gefitinib versus all doublet chemotherapies (gefitinib vs. pemetrexed/cisplatin OR 3.05, 95% CrI: 1.58–5.51). **CONCLUSIONS:** This adjusted indirect comparison suggests that gefitinib may have important ORR advantages over other first-line treatments in EGFR-TK M+ patients.

PCN12

EFFICACY OF SECOND LINE TREATMENTS IN PATIENTS WITH METASTATIC HORMONE REFRACTORY PROSTATE CANCER (MHRPC) IS NOT DEMONSTRATED BY PUBLISHED EVIDENCE FROM NON-RANDOMIZED TRIALS

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OBJECTIVES: Standard first-line treatment for patients with mHRPC is Docetaxel(D)-based chemotherapy. Published results from randomized clinical trials of second-line treatments after D failed to provide definitive conclusions about clinical efficacy largely due to paucity of data. This study sought to identify nonrandomized trials of second-line chemotherapy in mHRPC patients pretreated with D and present related survival and clinical benefits. **METHODS:** Pubmed and Embase were used to perform a systematic literature review (SLR) (2000–2010). Both comparative and noncomparative nonrandomized evidence were extracted from prospective and retrospective studies. Targeted population was patients with mHRPC failing previous D-based regimens. End points included overall-survival (OS), progression-free-survival (PFS), and PSA-response rate. **RESULTS:** Among the 825 records screened, 30 studies met the inclusion criteria, two of which were comparative. Of these, 10 addressed rechallenge with D and seven addressed mitoxantrone (MTX); the remaining 18 studies considered various other regimens. Treatment was with either single-agent or combination regimens. Ninety-three percent of studies included <50 patients. PFS and PSA response definitions varied between trials. For studies evaluating rechallenge with D, the median OS and PFS varied from 41 to 76 weeks and from 15 to 39 weeks respectively. For MTX, the median OS and PFS varied from 39 to 48 weeks and 13 to 16 weeks, respectively. For other chemotherapy regimens, the median OS and PFS varied from 51 to 104 weeks and 9 to 17 weeks, respectively. PSA response rates varied from 24% to 70% to D rechallenge, from 4% to 33% to MTX-based regimens and from 0% to 60% to other regimens. **CONCLUSIONS:** The SLR showed a lack of available non-randomized evidence, and among the selected studies, evidence was not strong enough due to small sample sizes, noncomparative nature and variable PFS and PSA response definitions. This literature review demonstrates that it is difficult to infer the clinical efficacy of mHRPC 2nd line chemotherapy.

PCN13

EFFECT OF ZOLEDRONIC ACID AND PAMIDRONATE ON SKELETAL-RELATED EVENTS AND MORTALITY IN WOMEN WITH BONE METASTASES FROM BREAST CANCER IN A MANAGED CARE PLAN: A RETROSPECTIVE DATABASE ANALYSIS

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OBJECTIVES: Patients with breast cancer (BC) and bone metastases are at risk for skeletal-related events (SREs) that are associated with significant morbidity, mortality, and reduced quality of life. The intravenous bisphosphonates (IVBPs) zoledronic acid (ZOL) and pamidronate (PAM) are approved for treating patients with bone metastases from BC. We compared incidence of SREs and mortality in women with BC who received ZOL or PAM, and assessed the long-term benefit of ZOL in a real-world setting. **METHODS:** A claims-based analysis of commercial and Medicare Advantage data from >45 US managed care plans was used to evaluate SRE rates and mortality in patients treated with ZOL or PAM. Inclusion criteria were age >18 years, BC with bone metastasis diagnosis between 01/01/01 and 12/31/06, continuous enrollment in the health plan, no evidence of bone metastasis or IVBP for 6 months before an index date of first receipt of ZOL or PAM. Patients were followed until disenrollment (including mortality) or study completion (12/31/07). Persistency was defined as the absence of a >45-day gap between treatments. SREs were defined as evidence of pathologic fracture, spinal cord compression, and radiotherapy or surgery to bone. **RESULTS:** Among 8757 patients (mean age, 58.1 ± 12.4 years) approximately 30% received ZOL, 15% received PAM, and 55% received no IVBP. Longer persistency with ZOL was associated with lower risk of fracture and of all SREs versus shorter persistency (trend test, $P = 0.0026$ and $P = 0.0216$, respectively). ZOL-treated patients had a moderately lower SRE incidence (36.2 vs. 40.0 per 100 person-years; $P = 0.0707$) and significantly fewer deaths (6.2 vs. 8.9 per 100 person-years; $P = 0.0130$) versus PAM-treated patients. **CONCLUSIONS:** In a real-world assessment of women with bone metastases from BC, ZOL reduced SRE incidence and significantly improved survival versus PAM. Longer ZOL persistency was associated with lower SRE risk, reinforcing the importance of regular monthly ZOL dosing.

PCN14

CLINICAL CONSEQUENCES OF PRIMARY PROPHYLAXIS WITH PEGFILGRASTIM VERSUS FILGRASTIM FOR THE PREVENTION OF FEBRILE NEUTROPENIA IN NON-HODGKIN LYMPHOMA AND STAGE II BREAST CANCER PATIENTS IN GERMANY

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OBJECTIVES: To assess the clinical consequences of primary prophylaxis (PP) with pegfilgrastim versus 6- or 11-day filgrastim (F6, F11) in the prevention of febrile neutropenia (FN) in non-Hodgkin lymphoma (NHL) patients receiving CHOP-14 chemotherapy and in breast cancer (BC) patients receiving TAC chemotherapy in Germany. **METHODS:** A lifetime Markov model was developed, consisting of two phases: 1) on-chemotherapy phase (OCP), where model cycle length equals chemotherapy cycle length (CHOP-14:14 days, TAC: 21 days), and 2) post-chemotherapy phase (PCP) with annual model cycles. PP is defined as prophylaxis initiated with the first chemotherapy cycle. Cycle 1 FN risk with no prophylaxis (NP) was estimated to be 21% for NHL CHOP-14 and 14% for BC TAC. All cycle relative risk of FN using PP with pegfilgrastim versus no PP, F6, and F11 was 0.25, 0.87, and 0.61. FN case fatality was estimated (NHL: 8.9%; BC: 3.6%). In PCP, all-cause mortality was estimated from German life-tables; NHL and BC mortality from US data; patients experiencing FN were assumed to have higher mortality due to reduced chemotherapy dose intensity. All inputs were estimated from clinical trials and published literature. The model estimates life-years, number of FNs, and number needed to treat (NNT) to prevent an FN. **RESULTS:** NNT to prevent an FN were 1.3, 6.2, 2.2 in NHL; 2.3, 11.1, 4.0 in BC for Pegfilgrastim, F6, and F11 compare to NP. Overall, FN episodes per patient were 0.15, 0.76, and 0.47 in NHL; 0.09, 0.43, and 0.27 in BC. Per-patient life-months gained using PP with Pegfilgrastim were 3.4 and 1.8 versus F6 and F11, respectively in NHL, and 2.2 and 1.2 in BC. **CONCLUSIONS:** Primary prophylaxis with pegfilgrastim results in a lower NNT, fewer FN events, and more life-years than with 6-day filgrastim or 11-day filgrastim in both NHL and BC.

PCN15

SYSTEMATIC REVIEW OF LAPATINIB PLUS LETROZOLE WITH OTHER FIRST LINE TREATMENTS FOR HORMONE POSITIVE (HR+) HER2+ ADVANCED OR METASTATIC BREAST CANCER (MBC)

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OBJECTIVES: To undertake a systematic review of lapatinib plus letrozole (LAP + LET) with other first-line treatments for HR+ HER2+ advanced or MBC in postmenopausal women who have not received prior therapy for advanced or metastatic disease. **METHODS:** Seven databases were searched through January 2009 for randomized controlled trials. Relevant interventions were lapatinib (alone/in combination), aromatase inhibitors (letrozole (LET), anastrozole (ANA), exemestane (EXE)), tamoxifen (TAM), and trastuzumab (TRAS) (alone/in combination). Outcomes included overall survival (OS), progression-free survival (PFS), time to progression (TTP), and objective response rate (ORR). From the available evidence, it was possible to directly compare LAP + LET with LET. Using a network meta-analysis, LAP + LET could be indirectly compared with the four other interventions. **RESULTS:** Eighteen studies (62 papers) met the inclusion criteria. LAP + LET was significantly superior to LET based on a direct head-to-head study in terms of PFS/TTP and ORR. In the indirect comparison with LAP + LET, TAM (hazard ratio [HR] = 0.45 [95% CI: 0.32, 0.65]), EXE (HR = 0.52 [0.34, 0.79]), and ANA (HR = 0.53 [0.36, 0.80]) scored significantly worse in terms of PFS/TTP and ORR (TAM: odds ratio [OR] = 0.25 [0.12, 0.53], ANA: OR = 0.27 [0.12, 0.58], EXE: OR = 0.47 [0.20, 1.09]). LAP + LET also seemed better, although not significantly, in terms of OS versus TAM: HR = 0.74 (0.49, 1.12), EXE: HR = 0.65 (0.39, 1.11), and ANA: HR = 0.71 (0.45, 1.14). LAP + LET when indirectly compared with TRAS + ANA, seemed to be better in terms of OS (HR = 0.85 [0.47, 1.54]), PFS/TTP (HR = 0.89 [0.54, 1.47]) and ORR (OR = 0.92 [0.24, 3.48]), although, none of these results were significant. **CONCLUSIONS:** Using indirect methods, LAP + LET appeared to be the best treatment in this HR+ HER2+ patient population. However, the results are based on a network analysis for which the basic assumptions of homogeneity, similarity, and consistency were not fulfilled. Therefore, despite the fact that these are the best available data, the results need to be interpreted with caution.

PCN16

MIXED TREATMENT COMPARISON OF BEVACIZUMAB-BASED THERAPIES RELATIVE TO DOUBLET-CHEMOTHERAPY COMBINATIONS TO ESTIMATE THE RELATIVE EFFICACY IN PROGRESSION-FREE SURVIVAL FOR TREATMENT OF FIRST-LINE ADVANCED OR METASTATIC NON-SMALL CELL LUNG CANCER (NSCLC)

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OBJECTIVES: To compare the efficacy in progression-free survival (PFS) of bevacizumab plus cisplatin and gemcitabine (BCG) and bevacizumab plus carboplatin and paclitaxel (BCP), relative to doublet-chemotherapy combinations for the treatment of

first-line advanced or metastatic NSCLC. **METHODS:** A systematic literature review identified randomized controlled trials (RCTs) reporting PFS for bevacizumab-based and doublet-chemotherapy combinations. Studies were evaluated for comparability of design and patient population. Reported PFS hazard ratios (HR) were analyzed simultaneously with a Bayesian mixed treatment comparison. The base-case analysis compared BCG and BCP with grouped platinum-based doublets (PLD) and grouped nonplatinum-based doublets (NPLD). Scenario analyses explored BCP and BCG versus different combinations of doublet treatments. **RESULTS:** Eight identified RCTs, considered comparable in design and patient characteristics, allowed for a comparison between bevacizumab-based therapies and grouped doublet-chemotherapy combinations. The expected PFS HRs relative to PLD, for BCP, BCG, and NPLD were 0.66 (95% interval: 0.57; 0.77), 0.80 (0.71; 0.89), and 1.05 (0.92; 1.19), respectively. BCP and BCG were ranked as the top two most efficacious treatments in terms of PFS across all included regimens. Scenario analyses confirmed the top ranking for BCP and BCG. When BCP and BCG were compared to individual doublet chemotherapies, BCP showed the greatest benefit (HR of 0.63 [0.45; 0.88]), followed by BCG 7.5 mg/kg (0.75 [0.64; 0.87]) and BCG 15 mg/kg (0.85 [0.73; 0.99]). Further analyses confirmed the robustness of the findings. **CONCLUSIONS:** Compared to all available doublet-chemotherapy combinations, bevacizumab-based therapy is expected to be more efficacious in terms of PFS, and could therefore be considered as the first treatment option in advanced or metastatic NSCLC.

PCN17

NO CONCLUSIVE EVIDENCE FROM RANDOMIZED CONTROLLED TRIALS (RCTS) FOR IMPROVED SURVIVAL WITH SECOND-LINE TREATMENT OPTIONS, IN PATIENTS WITH METASTATIC HORMONE-REFRACTORY PROSTATE CANCER (MHRPC) PREVIOUSLY TREATED WITH DOCETAXEL

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OBJECTIVES: A docetaxel (D)-based regimen is recommended first-line treatment for mHRPC patients. Currently, there are no recommended second-line treatments for D pretreated patients. This study sought to identify phase II and III RCTs of second-line treatments for mHRPC in D pretreated patients to provide information regarding survival. **METHODS:** PubMed and Embase were used to perform a systematic literature review (2000–2009). Primary and secondary efficacy end points were extracted. Safety outcomes were reviewed according to grade. **RESULTS:** Among 52 records screened, three trials were included and 47 were excluded (35 not clinical trials; four not second line to D; eight not comparative or randomized). Primary end points included overall survival (OS), progression-free-survival (PFS), PSA response rate, and objective tumor response (OTR). a phase III study comparing satraplatin plus prednisone (SP) to prednisone (P) alone (n = 950, 51% post-D) was identified. Two phase II trials compared ixabepilone (ixa) with mitoxantrone plus prednisone (MP) (n = 82), and custirsen in combination with prednisone plus D (DPC) versus curtisen plus MP (MPC) (n = 42). SP demonstrated significant improvements compared to P in PSA response (25% vs. 12%, $P < 0.001$), OTR (7% vs. 1%, $P < 0.002$), and pain response (24% vs. 14%, $P < 0.005$). Median PFS (11 weeks vs. 9.7 weeks), but median OS (66.1 weeks vs. 62.9 weeks) were similar. In the second trial (Ixa vs. MP), there was no significant improvement in either PSA response (17% vs. 20%) or OS. In the third trial, PSA response was better for DPC than MPC (40% vs. 27%); no OS data reported. Grade 3 or 4 neutropenia occurred in 54% and 63% with Ixa and MP respectively. **CONCLUSIONS:** This review found a limited number of published phase II and III RCTs second-line treatments for mHRPC in D pretreated patients. None demonstrated a survival benefit. Results should be interpreted with caution in terms of clinical benefits.

PCN18

RETROSPECTIVE DATABASE ANALYSIS OF THE EFFECT OF ZOLEDRONIC ACID ON SKELETAL-RELATED EVENTS IN MEN WITH PROSTATE CANCER AND BONE METASTASES

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OBJECTIVES: Patients with bone metastases from prostate cancer (PC) are at risk for skeletal-related events (SREs) including pathologic fracture, spinal cord compression, the need for radiotherapy or surgery to bone, and hypercalcemia of malignancy. Zoledronic acid (ZOL), an intravenous bisphosphonate (IVBP), has proven efficacy for reducing the incidence and delaying the onset of SREs in multiple tumor types. This retrospective study was designed to assess the fracture risk in patients receiving ZOL or no treatment, and to examine the benefit of long-term ZOL use in a real-world setting among men with PC and bone metastases. **METHODS:** Commercial and Medicare Advantage databases were used to evaluate fracture rates and medication persistency. Patients included in this analysis were ≥18 years old, had PC and bone metastasis diagnosed between January 1, 2001 and December 31, 2006, were continuously enrolled in the health plan, and had no evidence of bone metastasis or IVBP for 6 months before first infusion of ZOL. Patients were followed until discontinuation (including mortality) or study completion. Fractures were categorized as vertebral, hip, or other nonvertebral fractures. Persistency was defined as the absence of a >45-day gap between ZOL treatments. **RESULTS:** Among 4976 men (mean age, 70.9 ± 9.7 years), approximately 26% received ZOL and 74% received no IVBP. Regardless of fracture site, ZOL reduced the fracture rate compared with no IVBP (5.9 vs. 8.5 per 100 person-years; $P = 0.0003$). Longer persistency with ZOL was associated with a reduced fracture rate (trend test, $P = 0.0179$). The mortality rate was also significantly lower in ZOL patients versus patients receiving no IVBP (6.2 vs. 9.4 per 100 person-years; $P = 0.0018$). **CONCLUSIONS:** In men with bone metastases from PC, ZOL was associated with a significantly lower fracture rate and mortality compared with no IVBP. Furthermore, longer persistency with ZOL was associated with a lower fracture rate.

PCN19

SYSTEMATIC REVIEW OF ENDOSCOPIC SUBMUCOSAL DISSECTION VERSUS ENDOSCOPIC MUCOSAL RESECTION FOR EARLY GASTRIC CANCER

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OBJECTIVES: Endoscopic submucosal dissection (ESD) allows en bloc resection of the entire lesion which permits higher curative resection rate, lower local recurrence, and consequently, increases quality of life by minimizing the resection size compared to endoscopic mucosal resection (EMR). While ESD has been implemented in most university hospitals in Korea currently, potential complications of ESD like hemorrhage and perforation waver over the therapeutic decision on the ESD for early gastric cancer patients as well as the reimbursement decision-making. The study aims to address both effectiveness and safety outcomes of ESD versus EMR in early gastric cancer by systematic review. **METHODS:** MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), and Koreamed were searched using primary key words: "stomach neoplasm" and "endoscopic submucosal dissection" and "endoscopic mucosal resection." To assess the quality of selected studies, the methodological approach of Scottish Intercollegiate Guidelines Network were used. Five effectiveness-relevant and three safety-relevant outcome measures were extracted. Bibliography management and meta-analysis for each outcome were conducted using Review Manager 5.0. **RESULTS:** Three nonconcurrent cohort studies and nine retrospective cohort studies were identified. Meta-analyses showed significantly greater effectiveness of ESD as compared to EMR for en bloc resection (OR = 8.43, 95% CI: 5.20–13.67), complete resection (OR = 8.54, 95% CI: 4.44–16.45), curative resection (OR = 2.56, 95% CI: 1.68–3.91), local recurrence (RR = 0.13, 95% CI: 0.04–0.40), and all-cause mortality (RR = 0.65, 95% CI: 0.08–5.38). While intraoperative bleeding (RR = 2.16, 95% CI: 1.14–4.09) and perforation risk (RR = 3.58, 95% CI: 1.95–6.55) were significantly greater for ESD, overall bleeding risk (RR = 1.22, 95% CI: 0.76–1.98) and longer resection time (RR = 1.55, 95% CI: 0.74–2.37) were not significantly different between ESD and EMR. **CONCLUSIONS:** Considering bleeding risk was not significantly different between ESD and EMR, and the perforation risk usually does not lead to life-threatening disease, the effectiveness benefit of ESD can overweigh the overall harm compared to EMR on condition that ESD was performed by surgeons with certain experiences.

PCN20

MAINTENANCE ERLOTINIB VERSUS PEMETREXED FOR THE TREATMENT OF NON-SMALL CELL LUNG CANCER: INDIRECT COMPARISON APPLYING REAL-LIFE OUTCOMES

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OBJECTIVES: Recent clinical trials have established superior efficacy of both erlotinib and pemetrexed as first-line maintenance therapies for metastatic non-small cell lung cancer (mNSCLC) over placebo. Results indicated that erlotinib improved survival for all histology types and pemetrexed improved survival in nonsquamous patients. To date, there have been no head-to-head trials directly comparing the two agents. An indirect comparison analysis was performed to examine the relative efficacy of these two treatment regimens as maintenance treatment options following platinum-based first-line therapy. **METHODS:** An adjusted-matched indirect analysis approach was used to compare overall survival (OS) estimates in mNSCLC patients treated with erlotinib from SATURN versus pemetrexed patients from JMEN. Patient distributions of key characteristics between the two studies were unbalanced; JMEN trial patients had a better prognosis at baseline. Patient distributions observed in the pemetrexed study for race and smoking status were used to match erlotinib-treated patients using patient-level data from the SATURN trial, employing an adjusted matching approach to make the populations more comparable. a distribution of survival outcomes was derived from each of 1000 repeated random matching samples of the SATURN data, with 95% confidence intervals (CI) around the mean of the aggregate of all observed median OS survival estimates generated by ordering the outcome measures and identifying the 2.5 percentile observations. To indirectly compare treatments, the median ratio (MR) for OS was calculated to approximate the hazard ratio. **RESULTS:** The estimated median OS after adjusted-matching was 13.9 months (95% CI 10.9–16.8) for erlotinib, compared with the published median OS reported for pemetrexed of 13.4 months (95% CI: 11.9–15.9). Erlotinib patients had similar median OS compared to pemetrexed patients with an MR of 0.96 (0.95, 1.09). **CONCLUSIONS:** Erlotinib and pemetrexed are similarly efficacious in first-line maintenance NSCLC differing in other parameters than efficacy such as tolerability, administration, and patient convenience.