or 500mg. The indirect analysis did not show a statistically significant difference in OS between everolimus compared with fulvestrant.

PCN12

SMALL MOLECULE TARGETED THERAPIES FOR THE SECOND LINE TREATMENT OF METASTATIC RENAL CELL CARCINOMA (MRCC): A SYSTEMATIC REVIEW AND INDIRECT COMPARISON OF SAFETY AND EFFICACY

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OBJECTIVES: Patients with mRCC and a good performance status typically receive an anti-VEGFR TKI (sunitinib or pazopanib) as initial therapy. Upon disease progression or intolerance, there are four orally-administered agents approved in the 2nd - line setting (including cytokine-refractory). However, head to head comparative trial data are limited. In the absence of such data, mixed treatment comparison (MTC) models are a widely accepted statistical method for generating comparative effectiveness information. In this study, an indirect comparison on the safety and efficacy was undertaken between axitinib, sorafenib, pazopanib and everolimus for 2nd - line therapy in advanced RCC. **METHODS:** A systematic review of major databases was conducted from January 2005 to June 2013 for randomized controlled trials evaluating at least one of the four agents in 2nd- line mRCC. Bayesian MTC models were fitted to assess comparative effectiveness based on multiple endpoints: tumour response, progression free survival (PFS), grade III/IV toxicities such as diarrhea, fatigue, hand foot skin reaction, rash and stomatitis as well as treatment discontinuations. **RESULTS:** A total of four randomized trials meeting the inclusion criteria were appropriate for the statistical pooling exercise. All four agents seem able to induce tumour shrinkage and provide patients with a clinically meaningful PFS benefit. Axitinib was superior to pazopanib (HR = 0.64; 95%CrI: 0.42 to 0.96) and sorafenib (HR = 0.70; 95%CrI: 0.57 to 0.87) in terms of PFS. However, patients receiving axitinib would be at an elevated risk for fatigue and to a lesser extent, stomatitis. **CONCLUSIONS:** Keeping in the mind the caveats associated with cross-trial comparisons, axitinib appears to provide superior PFS benefits relative to pazopanib and sorafenib. However, this is at a cost of a higher frequency of some dose-limiting toxicities. Everolimus, an mTor inhibitor, is mechanistically distinct from the other agents evaluated and would be a useful option post anti-VEGFR TKI failure.

PCN13

TARGETED THERAPY IN TRIPLE-NEGATIVE METASTATIC BREAST CANCER (TNBC) - A SYSTEMATIC REVIEW AND META-ANALYSIS

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OBJECTIVES: To perform a systematic review and meta-analysis of all randomized controlled trials comparing the efficacy of targeted therapy to conventional CT in patients with metastatic Triple-Negative Breast Cancer (TNBC). **METHODS:** Several databases were searched, including MEDLINE, EMBASE, LILACS, and CENTRAL. The primary endpoint was progression-free survival (PFS). We performed a meta-analysis (MA) of the published data. The results were expressed as Hazard Ratio (HR) or Risk Ratio (RR), with their corresponding 95% confidence intervals (CI 95%). **RESULTS:** The final analysis included 12 trials comprising 2,054 patients with TNBC. It was evidenced studies with conventional CT plus targeted therapy including bevacizumab (Bev), sorafenib (Sor), cetuximab and iniparib. The PFS was higher in patients who received Bev plus CT compared to CT alone in previously untreated patients with TNBC (fixed effect: HR=0.62; CI 95%=0.51-0.75; p<0.00001). The PFS was also higher in one study with Bev plus CT in previously treated patients (fixed effect: HR=0.49; CI 95%=0.33-0.74; p=0.0006). Sor plus CT was available in first-line and second-line. The PFS was higher in the group with Sor versus CT alone (fixed effect: HR=0.69; CI 95%=0.49-0.98; p=0.04) and iniparib plus CT (fixed effect: HR=0.75; CI 95%=0.62-0.90; p=0.002). **CONCLUSIONS:** Bev, Sor and iniparib, when associated with the conventional CT, demonstrated gains in the PFS of patients with TNBC.

PCN14

ABIRATERONE AND ENZALUTAMIDE FOR THE TREATMENT OF METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (MCRPC) POST CHEMOTHERAPY: AN INDIRECT COMPARISON AND BUDGET IMPACT ANALYSIS

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OBJECTIVES: Abiraterone and enzalutamide are two new treatment options for patients with mCRPC after docetaxel-based chemotherapy. This study aims to understand the relative clinical and economic value of these therapies. **METHODS:** Two pivotal clinical trials were conducted to evaluate abiraterone and enzalutamide in post-docetaxel treatment of mCRPC: Study COU-AA-301 for abiraterone and the AFFIRM trial for enzalutamide. The PICO (population, intervention, comparison, and outcomes) construct was employed to assess the comparability of the trials, followed by an indirect treatment comparison (ITC) using the Bucher method and a mix treatment comparison using Bayesian statistics. An economic evaluation was performed based on the ITC results. **RESULTS:** Several key differences were identified between the COU-AA-301 and AFFIRM trials. First, the studies used different comparators. Abiraterone plus prednisone was compared with prednisone alone, while enzalutamide was compared with placebo. Second, the endpoints rPFS, PSA progression, and PSA response were defined differently between trials, and thus were not included in the analysis. To address the difference in comparators, the ITC was performed using data from COU-AA-301 and subjects receiving corticosteroids concurrently in the AFFIRM trial. OS was significantly improved with both abiraterone and enzalutamide (3.9 and 3.2 months respectively). The ITC results were HR = 0.949 (95% CI: 0.712-1.26) for abiraterone versus enzalutamide using the Bucher method, and HR = 0.948 (95% CI: 0.711-1.26) using the Bayesian method. Using the US price for abiraterone and enzalutamide (approved in the US only), and assuming 25% of patients received therapy following docetaxel, cost savings from using abiraterone would be >$10K/patient/year or $49.0M/year nationally. **CONCLUSIONS:** Differences in study design should be addressed when conducting an ITC. The evidence from this ITC shows that abiraterone and enzalutamide have similar efficacy in OS in mCRPC post chemotherapy. However, abiraterone is cost saving compared to enzalutamide in this analysis.

PCN15

DIFFERENCES IN MEDICAL COST AND SURVIVAL BETWEEN TRIAL AND NON-TRIAL PATIENTS WITH ACUTE MYELOID LEUKAEMIA – A UK POPULATION-BASED PROPENSITY ANALYSIS

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OBJECTIVES: Information about acute myeloid leukaemia (AML), including the costs of treatment and survival-estimates, are usually derived from clinical trial data. However, it is not known whether this information is generalizable to non-trial patients. This study was carried out to evaluate the differences in medical costs and survival between trial and non-trial patients with AML; and hence assess the external validity of trial data to the general patient population. **METHODS:** The Haematological Malignancy Research Network (HMRN, www.hmrn.org) is an established population-based patient cohort that registers around 2000 newly diagnosed patients each year. All adults (≥18) newly diagnosed with AML between September 2004 and August 2007 and treated with induction intent were included. Patients were followed until August 2012, and the comparative outcomes were medical costs and survival. Standard statistical analyses were used to measure unadjusted difference in outcomes, and propensity score analyses were applied to measure differences by adjusting for baseline imbalance in pre-treatment characteristics between trial and non-trial patients. **RESULTS:** Overall, 173 patients treated with induction intent were included, of which 106 were trial and 67 non-trial. Trial participation was associated with younger age, fewer comorbidities, better prognosis, and being treated at teaching hospitals. Before controlling for patients' characteristics, trial patients had better survival and incurred higher costs (p<.0001 for both). After controlling for patients' characteristics by carrying out propensity score analyses, these differences remained significant in both survival (median survival 28.7 vs. 8 months; p<.0001) and medical costs (mean costs £84,497 vs. £49,624; p<.0001). **CONCLUSIONS:** For AML patients treated with induction intent, significant differences were observed in treatment costs and survival according to trial status, both before and after controlling for patients' pre-treatment characteristics. Data generated solely from clinical trials may therefore not be generalizable to non-trial patients and should be treated with some caution when used to facilitate decision-making.

PCN16

THE EFFECT OF POSITIVE MARGINS ON OUTCOMES IN BREAST CANCER

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OBJECTIVES: To review the data available on excision margins following breast-conserving therapy (BCT), focusing on definitions of positive and clear margins, percentage of operations resulting in positive margins, the effect of positive margins on future treatment, and the relationship between positive margins and disease-free and overall survival. **METHODS:** Targeted searches of PubMed were conducted using a predefined search strategy. Data from robust systematic reviews and/or meta-analyses were given priority. **RESULTS:** Definitions of positive and negative margins are variable, but typically a clear margin of 2 mm is considered acceptable. Most studies indicate positive margins in 20%-40% of patients after wide local excision. Guidelines recommend that patients with positive margins after BCT undergo repeat surgery, and in surveys, most physicians said they would recommend re-excision when there is tumour within 1 mm of the margin. In the identified studies, 20%-30% of patients underwent re-excision and approximately 2% had multiple re-excisions (two or more); 10%-15% of patients who initially had lumpectomy later had a mastectomy. There is a significant association between margin status and local recurrence (in a recent meta-analysis, the odds ratio was 2.42 for positive vs. negative margin status; 95% confidence interval, 1.94-3.02; P<0.001). However, among patients with a clear margin, width is not clearly related to risk of local recurrence. Four studies that assessed the effect of margin status on overall or disease-specific survival were identified, three reported a significant association (e.g., cause-specific survival at 12 years significantly associated with margin status, P<0.001). **CONCLUSIONS:** Definition of adequate margins remains controversial. None-the-less, final margin status is a key prognostic factor following BCT. The data identified suggest that an intervention that reduces the rates of positive margins during BCT may have the potential to improve outcomes and reduce the burden on patients and health care providers.

PCN17

A MIXED TREATMENT COMPARISON (MTC) TO COMPARE PROGRESSION FREE SURVIVAL (PFS) ASSOCIATED WITH DIFFERENT CHEMOTHERAPY REGIMENS FOR PLATINUM-SENSITIVE OR PARTIALLY PLATINUM-SENSITIVE RECURRENT ADVANCED OVARIAN CANCER

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OBJECTIVES: This research was conducted during a review of the manufacturer's submission (MS) to the NICE Single Technology Appraisal programme for bevacizumab, a vascular endothelial growth factor (VEGF) inhibitor. Bevacizumab in combination with gemcitabine/carboplatin has recently been licensed for use in patients with platinum-sensitive or partially platinum-sensitive recurrent advanced ovarian cancer. This research compared this new triple therapy with treatments used in clinical practice in the UK: platinum monotherapy, gemcitabine/carboplatin, paclitaxel/carboplatin, pegylated liposomal doxorubicin hydrochloride (PLDH)/carboplatin. **METHODS:** Randomised controlled trials (RCTs) for inclusion were identified using the MS for bevacizumab. RCTs were assessed for comparability based on patient population, disease severity, platinum sensitivity, and treatments received. An MTC was conducted using a Bayesian Markov chain Monte Carlo simulation.