

literature review of MEDLINE, Embase, and Cochrane Library identified clinical trials that met the following criteria: 1) included adults with untreated advanced or metastatic NSCLC; 2) included an IO agent or a chemotherapy agent recommended in clinical guidelines; 3) reported efficacy outcomes; and 4) published no earlier than 2002. **RESULTS:** Among 110 clinical trials identified, 99 focused on chemotherapies, with median progression-free survival (PFS) and overall survival (OS) ranging from 2.6-9.2 months and 5.9-27.3 months, respectively. Eleven IO trials (3 pembrolizumab, 4 nivolumab, 3 atezolizumab, and 1 durvalumab) were identified, of which 9 were phase I/II studies. For the IO treatment arms that had reached median PFS by data cut-off, the range was 3.6-10.3 months for IO monotherapies, 4.9-10.6 months for IO-IO combination therapies, and 4.8-13.0 months for IO-chemotherapy combinations. Only three IO studies had reached the median OS. Three studies directly compared IO therapies with chemotherapies. KEYNOTE-024 demonstrated significantly longer PFS and OS for pembrolizumab compared with chemotherapy in programmed cell death ligand-1 (PD-L1)-positive patients, while CheckMate-026 did not show superior PFS or OS for nivolumab in the PD-L1-positive population. However, there was considerable heterogeneity in PD-L1 cut-offs and the assay used between these two studies. The third study (KEYNOTE-021 Cohort G) reported significantly longer PFS for pembrolizumab plus chemotherapy in non-squamous NSCLC irrespective of PD-L1 levels. **CONCLUSIONS:** The survival benefit of chemotherapies is limited for patients with untreated advanced or metastatic NSCLC. One IO monotherapy has demonstrated significantly improved survival over chemotherapy in patients expressing PD-L1. IO combination therapies are showing great potential in all comers, but more data are needed to confirm their superiority.

PCN14

EFFICACY AND SAFETY OF ENZALUTAMIDE IN METASTATIC PROSTATE CANCER PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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OBJECTIVES: Prostate cancer (PCa) is the sixth leading cause of cancer death and the second most common cancer in men across the world. An estimated 1.1 million men worldwide were diagnosed with prostate cancer in 2012. By 2030, PCa burden is expected to be 1.7 million new cases and 499,000 new deaths. The objective of this review is to evaluate the efficacy and safety of enzalutamide (ENZ) versus placebo in metastatic prostate cancer (mPCa) patients. **METHODS:** Literature searches were conducted in MEDLINE and the Cochrane Library. In addition, references of included studies and clinicaltrials.gov were searched for relevant studies. No language or date restrictions were imposed. Study quality of included trials was assessed using the Cochrane Risk of Bias Assessment Tool. Two authors were independently selected, extracted and assessed the quality of included studies and disagreements were resolved by discussion or by consulting a third reviewer. All randomized controlled trials (RCTs) examining the efficacy and safety of enzalutamide compared to placebo in mPCa patients were included. The primary outcomes were overall survival (OS) and progression-free survival (PFS). Secondary outcomes were objective response, any grade adverse events (AE) and the treatment discontinuation. **RESULTS:** A total of 3 RCTs with 1579 patients were included. ENZ showed significantly better OS (Hazard Ratio [HR] 0.668, 95% confidence interval [CI] 0.594-0.752), radiographic PFS (HR 0.291; 95%CI 0.152-0.558) and improved objective response (Risk Ratio [RR]=9.81, 95%CI 6.99-13.77) compared to placebo. There was no significant difference between the groups in terms of any grade AEs (RR=1.03, 95%CI 0.99-1.08). However, overall treatment discontinuation was lesser with ENZ (RR=0.66, 95%CI 0.55-0.78) compared to placebo. The most common adverse events in ENZ were fatigue, back pain, and hot flash. **CONCLUSIONS:** Enzalutamide is associated with significant improvement in OS, PFS, and OR with tolerable side effects compared to placebo in mPCa patients.

PCN16

APPROACHES FOR ESTIMATING THE COMPARATIVE EFFICACY OF TREATMENTS FOR PATIENTS WITH RECURRENT SMALL CELL LUNG CANCER (SCLC) WITHIN CONNECTED AND DISCONNECTED NETWORKS OF EVIDENCE

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OBJECTIVES: Nivolumab+ipilimumab is currently being evaluated for SCLC. We aimed to 1) estimate the comparative efficacy of treatments for SCLC after at least one prior line of chemotherapy/chemoradiotherapy using connected randomized controlled trials (RCTs); 2) identify methodologies to connect the single-arm, non-randomized SCLC cohort from the CheckMate032 trial to the network of RCTs. **METHODS:** A systematic literature review identified five SCLC RCTs that formed a connected network centered on intravenous (IV) topotecan. The Kaplan-Meier survival curves from these RCTs were synthesized using fractional polynomial network meta-analysis (NMA) models. Approaches to connecting CheckMate032 to the network were then considered. As only study-level results are currently available, we used aggregate-level matching, whereby CheckMate032 was connected to the closest RCT in terms of study design, inclusion criteria, and patient characteristics, to facilitate an indirect comparison including nivolumab+ipilimumab. **RESULTS:** Hazard ratios (HRs) (95% credible intervals) from the NMA of RCTs were: oral versus IV topotecan 0.85 (0.69-1.04); amrubicin versus IV topotecan 0.90 (0.76-1.07); and cyclophosphamide-doxorubicin-vincristine versus IV topotecan 0.81 (0.60-1.09). ACT-1 (amrubicin versus IV topotecan) was most similar to CheckMate032 based on aggregate matching and was used to connect CheckMate032 to the network. The proportional hazard assumption was not valid for nivolumab+ipilimumab versus IV topotecan in ACT-1. Therefore, time-varying HRs were estimated, which

showed that nivolumab+ipilimumab had more durable tumor response and better long-term survival versus IV topotecan and versus amrubicin. Sensitivity analyses were performed connecting CheckMate032 through other IV topotecan trials. **CONCLUSIONS:** Chemotherapies for SCLC evaluated in RCTs delivered poor outcomes and did not differ from each other in terms of survival. Aggregate-level matching can be used to connect single-arm studies to a network of RCTs when patient level data are not available; however, an analysis using individual patient data from CheckMate032 would better account for between study differences in patient characteristics.

PCN17

CABOZANTINIB VERSUS STANDARD OF CARE IN THE FIRST-LINE TREATMENT OF ADVANCED/METASTATIC RENAL CELL CARCINOMA: A NETWORK META-ANALYSIS

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OBJECTIVES: To assess the efficacy of cabozantinib versus standard of care in first-line treatment of adult patients with advanced/metastatic renal cell carcinoma (aRCC). **METHODS:** A systematic literature review in June 2017 identified all randomised controlled trials of licensed first-line therapies in aRCC. Studies were excluded if they did not report hazard ratios (HRs) for overall survival (OS)/progression-free survival (PFS), baseline prognostic classification or prior therapy use. Using a fixed-effects model, a network meta-analysis compared OS and PFS HRs for the intent-to-treat populations, and for intermediate- and poor-risk subgroups. HRs were calculated for comparators versus cabozantinib. **RESULTS:** 13 studies were eligible for inclusion; some trials were not powered to assess OS; patient populations were heterogeneous so sensitivity analyses were conducted for poor- and intermediate-risk sub-groups. Comparators were: sunitinib, pazopanib, interferon-alfa (IFN), sorafenib, bevacizumab+IFN, temsirolimus, and tivozanib. PFS was significantly higher for cabozantinib than for all other interventions. In ITT, the cabozantinib PFS HR [95% CI] was greatest for the following comparisons: IFN (HR=4.25 [2.61, 6.92]); temsirolimus (HR=3.15 [1.85, 5.35]); and still significantly higher for bevacizumab+IFN, sorafenib, pazopanib, tivozanib and sunitinib (HR=2.90 [1.75, 4.78], HR=2.76 [1.73, 4.40], HR=2.10 [1.33, 3.31], HR=2.09 [1.22, 3.57] and HR=2.08 [1.35, 3.22], respectively). In the intermediate-risk subgroup, PFS HR [95% CI] were IFN (HR=4.93 [2.81, 8.64]), bevacizumab+IFN (HR=2.71 [1.48, 4.98]), sorafenib (HR=2.19 [1.25, 3.83]), sunitinib (HR=1.92 [1.22, 3.03]). In the poor-risk subgroup: IFN (HR=6.09 [1.57, 23.55]), bevacizumab+IFN (HR=4.93 [1.14, 21.35]), temsirolimus (HR=4.50 [1.15, 17.70]), sunitinib (HR=3.23 [1.12, 9.33]). Covariate analyses showed that these conclusions held despite differences in the patient populations. In all analyses, OS HRs favoured cabozantinib but were not statistically significant. **CONCLUSIONS:** Cabozantinib significantly increases PFS in intermediate- and poor-risk patients when compared with standards-of-care. This network meta-analysis suggests that cabozantinib may be considered as an efficient treatment option in first-line aRCC.

PCN18

COMPARATIVE EFFECTIVENESS OF TREATMENTS IN EPIDERMAL GROWTH FACTOR RECEPTOR MUTANT (EGFR-MUTANT) NON-SMALL CELL LUNG CANCER (NSCLC) PATIENTS WHO FAILED ON PRIOR TARGETED THERAPIES: A SYSTEMATIC LITERATURE REVIEW (SLR)

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OBJECTIVES: EGFR mutations are found in 10-20% of Caucasian patients with NSCLC and patients who initially benefit from targeted therapies develop resistance within 9-13 months of therapy. We systematically reviewed published clinical evidence to assess the effectiveness and safety of available agents in refractory EGFR-mutant NSCLC. **METHODS:** Medline, Embase, and Cochrane databases were systematically searched for randomized controlled trials (RCTs) in refractory EGFR-mutant NSCLC published during January 2007-October 2017. 11,708 records were reviewed; 2671 full papers screened of which 11 were relevant. **RESULTS:** Eleven publications reported data on 10 RCTs in refractory EGFR-mutant NSCLC. Of the 10 RCTs, 3 included patients with ≥ 1 prior therapy, 4 RCTs with ≥ 2 prior therapies, and 3 RCTs with 0 to ≥ 3 prior therapies. Four RCTs focused on addition of tyrosine kinase inhibitors (TKIs; afatinib [1], erlotinib [2], gefitinib [1]) to chemotherapy or another TKI (cabozantinib); four on TKI monotherapy (afatinib [1], dacomitinib [1], osimertinib [2]); two included EGFR-mutant subgroups receiving programmed-death-ligand-1 inhibitors (PD-L1; nivolumab, pembrolizumab). Five of eight studies reporting progression free survival (PFS) showed significant improvement versus comparator: 2.7-10.2 months treatment versus 1.1-5.4 months comparator. In 5 RCTs that reported overall survival (OS), the comparator arm reported higher [4] or the same [1] median OS than the treatment arm: 7.2-14.2 months treatment vs. 7.5-19.5 months comparator. Neutropenia was observed only when TKIs were combined with chemotherapy, with 14% Grade 4 neutropenia noted in erlotinib+pemetrexed group. 30.8% patients receiving erlotinib+cabozantinib reported diarrhea, the highest rate across all selected RCTs. While <1% of patients reported grade ≥ 3 adverse events in PD-L1 RCTs, an improvement in efficacy versus docetaxel monotherapy was not demonstrated in these patient subsets. **CONCLUSIONS:** Although several therapies tested in RCTs showed a significant improvement in PFS, none demonstrated OS benefit versus a chemotherapy comparator in a population with refractory EGFR-mutant NSCLC.

PCN19

EFFICACY AND SAFETY ANALYSIS OF RADIUM-223 IN PATIENTS WITH PROSTATE CANCER CASTRATION-RESISTANT AND BONE METASTASIS

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OBJECTIVES: Radium-223 is a radiopharmaceutical with alpha waves emission. Recently, clinical discussion focus on using the combination of Radium-223 with abiraterone or enzalutamide, or previous chemotherapy. We aimed to evaluate the efficacy and safety of radium-223 in patients with prostate cancer castration-resistant and bone metastasis as an alternative choice of treatment. **METHODS:** We conducted a literature review at MEDLINE, Embase, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, LILACS, Cochrane Central Register of Controlled Trials, WHO International Clinical Trials Registry Platform, and ClinicalTrials.gov, which used the combination of terms related to the disease, intervention and comparators. We defined as outcomes the overall survival, progression free survival, tumor reduction, disease control ratio, adverse effects and quality of life. We included systematic reviews, meta-analysis and clinical trials, published before November 2017. Also, the quality of evidence was assessed by using quality-value international scales. Results of all included studies were described and no indirect comparison analysis was made. **RESULTS:** We identified 92 studies, 79 were excluded by title and abstract. Thirteen were selected for full text evaluation. Final analysis included two systematic reviews, one meta-analysis and five clinical trials. Trials compared radium-223 or its comparators with placebo. The meta-analysis showed that radiopharmaceutical reduces skeletal muscle events, and improves functionality and quality of life [OR 0.63 (95%CI 0.51-0.78; I²=27%, p=<0.0001)]. It also evidenced that radium-223 is less toxic and increased overall survival. A systematic review reported similar results to meta-analysis on quality of life. Other systematic review showed that radium-223 and bicalutamide improved overall survival, however the effect on progression free survival was not clear. **CONCLUSIONS:** According with the available information, radium-223 is effective by increasing overall survival. Also, it's safer than other radiopharmaceutical according to its pharmacological characteristics. Nevertheless, further studies are required to conduct head-to-head comparisons between radium-223 and other drugs.

PCN20

EMPHASIZING QUALITY OF LIFE IN TREATMENT RECOMMENDATIONS FOR NODE-POSITIVE STAGE III NON-SMALL CELL LUNG CANCER

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OBJECTIVES: Conflicting evidence from clinical trials has led to uncertainty about which treatment strategy maximizes quality-adjusted life expectancy for survivors of node-positive Stage III non-small cell lung cancer (NSCLC). This study addresses this uncertainty by comparing the survival benefits as well as the quality-adjusted life expectancy attributable to each strategy. We hypothesized that the strategy that maximizes survival differs from the strategy that maximizes quality-adjusted life expectancy. **METHODS:** Systematic review of the literature was conducted to identify clinical trials for node-positive Stage III NSCLC, and lung cancer utility studies. The meta-analysis was organized by treatment strategies, which included: neoadjuvant chemoradiation + surgery (NCR + S), neoadjuvant chemotherapy + surgery (NC + S), surgery + chemotherapy (S + C), surgery + chemoradiation (S + CR). A Markov cohort model was constructed to estimate survival benefits and quality-adjusted life expectancy for each strategy. **RESULTS:** Five clinical trials comprised the meta-analysis. S + C is the strategy with the greatest survival benefit (S + C > NCR + S > NC + S > S + CR), with an additional 6.4 ± 1.4 months more life expectancy than NCR + S. S + C is also estimated to lead to the greatest quality-adjusted life expectancy, with an additional 5.2 ± 1.1 months more quality-adjusted life expectancy than NCR + S. The strategy with the lowest survival benefit and the worst quality-adjusted life expectancy is S + CR, with 1.4 ± 1.1 fewer months of survival benefit and 1.9 ± 0.7 months lower quality-adjusted life expectancy than NC + S (10.8 ± 1.7 months and 8.5 ± 1.1 quality-adjusted months less than S + C). **CONCLUSIONS:** Surgery followed by chemotherapy for node-positive Stage III NSCLC is estimated to maximize survival, and it is projected to have the greatest health benefits in terms of quality-adjusted life expectancy.

PCN22

EVALUATING DIFFERENT INDIRECT TREATMENT COMPARISON APPROACHES: A CASE STUDY IN ACUTE MYELOID LEUKEMIA PATIENTS INELIGIBLE TO RECEIVE INTENSIVE CHEMOTHERAPY

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OBJECTIVES: The National Institute for Health and Care Excellence recommends two methods for adjusting between-trial population imbalances in indirect treatment comparisons (ITC): Matching-Adjusted Indirect Comparison (MAIC) and Simulated Treatment Comparison (STC). While neither method is recommended more, this case study compares both approaches plus standard (unadjusted) ITC among patients ineligible to receive intensive chemotherapy. **METHODS:** Using standard ITC, MAIC, and STC, results of the Phase II glasdegib with low-dose ARA-C (GLAS+LDAC) trial (n=116) were indirectly compared to published Phase III azacitidine (AZA) trial data, with LDAC alone as the common comparator. In MAIC, patient-level data for GLAS+LDAC were weighted to match mean baseline characteristics reported for AZA. In STC, GLAS+LDAC data generated a regression model with baseline characteristics as covariates, which was used to simulate outcomes for AZA trial participants. Overall survival (OS) hazard ratios (HR) with 95% confidence intervals (CIs) were estimated. **RESULTS:** Standard ITC demonstrated GLAS+LDAC superiority over AZA (HR=0.57; 95%CI: 0.35-0.91). Using MAIC, propensity score weighting reduced effective sample size to 32 (72% loss). MAIC estimated improved OS in favor of GLAS+LDAC, but did not reach statistical significance (HR=0.87; 95%CI: 0.48-1.58). In STC, adjusting for key population covariates found a similar yet stronger, more precise survival effect (HR=0.47; 95%CI: 0.26-0.85) without reducing sample size. **CONCLUSIONS:** In each ITC, GLAS+LDAC is associated with improved OS. Preserving sample size is important for subpopulations to minimize uncertainty around point estimates, improve model robustness, and derive more applicable results. While standard ITC and STC preserve the sample, only STC enables population-specific interpretations. In MAIC, significant results

and interpretations are severely limited by sample size loss. Although the literature reflects increasing MAIC use despite its limitations regarding sample size reduction, choosing an ITC method should be guided by characteristics of data available to ensure robust analyses and appropriate interpretation of the data.

PCN23

THE PROMISING ROLE OF PEMBROLIZUMAB IN THE MANAGEMENT OF PATIENTS WITH PD-L1-POSITIVE NON-SMALL CELL LUNG CANCER: A SYSTEMATIC REVIEW

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OBJECTIVES: Non-small cell lung cancer (NSCLC) is one of the most protruding forms of cancer with malignancies in lung tissues. As per the American Cancer Society, about 14% of all new cancers reported are the lung cancers and of them majority are the NSCLC. Pembrolizumab is a monoclonal antibody that blocks the PD-1 (programmed cell death protein 1) receptors located on lymphocytes, thus allowing the immune system to target cancer cells. It has been approved by USFDA in 2017, to cure metastatic solid tumours with certain genetic anomalies. **METHODS:** Clinical trials which included Pembrolizumab as an intervention for patients with advanced PD-L1-Positive NSCLC, were identified in databases such as, Cochrane, and MEDLINE (via PubMed). No language and publication year restrictions were applied. Two researchers independently reviewed studies using the Cochrane methodology for systematic reviews. Outcomes of interest included progression-free survival (PFS), overall survival (OS), overall response rate (ORR), and safety. **RESULTS:** In total, 98 potentially relevant studies were screened. Five clinical trials with 789 treated patients having NSCLC were included. Four clinical trials were randomized controlled studies with docetaxel /platinum-pemetrexed group as control, whereas remaining one was a single arm study. The ORR was significantly better in the pembrolizumab group (44.8-55%; 95% CI, 36.8 to 68) than in the platinum-pemetrexed (27.8%; 95% CI, 20.8 to 35.7) and docetaxel (9.3%; 95% CI, 6.5 to 12.9) groups. Pembrolizumab has a high OS (7.7 months) in single arm study as well. Overall, longer duration of progression-free survival was observed with pembrolizumab. Very few patients were reported with adverse events of grade 3 or higher. **CONCLUSIONS:** Pembrolizumab is a potential cure for patients with advanced NSCLC with good clinical activity and minimal side-effects. However, the results have to be interpreted cautiously due to limited evidence available

PCN24

DURATION OF TREATMENT AND ECONOMIC BURDEN IN PATIENTS WITH ANAPLASTIC LYMPHOMA KINASE POSITIVE (ALK+) NON-SMALL CELL LUNG CANCER (NSCLC) RECEIVING SECOND-LINE ALK INHIBITORS

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OBJECTIVES: To describe the real-world treatment patterns and economic burden of patients with ALK+ NSCLC treated with second-line ALK inhibitors. **METHODS:** This retrospective study used the Optum Research database to identify adult patients with a lung cancer diagnosis code (≥1 inpatient claim or ≥2 outpatient claims ≥30 days but ≤1 year apart) and use of a second-line ALK inhibitor (alectinib or ceritinib) after crizotinib, between January 2011 and March 2017. Study outcomes were time to discontinuation of second-line ALK inhibitors and probability of continued use at 6 months. Healthcare costs (2016 USD) were investigated in a subgroup analysis that included patients who had continuous enrollment in medical and pharmacy benefits for 6 months prior to second-line ALK inhibitor treatment. **RESULTS:** 532 patients with NSCLC received at least one ALK inhibitor during the study period. Use of a second-line ALK inhibitor (alectinib or ceritinib post-crizotinib) was observed in 111 patients (42 alectinib, 69 ceritinib). Median time to discontinuation was 4.9 months for second-line ALK inhibitor treatment, and probability of continued use at 6 months was 44.7%. Patient-per-month total healthcare costs were \$21,056 for second-line ALK inhibitor treatment; approximately 50% of costs were non-pharmacy related. **CONCLUSIONS:** Time to discontinuation was short and healthcare costs were high for ALK+ NSCLC patients receiving alectinib or ceritinib as second-line ALK inhibitors. This suggests an unmet medical need for novel therapy in these patients.

PCN27

THE COST-EFFECTIVENESS ANALYSIS OF RHTPO VERSUS IL-11 ON THE TREATMENT OF CHEMOTHERAPY-INDUCED THROMBOCYTOPENIA PATIENTS IN CHINA

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OBJECTIVES: Thrombocytopenia is a serious clinical conditions after cancer chemotherapy and the condition could result potential drug dose reduction and treatment delay. At the same time, thrombocytopenia can affect the quality of life of patients and increase healthcare cost substantially. In China, recombinant human thrombopoietin (rhTPO) was recommended to treat chemotherapy-induced thrombocytopenia (CIT) by China cancer chemotherapy expert panel in 2014. The objective of this study is to assess the cost-effectiveness of rhTPO versus IL-11 in treating Chinese CIT patients. **METHODS:** An economic model was constructed to assess the cost-effectiveness of rhTPO and IL-11 in the treatment of CIT. All data required by the model were derived from literature review and key opinion leader (KOL) survey. The clinical efficacy data were obtained from published literature. Cost data were collected from Chinese leading hospitals located in Beijing, Shanghai, Guangzhou, Jinan, Wuhan and Chengdu with a total of 51 experts interviewed in the 6 cities. A one-way sensitivity analysis was conducted. **RESULTS:** The total medical cost of rhTPO and IL-11 is RMB 8533.3 and RMB 6820.9 respectively. The incidence rate of grade III thrombocytopenia is 39.7%, 67.6% and grade IV thrombocytopenia is 11.1%, 35.2% respectively of rhTPO and IL-11 group. Compared with IL-11, the increased