tolerated at infusion volumes, intervals and rates comparable to pre-study administration.

250 PHARMACOKINETICS OF HUMAN IMMUNOGLOBULIN G, 10%, ADMINISTERED INTRAVENOUSLY (IGIV), SUBCUTANEOUSLY (IGSC) OR FACILITATED SUBCUTANEOUSLY WITH RECOMBINANT HUMAN HYALURONIDASE (IGHY) IN PATIENTS WITH PRIMARY IMMUNODEFICIENCIES

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Introduction: Immunoglobulin infusion, facilitated subcutaneously with recombinant human hyaluronidase (IGHy) improves bioavailability (area under the concentration-time curve [AUC]) vs IGIV, compared to IGSC vs IGIV, thereby decreasing need for multiple infusion sites and permitting infusion rates and treatment frequencies equal to IGIV.

Objective: To report the final pharmacokinetic analysis from a phase 3 study of IGHy in patients with primary immunodeficiencies (PI).

Methods: Patients continued with their pre-study IGIV dosage and frequency, followed by 12-month IGHy treatment. 75 U of rHuPH20/g IgG was given SC followed by IgG 10% (108% of IGIV dose). IgG dosing was adjusted based on trough level to target AUC equivalence to IGIV. Pharmacokinetic parameters of IGHy vs. IGIV and IGSC from the previous SC study are reported.

Results: Of the 83 patients treated with IGHy, pharmacokinetic analysis was performed on 60 patients aged ≥12 years. Ratio of IGHy to IGIV dose to achieve an equivalent AUC was 108%. AUC_{IGHy}/AUC_{IGIV} was pharmacokinetically-equivalent at 93.3%. IGHy required a lower dose than IGSC to reach the same AUC_{IGIV}. Median IgG peaks (mg/dL) were 1550 using IGHy vs 2190 and 1410 for IVIG and IGSC, respectively. Median trough using IGHy was 1040 vs 1010 and 1260 for IGIV and IGSC, respectively.

Conclusion: At 3-4-week intervals, IGHy provided bioavailability (per AUC) similar to IGIV at a lower median dose compared with IGSC. IGHy provides a lower peak IgG concentration compared with IGIV, similar to weekly SC, with trough levels similar to every 3- or 4-week IGIV treatment.

288 ESTIMATING THE PROTECTIVE CONCENTRATION OF ANTI-PNEUMOCOCCAL CAPSULAR POLYSACCHARIDE ANTIBODIES IN PAEDIATRIC PATIENTS WITH PRIMARY IMMUNODEFICIENCY DISEASE (PID) TREATED WITH INTRAVENOUS IMMUNOGLOBULIN (MULTIGAM®)

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Introduction: S.pneumoniae diseases are an important public health problem worldwide. Appropriate intravenous immunoglobulin (IVIG) replacement therapy in PID patients is important in preventing severe bacterial infections. How to estimate the trough level of protective anti-pneumococcal antibodies (APAb) is not established. Based on vaccine-efficacy studies, the APAb minimum protective levels (0.35/ 0.2 mg/ml according ELISA conditions) were determined (WHO, 2008).

Objective: A statistical assessment was performed of peak and trough specific APAb contents, in IVIG-treated PID paediatric patients in the context of a GCP prospective, multicenter, open label clinical study.

Methods: Twenty-two patients were treated during 6 consecutive IVIG infusions. Multigam® is produced from donations collected in Belgium. Peak and through APAbs were determined in plasma patients and in IVIG batches by a validated high-throughput quantifying process using 16 specific ELISAs ±22F-preincubation.

Results: In conditions known to measure protective APAbs against invasive pneumococcal disease, 90% trough patient samples contain ≥0.35 µg/ml for most serotypes, 88-85% of the samples for 9N, 1, 3 and 70-69% for 4 and 12F. With an additional 22Fpreabsorption, 90% trough patient samples contain ≥ 0.2 µg/ml for most serotypes, 87% for APAb1 and 65

to 33% for APAb 9V, 4 and 12F. All peak values complied with the WHO thresholds. Trough GMC APAbs 14, 6B, 19A, 19F concentration were ³1 μg/ml, a level thought to protect against pneumonia. A good relation was found (P< 0.001) between APAbs trough levels and their contents in IVIG.

Conclusion: IVIG-treated patient plasma contains the required protective serospecific APAb levels against IPD.

713 SAFETY AND TOLERABILITY OF HUMAN IMMUNE GLOBULIN SUBCUTANEOUS (IGSC), 20%: INTERIM ANALYSIS OF A PHASE 2/3 STUDY IN PATIENTS WITH PRIMARY IMMUNODEFICIENCIES (PI)

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Introduction: Immunoglobulin (IG) products formulated at higher protein concentrations allow for smaller subcutaneous (SC) infusion volumes compared with less concentrated products. IGSC, 20% is a new ready-for-use, sterile, liquid preparation of highly purified, functionally intact human IgG formulated specifically for SC administration. In order to develop IGSC, 20% as a treatment option, a phase 2/3 study was initiated in patients with PI in Europe.

Objective: To report safety and tolerability results from an interim analysis of a data snap-shot in July 2012.

Methods: This is a prospective, open-label, non-controlled, multicenter study in approximately 47 patients with PI aged ≥2 years. Study duration is as follows: Epoch 1; IGSC 16% or IVIG 10% treatment for 3 months at pre-study doses and intervals, and Epoch 2; treatment period with once-weekly IGSC 20% for 12 months. Twenty-three of twenty-seven patients who have started on the study are currently in Epoch 2. During the study, IgG trough levels >5 g/L are to be maintained. The primary endpoint is acute serious bacterial infection rate. Efficacy, safety, and pharmacokinetic parameters will be evaluated at study completion.

Results: The interim analysis will include number and rate of serious or severe related AEs; temporally associated local or systemic AEs classified by severity; all infections; number of infusions; percentage of infusions requiring adjustment or not completed. Additionally, infusion volumes per site and tolerability as well as IgG trough levels will be assessed.

Conclusion: Data assessing the safety and tolerability of IGSC 20% in patients with PI will be reported.

741 POSACONAZOLE AS SUPPRESSIVE ANTIFUNGAL THERAPY IN CHILDREN WITH CHRONIC GRANULOMATOUS AND INVASIVE FUNGAL DISEASE

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Introduction: Invasive fungal disease (IFD) is a feared complication in CGD patients. Posaconazole (PSZ) has been used as rescue therapy in this setting, but data on its usefulness as primary or secondary prophylaxis are scarce. Routine therapeutic drug monitoring (TDM) is desirable in children receiving PSZ. Trough levels are currently recommended to be > 0.5-0.7 μg/ml.

Objective: To describe the efficacy, tolerability and compliance of PSZ as suppressive therapy in our CGD paediatric cohort, emphasizing the importance of TDM.

Methods: Data from all patients who suffered an IFD in the last 10 years were collected. Patients were initially receiving PSZ following pediatric preliminary dosing recommendations. PSZ-C_{trough} levels were quantified using HPLC and considered to be effective if >0.5 μg/ml. Initial dosage was proportionally adjusted to reach this target level, depending on tolerability.

Results: Eight out of 20 children presented at least one episode of IFD, two of them under primary prophylaxis with itraconazole. When PSZ was instituted as suppressive therapy, plasma levels were under target at least once in five patients, thus dosage adjustment was needed. During the study period, only one patient presented a new IFD episode (*Scedosporium apiospermum* invasive pulmonary infection), despite PSZ-C_{trough} levels of 0.57μg/ml and the strain has been inhibited *in vitro* by posaconazole (MIC: 0.19 μg/ml).