ANALYSIS GROUP

Raising the Standard in HEOR

Analysis Group Posters and Presentations

ISPOR EUROPE 2023 | NOVEMBER 12–15 | COPENHAGEN, DENMARK

Analysis Group's health economics and outcomes research professionals have extensive experience helping clients quantify product value in a dynamic and rapidly changing marketplace.

This year, we are pleased to present an educational symposium, a podium presentation, and 13 research posters. Please find details below.

Please stop by and say hello to our team at Booth #C3-093

ISPOR Europe 2023 Analysis Group Educational Symposium

EDUCATIONAL SYMPOSIUM

Tuesday, November 14 | 11:45 a.m.–12:45 p.m. | Bella Center Copenhagen, Room C1

Advancing Real-World Evidence Generation: Insights from Europe, the US, and China

Real-world evidence (RWE) plays a pivotal role in healthcare decision making, exerting a profound impact on regulatory approvals, health technology assessment (HTA) evaluations, policy formulation, and clinical guideline development. While RWE holds immense potential in shaping multi-dimensional aspects of healthcare, its implementation and utilization vary across different regions. Understanding regional contexts and strategies is crucial for fostering international research collaboration, accelerating medical innovation, and improving patient outcomes. The presenters will discuss the expanding significance of RWE in healthcare, with examples of experiences and practices observed in Europe, the US, and China.

Moderator: Eric Q. Wu, Ph.D., *Managing Principal, Analysis Group*

Panelists: Min Yang, M.D., Ph.D., *Vice President, Analysis Group*

Jia Zhong, Sc.D., *Vice President, Analysis Group*

Grégoire Mercier, M.D., Ph.D., *Head of Data Science and Economic Evaluation, University Hospital of Montpellier*

ISPOR Europe 2023 Analysis Group Podium Presentation

PODIUM PRESENTATION

Wednesday, November 15 | 10:00–10:15 a.m. | Bella Center Copenhagen, Hall C, Theater 1

Comparability of Overall Survival in Real-World and Clinical Trial Data for BRAF+ Advanced Melanoma

Objectives: External controls based on real-world data (RWD) are increasingly used to complement clinical trial data when assessing effectiveness of treatments in oncology. In the absence of randomization, comparisons between clinical trial and RWD have well-recognized risk of bias, arising from potential differences across these settings in patient populations, diagnostic testing, background therapies, and outcome assessments. Suitability of RWD as external controls should be determined on a case-by-case basis considering the RWD source, study outcomes compared, and study design and analysis steps employed to address bias. Empirical assessment of consistency in outcomes across trial and RWD settings can also help assess suitability of external controls based on RWD.

Methods: We compared overall survival (OS) in patients with metastatic BRAF V600-mutant melanoma treated with encorafenib plus binimetinib (ENCO+BINI) drawn from the phase 3 COLUMBUS trial and from Flatiron Health, an electronic medical records-derived database of primarily community oncology clinics in the US.

Results: After applying key trial inclusion/exclusion criteria to the RWD, imputing missing baseline prognostic factors using multiple imputation, and adjusting for baseline prognostic factors, OS was similar in ENCO+BINI-initiating patients across trial (n=192) and RWD (n=83; hazard ratio (HR): 1.03; 95% CI: 0.53, 1.54) settings. Similar OS between trials (n=241) and RWD (n=816) from Flatiron was also reported in a previous analysis of patients with metastatic melanoma, regardless of molecular testing status, treated with ipilimumab (HR: 0.98 (0.75, 1.26)).

Conclusions: These findings of consistent OS with clinical trials after applying equivalent I/E criteria, and adjusting for differences in patient profiles and missing data are encouraging for the use of RWD from Flatiron to construct external controls for OS in BRAF+ metastatic melanoma. RWD may augment randomized control arms, provide a reference arm in long-term extension periods, contextualize trial outcomes, or be pooled with trial data to facilitate analyses based on more comprehensive evidence.

Authors: Managing Principal James Signorovitch, Vice President Gautam Sajeev, Associates Sarah Kalia and Ryan Simpson, Analysts Dana Christensen and Daisy Liu, and researchers from Pfizer and the USC Norris Comprehensive Cancer Center

ISPOR 2023 Analysis Group Research Posters

POSTER SESSION 1

Monday, November 13 | 10:30 a.m.–1:30 p.m.

Progressive Disease Milestones and Survival in Duchenne Muscular Dystrophy (DMD): A Model-Based Synthesis for Extrapolating Lifetime Treatment Effects From Clinical Trial Results

Objectives: Randomized controlled trials of gene therapies in Duchenne muscular dystrophy (DMD) have studied effects on ambulatory function limited to one year using the North Star Ambulatory Assessment (NSAA). However, the projected lifetime effects of these therapies will need to be considered in health economic evaluations. Drawing on natural history data, we developed a model-based synthesis for projecting plausible effects on longer-term disease milestones, including mortality, based on one-year outcomes from clinical trials.

Conclusions: Lifetime effects of novel therapies for DMD will ultimately be determined based on real-world evidence over several decades. In the near-term, the NH model presented here, which incorporates NH data, published evidence, and plausible assumptions, can complement and supplement the lifetime projections used in health economic evaluations.

Authors: Managing Principal James Signorovitch, Vice President Michaela Johnson, Associate Andres Gomez-Lievano, Senior Analyst Adina Zhang, Analyst Aarushi Sharma, and researchers from Duke University and Pfizer

Real-World Comparison of Healthcare Resource Utilization and Costs Between Patients with Chronic Lymphocytic Leukemia Treated with First-Line Ibrutinib or Acalabrutinib

Objectives: To compare real-world healthcare resource utilization (HRU) and costs between patients with chronic lymphocytic leukemia (CLL) initiated on first-line (1L) ibrutinib or acalabrutinib.

Conclusions: 1L CLL patients treated with ibrutinib had lower number of days with outpatient services and lower costs compared to acalabrutinib. These findings have important implications for optimal 1L BTKi selection. Additional research is warranted to understand reasons behind differences in HRU/costs between 1L ibrutinib and acalabrutinib.

Authors: Vice Presidents Bruno Émond and Marie-Hélène Lafeuille, Associate Priyanka Gogna, and researchers from The Ohio State University, Janssen Scientific Affairs, and the Perelman School of Medicine at the University of Pennsylvania

POSTER SESSION 2

Monday, November 13 | 3:30–6:30 p.m.

Feasibility Assessment of an Indirect Treatment Comparison (ITC) of Sacituzumab Govitecan (SG) Vs Trastuzumab Deruxtecan (T-DxD) in HR+/HER2– Metastatic Breast Cancer (mBC)

Objectives: In the TROPiCS-02 trial, SG provided statistically significant and clinically meaningful improvement in progression-free survival and overall survival versus chemotherapy in patients with hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2-) (IHC 0, 1+, 2+/ISH-) mBC. Separately, T-DxD also demonstrated clinical benefits in patients with HR+/HER2 low (IHC 1+, 2+/ISH-) mBC in the Destiny Breast-04 (DB04) trial. A feasibility assessment for an ITC was needed to understand whether outcomes could be compared indirectly between SG and T-DxD without biases.

Conclusions: An ITC between these two treatments using data from currently available trials is not feasible due to heterogeneity in study designs, populations, and lack of data on prognostic factors in the directly overlapping population. Therefore, no comparative conclusions can be made from an ITC between these two treatments among HR+/HER2- mBC patients.

Authors: Manager David Proudman and researchers from Gilead Sciences, Gilead Sciences Europe, and Institut de cancérologie de l'Ouest

Gastrointestinal Manifestations and Incontinence Products in the Real World Among Patients with Rett Syndrome in the United States

Objectives: Rett syndrome (RTT) is a rare neurodevelopmental disorder that almost exclusively affects females. Patients with RTT experience burdensome GI manifestations and may require durable medical equipment (DME) incontinence products. This study describes GI manifestations and DME incontinence products among female patients with RTT in the United States (US).

Conclusions: Over a quarter of patients with RTT experience constipation and nearly half of all pediatric and adult patients require incontinence products. These findings suggest that patients with RTT require management of GI manifestations, which may be supplemented with DME incontinence products.

Authors: Managing Principal Patrick Lefebvre, Manager Kalé Kponee-Shovein, Associate Malena Mahendran, and researchers from Acadia Pharmaceuticals

Matching-Adjusted Indirect Comparison (MAIC) of Nivolumab + Relatlimab (NIVO+RELA) Vs. BRAF/MEK Inhibitors for First-Line Treatment of BRAF-Mutant Advanced/Metastatic Melanoma (AMEL)

Objectives: Due to lack of head-to-head randomized clinical trials comparing NIVO+RELA vs BRAF/MEK inhibitors for first-line treatment of BRAF-mutant aMel, we evaluated the efficacy of NIVO+RELA vs dabrafenib+trametinib (DAB+TRAM), encorafenib+binimetinib (ENCO+BINI), and vemurafenib+cobimetinib (VEM+COBI) via MAICs.

Conclusions: These MAICs suggest long-term (after 12 months) OS advantage of NIVO+RELA over DAB+TRAM, ENCO+BINI, and COBI+VEM for first-line treatment of BRAF-mutant aMel.

Authors: Vice Presidents Jenny Zhou and Viviana García-Horton, Analyst Matthew Mattera, and researchers from Bristol Myers Squibb

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Model-Projected Long-Term Clinical Outcomes of Exagamglogene Autotemcel (exa-cel) Gene-Edited Therapy in Patients with Sickle Cell Disease with Recurrent Vaso-Occlusive Crises in the United Kingdom

Objectives: Exagamglogene autotemcel (exa-cel) is a one-time potentially curative gene-edited therapy being evaluated for patients with sickle cell disease (SCD) with recurrent vaso-occlusive crises (VOCs). The standard of care (SOC) for SCD includes hydroxyurea and red blood cell transfusions. A model was developed to assess the potential long-term clinical outcomes of exa-cel versus SOC in the United Kingdom for patients with SCD with recurrent VOCs.

Conclusions: The model projected that patients treated with SOC had a mean age of death of 44.6 years; exa-cel is projected to substantially increase survival by 25.2 years (to 69.7 years). Patients treated with exa-cel, compared to SOC, experienced 88 fewer VOCs over lifetime (exa-cel: 9 vs SOC: 97). Patients treated with exa-cel also experienced fewer acute complication events over a lifetime, including acute infections (exa-cel: 0.75 vs SOC: 7.39) and leg ulcers (exa-cel: 0.32 vs SOC: 3.11). Over lifetime, exa-cel substantially lowered the proportion of patients developing chronic complications compared to SOC, including avascular necrosis (exa-cel: 12.2% vs SOC: 52.9%) and chronic kidney disease (exa-cel: 6.2% vs SOC: 34.6%).

Authors: Managing Principal Hongbo Yang, Associate Yanwen Xie, and researchers from Vertex Pharmaceuticals

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Model-Projected Long-Term Clinical Outcomes of Exagamglogene Autotemcel (exa-cel) Gene-Edited Therapy in Patients with Transfusion-Dependent Beta-Thalassemia in the United Kingdom

Objectives: Exagamglogene autotemcel (exa-cel) is a one-time potentially curative gene-edited therapy being evaluated for patients with transfusion-dependent ß-thalassemia (TDT). The standard of care (SOC) for TDT includes regular red blood cell transfusions (RBCTs) and iron chelation therapies from early childhood. A model was developed to assess the potential long-term clinical outcomes of exa-cel versus SOC in the United Kingdom for patients with TDT.

Conclusions: Model projections suggest exa-cel could considerably improve survival, lower the prevalence of TDT-related complications, and reduce disease burden in patients with TDT compared to treatment with SOC.

Authors: Managing Principal Hongbo Yang, Manager Honghao Fang, and researchers from Vertex Pharmaceuticals

POSTER SESSION 4

Tuesday, November 14 | 3:30–6:30 p.m.

Prospects for Automation of Systemic Literature Reviews (SLRs) With Artificial Intelligence and Natural Language Processing

Objectives: This research explores the performance of the latest artificial intelligence (AI) techniques to assist with SLRs, with the goal of improving review time while maintaining high accuracy.

Conclusions: Recent AI developments show promise in creating significant reductions in the time associated with conducting SLRs by better targeting abstracts for human review. In particular, human reviewers can focus on the more uncertain/inconclusive AI recommendations while the AI rapidly trims the screening set by dropping high-confidence irrelevant abstracts.

Authors: Managing Principal Eric Q. Wu, Principal Jimmy Royer, Vice President Rajeev Ayyagari, Data Science Director Stefano Parravano, Senior Data Scientist Upamanyu Pathare, and Analyst Magda Kisielinska

Treatment Patterns and Disease Burden of Patients With Hypereosinophilic Syndrome (HES) and Eosinophilic Granulomatosis With Polyangiitis (EGPA) Across Five European Countries

Objectives: HES and EGPA are two rare eosinophilic diseases with overlapping symptoms, diagnostic challenges, and treatments. This pooled sub-analysis characterized European country-by-country differences in management and healthcare resource use (HCRU) of patients with HES or EGPA.

Conclusions: Despite variations in diagnostic testing, treatment, clinical manifestations, and HCRU, overall disease characteristics and management approaches were mostly consistent between countries. Oral corticosteroid use was high, and hospitalizations and emergency visits were common, suggesting opportunities to optimize care for HES and EGPA.

Authors: Managing Principal Mei Sheng Duh, Vice President Lynn Huynh, and researchers from GSK and Cincinnati Children's Hospital Medical Center

POSTER SESSION 5

Wednesday, November 15 | 9:00–11:30 a.m.

Economic Burden of Propionic Acidemia by Age Stratum in the United States

Objectives: To estimate the economic burden of propionic acidemia (PA), a rare inherited metabolic disorder, in the United States by age stratum.

Conclusions: Patients with PA had significant HRU and economic burden compared to controls without PA across age strata, primarily driven by a higher burden of hospitalization. Development of efficacious treatments for PA to help reduce the burden is needed.

Authors: Vice President Fan Mu, Manager Erin Cook, Associate Mu Cheng, Senior Analyst Adina Zhang, Analysts Jessie Lan and Lin Zou, and researchers from Moderna

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Identifying Relevant Clinical Regulatory and Health Technology Assessment (HTA) Precedents via Artificial Intelligence (AI)

Objectives: As drug developers or evaluators consider new medical product submissions, e.g., for clinical regulatory agencies or HTAs, an effective process for all stakeholders requires understanding of regulatory precedents for study designs, data sources, outcome measurements, analytical methodology, interpretations of findings, and other diverse and interrelated topics. Human expertise is central to this process, but subject to time and resource constraints, especially when relevant precedents (1) span multiple therapeutic areas and decision authorities, (2) exist only as short passages within large documents, or (3) involve topics poorly suited to keyword searches. We developed and assessed AI-based approaches to identifying relevant regulatory precedents.

Conclusions: Artificial intelligence can augment human expertise to simultaneously increase the efficiency, breadth, and depth of understanding of regulatory precedents in drug development applications.

Authors: Managing Principal James Signorovitch, Vice Presidents Christopher Llop and Yan Song, Data Science Director Stefano Parravano, Senior Data Scientist Upamanyu Pathare, and Data Scientist Simon Fortier

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Impact of Valoctocogene Roxaparvovec on the Economic Burden of Adults with Severe Hemophilia A Managed with Prophylaxis in the United States

Objectives: To estimate the reduction in societal economic burden among patients with severe hemophilia A without inhibitors currently managed with prophylaxis in the US after the introduction of valoctocogene roxaparvovec.

Conclusions: While the initial, one-time cost of valoctocogene roxaparvovec is significant, its use will reduce the overall societal economic burden of severe hemophilia A that would otherwise be managed with prophylaxis and result in cost savings after 4 years.

Authors: Managing Principal Noam Kirson, Vice President Keziah Cook, Manager Taiji Wang, Senior Analyst Cassie Regan, and researchers from BioMarin Pharmaceutical, Enlightenment Bioconsult, and the Institute for Policy Advancement

Resource Utilization of Different Remission and Relapse Profiles in Chronic Urticaria—Results From Predict-CSU Real-World Study in the United States

Objectives: Published evidence indicates that patients with chronic urticaria (CU) exhibit diverse remission and relapse rates. The objective of this study was to quantify resource utilization among patients with CU when grouped by differing patterns of remission and relapse.

Conclusions: Patients with lower remission and higher relapse rates had higher resource utilization. This clustering algorithm could support the development of a prognostic model to aid clinicians by adjusting treatment decisions for specific patient profiles.

Authors: Managing Principal James Signorovitch, Vice President Irina Pivneva, Manager Thomas Cornwall, Data Scientist Kathleen Chen, and researchers from Novartis Pharma AG, Novartis Pharmaceuticals Corporation, Novartis Healthcare Pvt. Ltd., AllerVie Health-Alabama Allergy & Asthma Center, and the University of Manchester