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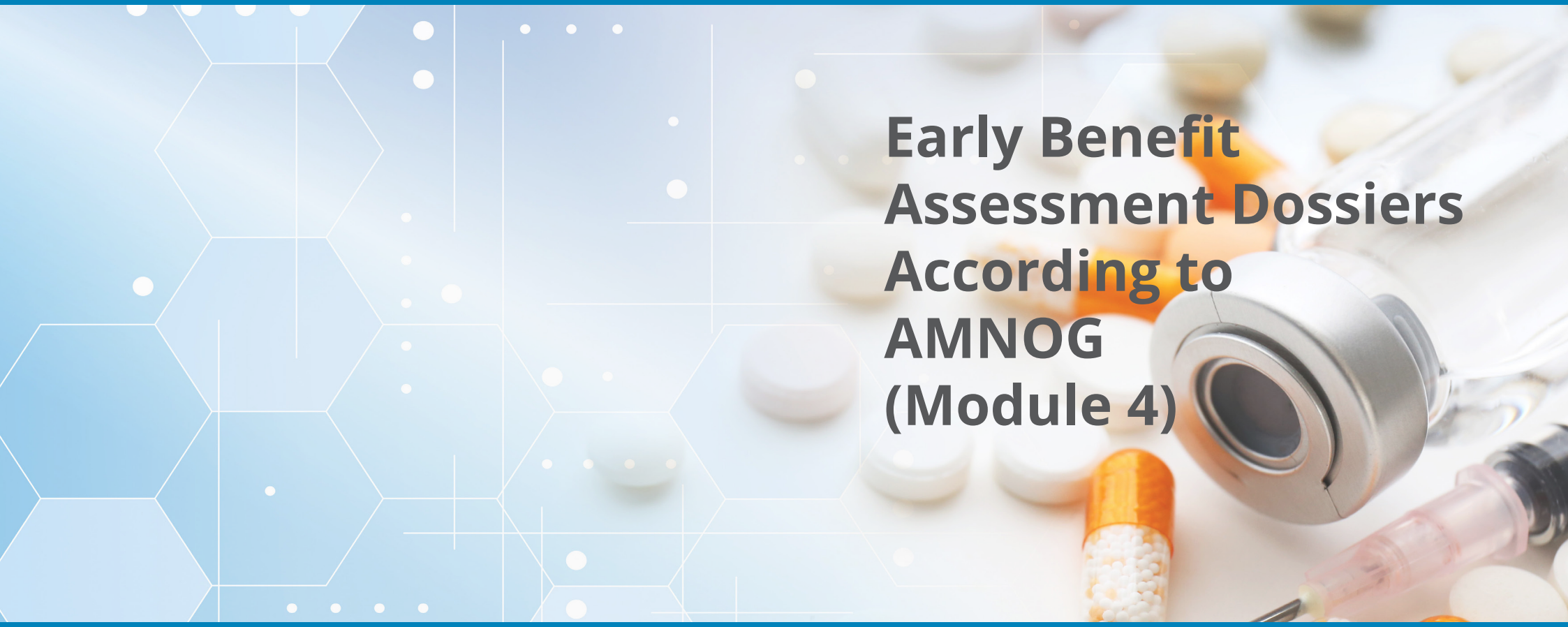
numerus

Discover the power of statistics



Early Benefit Assessment Dossiers According to AMNOG (Module 4)

AMNOG Gesetz zur Neuordnung des Arzneimittelmarktes
IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
G-BA Gemeinsamer Bundesausschuss

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The Numerus Advantage

Rely on experience

As a highly specialised CRO (founded 15 years ago), our services range from statistical consultancy to provision of the comprehensive AMNOG Dossier Module 4 statistical analysis (since 2012). Standard Service Scope typically includes a thorough data gap analysis, development of a Statistical Analysis Plan (SAP), its implementation, execution, documentation and reporting.

Profit from a unique, cutting-edge analytical approach

Our clients need to present their drugs' real benefits in a favourable light. Therefore, right at project start, we ask a few questions: Under the specific perspective of AMNOG/IQWiG, will the numbers support the value story? How can we apply cutting-edge stats technology in order to maximize the chance of successfully showing additional benefit? The numbers tell the story. We strive to let it shine. In a true, fair and positive light - because it's worth the effort.

Take advantage of our outstanding methodical skills

Our statisticians are among the frontrunners of applied statistics in the industry. They contribute to relevant studies, meetings, congresses and publications on an ongoing basis. All deliverables undergo meticulous quality checks before submission. We take pride in outmatching standard methodology whenever it is to our clients' benefit.

Boost your projects with operational flexibility and speed

In order to facilitate project implementation and meet tight timelines, customers require flexibility and speed. We claim to be a straightforward, enthusiastic business partner, responding fast and friendly.

Use in-depth know-how of German healthcare authorities, guidelines and procedures

With respect to all our statistical deliverables, we guarantee full compliance with the IQWiG* General Methods Guidance and G-BA* templates, as well as with AMNOG (and related) regulation. We are always up to date and able to execute in native English and native German.

Gain momentum with interface skills

Ever stumbled across the communicative cracks and crevices between statistical and clinical or market access teams? We can provide necessary interface skills and help transform the message of the numbers into a consistent narrative. The **Numerus Value Story Explorer Board** facilitates the interpretation of tables, listings, figures (TLF) and helps to select and focus in subsequent process stages.

Indication	Details	Outcomes	Methodology Applied
Multiple Sclerosis (including Paediatric Multiple Sclerosis)	More than 10 individual projects since 2015, ongoing. Standard Service Scope with regards to AMNOG Early Benefit Assessment Dossier Module 4.	Morbidity (e.g. 3mCDP, ARR, TTFR, Relapse Characteristics, MSFC, EDSS et al.) QoL (e.g. EQ-5D et al.) Safety (e.g. AE by SMQ et al.)	Standard Methodology; plus: Multi-Level Analysis of (> 10) Subgroups according to G-BA requirements Graphical visualisation of (subgroup) results (e.g. forest plots et al.)
Pulmonary Arterial Hypertension (PAH) & Chronic Thromboembolic Pulmonary Hypertension (CTEPH)	Multiple projects since 2014. Standard Service Scope with regards to AMNOG Early Benefit Assessment Dossier Module 4.	Mortality (Time to Death all causes, Time to Death due to PAH) Morbidity (e.g. Time to hospitalisation, Time to Clinical Worsening, 6mWD, WHO FC et al.) QoL (e.g. SF 36, EQ-5D et al.) Safety (e.g. AE by SMQ et al.)	Standard Methodology; plus: Combination of multiple studies (> 3) Creation of customer-specific report tables that could be directly embedded into running text
Migraine	Standard Service Scope with regards to AMNOG Early Benefit Assessment Dossier Module 4.	Morbidity (e.g. Monthly Migraine Days, Monthly Migraine Attacks, Monthly Acute Migraine-Specific Medication, Proportion of Responders, et al.) Safety (e.g. AE, AE of special interest et al.)	Standard Methodology; plus: Bucher Indirect Treatment Comparison following Fixed Effects Meta-Analysis methodology. Output > 70 report tables. Network Meta-Analysis (NMA) for a Mixed Treatment Anchored Comparison (3 substances) Bayesian Random Effects Model using the MCMC (Markov Chain Monte Carlo Simulation) Validation of input data (Data Extraction Table DAT) for meta analyses and indirect treatment comparison Test for Heterogeneity of Treatment Effects between studies
Relapsed and Refractory Multiple Myeloma	Standard Service Scope with regards to AMNOG Early Benefit Assessment Dossier Module 4.	Mortality (Time to Death) Morbidity (e.g. Time to Progression, Progression-free survival, Time to Treatment Failure, Time to Subsequent Anti-Myeloma Therapy et al.) QoL (e.g. ETORC-QLQ-C30, ETORC-QLQ-MY20, Clinically Meaningful Deterioration et al.) Safety (e.g. AE, Second Primary Malignancies et al.)	Standard Methodology; plus: Multi-Level Analysis of (> 20) Subgroups according to G-BA requirements Two Stage Model (Latimer et al.) to adjust for treatment switching including re-censoring and bootstrapping sensitivity analyses QoL AuC, adjusted for observation time Exposure Adjusted Incidence Rates Analysis using a Poisson-Regression Model All-AE Analysis performed by CTC Grade
Renal Anaemia	Devised analytical strategy and developed SAP Extracted and merged clinical study data, consistency & quality checked Conducted (Network) Meta-Analysis	Mortality (Time to Death) Morbidity (e.g. Hb Change from Baseline, Hb Response after 24w, MACE, MACE+, Use of Rescue Therapy, Use of RBC Transfusion, Disease Related Hospitalisation et al.) QoL (e.g. EQ-5D-5L (VAS), FACT-Anaemia, PGIC, SF 36 et al.) Safety (e.g. AE et al.)	Standard Methodology; plus: Meta-Analysis (9 global studies) using one-stage and two-stage fixed-effects and random-effects methods, using IPD. Test for Heterogeneity of Treatment Effect between studies. Mixed Model of Repeated Measures (MMRM) Logistic Regression Analysis of proportions Analysis of Rates using Poisson-Regression Model
Hormone-Sensitive Prostate Cancer	Devised the analytical strategy, developed SAP, collaboration and instruction of client's stats programming service provider Prepared the experts' response ("Stellungnahme") to the IQWiG dossier assessment ("Dossierbewertung"), in close collaboration with client Provided expert consulting, preparing of client's staff for official G-BA authority hearing	Mortality (Time to Death) Morbidity (e.g. Radiographic progression free Survival (Rfps), Time to First Symptomatic Skeletal Event, Mean Pain Interference and Severity Score (BPI-SF), Time to First use of Cytotoxic Chemotherapy et al.) QoL (e.g. EQ-5D-5L (VAS), FACT-Anaemia, PGIC, SF 36 et al.) Safety (e.g. AE et al.)	Standard Methodology; plus: Indirect Treatment Comparison (5 global studies) Fixed Effects Meta-Analysis, followed by a Bucher pairwise Indirect Treatment Comparison Extract of treatment effects data from app. 20 publications based on a Systematic Literature Review.
Acute Myeloid Leukaemia	Standard Service Scope with regards to AMNOG Early Benefit Assessment Dossier Module 4.	Mortality (Time to Death) Morbidity (e.g. Event-Free Survival, CA/TAh rate, Leukaemia-Free Survival, Transfusion Rate, Transplantation Rate et al.) Quality of Life (e.g. Brief Fatigue Inventory BFI, ECOG Performance Score, EQ-5D, FACET-Dys-SF et al.) Safety (e.g. AE et al.)	Standard Methodology, plus: Several subpopulations analysed Analysis according to the new and changed G-BA dossier template (Q1-2019) in revised version. Significantly increased amount of report requirements (tables, listings, figures).
Psoriatic Arthritis	Devised and developed SAP, external review and quality check (QC) of analyses (by third party CRO) to support AMNOG module 4 Documented review findings and QC findings; documented the extent of additional benefit ("Zusatznutzen") for each endpoint and subgroup. Categorized results based on p value and effect size, interpreted and classified study results	Morbidity (e.g. PASI 75/90/100, Relapse and Rebound Rates et al.) Quality of Life (e.g. EQ-5D, DL-QI Score, HAQ-DI Score et al.) Safety (e.g. AE, AE of Special Interest et al.)	Standard Methodology