

# ISPOR Europe 2022

6-9 November | Vienna, Austria and Virtual



## Poster Tour Guide Packet

Poster Session:	In-Person and Virtual Poster Session 4
Tour Name:	Rare and Orphan Diseases
Tour Date/Time:	Tuesday, 8 November 2022, 2022, 17:45 - 18:30
Tour Area:	Area B, Hall X2, Level -2

Acceptance Code:	CO15
Board Number:	1B
Abstract Title:	A Matching-Adjusted Indirect Comparison of Efgartigimod Versus Ravulizumab for Generalized Myasthenia Gravis
Presenting Author:	Lorenzo Celico

### Abstract Body:

**OBJECTIVES:** In the absence of head-to-head trials, a matching-adjusted indirect comparison (MAIC) was conducted to compare the efficacy of efgartigimod vs ravulizumab in adult patients with generalized, acetylcholine receptor autoantibody positive (AChR+) myasthenia gravis (gMG).

**METHODS:** The MAIC was based on the published aggregate data for ravulizumab from CHAMPION and the individual patient data (IPD) from ADAPT for efgartigimod. The ADAPT population was restricted to align with the inclusion criteria of CHAMPION (n=110 and n=175, respectively). ADAPT IPD were then weighted to match the baseline characteristics of the population in CHAMPION for treatment effect modifiers, including baseline MG-ADL score, time from diagnosis, use of glucocorticoids and of non-steroidal immunosuppressive drugs. The endpoint of interest was the difference in least square (LS) mean change from baseline in MG-ADL vs placebo, estimated using a mixed model for repeated measures. The efficacy of efgartigimod vs ravulizumab was compared at time of best-response (week 4 for efgartigimod and week 26 for ravulizumab). The number needed to treat (NNT) to have one more patient with minimum two points improvement in MG-ADL (minimum clinically meaningful significant improvement) compared with placebo was estimated for efgartigimod and ravulizumab at time of best response.

**RESULTS:** The effective sample size of the reweighted ADAPT population was 102.4, indicating good study feasibility. After adjustment, efgartigimod was associated with significantly greater improvement in MG-ADL compared with ravulizumab at time of best-response (-1.4; 95%CI=[-2.8,0.0], p<0.05). The NNT to have one more patient with minimum two points improvement in MG-ADL was 3.2 for efgartigimod and 9.2 for ravulizumab.

**CONCLUSIONS:** The MAIC suggested an improved efficacy with efgartigimod compared with ravulizumab in adult patients with gMG and AChR+.

**Tour Guide's Questions for Starting Q&A** (Each poster will have ~5 minutes for Q&A with attendees/Tour Guide)

1. \_\_\_\_\_

2. \_\_\_\_\_

# ISPOR Europe 2022

6-9 November | Vienna, Austria and Virtual



## Poster Tour Guide Packet

Poster Session:	In-Person and Virtual Poster Session 4
Tour Name:	Rare and Orphan Diseases
Tour Date/Time:	Tuesday, 8 November 2022, 2022, 17:45 - 18:30
Tour Area:	Area B, Hall X2, Level -2

Acceptance Code:	EE382
Board Number:	2B
Abstract Title:	Cost-Utility Analysis of Avacopan for the Treatment of Anca-Associated Vasculitis (AAV) Patients in the UK
Presenting Author:	Antonio Ramirez de Arellano Serna

### Abstract Body:

**OBJECTIVES:** The objective of this study was to evaluate the cost-utility of avacopan in combination with cyclophosphamide or rituximab compared with glucocorticoids (GC) and cyclophosphamide or rituximab for patients with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) in the UK National Health Service (NHS).

**METHODS:** A state-transition Markov model was designed to reflect clinical practice for induction of remission in patients with ANCA-associated vasculitis, with up to three induction courses. The model comprises 9 health states: an active disease state where patients start, three remission and three relapse states, end-stage renal disease (ESRD) and death. Additionally, patients can experience GC-related adverse events. The clinical efficacy for avacopan was based on the ADVOCATE trial, and included disease remission at 26, 52 and 60 weeks, change in estimated glomerular filtration rate (eGFR) and health-related quality of life. The transition probabilities to ESRD were sourced from literature. Cost data were obtained from published literature, including adverse events, and clinical management of AAV. Benefits were expressed as quality-adjusted life years (QALYs). Costs were reported in 2021 British pounds (£).

**RESULTS:** The incremental cost and incremental QALY of a regimen including avacopan compared to GC, both as an add on to cyclophosphamide (35%) or rituximab (65%), were £5,100 and 0.26 QALY, respectively. The results show an incremental cost-effectiveness ratio of £19,615 per additional QALY gained, which is lower than the willingness-to-pay threshold of £20,000 per QALY in the UK. The model results were sensitive to the eGFR improvement reported in the ADVOCATE trial. Other parameters which contributed to model uncertainty were the discount rate for outcomes and costs, and the cost of maintenance dialysis, which is the main component of the cost of ESRD.

**CONCLUSIONS:** Avacopan in combination with cyclophosphamide and rituximab is a new cost-effective option for AAV patients in the NHS.

**Tour Guide's Questions for Starting Q&A** (Each poster will have ~5 minutes for Q&A with attendees/Tour Guide)

1. \_\_\_\_\_

2. \_\_\_\_\_

# ISPOR Europe 2022

6-9 November | Vienna, Austria and Virtual



## Poster Tour Guide Packet

Poster Session:	In-Person and Virtual Poster Session 4
Tour Name:	Rare and Orphan Diseases
Tour Date/Time:	Tuesday, 8 November 2022, 2022, 17:45 - 18:30
Tour Area:	Area B, Hall X2, Level -2

Acceptance Code:	EE274
Board Number:	3B
Abstract Title:	Orphan Drug Pricing Comparisons in Low-, Middle- and High-Income Countries
Presenting Author:	Charles Brown

### Abstract Body:

**OBJECTIVES:** Most of the world's population resides in low- and middle-income countries (LMICs), many of which do not have orphan drug policies. Thus, access to treatments for rare diseases in LMICs represents a large global unmet need. We sought to assess orphan drug availability and pricing patterns in low-, middle-, and high-income countries.

**METHODS:** We identified rare-disease treatments using the US Food and Drug Administration's Orphan Drug Designations and Approvals list. For pricing analysis, we selected treatments approved between January 1, 2012, and January 1, 2022, that were available in >20 markets, including >2 LMIC markets. We classified countries as low, middle, or high income according to the World Bank's income classification criteria. We obtained pricing data from NAVLIN by EVERSANATM (a Web-based pricing subscription service). We analyzed prices by country income classification to identify potential pricing patterns between income classes and used the chi-squared test to determine statistically significant differences in prices between income groups.

**RESULTS:** Twelve treatments met analysis criteria. Of these, none were approved in low-income countries, whereas availability ranged from 26% in middle-income countries to 64% in high-income countries. No statistically significant differences in prices for orphan drugs between middle- and high-income countries were identified.

**CONCLUSIONS:** Orphan drugs have very limited presence in LMICs. When these rare-disease treatments are available in LMIC markets, prices are similar to those in high-income countries. Although the pharmaceutical industry has emphasized drug development for rare diseases, the benefits of these advancements have not yet reached many patients. The pharmaceutical industry's technological innovation must be matched with novel pricing strategies and funding mechanisms, as well as tailored contracting approaches, to facilitate and maximize orphan drug access for patients in LMICs.

**Tour Guide's Questions for Starting Q&A** (Each poster will have ~5 minutes for Q&A with attendees/Tour Guide)

1. \_\_\_\_\_

2. \_\_\_\_\_

# ISPOR Europe 2022

6-9 November | Vienna, Austria and Virtual



## Poster Tour Guide Packet

Poster Session:	In-Person and Virtual Poster Session 4
Tour Name:	Rare and Orphan Diseases
Tour Date/Time:	Tuesday, 8 November 2022, 2022, 17:45 - 18:30
Tour Area:	Area B, Hall X2, Level -2

Acceptance Code:	EE147
Board Number:	4B
Abstract Title:	Estimating the Causal Effect of Early Use of Erythropoietic Stimulating Agents in Intermediate-1 to Low-Risk MDS Patients: An Application of the Longitudinal Targeted Maximum Likelihood Estimation
Presenting Author:	Yingying Zhang

### Abstract Body:

**OBJECTIVES:** To demonstrate the use of Longitudinal Targeted Maximum Likelihood Estimation (LTMLE) methods to derive causal average treatment effect estimates for survival and health-related quality of life (measured by the EQ5D) outcomes from longitudinal real-world data with risk of bias from immortal-time and time-varying confounding.

**METHODS:** LTMLE is a double-robust method that accounts for time-varying confounding by modelling both treatment and outcome mechanisms, and produces an unbiased estimate of the causal treatment effects if either one of the mechanisms are correctly specified. Machine Learning algorithms can be used to estimate components of the treatment and outcome mechanisms, to increase the likelihood of correct model specification while retaining valid statistical inference. We apply LTMLE to data from the European Myelodysplastic Syndromes (EUMDS) registry and estimate causal average treatment effects of erythropoiesis-stimulating agents (ESA) for intermediate-1 to low-risk Myelodysplastic Syndromes patients. To account for the challenge of repeated measurements, long follow up and relatively small sample, we restrict the treatment and outcome models to only use a maximum of or two lags of covariates.

**RESULTS:** Accounting for time-varying confounding changes the predicted intervention-specific mean (counterfactual) outcomes and causal average treatment effects compared to a naïve analysis. We find no statistically significant effect of using ESA on patients' EQ5D scores or on cumulative survival. These results hold with and without using machine learning for the treatment and outcome models.

**CONCLUSIONS:** This study demonstrates the appropriate use of longitudinal causal methods in studying the treatment effect of therapies under sustained exposure, accounting for immortal-time and time-varying confounding risk of bias, which are usually neglected in these analyses. The challenges highlighted in the paper provide a lesson for future analyses that attempt to apply LTMLE in complex real-world data settings, especially in the case of a small sample size with a long follow-up period.

**Tour Guide's Questions for Starting Q&A** (Each poster will have ~5 minutes for Q&A with attendees/Tour Guide)

1. \_\_\_\_\_

2. \_\_\_\_\_



# ISPOR Europe 2022

6-9 November | Vienna, Austria and Virtual



## Poster Tour Guide Packet

Poster Session:	In-Person and Virtual Poster Session 4
Tour Name:	Rare and Orphan Diseases
Tour Date/Time:	Tuesday, 8 November 2022, 2022, 17:45 - 18:30
Tour Area:	Area B, Hall X2, Level -2

Acceptance Code:	HPR17
Board Number:	5B
Abstract Title:	Changing Landscape of Orphan Drug Reimbursement - Evidence From EU-4 and England
Presenting Author:	Graham Foxon

### Abstract Body:

**OBJECTIVES:** This study compares the rates of positive reimbursement decisions in EU-4 and England for ODs approved by the European Commission (EC) in 2015 and 2020 to determine whether patient access to Orphan Drugs (ODs) is improving.

**METHODS:** ODs approved by the EMA in 2015 and 2020 were identified. Their reimbursement status in EU-4 and England was recorded as of June 2017 and June 2022 respectively. Time to Reimbursement (TTR) was calculated for reimbursed ODs.

**RESULTS:** 12 ODs approved by EMA in 2015 and 22 ODs approved in 2020 were analysed. The percentage of positive recommendations (out of those which entered the HTA process) remained the highest in Germany (92%→100%), increased in Italy (50→73%) and England (20%→41%), and decreased in Spain (45%→39%). A decrease was also noted in France (64%→33%), however, thanks to the early access program (ATU), patients could access respectively 81% and 94% of assessed ODs. Germany remained the country with the shortest median TTR (1.1→1.3 months). For the remaining countries, an overall improvement can be seen in median TTR in Italy (13.6→10.1 months) and France (14→11.1 months), while median TTR in Spain (12.6→18 months) and England (8.7→12.2 months) increased.

**CONCLUSIONS:** Germany continuously provides the most robust patient access to ODs, owing to the strategy of not limiting the access during the price negotiation. Wide access to ODs is maintained in France despite an increased percentage of ODs still in the price negotiation due to the Early Access programme. The largest improvement can be seen in Italy which corresponds to the legislative changes in the pricing negotiation process and their COVID-19 mitigating strategies. In England, the increased percentage of positive recommendations coincides with the increased median TTR, presumably due to the higher number of ODs in the reimbursement process. With issues identified in previous research prevailing, Spain remains the most challenging market.

**Tour Guide's Questions for Starting Q&A** (Each poster will have ~5 minutes for Q&A with attendees/Tour Guide)

1. \_\_\_\_\_

2. \_\_\_\_\_

# ISPOR Europe 2022

6-9 November | Vienna, Austria and Virtual



## Poster Tour Guide Packet

Poster Session:	In-Person and Virtual Poster Session 4
Tour Name:	Rare and Orphan Diseases
Tour Date/Time:	Tuesday, 8 November 2022, 2022, 17:45 - 18:30
Tour Area:	Area B, Hall X2, Level -2

Acceptance Code:	SA73
Board Number:	6B
Abstract Title:	Addressing Unmet Needs of Patients With Neuronopathic Gaucher Disease Type 2 and Type 3: Creation of the GARDIAN Patient Registry
Presenting Author:	Tanya Louise Collin-Histed

### Abstract Body:

**OBJECTIVES:** Gaucher Disease (GD) is a rare inherited metabolic disorder. Type 2 and Type 3 are neuronopathic and often result in infant death or progressive neurological deterioration. Current drug therapies do not cross the blood brain barrier and thus do not treat neuronopathic GD (nGD). GARDIAN data will generate real-world evidence on the natural history and impact of disease and will inform clinical trial design and healthcare decision making. The objective is to describe the development of a patient registry specific to nGD.

**METHODS:** The International Gaucher Alliance, patients, caregivers, clinicians, and researchers partnered to develop a web-based platform for patients with nGD and their caregivers. Baseline and follow-up questionnaires were designed to capture data relevant to patients, including newly developed nGD-specific Patient Reported Outcome (nGD-PRO) and Observer Reported Outcome (nGD-ObsRO) instruments to be validated within the registry. Qualitative interviews were conducted to ensure the use of terminology relevant to patients. Diagnosis confirmation processes were informed by clinicians.

**RESULTS:** The patient-initiated Gaucher Registry for Development Innovation and Analysis of Neuronopathic Disease (GARDIAN) used stakeholder-identified objectives. It was designed as a worldwide, prospective patient registry available in English, French, German, Spanish, Arabic, Japanese and Chinese. Data collection timepoints are at baseline and every 6 months for 3 years, and include patient-reported enzyme/genetic results, patient characteristics, symptoms, medical history, treatment, and comorbidities. Patient- and caregiver-reported outcomes include the PedsQL, PGI-S, GAD-7, PHQ-9 and the nGD-PRO/nGD-ObsRO. GARDIAN was approved by institutional review boards. Patient enrollment began in April 2022.

**CONCLUSIONS:** The systematic and standardized collection of real-world data will provide a research platform for improving disease understanding, advancing disease management, designing treatments, and improving patient outcomes. Patient engagement in the development of GARDIAN optimizes its value as a real-world data source to inform healthcare decisions and address the unmet needs of patients.

**Tour Guide's Questions for Starting Q&A** (Each poster will have ~5 minutes for Q&A with attendees/Tour Guide)

1. \_\_\_\_\_

2. \_\_\_\_\_