the receiver operating characteristic curves (ROC), sensitivity, and specificity measures with Bonferroni adjustment for multiple testing applied were performed to compare the models' performance. ***Results:*** Among 15964 identified patients, a MALE occurred in 26.02% of patients, and death occurred in 18.82% of patients. The most effective predictive model for MALE, as determined by the AUC, was the gradient boosted decision tree (AUC= 0.7539) followed by the LASSO regulated GLM (AUC= 0.749). The most effective predictive model for mortality was the LASSO regularized GLM (AUC=0.7930) followed by the GLM model (AUC=0.7922). The GLM, LASSO regularized GLM model, and gradient boosted decision tree produced similar ROC. ***Conclusions:*** All models showed acceptable discrimination, with an AUC greater than 0.7, when predicting MALE and mortality among patients receiving treatment for lower extremity peripheral artery disease. The machine learning techniques outperformed traditional regression-based techniques and can be leveraged to generate robust predictive models within the clinical space of lower extremity PAD.

Comparative Effectiveness Studies

CE1
A MODELED HEALTH OUTCOMES EVALUATION OF DAROLUTAMIDE PLUS ANDROGEN DEPRIVATION THERAPY FOR HIGH-RISK NON-METASTATIC CASTRATION-RESISTANT PROSTATE CANCER IN CHINA

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Objectives: Novel antiandrogens have demonstrated clinical benefit for patients with non-metastatic castration resistant prostate cancer (nmCRPC). We modeled the incremental life-years and QALYs of darolutamide+ADT compared to apalutamide+ADT and enzalutamide+ADT, for high-risk nmCRPC, in a Chinese setting. ***Methods:*** A partitioned survival model with three health states (nmCRPC, metastatic CRPC and death) was devised. Data from the ARAMIS, PROSPER and SPARTAN trials were used, in the absence of head-to-head studies. Hazard ratios (HRs) characterizing overall survival (OS) were derived from formal indirect treatment comparisons of the OS HRs between the three trials; the point estimates of the OS HRs characterizing the indirect comparison of darolutamide+ADT vs apalutamide+ADT and enzalutamide+ADT were 0.88 and 0.95, respectively. Parametric survival functions were selected for extrapolation based on the goodness of fit. The baseline characteristics, treatment patterns and utilities for this modeled Chinese cohort were validated with 12 urologists from 11 hospitals. A discount rate of 5% was applied. Univariate and probabilistic sensitivity analyses were performed. ***Results:*** With a 20-year modeling horizon, darolutamide+ADT yielded more life years (5.98LYs) and QALYs (4.61QALYs) than both apalutamide+ADT (5.64LYs, 4.43QALYs) and enzalutamide+ADT (5.82LYs, 4.55QALYs). The incremental QALY gains with darolutamide+ADT vs. apalutamide+ADT (+0.18QALYs) and vs. enzalutamide+ADT (+0.06QALYs) were mainly driven by the improved life years during post-progression survival (+0.92LYs vs. apalutamide+ADT and +0.65LYs vs. enzalutamide+ADT). Results were sensitive to the HRs and utility inputs; however, the probabilities of darolutamide+ADT having incremental QALYs reached 70.4% and 56.8% when compared to apalutamide+ADT and enzalutamide+ADT, respectively. ***Conclusions:*** This modeled evaluation indicates that darolutamide+ADT is likely to be associated with incremental health outcomes over apalutamide+ADT and enzalutamide+ADT, for a high-risk nmCRPC Chinese cohort, over a 20-year time-frame.

CE2
EFFECT OF DIFFERENT VARIANCE ESTIMATION METHODS WITH INVERSE PROBABILITY TREATMENT WEIGHTS (IPTW) ON COMPARATIVE EFFECTIVENESS MEASURE IN MULTIPLE SCLEROSIS

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Objectives: The Inverse Probability Treatment Weighting (IPTW) method provides marginal treatment effects that are more generalizable than other propensity score (PS) methods. The objective of this study was to compare the treatment effects from three different variance estimation methods with stabilized IPTWs on comparative effectiveness between oral fingolimod and injectable Disease Modifying Agents (DMA) users in Multiple Sclerosis (MS). ***Methods:*** This longitudinal retrospective study used adults(≥18 years) with MS diagnosis (ICD-9-CM:340) and a DMA prescription from the IBM MarketScan Commercial Claims and Encounters Database from 2010–2012. Patients were classified into fingolimod or injectable users based on their initial DMA prescription. The composite endpoint (time-to-relapse/DMA switch) was assessed during the one-year follow-up period after DMA initiation. The stabilized IPTW-Cox Proportional Hazards regression model was used to evaluate the composite endpoint with three different variance estimators – (i)Naïve, (ii)Robust sandwich-type, and (iii)Bootstrapping(200 replications). Patients who died/were lost from follow-up due to the lack of insurance coverage were censored. ***Results:*** The new DMA user study cohort consisted of 1,700 MS patients who were initiated with oral(15.82%) or injectable(84.18%) DMAs during 2010-2011. The proportion of patients who had a composite endpoint in fingolimod and injectable DMA users was 16.72% and 27.16%, respectively. The stabilized IPTW-Cox model with naïve and bootstrapping variance estimators revealed that oral fingolimod users were superior to injectable DMAs in reducing the risk of composite endpoint (Naïve estimator: Adjusted Hazards Ratio [aHR]-0.67, 95%CI:0.51-0.87; Bootstrapped estimator: aHR-0.68, 95%CI:0.39-0.97). However, the findings were not significant in the IPTW-Cox model with robust sandwich estimator(aHR-0.67, 95%CI:0.43-1.03). ***Conclusions:*** The analyses revealed that the significance of treatment effect estimates could vary depending on the choice of variance estimation method. Hence, researchers should pay attention to the selection of variance estimation method with small samples in addition to handling of extreme weights while using IPTWs for time-to-event analyses.

CE3
SYSTEMATIC REVIEW AND INDIRECT COMPARISON OF PD-(L)1 INHIBITORS IN COMBINATION WITH PLATINUM-BASED DOUBLET CHEMOTHERAPY (PT-DC) FOR THE FIRST-LINE TREATMENT OF NON-SQUAMOUS, NON-SMALL-CELL LUNG CANCER (NSQNSCLC)

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Objectives: To evaluate relative efficacy and safety of sintilimab compared with other PD-(L)1 inhibitors in combination with platinum-based doublet chemotherapy (PT-DC) for the first-line treatment of nsqNSCLC. ***Methods:*** A systematic literature search was conducted based on published studies in electronic databases up to December 2020. Eligible randomized controlled trials (RCT) that investigated untreated locally advanced or metastatic nsqNSCLC without activating EGFR mutations or ALK translocations patients were analyzed. Outcomes evaluated by adjusted indirect treatment comparison (ITC) using Bucher method mainly included progression-free survival (PFS), objective response rate (ORR), time to response (TTR) and safety profile. Taking the heterogeneity into account, random-effect model will be applied if the p-value of Chi-square test greater than 0.05. ***Results:*** Seven RCTs involving 3,559 patients were included. ITC results suggested that combined PT-DC with sintilimab had a comparable PFS compared with that of combined PT-DC with pembrolizumab (HR=1.00, 95%CI: 0.71 to 1.41), atezolizumab (HR=0.81, 95%CI: 0.59 to 1.10), tislelizumab (HR= 0.75, 95%CI: 0.48 to 1.16), camrelizumab (HR=0.80, 95%CI:0.54 to 1.20) and nivolumab (HR=0.72, 95%CI : 0.51 to 1.02). Little differences were found in ORR between combined PT-DC with sintilimab and combined PT-DC with pembrolizumab (OR=0.66, 95%CI: 0.37 to 1.20), atezolizumab (OR=1.23, 95%CI: 0.70 to 2.14), tislelizumab (OR=1.11, 95%CI: 0.58 to 2.11), camrelizumab (OR=1.05, 95%CI: 0.58 to 1.90) and nivolumab (OR=1.14, 95%CI: 0.64 to 2.00). Incidence of all grades or grades ≥3 adverse events (AE) were comparable between combined PT-DC with sintilimab and other PD-(L)1s. For AE leading to discontinuation, the incidence of sintilimab in combination with PT-DC is significantly lower than that of pembrolizumab in combination with PT-DC (OR=0.27, 95% CI: 0.11 to 0.67). ***Conclusions:*** Combined PT-DC with sintilimab and other PD-(L)1 inhibitors had comparable efficacy and safety profile for the first-line treatment of locally advanced or metastatic nsqNSCLC patients.

CE4
EXPANDING EVIDENCE BASE VS INTRODUCING HETEROGENEITY IN NETWORKS FOR NETWORK META-ANALYSES: A SIMULATION STUDY

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Objectives: Network meta-analyses (NMAs) are widely used to estimate the relative treatment effect between treatments that have not directly been compared in clinical trials. Challenges arise in precision medicines, where only small networks of evidence are available. This study aimed to explore the trade-off between increasing the evidence base by including additional studies and increasing the level of heterogeneity in the network considered. ***Methods:*** Data were simulated to reflect a small network including four treatments. Four scenarios were simulated with increasing number of studies per direct comparison. Each study was assumed to add an additional level of heterogeneity in the network, that was partly explained by an observable covariate. Scenario 1 represented a small network with a low level of heterogeneity while scenario 4 was a bigger network with a higher heterogeneity level. Standard NMAs were conducted and the mean relative difference (MRD) between the NMA estimates

and the true treatment effects were used to compare the scenarios. For the two largest networks, meta-regressions were also conducted to adjust partially on the heterogeneity. ***Results:*** From scenarios 1 to 3, including additional studies in the networks while increasing the heterogeneity level reduced the MRDs when conducting standard NMAs (respectively 48.2%, 21.3% and 18.6%). However, a higher MRD was obtained for the largest network (scenario 4: 24.4%) compared to scenarios 2 and 3. Conducting meta-regressions markedly reduced the MRDs for the scenario 3 (7.2% with meta-regression vs. 18.6%) and scenario 4 (9.1% with meta-regression vs. 24.4%). ***Conclusions:*** This simulation study shows that including additional studies in case of a small network in a NMA context can be relevant, especially if it allows for a meta-regression to be conducted.

Oncology Studies

CN1
PATTERNS OF UTILIZATION AND IMPLEMENTATION EXPERIENCES OF ONCOLOGY MONOCLONAL ANTIBODIES (MABS) BIOSIMILARS IN THE U.S.: FROM BOTH PAYERS AND HEALTHCARE PROFESSIONALS (HCPS) PERSPECTIVES

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Objectives: Biosimilars are highly similar to an originator biologic, with no clinically meaningful differences in safety or efficacy. The adoption of biosimilars might provide an opportunity to lower costs and increase patient access to biologics. The current study sought to understand real-world implementation experiences associated with oncology MAbs biosimilars (trastuzumab, rituximab, and bevacizumab) from both payer and healthcare professional (HCP) perspectives. ***Methods:*** In-depth qualitative telephone interviews with 20 each of US HCPs (including 3 practice managers) and payers were conducted. The HCPs were either affiliated with a healthcare network or were community-based. They specialized in hematology/oncology and had experience prescribing oncology biosimilars. Participating payers included Managed Care Organizations (MCOs), Integrated Delivery Networks (IDNs) and Pharmacy Benefit Managers (PBMs). Audio transcripts of the interviews were coded using MaxQDA software. ***Results:*** Over 80% of HCPs interviewed perceived biosimilars to be highly comparable to originators in efficacy and safety. About 70% of HCPs reported using biosimilars in $\geq$50% of their treatment-naïve patients and were comfortable with use of biosimilars in all approved indications. To encourage utilization, approximately 75% of MCO/PBM payers preferred biosimilars over originators in treatment-naïve patients, which was implemented through step therapy. HCP involvement in choosing a biosimilar for their patients was minimal, and biosimilars were often automatically ordered by pharmacists or administrators based on practice protocols or patients' cost due to insurance preferences. The major factor that influenced both payers' coverage decisions and HCP adoption of biosimilars was potential cost savings. Moreover, payers considered HCPs' clinical confidence with biosimilars as a factor influencing their biosimilar coverage decisions. ***Conclusions:*** Both HCPs and payers in the US have favorable views of oncology MAbs biosimilars, particularly among treatment-naïve patients. A framework for biosimilars integration into oncology practice is developing, which is primarily driven by insurance coverage policy, contracting, and cost benefits.

CN2
ELICITING UNREPORTED SUBGROUP-SPECIFIC SURVIVAL FROM AGGREGATE RANDOMIZED CONTROLLED TRIAL DATA

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Objectives: Subgroup analyses are vital components of health technology assessments but randomized controlled trials (RCTs) do not commonly report survival distributions for subgroups. This study developed an analytical framework to elicit unreported subgroup-specific survival information from aggregate RCT data. ***Methods:*** Assuming exponentially-distributed subgroup survival times, we developed an optimization model which aimed to approximate the restricted mean survival time (RMST) for the overall population via weighted average of the RMSTs of two mutually exclusive and exhaustive subgroups in each arm. Reported hazard ratios from the forest plots between the arms were used to enforce the relationship among subgroups' hazard rates in the model. The performance of the model was tested in a case study consisting of 8 RCTs in advanced stage gastrointestinal tumors (3 in hepatocellular carcinoma, 3 in gastric/gastroesophageal junction/esophageal cancer and 2 in colorectal cancer) which also reported Kaplan-Meier (KM) curves for overall survival (OS) for 40 subgroups in total. For each subgroup, predicted median survival, OS rates and the RMSTs were compared against the actual OS rates, median survival and the RMSTs as well as their 95% confidence intervals (CIs). ***Results:*** - Predicted median survivals and RMSTs were within the 95% CIs of the reported values in 32 and 35 out of 40 subgroups, respectively. In 8 of the subgroups, the gap between the estimated RMSTs from the predicted and the reported survival curves was less than 5%. In 6 of the subgroups, predicted survival curves laid within the 95% CIs of reported KM-curves in at least 90% of the time. Across all subgroups, on average, predicted survival curves laid within the 95% CIs of reported KM-curves in 71% of the time. ***Conclusions:*** Our study offers a useful and reliable approach for extracting subgroup-specific survival from aggregate RCT data to better inform economic and comparative effectiveness analyses for subgroups.

CN3
IT'S ALL IN THE FAMILY: MICROSIMULATION MODELLING OF GENETIC TESTING

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Objectives: Around 20-25% of ovarian cancers and 5-10% of breast cancers are due to an inherited predisposition. The primary clinical and economic benefit of hereditary breast and ovarian cancer (HBOC) testing is from preventing cancers in unaffected relatives who present for predictive/cascade testing for a known pathogenic variant in the family. Population-based genetic testing (GT) as an alternative to current practice has been gaining momentum, as it enables identification of high-risk women before they develop cancer. Existing evaluations of population-based GT mostly rely on heavily simplified comparators, and are based on selected point estimates for probabilities of identifying relatives and cascade testing uptake. This likely overestimates the benefit of population-based testing. ***Methods:*** We developed a microsimulation model for evaluating HBOC testing that includes individuals linked within family structures (thus a more sophisticated cascade testing component). Family structures are modelled using an analysis of 11,143 pedigrees from an Australian genetics clinic. The genetic component includes Mendelian inheritance of pathogenic variants for eight high- and moderate-risk genes. HBOC risk associated with single nucleotide polymorphisms was incorporated through polygenic risk scores. Life histories for individuals are generated, considering their gender, age, and genetic risk. ***Results:*** This microsimulation model, called NEEMO, more accurately reflects current practice using a simulated family-based approach. It has been validated for gene-specific cancer incidence, mortality, pathology, and uptake of cancer risk management. It has also been validated for genetic testing referral rates, and uptake of predictive GT in relatives. ***Conclusions:*** Modelling GT presents challenges due to the nature of inheritance and interaction between individuals. Clinical genetics is complex and highly specialised, with a commonly cited barrier to GT being a lack of awareness or understanding in non-genetics specialists around eligibility and management. The NEEMO model will be useful for evaluating changes in risk assessment, target GT populations, and modifying cancer prevention strategies.

CN4
PATIENT-REPORTED OUTCOMES FROM THE PHASE 3, RANDOMIZED STUDY OF ACALABRUTINIB WITH OR WITHOUT OBINUTUZUMAB VERSUS CHLORAMBUCIL PLUS OBINUTUZUMAB FOR TREATMENT-NAÏVE CHRONIC LYMPHOCYTIC LEUKEMIA (ELEVATE-TN)

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Objectives: Report patient-reported outcomes of fatigue and health-related quality of life (HRQoL) from the randomized, phase 3, ELEVATE-TN study (NCT02475681) in patients with treatment-naïve chronic lymphocytic leukemia (CLL). ***Methods:*** Patients received acalabrutinib alone (A), A plus obinutuzumab (AO), or chlorambucil plus obinutuzumab (CO). Assessments included the FACIT-Fatigue Global Fatigue Score (GFS) (scale: 0–52; lower score=worse outcome [clinically meaningful improvement: $\geq$+3]) and the EORTC QLQ-C30