COMPARATIVE COST OF ABLATION IN ATRIAL FIBRILLATION PATIENTS STRATIFIED BY PROCEDURAL SUCCESS VERSUS FAILURE: IMPLICATIONS FOR RESOURCE UTILIZATION IN MEDIACRE-AGED ABLATION CANDIDATES IN THE UNITED STATES
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OBJECTIVES: Carotid ablation is increasingly used to maintain sinus rhythm in atrial fibrillation (AF) patients unresponsive to antiarrhythmic drugs (AADs). We compared medical costs in Medicare-eligible AF patients following successful vs unsuccessful ablation. METHODS: In this retrospective study, AF pts with 1) an index ablation, 2) ≥12 months’ medical/pharmacy coverage before and after index ablation, and 2) AF inpatient/outpatient visits within 6 months and AAD treatment within 12 months of index ablation were identified from the MarketScan® Medicare database (January 2002-June 2007). Ablation success was defined as absence of AAD treatment 6–12 months post-ablation. RESULTS: A total of 135 AF patients (67% men, mean 73 yrs) were included; ablation was successful in 69 and failed in 66 patients. Most patients (97% with successful vs 94% with failed ablation) underwent only 1 ablation procedure during the 12-month study. After successful ablation, patients discontinued AAD in (mean) 14 days. Use of rate-control and anti-coagulant drugs declined after successful ablation (67% vs. 87% and 64% vs. 86% patients, respectively), but remained largely unaltered after failed ablation (70% vs. 74% and 82% vs. 88% patients, respectively). Mean (median) per-patient costs per ablation were $13,635 ($11,795) for successful vs. $17,294 ($11,778) for failed ablation. Other AAD-related costs over 1 year after index ablation were $23,594 ($76,877) for successful vs. $2703 ($4478) for failed ablation. Overall annual per-patient costs were lower in patients with successful (mean $16,049; median $17,135) vs. failed ($19,997; $26,631) ablation (P = 0.07). CONCLUSIONS: Ablation failed in half of ‘real-world’ Medicare-aged-AF patients, and treatment of recurrent ablation. Overall costs were higher for successful ablation patients, possibly because of differences in AF-related issues, complications, and ablation methods. Over time, this cost differential would likely increase if failed ablation patients underwent repeat procedures. Identification of predictors for ablation success may reduce medical costs.

PODIUM SESSION III: PERSONALIZED MEDICINE STUDIES

PM1 RISK-BENEFIT FRAMEWORK FOR EVALUATION OF GENE EXPRESSION PROFILING IN WOMEN WITH EARLY STAGE BREAST CANCER: A DEVELOPMENTAL MODEL DEVELOPED IN COLLABORATION WITH STAKEHOLDERS
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OBJECTIVES: To develop a parsimonious risk-benefit model to assist stakeholders in evaluating gene expression profiling (GEP) to guide use of adjuvant chemotherapy in early stage breast cancer compared to clinical guidelines. METHODS: A decision model was developed to estimate comparative benefits and harms of using GEP relative to NCCN guidelines, including disease recurrences, adverse events, life years, and quality-adjusted life years (QALYs). Model structure and output were developed through a collaborative feedback process with stakeholders. The model’s interactive structure allows users to specify the GEP, adjuvant chemotherapy regimens, and prognostic and predictive risk stratification. A Markov process was utilized to estimate clinical outcomes, and parameter uncertainty was evaluated through one-way and probabilistic sensitivity analysis. The base case patient was a pre-menopausal woman of age 44. The prognostic and predictive properties of the GEPs were derived from published retrospective analyses of RCTs. Adjuvant chemotherapy regimen-specific utility decrements were incorporated based on trial-based adverse event rates. RESULTS: Preliminary analyses indicate that a GEP that provides prognostic information only would identify 61% of women to receive adjuvant chemotherapy, while 96% would be identified by clinical guidelines. Based on these estimates, GEP and clinical guidelines would prevent 29% and 34% of distant recurrences, respectively. These findings suggest that GEP may lead to a net harm, with 8.86 QALYs for GEP versus 10.08 for clinical guidelines, due to increased risk of disease recurrence, despite the avoidance of chemotherapy and side effects in 39% of women. Analyses of other risk stratification approaches are ongoing. CONCLUSIONS: We found that use of GEP to guide use of adjuvant chemotherapy in early stage breast cancer could lead to a decrease in QALYs relative to the use of clinical guidelines if chemotherapy predic- tive information is not available. Ongoing efforts are focused on collaboration with stakeholders to align model structure and output with stakeholder needs.

PM2 EFFECTS OF PRIMARY PROPHYLACTIC G-CSF USE AND DURATION OF USE ON NEUTROPHIL HOSPITALIZATIONS FOR ELDERLY BREAST CANCER PATIENTS RECEIVING CHEMOTHERAPY
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OBJECTIVES: Systemic chemotherapy is a vital component of breast cancer care. However, early-onset chemotherapy-toxichies like neutropenia hinder chemotherapy use in breast cancer patients, especially in the elderly. Depending on the severity, neutropenia management requires hospitalization and aggressive systemic antibiotic administration, and involves reduction or discontinuation of chemotherapy. Primary prophylactic granulocyte-colony stimulating factors (G-CSF), especially when administered over adequate duration, help prevent neutropenia. Nevertheless, evidence supporting the effectiveness of G-CSF in the elderly is limited, and in the ASCO guidelines for G-CSF-use and specifications for duration of its use in the elderly are not explicit. This study analyzed the effects of G-CSF and adequate duration of PPG-CSF on the occurrence of chemotherapy-induced neutropenia hospital- izations in elderly breast cancer patients. METHODS: A retrospective observational study for patients newly diagnosed with primary breast cancer between the years 1994 to 2002 using the SEER-Medicare data was performed. To account for the non-random nature of the observational data a non-parametric covariate genetic matching strategy was used to pre-process and post-process data before performing Mendelian randomization to estimate the treatment effects. RESULTS: Administration of PPG-CSF during the first course of chemotherapy reduced neutropenia hospitalizations by 15% within the first three months and 16% within the first six months of chemotherapy initiation (p < 0.01). Hospitalizations within the first one and six months were also considerably lower with longer PPG-CSF duration (3±days) (p < 0.10). CONCLUSIONS: PPG-CSF use is associated with reduction in occurrence of severe neutropenia and reduced in-patient health care utilization. These findings have implications for ASCO guidelines and Medicare coverage policies for PPG-CSF administration and duration of administration in elderly breast cancer patients.

PM3 ECONOMIC EVALUATION OF GENETIC TEST IN COMBINATION WITH PREVENTIVE DONEPEZIL TREATMENT FOR AMNESTIC MILD COGNITIVE IMPAIRMENT PATIENTS: LIFE-TIME IMPACT
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OBJECTIVES: Amnestic Mild Cognitive Impairment (AMCI) patients with Apolipo- protein-e4 allele (APOE-e4), a type of genetic mutation, have higher rates of progress- ion to Alzheimer Disease (AD) than patients without genetic mutation. Some studies suggest that early diagnoses and treatment in APOE-e4 carriers will delay their progression to AD. Objective is to evaluate the cost-effectiveness of APOE-e4 testing in combination with preventive Donepezil treatment in AMCI patients in Canada. METHODS: We performed a cost-effectiveness analysis using a Markov model used on a formal literature review. The base case was assumed to be a 70-year-old AMCI individual with problems in the memory domain. The model used a societal perspec- tive and a time horizon of 30 years. Two strategies were evaluated: genetic testing and preventive Donepezil treatment for APOE-e4 gene carriers vs. no testing (the current standard of care in Canada). Outcome measures were quality-adjusted life years (QALYs), lifetime costs, and the incremental cost-effectiveness ratio (ICER). RESULTS: The genetic testing and Donepezil treatment combination strategy resulted in the gain of 0.047 life years, when compared to not testing. The Incremental cost was CAD $ 1010 with Donepezil treatment; consequently, the ICER for the base case is estimated to be $ 21,586. The prevalence of genetic mutations, cost of genetic test and cost of Alzheimer disease had a small effect on the cost-effectiveness results; however, the ICER is sensitive to APOE e4 carriers, rate of progression to AD, APOE e4 surveillance cost, efficacy and cost of Donepezil preventive treatment. We conducted a sub-analysis by sex, and found that the ICER was lower for females than for males. CONCLUSIONS: Genetic testing in combination with preventive donepezil treatment for AMCI patients may be economically attractive in the current setting. Our preliminary findings are limited by substantial uncertainties surrounding the long-term efficacy of Donepezil preventive treatment and the rate of progression to AD.

PM4 TRANSLATIONAL AND POLICY RESEARCH IN PERSONALIZED MEDICINE FOR CANCER
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Personalized medicine (PM) targets interventions to patients who are most likely to benefit based on genetic clinical markers or genomic information. There is little research on the translation of genomics into clinical practice and health policy; this lack of evidence on the use, effectiveness and efficiency of targeted technologies is a key challenge to their appropriate adoption and utilization. Our conceptual approach to translation of PM research into practice incorporates utilization, patient and provider preferences, and health economic evaluation in breast (BC) and colorectal cancer (CRC). We are documenting testing and treatment patterns in Canadian and US patients, including which patients receive testing, with which test(s) and test sequenc- ing when confirmatory testing is performed. We are also measuring patient and provider preferences with discrete choice experiments to understand choice tradeoffs for testing and treatment. In the third component of our research, we develop decision-analytic modeling methods to evaluate the sequence of test-treat options. This analytical framework will characterise the cost-effectiveness of targeted therapy to estimate the value of PM interventions. Using our utilisation data, we will also...
compare guideline-adherent and routine clinical practice. Value of information analysis will be employed to identify areas for future research. We are applying this translational approach to various current and developed examples of PM in cancer: 1) trastuzumab for human-epidermal growth factor receptor-2 positive BC; 2) gene-expression profiling to identify patients who will benefit most from adjuvant treatments in BC; 3) cytotoxic PS2 D6 testing to select patients for adjuvant tamoxifen therapy in BC; and 4) testing for Lynch Syndrome in CRC patients and their family members to inform treatment and preventative interventions. This research will develop evidence-based information for patients, providers, industry, researchers and policymakers to objectively assess how PM can be beneficial and efficient in improving cancer outcomes.

PODIUM SESSION III: RESEARCH ON THE USE OF UTILITY MEASUREMENT

ASSOCIATION BETWEEN UTILITY AND TREATMENT AMONG PROSTATE CANCER PATIENTS

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OBJECTIVES: To analyze the association between utility, treatment and generic and prostate-specific health related quality of life (HRQoL) utility scores for prostate cancer patients. METHODS: In this longitudinal cohort study we recruited 201 (c45 yrs) newly diagnosed prostate cancer patients from urology clinics of an urban academic hospital. Participants completed Quality of Wellbeing (QWB-SA), generic (SF-36) and prostate-specific (UCLA-PC) HRQoL surveys prior to treatment and up to 24 months post-treatment. Baseline and demographic data were obtained via medical chart review and utility scores were computed using QWB-SA. To analyze the relationship between treatment and utility we used linear mixed effects models, after adjusting for covariates. Similar models were used to examine association between generic and prostate-specific HRQoL and utility. RESULTS: Mean baseline utility was comparable between radical prostatectomy (RP) and external beam radiation therapy (EBRT) groups (0.73 vs. 0.69, p = 0.175). Mixed effects models indicated that RP was associated with higher utility at 24 month (OR = 1.12, p = 0.027), after controlling for covariates. RP was associated with improved functioning for role physical, role emotional, vitality, mental health and bodily pain and impaired urinary function. Higher scores on generic health subscales were indicative of higher utility. Also, for prostate-specific HRQoL, higher scores on bowl function, sexual function, urinary bother and bowel bother were associated higher utility. CONCLUSIONS: Treatment appears to have significant association with post-treatment utility. Thus, utility assessment provides an approach to various current and developing examples of PM in cancer: 1) reduction in hours “on duty,” and 2) reduction in hours “doing things.” To estimate appropriate WTP values for each TAP outcome measure, we identified three studies which met these inclusion criteria: 1) published studies in the past 5 years using contingent valuation methodology to identify WTP; 2) a dementia-related intervention that required an out-of-pocket expenditure, and 3) asked caregivers what they would be willing to pay for an outcome of reducing caregiver burden. We also assessed WTP based on the potential financial savings caregivers could achieve from purchasing TAP. To assess proportion of time TAP was cost-effective, we built a Monte Carlo simulation to test the four WTP values identified. RESULTS: For the outcome measure “on duty” WTP varied between $1.06/ hr-$4.38/ hr. WTP for the outcome measure “doing things” varied between $22.1/ hs-$9.57/ hr. Applying WTP values to TAP indicates TAP cost-effectiveness varies between 50%-80% for both outcome measures. CONCLUSIONS: If WTP data can not be collected prospectively or societal values can not be applied, evaluating WTP using comparable studies appears to be an acceptable method for informing decisions makers of potential cost-effectiveness. Application of WTP to TAP shows potential cost-effectiveness that can be expected under different WTP scenarios.

COMPARISON OF HEALTH STATE UTILITY ESTIMATES IN SIGNIFICANT ASSOCIATION WITH POST-TREATMENT UTILITY. Thus, utility assessment provides an approach to various current and developing examples of PM in cancer: 1) trastuzumab for human-epidermal growth factor receptor-2 positive BC; 2) gene-expression profiling to identify patients who will benefit most from adjuvant treatments in BC; 3) cytotoxic PS2 D6 testing to select patients for adjuvant tamoxifen therapy in BC; and 4) testing for Lynch Syndrome in CRC patients and their family members to inform treatment and preventative interventions. This research will develop evidence-based information for patients, providers, industry, researchers and policymakers to objectively assess how PM can be beneficial and efficient in improving cancer outcomes.

RELIABILITY OF HEALTH UTILITIES INDEX (HUI) SCORES: PATIENT AND PARENT INTER-RATER AGREEMENT ACROSS TWO CLINICAL TRIALS OF TREATMENT FOR ACUTE LYMPHOBlastic Leukemia (ALL) IN CHILDHOOD

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OBJECTIVES: To assess differences in the reliability of HUI Mark 3 (HUI3) health-related quality of life (HRQoL) utility scores for patients between self and parent assessments across two Dana-Farber Cancer Institute (DFCI) clinical trials for treatment of ALL during childhood. METHODS: Patients were enrolled in either the DFCI 95-001 or 00-001 trial, and were ≥12 years of age at the time of HUI survey. Patients, parents, and blind to each other, completed HUI questionnaires at each of 5 trial phases: induction; CNS prophylaxis; intensification; continuation; and post-treatment. Reliability was assessed in terms of inter-rater agreement of individual scores and utilities in mean scores. Agreement was quantified using the single-way mixed model intra-class correlation coefficient (ICCs). An ICC of 0.41–0.60 represents moderate reliability, 0.61–0.80 good reliability, and 0.81–1.00 very good reliability. Mean differences of ±0.03 are clinically important. Statistical significance was set at p < 0.05. RESULTS: The number of patient and parent paired assessments varied by assessment phase for both the 95-001 (minimum = 29, maximum = 30) and the 00-001 (minimum = 28, maximum = 34) trials. ICCs in the two trials ranged from 0.49 (p = 0.05) to 0.88 (p < 0.05). There was substantial overlap of ICC 95% confidence bounds across the two trials at each of the five assessment phases. There was no significant difference (p > 0.06) between patient-parent pairs of scores at any assessment phase in either trial. The difference between trials in mean patient-parent scores was ±0.03 and insignificant (p > 0.08) for each of the 5 assessment phases. CONCLUSIONS: Agreement between patient and parent scores was moderate or better for all assessment phases in both trials. There were no important differences in mean patient and parent scores for any of the assessment phases of the two trials. Inter-rater reliability of scores was similar across the two trials. Parental assessments provide acceptable and consistent estimates of HRQoL for children.