PHM15

**HEMATOLOGICAL DISORDERS—Methods and Concepts**

**OBJECTIVES:** Investment views have been more or less neglected in economic evaluations. Fortunately, investments can be efficiently and easily assessed by evaluating the most uncertain feature of investment—Time—from two perspectives. The innovation, Positive Investment Interval (PII), its estimation and interpretation are presented here in relation to Payback Period (PP) with a safety example of Hemophilia A (HA), where the best safety is achieved using plasma/albumin-free methods (PFM). **METHODS:** PII estimates the interval when sc. safety costs are compensated by the treatment costs of adverse event/ events (AE). PP, on the other hand, estimates the time when the safety costs become compensated by the AE treatment costs. **RESULTS:** Both PII and PP are acceptable if the effectiveness of treatment options is equal. PII estimates the interval when investment to e.g. safety offers positive margin. In simple terms, PII is interval when no security threats should occur, if more risky treatment is used. Mathematically, PII compares the incremental costs of new minus old therapy (e.g. safety costs) to the incremental AE costs of old minus new therapy in a given interval (e.g. annual budgeting period). PP is the reversed version of PII. Stochastic PII can be presented in an AE costs-safety costs plane. In HA case, when base-case PII for annual PFM Advate vs. non-PFM Kogenate investment were 1–7 years depending on patient’s weight, age, and treatment modality, were PPs 2–11 years depending on the number of transfusion-dependent patients and unit costs of EC. **CONCLUSION:** A comprehensive cost-of-illness study covering all settings of care is necessary to learn about MDS resource consumption and economic consequences. Rational allocation of blood will be of special public health interest in the future due to the demographic development in Germany. The increasing scarcity of blood creates a strong need for therapies which terminate or reduce transfusion dependency. Due to the fact that innovative therapeutics for MDS will be available soon, it is important to evaluate their economic consequences with a special focus on their blood-sampling potentials.

**POSITIVE INVESTMENT INTERVAL (PII) AND PAYBACK PERIOD (PP) OFFER DIFFERENT INTERPRETATIONS IN HEALTH TECHNOLOGY INVESTMENT DECISIONS: PII IS A MATTER OF BEING AND PP IS A MATTER OF TURNING BENEFICIAL—A CASE OF HEMOPHILIA A**

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**PHM16**

**PHARMACOKINETIC-PHARMACODYNAMIC-PHARMACOECONOMIC (P3) MODELING TO INFORM PHARMACOGENOMIC TRIAL DESIGN AND RISK MANAGEMENT**

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**OBJECTIVES:** Our objective is to develop a quantitative, model-based protocol simulation approach for evaluating the clinical and economic effects of adverse drug outcomes related to genetic variation at early stages of drug or test development, using warfarin pharmacogenomics as a case-study. **METHODS:** We implemented a previously published (Hamberg et al. (2007)) population pharmacokinetic/pharmacodynamic (PK/PD) model of warfarin distribution and effect that incorporates the effects of genetic variation in the *CYP2C9* and *VKORC1* genes and other relevant demographic variables. We simulated outcomes (INR distribution) of a non-pharmacogenomic-based warfarin dosing protocol, and plan to simulate various pharmacogenomic-based dosing protocols and then integrate these results with pharmacoeconomic simulation models. **RESULTS:** INRs were modeled for 500 simulated patients using the same patient demographics (median and range) as those reported in the Hamberg analysis. The 5 mg/daily INR nomogram of Kovacs et al. (2003) was simulated. Baseline INRs were uniformly distributed over a range of 0.9 to 1.3. The INR at day 6 after initiation of therapy ranged from 0.97 to 10.31 with a median of 3.61. Median INR grouped by *CYP2C9* expression ranged from 3.17 for *1*1 patients to 5.29 for *3*3 patients. INR variations are linked to the risks of bleeding and stroke, and ultimately to the pharmacoeconomic outcomes of costs and quality-adjusted life years. **CONCLUSION:** P3-cubed (P3) modeling will be feasible only when sufficient population PK/PD data are available and valid long-term linkages can be made. It may serve as a tool to explore the robustness of such linkages and probe alternative therapeutic scenarios. Although our findings are preliminary to date, P3-modeling may provide a useful quantitative framework to help inform pharmacogenomic trial design, regulatory decisions, and potentially clinical guidelines and reimbursement policies.

**PHM17**

**RECOMBINANT ACTIVATED FACTOR VII (RFVIIa) VS. ACTIVATED PROTHROMBIN COMPLEX CONCENTRATE (APCC) FOR ON-DEMAND TREATMENT OF JOINT BLEEDS IN HEMPHILICS WITH INHIBITORS: A SYSTEMATIC REVIEW AND BAYESIAN META-REGRESSION SURVIVAL MODEL WITH TIME-DEPENDENT COVARIATES**

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**OBJECTIVES:** The recent FENOC 2006 comparative trial reported comparable efficacy for RFVIIa and APCC in the treatment of joint bleeds in hemophiliacs with inhibitors. A literature-based Bayesian meta-regression analysis was carried out to place these results within the context of earlier, non-comparative studies and to identify key variables influencing treatment efficacy. **METHODS:** A systematic search of the literature identified 15 studies reporting usable and relevant data, which were pooled in a Bayesian random-effects survival model. A repeating Gompertz hazard function was selected to model an initial increase in the hazard of bleed resolution after each injection, followed by a decrease until the next injection was administered. Model covariates included medication type and the combination of the time-