

each of the review methods address a slightly different research question, we assumed the underlying goal was to approximate the results from a standard connected network. The purpose of the study was therefore to assess the assumptions required for each approach that would provide unbiased estimates of the comparative effectiveness of included agents. **Results:** Armstrong et al. did not analyze comparative RCT data but instead removed placebo arms with cross-over, pooled individual active arms from 23 RCTs, and conducted naïve indirect comparisons between pooled arms (which assumes that all trials are equivalent in terms of prognostic factors, an unlikely assumption). Sawyer et al. analyzed a largely disconnected network with four comparative RCTs, as well as a larger network that was connected through 17 comparisons that assumed placebo response rates observed during induction period were maintained to week 52. Diels et al. only included comparative RCTs in their NMA and constructed a network of 11 RCTs by assuming a class-effect among TNF $\alpha$  inhibitors (i.e., all TNF $\alpha$  inhibitors have similar efficacy). **Conclusions:** Recent analyses assessing long-term comparative efficacy in psoriasis have methodological limitations and should be interpreted with caution. Future studies should consider the assumptions underpinning NMAs and assess how alternative NMA methods can be leveraged to yield more rigorous long-term indirect treatment comparisons.

## CE2

### APPLICATION OF PROPENSITY SCORE MATCHING AND BAYESIAN HIERARCHICAL DESIGN METHODS TO INTEGRATE SINGLE-ARM STUDIES INTO NETWORK META-ANALYSES (NMAs): OPPORTUNITIES AND PITFALLS ILLUSTRATED IN A CASE STUDY ASSESSING ABLATION/RADIATION THERAPIES IN LUNG CANCER

Qadeer R,<sup>1</sup> Ghosh S,<sup>2</sup> Clymer JW,<sup>2</sup> Wright G,<sup>1</sup> Ferko N,<sup>1</sup> Cameron C<sup>3</sup>  
<sup>1</sup>EVERSANA, Burlington, ON, Canada, <sup>2</sup>Ethicon Inc., Cincinnati, OH, USA, <sup>3</sup>EVERSANA, Sydney, NS, Canada

**Objectives:** Network meta-analyses (NMAs) generally include direct comparative evidence from randomized controlled trials (RCTs) and/or comparative observational studies; however, comparative evidence is limited in many disease/treatment areas. The objective of this analysis was to discuss opportunities and pitfalls associated with incorporating single-arm studies into NMAs, illustrated in a case study assessing the effectiveness of ablation/radiation therapies in lung cancer. **Methods:** A systematic literature review was conducted to identify RCTs, comparative observational studies, and single-arm studies assessing ablation/radiation therapies among adults with lung cancer. The outcomes were local tumor recurrence, overall survival, and complications. First, Bayesian hierarchical NMAs using direct comparative studies, down-weighting lower quality evidence, were conducted. Second, simulated comparative studies were obtained by matching relevant single-arm studies using optimal 1:1 matching; propensity scores were estimated by fitting a logistic regression model that included age, sex, tumor type, tumor size, and average number of tumors as covariates. Third, Bayesian hierarchical NMAs using both comparative and simulated comparative studies, down-weighting lower quality evidence, were conducted. **Results:** One RCT, 10 comparative observational studies, and 147 single-arm studies were identified. Seven to 22 simulated comparative studies were incorporated within each NMA, depending on the outcome. The conclusions of the Bayesian hierarchical NMAs were aligned between analyses using comparative or comparative and simulated comparative studies; however, differences in effect estimate magnitudes (0% - 44%) and treatment rankings were sometimes observed. Limitations of this analysis included sub-optimal reporting of covariates among single-arm studies limiting the ability to sufficiently match for cross-study differences and poor matching where cross-study differences existed. **Conclusions:** Thoughtful integration of single-arm studies in NMAs may offer opportunities to utilize all available evidence and be especially useful in disease/treatment areas with many single-arm studies and limited direct comparative evidence or incomplete evidence networks. However, studies should clearly state the methodological limitations and present results stratified by study design.



**Methods:** Bibliographic databases (Medline, Embase, and Central), regulatory documents (FDA and European Medicines Agency), and trial registries (ClinicalTrials.gov and EU trial register) were searched from inception to November 2019 for randomized controlled trials testing active drugs that added to androgen deprivation therapy (ADT) for mCSPC. Cochrane risk-of-bias tool version 2 were used to assess trial quality. Bayesian network meta-analysis (NMA) was used to estimate relative effects of competing strategies. In addition to combining published constant hazard ratios (HR), we reconstructed survival data from Kaplan Meier curves to enable parametric survival NMA and that allows time-varying HR. **Results:** Seven trials with 7,236 patients were included. Risk of bias is a concern for trials with open label, missing data, or unpre-specified analysis. Ordered from the most to the least effective, treatments that improved the overall survival are abiraterone, apalutamide, and docetaxel, HR (95% credible interval [CrI]) 0.64 (0.56-0.73), 0.67(0.51-0.88), and 0.80 (0.72-0.89); treatments that improved radiographic progression-free survival (rPFS) are: enzalutamide, abiraterone, apalutamide, and docetaxel, HR (95% CrI) 0.39 (0.30-0.51), 0.45 (0.40-0.51), 0.48 (0.39-0.59), and 0.67 (0.61-0.74). Allowing time-varying HR produced similar treatment rankings. Serious adverse events (SAE) were substantially increased for docetaxel and slightly increased for abiraterone, odds ratio (95%CrI) 104.17 (24.85-1012.32) and 1.42(1.11-1.83). **Conclusions:** Abiraterone provided the largest OS benefit with slightly increased risk of SAE. Apalutamide offered comparable OS benefit with abiraterone without increasing SAE risk. Enzalutamide, although delayed rPFS to the greatest extent, did not show OS benefit based on the available evidence.

## CE4

### ANALYSIS OF FACTORS INFLUENCING ACCEPTANCE OF DATA FROM MATCHING-ADJUSTED INDIRECT COMPARISONS BY NICE

Lach K,<sup>1</sup> Smith N<sup>2</sup>

<sup>1</sup>Maple Health Group, LLC, Krakow, Poland, <sup>2</sup>Maple Health Group, LLC, New York, NY, USA

**Objectives:** The objective of this study was to identify factors related to acceptance of findings from matching-adjusted indirect comparisons (MAICs) in appraisals performed by the National Institute for Health and Care Excellence (NICE). **Methods:** NICE Single Technology Appraisal documents were searched as of 31 December, 2019 to identify appraisals where MAICs were performed to provide clinical or economic data as part of the submission. Publicly available appraisal consultation documents and committee papers were then reviewed to identify MAIC methodological considerations such as rationale for use of the MAIC methodology, use of unanchored/anchored analyses, covariates included and rationale for inclusion, reductions in effective sample size. The perspective of the Evidence Review Group / committee was also analyzed to determine NICE's perspective on the MAIC results based on the methodology employed. **Results:** A total of 17 STAs were identified and included as part of the analysis, with nearly all of identified MAICs were performed in the oncology setting (94%; 16/17). The majority of MAICs were performed due to the single-arm nature of the clinical evidence available (36%; 5 of 14 where information are available), though other commonly stated reasons included lack of connection to a relevant comparator (29%; 4/14), and a desire to match for inclusion/exclusion criteria and other prognostic variables (21%; 3/14). Reductions in effective sample size (when reported) ranged from 9.52% to 99%. Ultimately, data produced by most MAICs was rejected by NICE (57%; 8/14). Common reasons for rejection included lack of inclusion of all relevant prognostic variables, variable and uncertain results due to selection of different prognostic variables, and concerns about small effective sample size. **Conclusions:** Though MAICs are increasingly utilized by manufacturers in submissions to NICE, careful consideration must be taken to covariate selection and effective sample size in order to secure acceptance of findings.



## Oncology Studies

### CN1

#### HEALTH RELATED QUALITY OF LIFE AMONG PATIENTS WITH EARLY BREAST CANCER: A MULTINATIONAL STUDY

Law E,<sup>1</sup> Spurden D,<sup>2</sup> Piercy J,<sup>3</sup> Williams R,<sup>4</sup> Corsaro M,<sup>1</sup> Pike J,<sup>5</sup> Criscitiello C<sup>6</sup>

<sup>1</sup>Pfizer, New York, NY, USA, <sup>2</sup>Pfizer Limited, Tadworth, SRY, UK, <sup>3</sup>Adelphi Real World, Bollington, UK, <sup>4</sup>Sunovion Pharmaceuticals, Marlborough, MA, USA,

<sup>5</sup>Adelphi Real World, Manchester, UK, <sup>6</sup>European Institute for Oncology, Milan, Italy

**Objectives:** To describe and characterize health-related quality of life (HRQOL) as measured by the EQ-5D-5L among patients with early-stage HR+/HER2- breast cancer across clinically relevant patient sub-groups. **Methods:** A multinational (France, Germany, Italy, Japan, Spain, UK and US) survey of patients with stage I-III HR+/HER2- breast cancer, either receiving adjuvant treatment or under surveillance, was performed from June to October 2019. Patients meeting these criteria were

## CE3

### COMPARATIVE EFFECTIVENESS OF SYSTEMATIC THERAPIES FOR METASTATIC CASTRATION-SENSITIVE PROSTATE CANCER: A PARAMETRIC SURVIVAL NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

Wang L,<sup>1</sup> Paller C,<sup>2</sup> Hong H,<sup>3</sup> Alexander C,<sup>4</sup> Brawley O<sup>1</sup>

<sup>1</sup>Johns Hopkins School of Public Health, Baltimore, MD, USA, <sup>2</sup>Johns Hopkins School of Medicine, Baltimore, MD, USA, <sup>3</sup>Duke University, Durham, NC, USA,

<sup>4</sup>Johns Hopkins School of Public Health and School of Medicine, Baltimore, MD, USA

**Objectives:** Treatment decision-making for metastatic castration-sensitive prostate cancer (mCSPC) is challenged by unclear comparative effectiveness and widely varied costs of multiple competing strategies. The objective of this study is to compare the effectiveness and safety of systematic therapies for mCSPC.

