Abstracts

needs to be taught in small friendly doses tied to practical problems. Each analysis note presented by Doug Gaus has sketches drawn by artist Pat Gaus.

CONCEPTUAL PAPERS & RESEARCH ON METHODS – Study Design

PMCa

METHODS FOR IDENTIFYING CASE REPORTS OF SUSPECTED ADVERSE DRUG REACTIONS: AN EVALUATION OF THE EFFICIENCY OF ALTERNATIVE SEARCH STRATEGIES IN MEDLINE AND EMBASE

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To illustrate the precision and sensitivity of identifying case reports of adverse events (AE) in MEDLINE and EMBASE, eight searching methods were created and applied to two systematic reviews of case reports. Search methods included use of indexing and text words for synonyms of AE and related terms, as well as drug, disease, and study design. All eight methods combined the drug and combinations of other search strings and ranged from broad to very specific. Searches were developed for MEDLINE and EMBASE, with each approach being checked against a “gold standard” (GS) of case reports previously identified in two systematic reviews (75 anti-TNF agent, 57 baclofen case reports). Sensitivity and precision of each method were calculated. The broadest search, using drug terms alone, yielded over 11,000 and over 3,600 references for each systematic review topic. Sensitivity decreased as search methods became narrower; precision was consistently low (generally <6%). The search method for drug terms alone had 100% sensitivity for both systematic review topics with very low precision (<1.6%). Precision was highest when drug, disease, case report and AE were combined. From MEDLINE, 7% and 18% from TNF agent and baclofen case reports respectively were not indexed as case reports. Sensitivity search methods able to identify relevant case reports are important, but when a sensitive search was constructed, this lead to low precision. A sensitive search method must be broad, and search both databases. Precision remains low with each combination of approaches, making accurate identification of case reports rather labor intensive. This illustration demonstrated the extent to which decisions made when developing search methods impact the comprehensiveness of reviews. Further work is ongoing to confirm the generalizability of these findings to other drugs.

CANCER – Clinical Outcomes Studies

PCN1

USE OF WHITE BLOOD CELL GROWTH FACTORS AND RISK OF ACUTE MYELOID LEUKAemia OR MYELODYSPLASTIC SYNDROMES AMONG ELDERLY NON-HODGKIN’S LYMPHOMA PATIENTS

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OBJECTIVES: Therapy-related myelodysplastic syndromes and acute myeloid leukaemia (t-MDS/AML) are devastating long-term complications of cancer therapy. Evidence suggests that white blood cell growth factors (CSFs) may increase risk of t-MDS/AML among patients (pts) receiving chemotherapy, possibly because they stimulate the proliferation and differentiation of hematopoietic stem cells and also interfere with apoptosis. The purpose of this retrospective study was to evaluate the association between CSF use and t-MDS/AML among a large population-based cohort of elderly non-Hodgkin’s lymphoma (NHL) pts treated with chemotherapy.

MATERIALS AND METHODS: t-MDS/AML cases were identified from the Surveillance, Epidemiology, and End Results-Medicare database diagnosed from 1992 to 2002 who received chemotherapy within 12 months of diagnosis. Pts were followed from their initial chemotherapy until t-MDS/AML development, death, or end of study period (December 31, 2006). Kaplan-Meier Cox proportional hazards analyses were used to evaluate the association between CSF use and t-MDS/AML. RESULTS: A total of 13,203 pts were identified. Overall, 40% (n=5,266) received CSF. 272 (5.2%) pts receiving CSF developed t-MDS/AML vs. 230 (2.9%) who did not receive CSF (log-rank p=0.0001). In a multivariable Cox regression analysis adjusting for gender, histology, stage, comorbidities, chemotherapy dates, and chemotherapy agent, use of CSF was independently associated with a 33% increased risk of t-MDS/AML (HR 1.33; 95% CI 1.19–1.48). A dose-response relationship was observed, with t-MDS/AML risk increasing by quartile of CSF claims. In an analysis of plausible biologic interactions, we found that 18% of anti-CSF and antimitabolite chemotherapy (n=1,567 pts) had a 2.5 fold increased risk of t-MDS/AML (HR 2.49; 95% CI 1.91–3.26) vs. pts who received neither agent (p-interaction = 0.04). CONCLUSIONS: Our findings suggest that CSF use among elderly NHL chemotherapy pts may increase risk of t-MDS/AML, even though absolute risk is low. Future studies are necessary to verify these results and to determine the clinical implications of the observed interaction between CSF use and antimitabolite chemotherapy.

PCN2

DIABETIC MEDICATIONS AND ITS ASSOCIATION WITH MORTALITY IN HOSPITALIZED CANCER PATIENTS

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OBJECTIVES: The effect of diabetes and diabetic medications on the morbidity and mortality in hospitalized cancer patients is a serious concern. We examined the association of diabetic medications with the transfer to ICU and inpatient mortality.

METHODS: Electronic patient records were prospectively collected in 5489 hospitalizations to UT MD Anderson Cancer Center from May 1st, to July 31st, 2006. For each record demographic, laboratory and pharmacy data were reviewed. To assess the effect of diabetic medications, we selected only diabetic patients, which were 36.3% (1911) of the total hospitalization. Descriptive and logistic regression analyses were performed. RESULTS: Out of 1991 hospitalizations for diabetic cancer patients, fifty-seven percent were male, sixty-nine percent were White with median age 65 years. These patients were on different diabetic medications and thirty one percent were only on sliding scale insulin (SSI). After controlling for socio-demographic variables and other medications like chemotherapy, we found cancer patients who were only on SSI were more likely to be transferred to intensive care unit (ICU), (OR 2.31, CI 1.7–3.2; P<0.001) and die during hospitalization (OR 1.88, CI 1.3–2.7; P<0.001). Glucocorticoids administration was also significantly associated with inpatient mortality (OR 5.91, CI 3.5–9.8; (p<0.001)). CONCLUSIONS: We found strong associations between the method of administration of insulin (SSI) and transfer to ICU and inpatient mortality in cancer patients with diabetes. Drug dosage and administration in inpatient settings should be tailored to the need of the patients to optimize the medication effect and minimize the side effects.

RELIABILITY OF CLINICIAN VS. CLINICIAN ADVERSE SYMPTOM REPORTING

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OBJECTIVES: Adverse symptom reporting is essential in clinical trials and drug labeling to assess and ensure patient safety. The standard approach to collecting adverse symptoms in cancer trials is clinician reporting using the Common Terminology Criteria for Adverse Events (CTCAE), which rates symptoms based upon descriptive clinical criteria. Despite the importance of this information, the reliability of these ratings has not been verified. At Memorial Sloan-Kettering Cancer Center, symptoms in cancer trials are routinely evaluated via CTCAE items by a clinician in an office suite, and again shortly thereafter by a second clinician in a chemotherapy suite, with no information passed between clinicians. METHODS: To measure the reliability of these evaluations, a retrospective analysis of medical charts was completed in a sample of 433 patients aged 26–91 (M=62.39; 41.8% male) receiving chemotherapy, who were enrolled in an observational study conducted between March 2005 and August 2009. Cancer diagnoses included lung (N=153), prostate (N=127), and gynecologic (N=153). RESULTS: For the first post-chemotherapy visit, interclass correlation coefficients were moderate for fatigue (0.52), dyspnea (0.75), nausea (0.55), vomiting (0.50), diarrhea (0.63), constipation (0.48) and neuropathy (0.73). The average time between evaluations was 70.42 minutes (range 67.97–72.88). These values were stable over up to six subsequent visits and did not differ based on age, gender, or elapsed time between evaluations. CONCLUSIONS: Given the short period of time and lack of interventions between reporting time points, the most likely cause of this lower than expected agreement between different clinicians is limited reliability of clinician reporting of this information. This finding has implications to clinical trials, as it brings into question the reliability or accuracy of symptom safety information. The investigators are currently evaluating patient-reported outcomes as an alternative and potentially more reliable method for collecting this information.

PCN3

INSULINS AND RISK OF CANCER AMONG TYPE 2 DIABETICS: A SYSTEMATIC REVIEW

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OBJECTIVES: There have been reports which suggest that insulin glargine use may contribute to increased cancer risk in some type 2 diabetic populations, in addition to the fact that diabetes mellitus is also associated with certain types of cancer. Therefore, the objective of the present study is to conduct a review of published studies on insulins and the risk of cancer in patients with type 2 diabetes and summarize the findings. METHODS: Several databases such as Medline and PubMed were used for publication searching. Key words included insulin, tumor, cancer, type 2 diabetes, and specific insulin names such as glargine, lantus, lispro, aspart, etc. Only English language literature was considered for articles looking at the increased risk of cancer among type 2 diabetic patients using insulins. RESULTS: About 30 articles were selected, among those, 4 studies were conducted in humans using secondary database. All were historic cohort studies, and they used Cox regression for analysis. Two articles established a positive association between cancer incidence and insulin glargine, while the other two found no association. Three studies also showed that several insulins other than glargine are not associated with an increased risk of cancer.
LIMITATIONS OF THESE STUDIES INCLUDE FAILURE TO CONTROL FOR IMPORTANT CONFUNDERS, SMALL SAMPLE SIZE AND SHORT STUDY PERIOD, WHICH MAY HAVE IMPACT ON THE RISK OF CANCER. CONCLUSIONS: GIVEN THE FACT THAT CANCERS ARE RARE AND OFTEN TAKE A LONG TIME TO DEVELOP, FURTHER STUDIES REQUIRE VERY LARGE POPULATIONS WITH LONG FOLLOW UP TIMES TO HAVE SUFICIENTLY POWERED TO DETECT A PRACTICALLY SIGNIFICANT DIFFERENCE. THIS COMBINED WITH SMALL PROPORTIONS OF INSULIN USERS WHO WERE EXPOSED TO GLARGINE, MAY BE A REASON TO STUDIES THAT FOUND NO ASSOCIATION, WHICH LEAVES A QUESTION OF A CLASS EFFECT. FUTURE STUDIES TO EXPLAIN THE EFFECT OF ALL OTHER INSULINS AND THE POSSIBLE MECHANISM MAY HELP TO UNTANGLE THIS QUESTION.

ASSESSMENT OF NEUROPATHY IN CLAIMS DATA AND THE ASSOCIATION WITH DOCEXAL (DC) AND PACLATUX (PC) IN ADJUVANT BREAST CANCER (BC)

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OBJECTIVES: Neuropathy, a common side effect of taxanes, is often dose-limiting and may result in changes in treatment. This study examined the occurrence of neuropathy in claims data from commercially insured US patients with BC treated with adjuvant DC or PC. METHODS: This retrospective database analysis used eligibility, medical and pharmacy claims data from a large US health care organization, including medical and pharmacy claims data from a large US health care organization, including adjuvant DC or PC.

RESULTS: A total of 3619 subjects were identified and conducted comprehensive chart reviews to confirm that these patients did not have any of the comorbidities of interest. Negative predictive values (true negatives / true negatives + false negatives) were calculated. RESULTS: Using our 2-phased search of the EMR, we found an overall prevalence of comorbidities of 22%. The most commonly identified conditions were COPD, cerebrovascular disease, paralyis, diabetes, peripheral vascular disease (PVD), myocardial infarction (MI), liver disease, and AIDS. The search was conducted in 2 phases. Initially, a series of programmatic queries were conducted to search standardized information on comitant illnesses, patient history, review of systems, and diagnoses other than cancer. In a second phase, keyword searches of text-based fields (i.e., physician dictation notes, problem lists, etc.) were conducted.

EVALUATION OF THE RELIABILITY OF ELECTRONIC MEDICAL RECORD DATA IN IDENTIFYING COMORBID CONDITIONS AMONG PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC)

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OBJECTIVES: Traditional methods for identifying comorbidities in retrospective observational research have relied primarily on claims data. The purpose of this study was to validate a 2-phased strategy to search EMR data to identify comorbidities among cancer patients. METHODS: Advanced stage NSCLC patients (N = 2513) who received chemotherapy from July 1, 2006–June 30, 2008 were identified using iKnowMed, US Oncology’s proprietary oncology-specific EMR system. EMR data were searched for documentation of the following comorbidities: moderate/severe renal disease, congestive heart failure (CHF), dementia, chronic obstructive pulmonary disease (COPD), cerebrovascular disease, paralyis, diabetes, peripheral vascular disease (PVD), myocardial infarction (MI), liver disease, and AIDS. The search was conducted in 2 phases. Initially, a series of programmatic queries were conducted to search standardized information on conitant illnesses, patient history, review of systems, and diagnoses other than cancer. In a second phase, keyword searches of text-based fields (i.e., physician dictation notes, problem lists, etc.) were conducted.

A COMPARISON OF INTRAVENOUS AND ORAL FORMULATIONS OF FLUDARABINE IN THE TREATMENT OF CHRONIC LYMPHOCYTIC LEUKEMIA

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OBJECTIVES: Fludarabine (F) has been proven to be highly effective in the treatment of chronic lymphocytic leukemia (CLL). Both oral and IV F are used internationally. Recently, the oral formulation of fludarabine was approved in the US for treating CLL, which may offer advantages for providers, payers and patients. This study is a systematic review of clinical trial and retrospective data for oral and IV fludarabine, focusing on differences in efficacy, complications, resource utilization and patient preference. METHODS: PubMed and manual bibliographic searches were conducted to identify relevant publications for oral and IV F. Studies were included if they were: 1) published after January 1, 2000, 2) derived from human subjects, 3) written or translated in English 4) focused on CLL, and 5) evaluated oral or IV F in randomized trials.

IMPACT OF 5-HT3-RECEPTOR ANTAGONIST STEP THERAPY ON CHEMOTHERAPY INDUCED NAUSEA AND VOMITING ASSOCIATED HOSPITAL AND EMERGENCY ROOM EVENTS

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OBJECTIVES: To explore the impact of step therapy policies requiring the use of a 1st generation 5-hydroxytryptamine- receptor antagonist (5-HT3-RA) treatment before palonosetron (a 2nd generation 5-HT3-RA) on the incremental risk of chemotherapy induced nausea and vomiting (CINV) associated with a hospital or emergency room (ER) event. METHODS: Claims data were used to identify patients newly enrolled adult patients diagnosed with breast cancer (BC) and initiated on cyclophosphamide-based chemotherapy (CT) within 4 months post-diagnosis or with lung cancer (LC) and initiated on carboplatin-based CT. Patients were stratified into those initiated and maintained on palonosetron throughout CT (Group 1) versus those treated on day 1/cycle 1 with any other 5-HT3-RA regimen (Group 2). Risks and frequency for CINV-associated hospital or ER events identified through ICD-9-CM codes for nausea, vomiting, and/or dehydration during a 6-month follow-up period were estimated using Poisson and Poisson regression models, controlling for age, gender (LC only), comorbidity, and CT days. RESULTS: Of 3606 BC and 4497 LC identified patients, 1864 BC (52%) and 1806 LC (40%) initiated palonosetron. Groups 1 and 2 had comparable comorbidity and CT treatment days. Compared to Group 2 patients, group 1 patients had a significantly lower probability of CINV-associated hospital or ER events (3.5% vs. 5.5% in BC and 9.5% vs. 12.8% in LC), had 47.4% (BC) and 29.1% (LC) fewer hospital or ER days with CINV, and fewer 5-HT3-RA claims (mean ± SD 6.2 ± 3.5 vs. 7.9 ± 4.1 in BC and 7.7 ± 4.9 vs. 10.3 ± 6.4 in LC), all at p < 0.05. Risk for CINV was 48% (BC) and 29% (LC) lower for group 1 patients (Odds Ratio = 0.62 in BC and 0.71 in LC, p < 0.05). CONCLUSIONS: LC or BC patients initiated and maintained on palonosetron throughout CT were at significantly lower risk for costly CINV versus those on any other 5-HT3-RA on day 1/cycle 1 of CT treatment.

USING PROPENSITY SCORES TO REDUCE SELECTION BIAS IN AN OBSERVATIONAL STUDY COMPARING RASBURICASE TO ALLOPURINOL IN THE US

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OBJECTIVES: Rasburicase (RA) reduces uric acid (UA) elevation otherwise resulting from tumor lysis syndrome. The PS is the probability of receiving RA, otherwise receiving allopurinol. RESULTS: There were 17 articles that met inclusion criteria. Results indicated that the pharmacokinetic profile of oral and IV F were similar, with 25 mg/m² of IV being equivalent to 40 mg/m² of oral. Oral F has similar efficacy and safety to IV F, and eliminates infusion related adverse events and administration costs. Studies indicated that providing oral F was more convenient for patients and nurses due to the absence of IV administration. No cost or pharmacoeconomic data were found. CONCLUSIONS: Oral and IV F were found to have similar clinical efficacy and safety. The oral formulation may potentially lead to substantial economic benefits which may be possible reductions in infusin related administration and adverse events. Future studies need to compare real-world clinical outcomes and economic impact of oral vs. IV F, taking into account decision-making in clinical practice of both health care providers and patients.

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