PCN8

REAL LIFE OUTCOMES IN 1ST LINE NON-SQUAMOUS NON-SMALL CELL LUNG CANCER (NSCLC): A PILOT STUDY IN FRANCE AND GERMANY ANALYSING BEVACIZUMAB-BASED VERSUS NON-BEVACIZUMAB-BASED TREATMENTS

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BACKGROUND: Bevacizumab has been used in NSCLC in Europe since its regulatory approval in 2007. Bevacizumab has demonstrated significantly improved survival in randomized phase III trials. The real life outcomes have so far, however, been assessed only in the US with evidence from routine clinical practice not previously available in Europe. **OBJECTIVES:** To investigate Time to Progression (TTP) in two pilot countries and thus assess the feasibility of such studies in a wider European setting. The primary comparison was bevacizumab-based therapy versus non-bevacizumab-based therapy in first-line non-squamous NSCLC. **METHODS:** Data were drawn from the Adelphi NSCLC Disease Specific Programme, a large cross-sectional study of consecutively presenting patients in France and Germany in 2010. Physicians provided retrospective information regarding disease status and treatment patterns. TTP was defined as time from start of treatment to physician-reported disease progression or two weeks before the start of second-line therapy. A log rank test was applied to test for differences between the two comparison groups. Cox Proportional Hazard Models were fitted to the data. Sensitivity analyses were run to analyse if age was a prognostic factor for treatment benefit between the two groups. **RESULTS:** A total of 895 non-squamous patients were included in the analyses, of whom 421 had experienced disease progression. The median time to progression for bevacizumab-treated patients was 8.5 months compared with 6 months in the comparison group ($p<0.001$). The Hazard ratio relating to the treatment effect (bevacizumab-based versus non-bevacizumab based) was 0.65 (95% CI 0.52 to 0.81). The differences in TTP remain significant between the two first-line therapy groups even after controlling for age. **CONCLUSIONS:** The feasibility of using real life oncology studies in Europe to demonstrate extended TTP for bevacizumab-based versus non-bevacizumab therapy was shown and was consistent with findings of two phase III trials and real life outcomes from a US study.

PCN9

VALUE OF RESEARCH ANALYSES IN RESEARCH PRIORITIZATION OF CANCER GENOMIC APPLICATIONS

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OBJECTIVES: The objective of this study, as part of the Center for Comparative Effectiveness Research in Cancer Genomics (CANCERGEN), was to establish and evaluate a process for incorporating formal value of research (VOR) analyses into a stakeholder-informed research prioritization process for genomic applications for study in a prospective, randomized comparative effectiveness trial within the SWOG clinical trials cooperative. **METHODS:** Six candidate genomic applications, identified through a landscape-analysis, were prioritized by 13 stakeholders based on 9 criteria: population impact, adequacy of standard care, analytic and clinical validity, benefits, harms, economic impact, evidence of need, clinical trial feasibility, and market factors. We developed decision-analytic based models for the top three candidates, performed expected value of perfect information calculations, and presented the results to stakeholders. We evaluated the impact of the VOR analyses on the test ranking and stakeholder perceptions about the usefulness of VOR using an online survey. **RESULTS:** The top three genomic applications based on the initial rankings were: 1) ERCC1 testing in early stage non-small cell lung cancer (NSCLC), 2) EGFR mutation testing in advanced NSCLC, and 3) tumor marker testing to detect recurrence in early stage breast cancer (BC). The VOR was estimated to be: $2.2 to $2.8 billion, $33 million, and $2.1 billion, respectively. After presentation of the results, the stakeholders changed their ranking to 1) ERCC1, 2) BC markers, and 3) EGFR. The majority of stakeholders found the VOR information to be useful (69%), with 53% changing their ranking after consideration of the VOR findings. In addition, all stakeholders indicated that they would use VOR analyses in future research prioritization processes. **CONCLUSIONS:** Stakeholder-informed research prioritization of genomic applications is a function of many evidence domains. Our study suggests that with adequate resources, VOR analyses can be incorporated into this process and provide useful information for research prioritization.

PCN10

ARE FURTHER STUDIES OF BREAST CANCER TUMOR MARKERS TO DETECT RECURRENCE WORTHWHILE? A VALUE OF RESEARCH ANALYSIS

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OBJECTIVES: To assess the value of additional research for testing carcinoembryonic antigen (CEA), cancer antigen (CA)15-3 and CA 27.29 biomarkers for earlier detection and treatment of recurrent breast cancer. **METHODS:** We developed a decision-analytic model to estimate the expected value of perfect information (EVPI) and expected value of sample information (EVSI) for a treatment strategy involving biomarker testing every 3-6 months for the five years following completion of primary therapy (in addition to standard care), versus standard care alone. Model parameters and uncertainty ranges were derived from published literature and expert opinion. EVPI and EVSI were assessed at various willingness-to-pay thresholds. The affected population was estimated from published recurrence data over a discounted 10-year time horizon. **RESULTS:** At a willingness-to-pay of $150,000 per quality-adjusted life year, the biomarker strategy and standard-care strategy resulted in average net-benefits of $598,000 and $600,000, respectively. The standard care strategy produced greater net-benefit in 57% of simulations. Among the 43% of simulations where standard care produced greater net-benefit, the average difference was $11,200. With an affected population of approximately 417,000 patients, the EVPI was $2.1 billion. Preliminary EVSI estimates range from $36 to $76 million at sample sizes between 500 to 5,000 patients per arm, respectively. **CONCLUSIONS:** Our findings indicate that research assessing the use of breast cancer recurrence biomarkers and consequent earlier treatment could be highly valuable. The EVPI of approximately $2.1 billion represents the upper bound of the value of additional research, and is driven by the affected population, testing sensitivity and specificity, costs, and uncertainty in the choice of optimal strategy. We are currently conducting EVSI analyses for various trial designs, compared to the cost of conducting these trials. Our analysis allows decision makers to quantitatively assess and prioritize research efforts in biomarker testing for breast cancer recurrence relative to alternative research investments.

PCN11

COMPARATIVE EFFECTIVENESS RESEARCH: ERECTILE DYSFUNCTION LONGITUDINAL COSTS ACROSS TREATMENTS FOR PROSTATE CANCER

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OBJECTIVES: Prostate cancer treatments are comparable in long-term outcome; but associated with different health-related-quality-of-life (HRQOL) outcomes, including erectile dysfunction(ED). We studied influence of changes in sexual function(SF) and bother(SB) on 3-monthly-ED cost over 13.5 years and estimated predictors of ED costs across and within treatments. **METHODS:** Data were from CaPSURE, a national disease registry of 3,276 men with prostate cancer from 31 urology practices completing questionnaires including risk, healthcare utilization and HRQOL. SF and SB scores(0-100) were measured by UCLA Prostate Cancer Index. ED 2009 costs included drugs, vacuum erection devices and penile implants. Bootstrapped regression models determined influence of age, BMI, race, marital status, risk, baseline and changes in SF/SB scores, and co-morbidities on ED costs. **RESULTS:** 62% had prostatectomy(RP), 48% were low-risk, and mean age was 64.3(64.1-64.6)years. Baseline SF score was 53.8(52.8-54.8) and SB 62.3(61-63.6). Mean ED cost was highest for RP ($78.6;$71.1-$86.1), followed by Brachytherapy ($42.7;$30.8-$54.6), Radiation ($35.5;$18-$53) and watchful waiting(WW)($25.5;$8.2-$42.9). Increasing baseline SF ($0.61,$p<0.001$), SF decline ($30,$p<0.001$), ≥1co-morbidity ($72,$p<0.001$), treatment type ($p=0.01$), increasing age ($p=0.07$), being married ($22,$p=0.002$), and being non-white ($133,$p<0.001$), significantly predicted ED costs. RP had $42 significantly higher ED cost than WW while Brachy and Radiation had $15 more. Individuals 70 and older had $32 lower ED costs than ≤50year olds. For WW, increasing age ($3,$p=0.05$) and higher BMI ($42,$p=0.03$) significantly predicted lower ED costs. For RP, higher baseline-SF ($0.66, $p<0.001$), declining-SF ($48,$p<0.001$), improved/no-change SB scores ($15,$p=0.05$), ≥1co-morbidity ($93,$p<0.001$), married ($34,$p=0.007$), and non-white ($165,$p<0.001$) significantly predicted higher ED costs. For Brachytherapy, increasing baseline-SF ($0.42,$p=0.001$) and for radiation, higher BMI ($32,$p=0.06$) predicted higher ED costs. **CONCLUSIONS:** Treatment type and age were strongest ED cost predictors with the younger RP patients showing highest ED costs and the older WW group with lowest ED costs. These results can guide physicians and patients deciding on prostate cancer therapies.

PCN12

RESOURCE UTILIZATION AND PERCEPTIONS OF MAJOR MOLECULAR RESPONSE IN CHRONIC MYELOID LEUKEMIA (CML): RESULTS OF A DELPHI PANEL STUDY

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OBJECTIVES: To understand factors that impact therapeutic decisions and to understand healthcare resource utilization. **METHODS:** A modified Delphi panel study was conducted, utilizing in-depth interviews with 16 CML-treating physicians to develop key themes and questions for testing, followed by an on-line survey to capture initial estimates. Results were discussed at a live meeting with 7 CML-treating physicians to develop consensus and complete another round of surveying. **RESULTS:** The majority of panelists believe that 20-30% of patients are not treated in accordance with CML guidelines. An estimated (mean) 25% of patients are switched from imatinib to nilotinib or dasatinib during the first year. Community oncologists are more likely to switch treatment due to side effects, whereas academic clinicians primarily switch for efficacy-related concerns. Six panelists indicated major molecular response (MMR) is a superior endpoint to complete cytogenetic response (CCyR) with credible evidence to support that MMR provides superior protection from progression. Panelists believe that molecular monitoring is less intensive and less time-consuming and is a better predictor of

progression-free survival. Timing of molecular testing via polymerase chain reaction (PCR) varies. Once patients have achieved and maintained MMR ≥12 months, 3 panelists would reduce the frequency of cytogenetic testing and 3 would cease cytogenetic testing. Mutational analysis is not routinely conducted in responding patients; however, when performed in the second- and third-line settings, mutational analyses are generally conducted once or twice yearly. Healthcare resource utilization was higher in patients with advanced-phase disease and was 2-3 times higher in nonresponders than responders. **CONCLUSIONS:** CML treatment and monitoring practices may not align with guidelines; furthermore, patient management may differ markedly between treatment settings. Monitoring disease burden using PCR is expected to become increasingly important with standardization, and new therapies are anticipated to yield deeper responses.

PCN13

REAL LIFE OUTCOMES IN 2ND LINE ADVANCED OR METASTATIC NON-SMALL CELL LUNG CANCER (NSCLC): A PILOT STUDY IN FRANCE AND GERMANY ANALYSING ERLOTINIB VERSUS CHEMOTHERAPY

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BACKGROUND: Erlotinib is an EGFR TKI inhibitor used as monotherapy in second-line NSCLC patients. Clinical studies have demonstrated the survival benefits of erlotinib, however outcomes from routine clinical practice have not previously been assessed in Europe. **OBJECTIVES:** To investigate Time to Progression (TTP) and thus to assess the feasibility of such studies in a European setting. The primary comparison was erlotinib versus chemotherapy in second-line NSCLC. **METHODS:** Data were drawn from the Adelphi NSCLC Disease Specific Programme, a large cross-sectional study of consecutively presenting patients in France and Germany in 2010. Physicians provided retrospective information regarding disease status and treatment patterns. TTP was defined as time from start of second-line treatment to physician-reported disease progression or two weeks before the start of third-line therapy. A log rank test was applied to test for differences between the two comparison groups. Sensitivity analyses on the treatment effect were run on EGFR mutation wild-type and non-tested patients. **RESULTS:** 521 patients receiving second line therapy were included in the analyses, of which 123 were receiving erlotinib and 398 were receiving other chemotherapy regimens. 60 patients were EGFR mutated, 150 were EGFR wild type and 311 were not tested. Only 19 erlotinib and 83 non-erlotinib patients had progressed. The median time to progression for erlotinib patients was 17 months compared with 9.5 months in the comparison group. The Hazard ratio relating to the treatment effect (erlotinib versus non-erlotinib) was 0.63 (95% CI 0.38 to 1.05) p=0.07. The results of the sensitivity analysis on the EGFR mutation wild-type and non-tested patients resulted in a Hazard ratio of 0.65, p=0.13. **CONCLUSIONS:** The feasibility of using real life oncology data has been demonstrated. TTP observed for erlotinib and chemotherapy was similar, independent of mutation status, in second-line NSCLC.

PCN14

UNMET NEED IN METASTATIC PROSTATE CANCER PATIENTS: RESULTS FROM A SYSTEMATIC REVIEW

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OBJECTIVES: Docetaxel (D) + prednisone (P), mitoxantrone (MTX), estramustine (E) and sipuleucel-T (S) are authorized in the US for castrate-resistant prostate cancer (CRPC) treatment. New agents such as abiraterone and zibotentan are being investigated. This systematic review aims to assess current clinical evidence of treating metastatic CRPC (mCRPC). **METHODS:** MEDLINE, Embase, and Cochrane were searched to March 22, 2010, as were abstracts from ASCO, ASCO GU, AUA, ESMO, and EAU (2006 – March 2010). RCTs and observational studies (English) were included. Endpoints extracted include overall survival (OS), progression-free survival (PFS), prostate-specific antigen (PSA) response, and adverse events (AEs). **RESULTS:** A total of 171 studies (331 publications) were included: prechemotherapy patients (71 RCTs, 15 observational), postchemotherapy patients (6 RCTs, 71 observational), and mixed populations (8 RCTs). D, P, and E were most commonly investigated. In postchemotherapy RCTs, D + P + custirsen (14.7 mos) and cabazitaxel + P (15 mos) exhibited a relatively high OS compared to other regimens. Regimens with D and MTX showed longer PFS versus other regimens. D regimens were associated with a high PSA response (40%). In postchemotherapy observational studies, D + bevacizumab showed a relatively high OS (17.5 mos) and PFS (8.9 mos). In prechemotherapy RCTs, S (26 mos) and D + P (27 mos) showed a high OS. D + P showed a favorable PFS (11 mos), as did E + etoposide (15 mos). Overall, PRO, bone pain, and skeletal-related events were rarely reported in these studies. Nausea, anemia, diarrhea, neutropenia, and thrombocytopenia were common across trials. Grade 3/4 AEs were frequently reported with D-based regimens. **CONCLUSIONS:** mCRPC remains a clinical challenge. D was frequently investigated. D improved survival but produced significant AEs. New treatments for D-refractory patients are needed.

PCN15

CORRELATES FOR HUMAN PAPILLOMA VIRUS VACCINATION UPTAKE IN A LARGE HEALTH ORGANIZATION IN ISRAEL

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OBJECTIVES: To assess the coverage of HPV immunizations two years since their introduction, and to determine factors associated with vaccination. **METHODS:** The present research has been conducted in Maccabi Healthcare Services, the second largest HMO in Israel. The study population consisted of women aged 8 to 43. Multivariate analyses were used to determine independent association of various factors with vaccination. **RESULTS:** The study population included 482,748 women, of which 3.8% purchased at least one HPV vaccine dose. HPV vaccine initiation was strongly associated with socioeconomic level, with chances for immunization being approximately 35-fold higher in the highest SES index as compared to the lowest. High proportion of women aged 21-25 were vaccinated, but the rate in younger girls, who are the target population were much lower. **CONCLUSIONS:** HPV immunizations, which are not part of the current Israeli immunization program, are purchased mainly by women older than 20 years from high socio-economic classes.

PCN16

MAJOR CHANGES IN CHEMOTHERAPY REGIMENS ADMINISTERED TO BREAST CANCER PATIENTS DURING 2000-2008

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OBJECTIVES: To determine the trends in type of chemotherapy regimens administered to early stage or metastatic breast cancer patients in daily practice, as this information is lacking in published literature. **METHODS:** Newly diagnosed breast cancer patients in the period 2000-2008 who received chemotherapy were selected from the Dutch ECR-PHARMO cohort. The ECR (Eindhoven Cancer registry) records data on all newly diagnosed cancer patients in the Southeastern Netherlands whereas the PHARMO RLS (PHARMO Record Linkage System) includes data on, among other things, in- and outpatient drug use. Chemotherapy regimens were classified based on the received combinations and sequences. Trends in the distribution of adjuvant chemotherapy regimens (for early stage breast cancer) and palliative chemotherapy regimens (for metastatic breast cancer) were determined and stratified by Her2/neu status when possible. **RESULTS:** In this study, 422 patients diagnosed with early stage breast cancer received adjuvant chemotherapy. The use of CMF decreased from 90% in 2000 to almost none since 2005. Administration of anthracyclines (without taxanes) increased from 4% in 2000 to 94% in 2005, but lowered to 60% in 2008, being replaced by both trastuzumab and taxanes (with or without anthracyclines). Among the 82 breast cancer patients who received palliative chemotherapy at diagnosis or after breast cancer recurrence, the use of CMF and anthracyclines (without taxanes) decreased (0% and 15% in 2008, respectively), while the use of taxanes (with or without anthracyclines) increased (26% in 2008). Trastuzumab was used as palliative chemotherapy from 2003 onwards, with 22% of the metastatic breast cancer patients receiving trastuzumab containing regimens in 2008, and bevacizumab was administered since 2007 with 19% of the patients receiving bevacizumab containing regimens in 2008. **CONCLUSIONS:** Key findings on chemotherapeutic treatment for breast cancer patients from large clinical trials have been incorporated in the Dutch guidelines resulting in major changes in patient care.

PCN17

MULTI-COHORT MODEL OF PREVALENCE ESTIMATION OF ADVANCED MALIGNANT MELANOMA IN THE UNITED STATES: RESULTS COMPARED TO SEER DATA

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OBJECTIVES: There is an increase in incidence of malignant melanoma (MM). However, there is no systematic estimation of prevalence of advanced MM in the US. The SEER registry does not provide prevalence by tumor stage or data on tumor recurrence rates. This study takes a public health approach in reporting MM prevalence rate and future trend by tumor stage and age. The objective of this study is to build upon SEER data to inform public health interventions. **METHODS:** An excel-based, multi-cohort natural history model was developed. It employed age- and stage-specific incidence, recurrence, and all-cause mortality rates, and the US Census data from up-to-date SEER data and literature. The estimations were projected to 2015. **RESULTS:** Our model estimated that there were approximately 1.2 million MM cases (376 per 100,000 people) in the US in 2010. Of which, (24.4%) were in advanced stages (regional: 169,975 (14.6%); distant: 114,666 (9.8%)). The estimated prevalence rate of advanced MM in 2010 was 92 per 100,000 people. Among these advanced cases, 149,148 cases (52.4%) were in the elderly (≥ 65y). The total cases of MM of all stages and advanced cases were projected to increase from 2010 to 2015 by 38.4% and 57.9%, respectively. When compared to the latest SEER reported national MM prevalence of all stages in 2007 (793,283 cases), our estimate for the same year was 965,933 cases, or 21.8% higher, due to difference in projection methodology. Of these 2007 MM cases, 332,149 (41.9%) and 429,479 (44.5%) were estimated to be in the elderly. **CONCLUSIONS:** Prevalence of advanced MM is projected to increase in the next five years. These estimates help enhance public health awareness. An accurate estimation of disease burden is essential in prioritizing health care resource allocation and in identifying unmet needs from disease prevention to treatment.