PCN21

FIRST-LINE BEVACIZUMAB-BASED THERAPY VERSUS PEMETREXED + CISPLATIN FOR THE TREATMENT OF ADVANCED ADENOCARCINOMA NONSQUAMOUS NON-SMALL CELL LUNG CANCER: INDIRECT COMPARISON APPLYING REAL-LIFE OUTCOMES

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OBJECTIVES: In the absence of head-to-head clinical trial data, an indirect comparison of bevacizumab (BEV) versus pemetrexed (PMX) was conducted to compare survival outcomes among adenocarcinoma nonsquamous metastatic Non-Small Cell Lung Cancer (mNSCLC) patients. **METHODS:** An adjusted matched indirect analysis was conducted to estimate overall survival (OS) in adenocarcinoma mNSCLC patients treated with BEV + cisplatin doublet therapy using patient-level data from SAiL (ECCO/ESMO 2009). These estimates were indirectly compared to previously published survival outcomes for PMX + cisplatin-treated patients (*Oncologist* 2009;14:253–263) by calculating the median ratio (MR) for OS. a subset of the SAiL population was selected to more closely approximate the PMX population by excluding patients who did not have cisplatin doublet as their baseline treatment, those with a baseline Eastern Cooperative Oncology Group (ECOG) performance status (PS) of > = 2, and those with non-adenocarcinoma histology. This sample of BEV patients was matched to the adenocarcinoma subgroup from the PMX trial on stage of disease and ECOG PS. One thousand repeated random matched samples of the SAiL data were produced to generate a distribution of survival outcomes and infer a 95% confidence interval (CI) around the mean of all sampled median survival estimates. **RESULTS:** After adjusted matching, the estimated median OS benefit for BEV patients was 15.6 months (95% CI: 15.0, 16.5) compared to the published median OS of 12.6 months (95% CI: 10.7, 13.6) for PMX patients. BEV patients had longer median OS with an MR of 0.81 (95% CI: 0.71, 0.82). **CONCLUSIONS:** Results from this indirect comparison show that BEV-based therapy provides superior overall survival outcomes when compared to PMX in adenocarcinoma mNSCLC patients.

PCN22

EFFICACY AND CARDIAC SAFETY OF TRASTUZUMAB (T) IN THE ADJUVANT TREATMENT OF HER2-POSITIVE EARLY-STAGE BREAST CANCER: A SYSTEMATIC REVIEW (SR) AND META-ANALYSIS (MA)

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OBJECTIVES: Trastuzumab (T) is now part of the standard adjuvant treatment for HER2 positive, breast cancer patients. However, the results of the studies are not uniform and there are still doubts about the ideal indication and schedule for its use. Our objective was to perform a systematic review (SR) and meta-analysis (MA) of all randomized controlled trials (RCT) comparing efficacy of Chemotherapy (CHEM) plus T versus CHEM plus observation in the adjuvant treatment of HER2-positive early-stage breast cancer. **METHODS:** Several databases were searched, including MEDLINE, EMBASE, LILACS, and CENTRAL. The primary end points were progression-free survival (PFS) and overall survival (OS). a subgroup analysis was performed to evaluate the influence of the use of T concurrent or sequential to CHEM. **RESULTS:** Overall, 730 references were identified and screened. The final analysis included six trials comprising 13,940 patients. The PFS was higher in the group of patients treated with CHEM plus T (fixed effect: HR = 0.61, CI 95% = 0.56 to 0.66; $P < 0.00001$) with significant heterogeneity ($\chi^2 = 13{,}33$ $df = 5$ ($P = 0.02$); $I^2 = 62\%$). This result remained favorable to the use of T after the random-effects model analysis was performed (HR = 0.63, CI 95% = 0.54 to 0.73; $P < 0.00001$). OS was better for patients who received T (fixed effect: HR = 0.71, CI 95% = 0.62 to 0.81; $P < 0.00001$ and random-effects: HR = 0.71, CI 95% = 0.60 to 0.84; $P < 0.0001$) with moderate-level heterogeneity ($\chi^2 = 7{,}12$ df = 5 ($P = 0.21$); $I^2 = 30\%$). There was a significant interaction between the concurrent and sequential use of T and CHEM, suggesting that the concurrent use may be more effective. **CONCLUSIONS:** Trastuzumab increased progression-free survival and overall survival of patients especially when administered concomitantly to chemotherapy.

PCN23

SIMULATION AND COMPARISON OF PROGRESSION-FREE-SURVIVAL OUTCOMES OF SEQUENTIAL TARGETED THERAPY IN METASTATIC RENAL-CELL CARCINOMA

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OBJECTIVES: The novel targeted agents bevacizumab (BEV), sorafenib (SOR), sunitinib (SUN), everolimus (EVR), and pazopanib (PAZ) have each demonstrated activity in metastatic renal-cell carcinoma patients. One of the remaining key questions is which therapy sequence provides the most valuable outcome in terms of progression-free-survival (PFS). **METHODS:** A Markov disease model was developed using pivotal trial evidence. All patients were assumed to be treatment-naïve, with a good or intermediate prognosis, and to enter the model in "PFS," receiving first-line treatment with either BEV + interferon-alpha-2a (IFN), SUN, PAZ, or IFN alone, taking into account current EMA licenses (e.g., BEV + IFN indicated only for first-line therapy). After initial treatment, patients were assumed to either die, progress to a subsequent line of therapy, or remain in PFS. Hence, in case of p. **RESULTS:** The most valuable therapy sequence in terms of total PFS was BEV + IFN → PAZ → SUN → SOR → EVR resulting in a mean PFS time of 33.2 months (95% confidence interval [CI]: 31.3–35.2). The sequence BEV + IFN → PAZ → SOR → SUN → EVR obtained comparable results (mean PFS 33.2; 95% CI: 31.3–35.1). The first-line PAZ sequences PAZ → SUN → SOR → EVR (mean PFS 28.6; 95% CI 26.6–31.2) and PAZ → SOR → SUN → EVR (mean PFS 28.6; 95%CI 26.6–31.2) were the second-best alternatives, followed by the most valuable IFN first-line sequence (IFN → PAZ → SUN → SOR → EVR; mean PFS 28.5; 95% CI 26.8–30.4) and the most valuable SUN first-line sequence (SUN → PAZ → SOR → EVR; mean PFS 26.7; 95% CI 24.4–29.1). The incremental PFS difference between the best therapy sequences (first-line BEV + IFN; mean PFS 33.2 months) and the second-best therapy sequences (PAZ first-line; mean PFS 28.6 months) of 4.6 months reached statistical significance ($P < 0.004$ for each possible comparison). Additional overall survival simulations have confirmed these findings. **CONCLUSIONS:** Modeling simulation indicates that patients' PFS outcomes could be improved significantly, if therapy started with first-line BEV + IFN compared to other first-line agents (PAZ, SUN, or IFN alone).

PCN24

EFFICACY OF ADJUVANT CHEMOTHERAPY WITH GEMCITABINE (GEM) COMPARED TO SURGERY-ONLY IN PATIENTS WITH RESECTED PANCREATIC CANCER: SYSTEMATIC REVIEW (SR) AND META-ANALYSIS (MA)

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OBJECTIVES: We aimed to perform a systematic review (SR) with meta-analysis (MA) of all randomized controlled trials (RCT) comparing the efficacy of adjuvant chemotherapy with gemcitabine (GEM) versus observation in patients with resected pancreatic cancer. **METHODS:** Several databases were searched, including MEDLINE, EMBASE, LILACS, and CENTRAL. The primary end points were progression-free survival (PFS) and overall survival (OS). The data extracted from the studies were combined by using hazard ratio (HR) with their corresponding confidence intervals of 95% (CI 95%). **RESULTS:** Overall, 233 references were identified and screened. The final analysis included two trials comprising 472 patients evaluated. The proportion of patients that underwent surgery with curative intent (R0 or R1 resection) was similar between the studies as well as their ages and nodal status. The progression-free survival was higher in the group of patients who were treated with adjuvant chemotherapy including GEM (fixed effect: HR = 0.59, CI 95% = 0.50 to 0.70; $P < 0.00001$) and no heterogeneity was found ($\chi^2 = 0.01$, $df = 1$ ($P = 0.94$); $I^2 = 0\%$). Overall survival was also higher in patients treated with GEM (fixed effect: HR = 0.81, CI 95% = 0.67 to 0.98; $P = 0.03$) yet again no heterogeneity was detected ($\chi^2 = 0.07$, $df = 1$ [$P = 0.79$]; $I^2 = 0\%$). **CONCLUSIONS:** Adjuvant chemotherapy with gemcitabine increased progression-free survival and overall survival of patients with resected pancreatic cancer.

PCN25

DID THE UPTAKE OF NEW TREATMENT OPTIONS CHANGE THE TREATMENT STRATEGY IN PATIENTS WITH COLORECTAL CANCER AND PRIMARY NONRESECTABLE METASTASES? THE RESULTS OF LARGE POPULATION-BASED SURVEY IN GERMANY 2006–2007

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OBJECTIVES: The survey was initiated to gain insights into the changes of treatment patterns in treatment of metastatic colorectal cancer and the implementation of the results of clinical trials in daily practice. **METHODS:** A representative sample of centers (82) was selected with regard to the distribution of treated prevalence in colorectal cancer in institutions (university hospitals, community hospitals, office-based oncologists) and regional population density. The physicians reported all pts. with a treatment decision in colorectal cancer in the respective reporting period May 2006 to April 2007. The database contains 3254 pts. with a retrospective record of their entire treatment history. The treatment patterns were analyzed in the whole patient group and in subgroups according to resectability of metastases, the treatment objectives (especially secondary resectability of metastases), used systemic treatment regimen, age, concomitant diseases, and performing institution type. The statistics were performed in SPSS by bivariate analyses with two-sided chi-square test. In the next step, the decisive parameters for treatment choice were defined by logistic regression in multivariate analysis. **RESULTS:** The clinical trial data were taken up very soon in clinical reality. The correlation of drug efficacy and resectability of metastases was transferred into the disease management of colorectal cancer. The patient share with treatment objective "secondary resection of metastases" increased significantly (18% 2004 vs. 27% 2006–2007, $P = 0.000\%$). In this subgroup, the patient share treated with targeted therapy was significantly higher than in patients with other treatment objectives (34% vs. 19%, $P = 0.000\%$). **CONCLUSIONS:** The method used for creation of the database and for the statistic analyses has been proven as appropriate for the objectives of this survey. The resectability of metastases is recognized as an important treatment objective. Therefore, targeted therapy was implemented more frequently in treatment regiments for patients deemed secondary resectable, compared to other treatment aims.