Global Health Status (GHS) score (scale: 0–100; lower score=worse HRQoL [clinically meaningful improvement: >+8]) in all patients (excluding those who progressed) and those with severe fatigue at baseline (GFS ≤34), analyzed using mixed-model repeated measures methodology. A post-hoc analysis assessed time to clinically meaningful deterioration (TTD; change ≤−3) in GFS. ***Results:*** Among 535 randomized patients, 449 completed the GFS (A, n=156; AO, n=152; CO, n=141) and 450 completed the GHS (A, n=157; AO, n=151; CO, n=142) at baseline. Overall, 151 randomized patients had severe fatigue (A, n=56; AO, n=53; CO, n=42); all completed both questionnaires at baseline. In all arms, GFS and GHS improvements were observed by week 4 (mean changes: 2.76 and 5.35 for A [n=136, n=137], 2.33 and 2.17 for AO [n=138, n=138], 1.26 and 2.53 for CO [n=121, n=122]) and maintained at 96 weeks (4.94 and 7.01 for A [n=81, n=82], 3.91 and 5.25 for AO [n=92, n=92], 3.86 and 2.41 for CO [n=38, n=38]); this benefit was larger in patients with severe fatigue. Median TTD in fatigue was longer in acalabrutinib-containing arms (A: 16.9 mo; AO: 16.7 mo) versus CO (5.7 mo [*P*=0.0376 vs A; *P*=0.1596 vs AO]). ***Conclusions:*** In ELEVATE-TN, all treatments improved fatigue scores; TTD of fatigue was significantly longer with acalabrutinib-containing treatment. The previously reported statistically significant progression-free survival increases with A/AO versus CO (*Lancet*. 2020;395:1278-91) were accompanied by clinically meaningful HRQoL benefits.

Clinical Outcome Assessment Studies

CO1
THE NATURAL HISTORY, CLINICAL OUTCOMES AND UNMET NEEDS OF PATIENTS WITH ARGINASE 1 DEFICIENCY (ARG1-D): A SYSTEMATIC REVIEW OF CASE REPORTS

Bin Sawad A,[1] Pothukuchy A,[1] Badeaux M,[1] Hodson V,[1] Bubb G,[1] Lindsley K,[2] Uyei J,[3] Diaz GA[4]
[1]*Aeglea BioTherapeutics, Austin, TX, USA,* [2]*IQVIA, WINDSOR MILL, MD, USA,* [3]*IQVIA, San Francisco, CA, USA,* [4]*Division of Medical Genetics and Genomics in the Department of Genetics and Genomic Sciences at the Icahn School of Medicine at Mount Sinai, New York, NY, USA*

Objectives: ARG1-D is a debilitating, progressive, inherited, metabolic disease characterized by hyperargininemia leading to significant morbidity and early mortality. The objective of this study was to systematically review the literature to assess the natural history, clinical outcomes, and unmet needs of patients with ARG1-D. ***Methods:*** We searched MEDLINE, EMBASE, and other databases for case reports describing patients with ARG1-D. Eligible studies reported natural history (patient demographics, diagnosis methods, clinical manifestations), treatments, and/or clinical outcomes (cognitive, motor, growth, death). Two individuals independently screened records, extracted data, and assessed study quality using the Joanna Briggs Institute Critical Appraisal Tool. ***Results:*** We included 90 studies that described 157 unique patients with ARG1-D. The most frequently reported and observed clinical manifestations were motor deficits (126/133; 95%), including lower limb spasticity (102/114; 89%); intellectual disability or cognitive impairment (87/112; 78%); and seizures (78/101; 77%). Most clinical manifestations were documented by 3 years of age; mean age of diagnosis was 6.4 years (median 5; range 0-27). Physician-prescribed dietary restriction was the most commonly reported intervention (62%), followed by use of nitrogen scavengers (45%), essential amino acids (21%), dialysis (5%), and liver transplantation (3%). Few studies reported clinical outcomes: 23 reported motor function (11 patients improved, 12 did not), 19 reported cognitive function (15 patients improved, 4 did not), and 10 reported growth (6 patients improved, 4 did not). Sixteen patients died, all but one before 25 years and six before age 2. ***Conclusions:*** This review describes the natural history of ARG1-D in terms of clinical presentation and diagnosis. It illustrates that the current standard of care is ineffective at managing the disease and does not improve clinical outcomes. The large sample of included cases highlights a significant disease burden, risk of mortality, and a clear unmet need for clinically effective treatment options for patients with ARG1-D.

CO2
HEALTHCARE UTILIZATION, COST, AND QUALITY AMONG HIGH-NEED, HIGH-COST MEDICARE BENEFICIARIES IN MEDICARE FEE-FOR-SERVICE VERSUS MEDICARE ADVANTAGE

Teigland C,[1] Pulungan Z,[2] Mohammadi I[3]
[1]*Avalere Health, an Inovalon Company, Washington, DC, USA,* [2]*Avalere Health - An Inovalon Company, Washington, DC, USA,* [3]*Avalere Health, Washington, DC, USA*

Objectives: More than one-third of Medicare beneficiaries are enrolled in a managed Medicare Advantage (MA) plan, yet there is little data comparing outcomes among MA Beneficiaries (MAB) compared to traditional Medicare Fee-for-Service Beneficiaries (FFSB). The objective of this study was to identify high-need, high-cost cohorts of MAB and FFSB and compare their healthcare resource utilization, costs, and quality outcomes. ***Methods:*** This retrospective study used data from a national sample of MA encounter data and 100% Medicare Parts A, B, and D claims data from 2015-2017. A validated algorithm was applied to identify distinct clinical cohorts of high-need, high-cost beneficiaries in FFS and MA, including disabled under age 65, frail elderly, and major complex chronic patients. Propensity score matching was used to assure the populations had similar demographic and clinical characteristics; matching resulted in a study sample of 1,262,180 patients in both cohorts. We compared performance on a discrete set of health outcomes selected as relevant indicators of the impact of care management practices. ***Results:*** Overall, MA performed better than FFS on 17 of 22 quality measures, including preventive care (e.g., 50% more likely to receive pneumonia vaccine; 18-27% more likely to be screened/treated for depression). MAB had 10% fewer inpatient stays, but higher use of outpatient and physician office visits. MAB were about 50% less likely to be hospitalized for potentially preventable complications. Total medical and pharmacy spend was 15% lower in MA. ***Conclusions:*** This study found significant differences in health outcomes of high-cost high-need MAB compared to similar FFSB. Enrollment in MA continues to rapidly expand, projected to reach 47% of Medicare by 2029. This study indicates the incentives in MA to better coordinate care and provide flexible medical/non-medical benefits are associated with better care at lower cost, which is the goal of value-based purchasing.

CO3
COMPARISON OF GOAL ATTAINMENT AND MEASURES OF FUNCTION IN TWO DEMENTIA CLINICAL TRIALS.

Stanley J,[1] Howlett SE,[2] Dunn T,[1] Stanojevic S,[1] Chapman C,[1] Rockwood K[2]
[1]*Ardea Outcomes, Halifax, NS, Canada,* [2]*Dalhousie University, Halifax, NS, Canada*

Objectives: Questionnaire-style outcome measures are often used in clinical trials. It is unclear whether this type of outcome measurement can capture change that is personally meaningful to individuals. In contrast, Goal Attainment Scaling (GAS) is an outcome measure where patients and clinicians develop and track an individualized set of treatment-related goals that are important to the patient. Here, we compared attainment of daily function goals to questionnaire-style measures of function in two mild-moderate dementia clinical trials. ***Methods:*** Data were from the Atlantic Canadian Alzheimer Disease Investigation of Expectations (ACADIE) and the Video Imaging Synthesis of Treating Alzheimer disease (VISTA) trials. Both used GAS as a primary outcome. ACADIE used the Functional Assessment Questionnaire, Lawton-Brody Physical Self-Maintenance Scale, and Lawton-Brody Instrumental Activities of Daily Living which we normalized to a 100-point scale. The VISTA trial used the 100-point Disability Assessment for Dementia to assess function. ***Results:*** Subjects were demographically comparable between ACADIE and VISTA (75.9±7.8, 76.3±7.6 years of age; 73%, 64% women; and baseline Mini-Mental State Examination scores 19.7±5.2, 20.8±3.3), respectively. Baseline function scores were near-normal in ACADIE (mean=46.8±15.2, median=44) and negatively skewed in VISTA (mean=76.3±19.7, median=83). Patient-rated daily function goal attainment correlated with change in questionnaire-based measures of function (ACADIE: r=0.25, p=0.022; VISTA: r=0.37, p=0.044) but clinician-rated daily function GAS was not correlated in VISTA (ACADIE: r=0.60, p<0.001; VISTA: r=0.07, p=0.7). There was no change in daily function GAS (ACADIE: mean=50.6±9.4, p=0.6; VISTA: mean= 51.5±14.2, p=0.5), but questionnaire-based measures of function declined (ACADIE: mean change=-3.6±10.0, p<0.001; VISTA: -5.2±11.8, p=0.003). ***Conclusions:*** Questionnaire-style outcome measures were correlated with patient-rated daily function GAS goals. However, GAS clearly showed that patients maintained important aspects of daily living when questionnaire-based measures showed net decline. Individualized outcome measures like GAS can detect meaningful change that could be missed by standard outcome assessments.

CO4
PREDICTORS OF INPATIENT RELAPSE IN MULTIPLE SCLEROSIS PATIENTS USING FIRST-LINE DISEASE MODIFYING THERAPIES: A MACHINE LEARNING STUDY OF REAL WORLD DATA

Icten Z, Friedman M, Menzin J
Panalgo, Boston, MA, USA

Objectives: Relapse among multiple sclerosis (MS) patients is associated with disability progression and worsening outcomes. This study aims to identify characteristics of inpatient MS relapse using claims data and machine learning techniques. ***Methods:*** MS patients with a new prescription or administration of a disease modifying therapy (DMT) were identified based on ICD-9/10 diagnosis codes in de-identified Optum® Clinformatics® Data Mart from 2000-2019. The first DMT date was the index date with >=2 MS diagnoses required in the preceding 6 months (baseline). Inpatient relapse was defined as an inpatient visit with a primary MS diagnosis code during the 12 months following the index date. Features included demographics, comorbidities, concomitant medications, healthcare resource utilization (HRU), DMT route of administration and proportion of days covered (PDC) for

DMTs. Five-fold cross validation was used to tune and evaluate traditional and regularized logistic regression, XGBoost, support vector machine, random forest and feed-forward neural network models. The best model was selected using the area under the ROC curve (AUC) and accuracy, recall, precision, F1-score and specificity were assessed. ***Results:*** Inpatient relapse was observed for 984 (5.2%) patients of 18,820 patients (mean age=44.2 years; females=75.8%). The XGBoost model had the best AUC (AUC=79.3%; accuracy=74.3%; recall=69.7%; precision=13.1%, F1=0.22, specificity=74.5%). Predictors of inpatient relapse included MS related HRU measures (previous IP or ER visit with MS diagnosis, number of MS related encounters, utilization of home care services and durable medical equipment), epilepsy/convulsions, paralysis, urinary tract infections, potential medication side effects (nausea and vomiting), use of muscle relaxants, anticonvulsants and antidepressants. Factors protective of relapse were increased PDC, older age, DMTs administered as infusion, Caucasian race and being female. ***Conclusions:*** Our study identified demographic and clinical predictors of inpatient MS relapse with high predictive accuracy. Our findings can potentially be utilized to better manage patients at high risk of relapse.

Economic Evaluation in Oncology Studies

EC1
A COST-EFFECTIVENESS ANALYSIS OF NIVOLUMAB PLUS IPILIMUMAB PLUS TWO CYCLES OF PLATINUM DOUBLET CHEMOTHERAPY VERSUS PLATINUM DOUBLET CHEMOTHERAPY IN THE FIRST-LINE TREATMENT OF STAGE IV OR RECURRENT NON-SMALL CELL LUNG CANCER IN THE UNITED STATES

Polyzoi M,[1] Sandhu H,[2] Maervoet J,[2] Yuan Y,[3] Chaudhary M,[3] Varol N,[4] Lee A,[4] Dale P,[2] Jones C,[5] Lubinga SJ,[3] Penrod JR[3]
[1]*PAREXEL International, Strängnäs, D, Sweden,* [2]*Parexel International, London, ESS, UK,* [3]*Bristol-Myers Squibb, Princeton, NJ, USA,* [4]*Bristol-Myers Squibb, Uxbridge, Middlesex, UK,* [5]*PAREXEL International, Stockholm, Sweden*

Objectives: To evaluate the cost-effectiveness of nivolumab plus ipilimumab plus two cycles of platinum doublet chemotherapy (NIVO+IPI+PDC) versus four cycles of PDC in the first-line (1L) treatment of stage IV or recurrent non-small cell lung cancer (NSCLC) from a health insurance perspective in the United States (US). ***Methods:*** A partitioned survival model with three health states (progression-free, progressed disease and death) was developed. Efficacy, safety and quality of life data were derived from the Phase-III CheckMate 9LA trial (CM9LA), with a minimum follow-up (FU) of 12.7 months for overall survival (OS)). Data from a more mature trial involving NIVO+IPI in 1L NSCLC, CM227 (37.7 months minimum FU for OS), were used to inform long-term OS over the 25-year (lifetime) horizon to capture the long-term survival effect observed from dual Immune-Oncology therapy. OS and progression-free survival was estimated based on CM9LA Kaplan Meier (KM) data up to 13 months then extrapolated using the conditional survival estimates from CM227. The CM9LA duration of treatment KM curves were used to estimate treatment costs. Resource use and direct medical costs (2020 USD) were included. EQ-5D based treatment-specific utility weights (US tariffs) were used. Annual discount rates of 3.5% for costs and outcomes were applied. Probabilistic sensitivity analyses (PSA) were conducted. ***Results:*** The incremental cost per quality-adjusted life-year (QALY) gained was $132,960. NIVO+IPI+PDC vs. PDC resulted in increased life-years (3.71 vs. 1.89), QALYs (2.86 vs. 1.37), and costs ($317,497 vs. 119,932). Drug acquisition cost for NIVO+IPI+PDC was the key driver of the difference in total costs. PSA results were consistent with the base case. ***Conclusions:*** NIVO+IPI+PDC offers a new cost-effective treatment option for patients in 1L NSCLC. Estimated incremental cost-effectiveness ratio is within the range of what is considered acceptable value for money within the metastatic cancer setting in the US.

EC2
MODELING APPROACHES TO ESTIMATE REALIZED REAL OPTION VALUE OF IPILIMUMAB IN METASTATIC MELANOMA

Lee W,[1] Li M,[2] Wong W,[3] To TM,[3] Garrison LP,[1] Veenstra D[1]
[1]*University of Washington, Seattle, WA, USA,* [2]*The University of Texas MD Anderson Cancer Center, Houston, TX, USA,* [3]*Genentech, Inc., South San Francisco, CA, USA*

Objectives: Real option value (ROV) is created when a drug enables a patient to live long enough to benefit from a future innovation, but few if any studies have quantified ROV observed in the real world. We aimed to estimate the realized ROV using real-world data (RWD) using ipilimumab in melanoma as a case study. ***Methods:*** We developed a framework for calculating ROV using RWD that accounted for the health gain in the standard therapy arm as well as the actual uptake of future innovative drugs. We developed a Markov model to estimate the quality-adjusted life-years (QALYs) gained with ipilimumab compared to chemotherapy for patients with or without subsequent cancer immunotherapy (CIT). The realized ROV of ipilimumab and chemotherapy was the additional health gain due to the CIT. To inform the model parameters, we used the nationwide Flatiron Health electronic health record-derived de-identified database to estimate real-world progression-free survival (PFS) and overall survival (OS) curves for patients stratified by the first- and subsequent-lines of therapy. Patients diagnosed with metastatic or advanced unresectable melanoma and started treatment between 1/1/2011 and date of 1st CIT approval (9/4/2014) were included. ***Results:*** The incremental QALYs gained for ipilimumab vs. chemotherapy without subsequent CIT were 1.74. With subsequent CIT, the incremental QALYs increased by 0.92, 0.60, 0.33, 0.18, 0.10, and 0.02 when CIT became available 0, 3, 6, 9, 12, and 24 months after the initiation of first-line ipilimumab, respectively. The results were sensitive to the survival benefit of ipilimumab, the survival benefit of subsequent CIT, and the uptake of CIT. ***Conclusions:*** This is the first study to demonstrate the realized ROV using RWD. The realized ROV was between 1%–54% of conventional value for patients diagnosed within 2 years before CIT availability. Further studies are needed to understand ROV in other diseases, particularly those with longer survival times.

EC3
ECONOMIC BURDEN OF CARDIOVASCULAR EVENTS IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA TREATED WITH NOVEL AGENTS

Malangone-Monaco E,[1] Ryan K,[2] Marchlewicz E,[1] Lo J,[2] Huntington S[3]
[1]*IBM Watson Health, Cambridge, MA, USA,* [2]*AstraZeneca, Gaithersburg, MD, USA,* [3]*Yale University School of Medicine, New Haven, CT, USA*

Objectives: Novel agent treatments (NATs) have improved survival in chronic lymphocytic leukemia (CLL), but can be associated with increased cardiovascular (CV) events. This analysis examined real-world healthcare costs associated with CV events in CLL patients treated with NATs. ***Methods:*** Using US-commercial administrative claims data (IBM MarketScan), we compared unadjusted healthcare costs among CLL patients taking NATs with and without a CV event during treatment (CV vs. noCV). Inclusion criteria were adult CLL patients, evidence of NATs (acalabrutinib, duvelisib, ibrutinib, idelalisib, venetoclax) between November 2013-November 2019 (index date=earliest fill date), continuous enrollment for 6-months pre-index (baseline), and no evidence of NATs or trial participation during baseline. Annual all-cause and CV-related healthcare costs (adjusted to 2019 US dollars) were measured in a fixed 12-month follow-up period while per-patient-per-month (PPPM) costs were compared in variable-length pre/post-CV event periods. ***Results:*** Of 1,886 CLL patients with NATs, 27.7% experienced a CV event during treatment, occurring a mean(SD) 103.0(93.9) days following NAT initiation. Almost half (47.1%) of CV patients had a CV event pre-index, the majority of which were hypertension. CV patients were older (71.7 vs. 65.8, $p<0.001$) and had a higher baseline NCI score (1.2 vs. 0.8, $p<0.001$) than noCV patients. Annual all-cause total healthcare costs were higher in the CV vs. noCV cohort ($203,349 vs. $165,144, $p<0.001$). Higher annual medical costs ($82,949 vs. $45,293, $p<0.001$) compensated for numerically lower NAT costs in CV vs. noCV cohort ($110,925 vs. $115,026, p=0.262). Pre-CV event, outpatient pharmacy PPPM costs contributed most to total healthcare costs; post-CV event, PPPM medical costs contributed more: outpatient pharmacy 74.8% vs. 38.8%, hospitalization 7.6% vs. 38.8%, and outpatient services 17.7% vs. 22.4%. ***Conclusions:*** In CLL patients with a CV event, higher medical costs compensate for decreased novel agent costs, suggesting increased medical management in addition to NAT discontinuation.

EC4
REAL-WORLD HEALTHCARE COSTS IN PATIENTS WITH CLASSICAL HODGKIN LYMPHOMA TREATED WITH PEMBROLIZUMAB AND NIVOLUMAB IN THE UNITED STATES

Laliberte F,[1] **Raut M,**[2] Germain G,[3] Desai K,[4] Nahar A,[5] Yang X,[6] MacKnight S,[3] Duh MS[7]
[1]*Groupe d'analyse, Ltée, Montreal, QC, Canada,* [2]*Merck & Co., Inc., Raritan, NJ, USA,* [3]*Groupe d'analyse, Ltée, Montréal, QC, Canada,* [4]*Merck & Co., Inc., Cranbury, NJ, USA,* [5]*Merck & Co., Inc., Kenilworth, NJ, USA,* [6]*Merck & Co., Inc., Rahway, NJ, USA,* [7]*Analysis Group, Inc., Boston, MA, USA*

Objectives: Patients with classical Hodgkin lymphoma (cHL) relapsed or refractory (R/R) disease incur substantial healthcare resource utilization and costs. The PD-1 inhibitors nivolumab and pembrolizumab were approved by the FDA (May 2016 and March 2017, respectively) as treatments for R/R cHL patients; however, literature on the healthcare costs of patients treated with these two medications is sparse. This retrospective study evaluated the medical costs of patients with cHL initiated on pembrolizumab compared to nivolumab in the US. ***Methods:*** Healthcare insurance claims from Symphony Health's Patient Integrated Dataverse® (07/2014-06/2018) were used to identify adult patients with cHL initiated on pembrolizumab or nivolumab (index date). Inverse probability of treatment weighting was used to adjust for differences in baseline patient characteristics between cohorts (evaluated in the 12 months prior to the index date). All-cause and cHL-related hospitalization and outpatient visit costs (based on provider charges) were reported per-patient-per-