of the routine clinical services provided by oncology pharmacist like drug information to clinicians and patients, adverse drug reactions detection and management, identification of medication errors in cancer therapy at different health care levels, chemotherapy preparation and mixing, inpatient pharmacy services to cancer patients and patient medication counselling, and also to understand research opportunities in oncology pharmacy.

During his training program he had opportunity to rotate in following departments;

- In-patient Medical Oncology
- Oncology Ambulatory Care
- Haematology Oncology & Bone Marrow Transplant
- Radiation Oncology
- Medication therapy management Services at Oncology Pharmacy
- Chemotherapy preparations and IV admixtures
- Paediatric Oncology & Clinical Trials
- Cancer Prevention Centre, Genetic Counselling, FINANCIAL Counselling and Breast Clinic



Mr. Himanshu Patel (in Apron) with staff of Oncology Pharmacy Department of Rutgers Cancer Institute of New Jersey, USA

Faculty Attended to International Training Course in Pharmacoepidemiology

Mr. Krishna Undela, Lecturer, Department of Pharmacy Practice has undergone training at 'Quality Use of Medicines and Pharmacy Research Centre (QUMPRC)', University of South Australia, Adelaide from 13th April to 10th July 2015. Krishna

Undela received 2015 Endeavour Executive Fellowship from Department of Education, Australian Government to undertake this training. During this period, he was trained in 'Veterans' Medicines Advice and Therapeutics Education Services (MATES) project'; it is one of the major funded projects of QUMPRC. Also he was trained in data mining using various Australian Government health care databases for Pharmacoepi demiological research. Additionally he learned about various statistical analyses methods used in data analysis of Pharmacoepidemiological studies.

Along with the training at QUMPRC, Krishna Undela also got an opportunity to observe the hospital and clinical pharmacy services at major hospitals in South Australia like Royal Adelaide Hospital, Repatriation General Hospital, Flinders Medical Centre and Port Augusta Hospital. He also observed pharmacy services in community settings like Medication Review at Disability Services, Aged Care Services and Nursing Home Facilities.

Mr. Krishna Undela (left) with Pharmacists from Different Hospitals of South Australia

A **Namibian team** visited the Department of Clinical Pharmacy on 20th August 2015 and they were briefed about the various activates of the department. Also the team interacted with the Department staff

Two staff members from Department of Pharmacy Practice, **Oxbridge College of Pharmacy, Bengaluru** visited the Department of Clinical Pharmacy during 3rd & 4th August 2015 for orientation on Clinical Pharmacy Services

Gerturrd Haitsma, from University of Groningen, Netherland visited the Department of Clinical Pharmacy during 4th to 7th August 2015. During her visis, she was oriented to various Clinical Pharmacy Services provided by the department. Also she interacted with staff and students of the Department of Clinical Pharamcy

Two students (Ms. **MUchechukuwu Ezeonyebuchi** and Ms. **Chelsie Morrison)** from **School of Pharmacy, Howard University, Washington, USA** underwent International Clinical Rotations at the Department of Clinical Pharmacy from 22nd June 2015 to 11th July 2015

Mr. Pramod Kumar A, Research Scholar, Department of Clinical Pharmacy received 'Best Poster Award' during "National Conference on Role of Clinical Pharmacists in Improving Medication Safety and Pharmacoeconomics" held at Krupanidhi College of Pharmacy Bengaluru on 22nd and 23rd August 2015

Abstracts of M. Pharm Project Work

Title : Adverse drug reactions in elderly patients: a systematic review and meta-analysis

Background: Several studies suggest that adverse drug reactions (ADRs) are commonly seen among hospitalized elderly and also found common causes of hospital admission leading to substantial morbidity and mortality among elderly. But no meta-analysis was conducted till date to estimate the overall incidence of ADRs among elderly.

Objectives: To estimate the overall incidence of ADRs in elderly patients along with incidence in different health care settings and continent-wise incidence.

Design: Meta-analysis and systematic review

Methods: Studies were identified through searching MEDLINE, Cochrane database of systematic reviews, Google scholar, Clinical key, Scopus (published up to March 2014), and by hand searching the reputed journals on Geriatrics and Gerontology, and references of included articles. Original peer-reviewed research articles published in English, defined ADRs according to WHO's or similar definition and assessed the incidence of ADRs in elderly or having sufficient raw data to determine the incidence were included. Disease or treatment specific studies were excluded. Before meta-analysis, the studies were evaluated for heterogeneity using Chi^2 and I^2 statistics. Overall incidence of ADRs among elderly with 95% confidence interval (CI) was determined using a random-effects model (DerSimonian and Laird method). Subgroup analyses were performed based on study settings and continent where the studies conducted. All the analyses were carried out by using Review Manager (RevMan, version: 5.3) software.

Results: Of the 5747 articles retrieved, 56 and 54 articles were included for systematic review and meta-analysis respectively. The overall incidence (95% CI) of ADRs among elderly population was found to be 12.94% (12.29 - 13.60%). Incidence of ADRs in in-patients, out-patients and patients hospitalized due to ADRs were 17.53%, 19.54% and 6.92%, respectively. The continent-wise incidences of ADRs among elderly were 12.15%, 22.94%, 12.34% and 18.76% in Asia, Australia, Europe and USA respectively. Electrolyte disorders and skin rashes were the common manifestations of the drugs. Cardiovascular drugs and NSAIDs were the most common causative agents for the ADRs among elderly. Polypharmacy was the major risk factor for ADRs in elderly population, irrespective of the type of healthcare settings and continents.

Conclusions: The incidence of ADRs in elderly was higher and is a significant healthcare burden in elderly. Appropriate prescribing, proper compliance and monitoring for ADRs are needed to decrease the incidence of ADRs in elderly patients. ***Dhaval B. Joshi***

Title : Assessment of occurrence of acute kidney injury among inpatients of a tertiary care teaching hospital

Background: Though the relative effects of acute kidney injury (AKI) on mortality, hospital length of stay have been studied extensively in western population, reports from India on occurrence and cost of management of AKI are scanty.

Objective: To determine the incidence of AKI and cost of management of AKI in a tertiary care teaching hospital.

Methods: It was a prospective observational study conducted in Departments of General Medicine, Surgery, Nephrology,

Abstracts of M. Pharm Project Work

Orthopaedic and Critical care Units of a tertiary care hospital. Admitted patients with a primary diagnosis of AKI, all in-patients with an abrupt increase in SeCr of ≥ 0.3mg/dL from baseline or diagnosed to have developed AKI during hospital stay were included. Study patients were followed throughout their hospital stay and all the required data were collected from case records, treatment chart, laboratory reports, and interviewing the healthcare professionals / patients. Data was subjected to analysis to determine the incidence and cost of management of AKI.

Results: Of the 9301 patients admitted to the medicine [n=3331] and surgery [n=1106], nephrology [n=1023], critical care [2971] and orthopedic units [870] from June 2014 - Feb 2015, 672 patients were diagnosed to have AKI. The over all incidence of AKI was found to be 7.1%. The incidences of hospital acquired AKI and Drug induced AKI were found to be 16% [n=108], and 14.6% [n=98] respectively. Pre-renal cause accounted for almost 50% of AKI. The Mean (SD) age was found to be 52.53 (15.87) years. Mean (SD) duration of hospital stay was 6.33 (2.95) days. Twenty five percent of patients underwent Renal Replacement Therapy. Mortality rates were 16.5%. Mortality was high in males and elderly. The mean (SD) direct cost for management of AKI was found to be INR. 7725 (4649).

Conclusion: AKI is associated with significantly increased mortality, length of stay, and costs across a broad spectrum of conditions. The results confirm that AKI definitely poses heavy burden to the patients in terms of suffering and costs. ***A. R. Radhika***

Title : A comparative study to evaluate treatment pattern and resulting utility in patients of head & neck cancers under private payment scheme and government scheme

Background: It is essential to evaluate treatment patterns of cancer patients treated under different reimbursement schemes. Such evaluation helps finding merits and demerits of various reimbursement schemes.

Objectives: To compare the treatment pattern and resulting quality adjusted life year (QALY) in patients of Head & Neck cancers under private payment scheme (PPS) and government scheme (GS).

Methods: Medication orders of patients on chemotherapy for head & neck cancers were reviewed prospective and patients were interviewed for six treatment cycles to assess treatment pattern in an oncology hospital having dedicated wards for patients under GS & PPS. Direct medical cost, indirect medical cost and non-medical costs associated with treatment were calculated for patients under PPS and GS and were compared. EQ-5D-5L instrument was administered to assess patient utility with treatment during each cycle. Utility was measured for patients of both groups and were compared.

Results: A total of 104 patients (n=49 under PPS, n=55 under GS) were enrolled in the study after obtaining their informed consent. Majority of the patients under PPS were on Paclitaxel based regimen (63%) followed by primary protocol (Docetaxel+ Cyclophosphamide+ Fluorouracil, (8%)). Most of the patients under GS were treated with Cisplatin with radiation therapy (82%) and none of the eligible patients under GS had privilege of treatment with primary protocol due to limited budget. Treatment compliance to National Comprehensive Cancer Network (NCCN) guidelines for patients under PPS and GS was 89% and 58% respectively. Common adverse events like vomiting, constipation, neutropenia, fatigue and myalgia were higher in patients under GS than PPS. Average cost of treatment for PPS and GS per cycle was US $125 and US $30 respectively. Quality-adjusted life-year (QALY) gained by patients under PPS and GS after six cycles was 0.024 and 0.014 respectively and the difference was found to be statistically significant ($p<0.05$).

Conclusion: Treatment pattern in patients under PPS were well compliant to NCCN guidelines. Limited budget of government scheme in a developing country does not allow clinicians to prescribe required anti-cancer medicines and supportive care. Patients under GS can be benefited with more utility with additional increment in the budget. ***Avinash Khadela***

Your suggestions are welcome. Please send your comments/suggestions to the editors at: dic.jsscp@jssuni.edu.in

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