PCN4

ASSESSMENT OF SERIOUS ADVERSE REACTIONS AMONG PATIENTS ON TYROSINE KINASE INHIBITORS: IDENTIFICATION OF SIGNIFICANT SIGNALS FOR GASTROINTESTINAL HEMORRHAGE AND PULMONARY REACTIONS

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OBJECTIVES: Tyrosine kinase inhibitors (TKIs) provide target-specific therapies for certain types of malignancies. TKIs may be associated with serious adverse drug reactions. We searched the Food and Drug Administration's Adverse Event Reporting System (FAERS) to identify specific adverse drug reactions associated with small molecule TKIs in the post-marketing setting. **METHODS:** The TKIs included were gefitinib, imatinib, lapatinib, nilotinib, erlotinib, pazopanib, sorafenib, and vandetanib. The adverse reactions evaluated were interstitial lung disease (ILD), pneumonitis, pleural effusion, and gastrointestinal hemorrhage, depression, and suicide. We searched FAERS for each TKI from their respective approval date and calculated empiric Bayesian geometric means (EBGM) to identify significant disproportionality signals of each drug and reaction. **RESULTS:** EBGM for ILD, pneumonitis, and pleural effusion were significant for gefitinib, imatinib, erlotinib, and sorafenib. EBGM for pleural effusion was also significant for nilotinib. The strongest EBGM signals were associated with gefitinib/ILD (25.4, n=320), gefitinib/pneumonitis (10.5, n=54), erlotinib/ILD (7.5, n=212), nilotinib/pleural effusion (7.0, n=101), erlotinib/pleural effusion (6.9, n=325), sorafenib/pleural effusion (6.4, n=70), imatinib/pleural effusion (6.3, n=413), gefitinib/pleural effusion (5.8, n=118), and erlotinib/pneumonitis (5.7, n=63). EBGM for gastrointestinal bleeding was significant for erlotinib (2.5, n=156) and sorafenib (4.3, n=63). No significant signals were found for depression or suicide with any of the TKIs. Mortality rates for the adverse reactions with significant signals were: ILD=50.8%, gastrointestinal bleeding=40.6%, pneumonitis=37.0%, and pleural effusion=31.5%. **CONCLUSIONS:** Serious pulmonary adverse reactions, with high rates of mortality, have been reported disproportionately more frequently with gefitinib, imatinib, erlotinib, nilotinib, and sorafenib. Gastrointestinal hemorrhage has been reported to FAERS disproportionately more often with erlotinib and sorafenib. Limitations of FAERS are that lack of signals among other TKIs may be due to less frequent use or reporting of these reactions to FAERS, or shorter post-marketing time periods. Physicians and pharmacists should inform and monitor patients on TKIs for these reactions.

PCN5

FACTORS INFLUENCING TREATMENT DURATION IN METASTATIC COLORECTIC CANCER PATIENTS TREATED WITH ZIV-AFLIBERCEPT: A REAL WORLD VIEW

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OBJECTIVES: Ziv-aflibercept (Ziv) is an anti-angiogenic agent used in combination with FOLFIRI (folinic acid, fluorouracil and irinotecan) to treat adults with metastatic colorectal cancer (MCC). The purpose of this study is to examine the impact of patient characteristics, complications, and comorbidities on treatment patterns and outcomes of Ziv-treated MCC patients in a real world setting. **METHODS:** A retrospective cohort study was conducted on Ziv-FOLFIRI treated MCC patients in the MedAssets health system data for inpatient and outpatient visits between January 2012 and April 2015. Age and gender, hospital characteristics, clinical comorbidities, and utilization measures (number of visits, treatment duration, and Ziv initiation) were described. Ziv related complications included neutropenia, proteinuria, hypertension, gastrointestinal (GI) hemorrhage, and thromboembolism. Multivariate regression models were developed to identify drivers of hospital utilization and treatment duration. **RESULTS:** The study population included 337 patients that were predominately male (55.4%) with an average age of 58.8 years. The mean Charlson comorbidity score was 7.51. Hospital utilization included over 12,000 visits which occurred primarily in the outpatient setting (96.2%) in teaching facilities (69.0%) with 300 or more beds (87.6%). Treatment complications included neutropenia (31.2%), proteinuria (6.2%), hypertension (48.7%), GI hemorrhage (7.4%), GI perforation (3.2%), and deep vein thrombosis (12.2%). Mean treatment duration was 523 days while the average days from colon cancer diagnosis to Ziv treatment was 218 days. After adjustments, neutropenia (HR: 0.771, p=0.0323) chronic renal disease (HR: 0.649, p=0.001), and hypertension (HR: 0.693, p=0.001) were found to significantly reduce treatment duration. Neutropenia (RR: 0.23, p=0.0135) and sever liver disease (RR: 0.035, p=0.0008) had a significant impact on total visits. **CONCLUSIONS:** Ziv related complications and comorbidities can significantly impact treatment viability and ultimately patient survival.

PCN6

EFFICACY AND SAFETY PROFILE OF COMBINED TARGETED THERAPY AGAINST EGFR AND VEGF IN PATIENTS WITH PREVIOUSLY TREATED ADVANCED NON–SMALL-CELL LUNG CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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OBJECTIVES: The objective was to evaluate the clinical efficacy and safety of combined targeted therapy against EGFR and VEGF pathways in patients with previously treated advanced Non–small-cell lung cancer (NSCLC). **METHODS:** Studies were retrieved from Embase, Pubmed and Cochrane databases using relevant search strategies. Randomized controlled trials which compared combined targeted therapy with control groups (including single EGFR or VEGF inhibition or/and chemotherapy) were selected as per pre-defined inclusion criteria. Outcomes assessed included overall survival (OS), progression free survival (PFS), objective response rate (ORR), and adverse events (AEs). Two reviewers independently extracted data from the included studies. Data was analysed using RevMan (v5.3). **RESULTS:** Of the 876 studies identified, seven studies with 3347 patients were included for meta-analysis. In total, 1688 patients were randomised to combination therapy and 1659 were randomised to control groups. Median OS (range 8- 13.7 vs. 4.5- 13.4 months), PFS (range 3.4- 4.7 vs. 1.9- 4.8 months) and ORR (range 4.6% -26.2% vs. 3.1% - 12.5%) was better with combination therapy vs. control group therapies. In two studies, patients on vandetinib and docetaxel combination therapy showed a significant improvement (p<0·0001) in PFS and overall response rate versus those randomly assigned to receive docetaxel only. Results of meta-analysis demonstrate that combined targeted therapy has better OS (WMD: 1.23 [95% CI: 0.06, 2.41], p = 0.04), PFS (WMD: 1.07 [95% CI: 0.7, 1.45], p < 0.00001) and ORR (OR: 1.85 [95% CI: 1.49, 2.31], p < 0.00001). The AE profile (gastrointestinal, vascular, infectious and blood disorders) was better in the control group therapies. **CONCLUSIONS:** Survival benefit and response rate with combined inhibition therapy against EGFR and VEGF was better than the VEGF or EGFR alone inhibition. Combination therapy was associated with increased toxicity resulting in low compliance and dose reduction or discontinuation.

PCN7

A SYSTEMATIC REVIEW TO ASSESS THE ASSOCIATION BETWEEN THE USE OF ANTIDEPRESSANTS AND MALE-ONLY CANCERS

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OBJECTIVES: To assess the association between antidepressants (ADs) use and male-only cancers. **METHODS:** Embase and PubMed were searched for relevant human studies published in English. Data was extracted for study population, study characteristics, interventions, and risk of male cancers (prostate [PC], testicular [TC], penile [PNC], and male breast cancer [MBC]). **RESULTS:** Of the 374 results that were obtained from the literature search, five case-control studies (three assessed PC risk and two assessed TC risk) and one case-report (assessed MBC risk) met the inclusion criteria. None of the included studies assessed PNC risk. In a population-based study, no significant association was found between selective serotonin reuptake inhibitors (SSRIs) use and PC (risk ratio [RR]=1.01 [95% CI: 0.82-1.25]). Similarly, no significant association was found between ADs use and PC risk in other two studies. Significantly positive association was found between tricyclic antidepressants (TCAs) use for 2-5 years and PC with a RR of 1.31 (1.14-1.51), 1.58 (1.29-1.93), and 2.42 (1.87-3.12) for the low, medium, and high average daily dose levels, respectively. However, authors acknowledged detection bias as possible reason for the observed association. SSRIs were found to be significantly associated with TC (fluoxetine RR=2.51 [1.39-4.53]; paroxetine RR=2.44 [1.25-4.74]) in one study. A four-year follow-up study re-tested the association with 12 ADs. In multivariate analyses in this study, neither fluoxetine (odds ratio [OR]=1.22 [0.88-1.71]) nor paroxetine (OR=1.19 [0.78-1.83]) or all SSRIs combined (OR=1.21 [0.92-1.58]) were significantly associated with TC risk. All TCAs (OR=1.06 [0.75-1.51]) and all ADs combined (OR=1.06 [0.85-1.32]) were also not associated with TC risk. In a report of three cases, authors reported an anecdotal association between SSRIs and MBC. **CONCLUSIONS:** The results do not indicate significant association between ADs use and risk of male-only cancers. In most cases, weak positive associations disappeared after adjusting for confounding factors.

PCN8

SERIOUS POST-OPERATIVE INFECTIONS INCREASE RESOURCE UTILIZATION, LENGTH OF STAY, AND INPATIENT MORTALITY IN PEDIATRIC PATIENTS UNDERGOING BRAIN TUMOR RESECTION

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OBJECTIVES: To assess the impact that serious post-operative infections (SPOI) have on hospitalization outcomes (i.e., resource utilization, length of stay, and inpatient mortality) in pediatric patients undergoing brain tumor resection. **METHODS:** Data from the 2003-2012 Nationwide Inpatient Samples (United States Agency for Healthcare Research & Quality) were analyzed for this study. Patients aged 20 and younger were eligible for inclusion if they had a malignant brain tumor (ICD-9 diagnosis codes 191.xx and/or 198.3) and underwent tumor resection (ICD-9 procedure code 01.59) during hospitalization. SPOI, including bacteremia (ICD-9 diagnosis code 790.7), septicemia (ICD-9 diagnosis code 038), pneumonia (ICD-9 diagnosis codes 481, 482, 483, 485, or 486), and wound infections (ICD-9 diagnosis codes 998.51 and/or 998.59) were also identified in the discharge summary. The impact of the serious SPOI on hospitalization outcomes were then assessed using bivariate and multivariate models. **RESULTS:** A total of 7,845 pediatric patients underwent brain tumor resection (Median Age: 8 years [IQR: 3-15]. Of these patients, 5.9% (N=461) had a SPOI, of which septicemia/bacteremia was the most common (N=312). SPOIs increased the odds of inpatient death nearly four-fold (unadjusted OR: 3.76 [2.62-5.40], p<.0001). When adjusted for patient characteristics, SPOIs were still associated with a nearly four-fold increase in the odds of inpatient mortality (adjusted OR: 3.73 [2.59-5.36]). Patients with SPOIs stayed significantly longer in the hospital (Median: 16 days [IQR: 6-33]) than those without SPOIs (Median: 5 days [IQR: 3-10]) (p<.0001). On average, patients with SPOIs underwent four additional procedures during the hospitalization stay (Median: 6 procedures [IQR: 2-8]) than those without SPOIs (Median: 2 procedures [IQR: 1-5]) (p<.0001). **CONCLUSIONS:** SPOIs significantly increase resource utilization, length of stay, and odds of inpatient mortality for pediatric patients undergoing brain tumor resection. Quality and process improvement efforts should be considered to minimize the risk of SPOIs in this patient population.

PCN9

CHANGES IN THE MORTALITY RATE DURING THE LAST DECADE IN THE FIELDS OF ONCOLOGY IN HUNGARY

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OBJECTIVES: Based on the data of the Hungarian Central Statistical Office the prevalence of oncological patients in Hungary is growing due to the modern diagnostic devices, the effectiveness of diagnostic screening methods and the increasing life expectancy. This study aims to assess information about the change in the mortality rate in the relevant patient population during the last decades. **METHODS:** This ret-