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CLINICAL EVIDENCE SUPPORTED BY A MODEL-BASED APPROACH AND REAL WORLD DATA FOR THE DEVELOPMENT OF C.E.R.A. (CONTINUOUS ERYTHROPOIETIN RECEPTOR ACTIVATOR) IN PEDIATRIC PATIENTS WITH ANEMIA DUE TO CHRONIC KIDNEY DISEASE

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Background C.E.R.A. indicated in Chronic Kidney Disease adult patients to correct and maintain hemoglobin (Hb) levels is approved in Europe and US since 2007; pediatric development is ongoing. A 20-week open-label Phase II study (NH19707) of intravenous (IV) C.E.R.A. in patients aged 5–17 years was conducted and data collected was analysed with adult data¹. Objectives were to determine the pharmacokinetic/pharmacodynamic (PK/PD) characteristics of C.E.R.A. in a broad population, to simulate treatment outcomes of C.E.R.A. administered IV and subcutaneous (SC) in pediatric patients and compare them to NH19707 data and Real World Data (RWD).

Methods PK and Hb data from 63 pediatric patients were pooled with 400 adult patients IV and SC data and analysed using models previously developed in adults². Simulations of treatment outcomes with C.E.R.A. administered IV and SC were performed. Assumptions on SC bioavailability in pediatric patients were based on previous darbepoetin data³. Model inferences were challenged versus RWD obtained in 158 pediatric patients receiving C.E.R.A. SC (N=126) or IV (N=32) from registries maintained by the International Pediatric Dialysis Network (IPDN, www.pedpd.org).

Results The adult PK and PK/PD models adequately described the pediatric data and indicated a similar exposure-response relationship in both populations. C.E.R.A. doses were adjusted to Hb levels during the simulation process to reflect clinical practice; simulated Hb levels matched observations. Furthermore, simulated median monthly C.E.R.A. doses following Hb stabilization were 105 µg (95% prediction interval 72–159 µg) for SC and 84 µg (60–123 µg) for IV, in good agreement with those reported in the IPDN registry: 100 µg and 80.4 µg, respectively.

Conclusion The PK/PD characteristics of C.E.R.A. are similar between adult and pediatric populations. Simulations of clinical outcomes in accordance with clinical trial data and RWD provided sufficient clinical evidence to support pediatric plans optimization subsequently approved by FDA and EMA.

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Disclosure(s) Chanu P is employee and holds stocks in F Hoffmann-La Roche Ltd, was employee of Certara Consulting Services, Certara, Princeton, NJ, USA and contractor to F Hoffmann-La Roche Ltd at the time of this work. Weichert A is employee of F Hoffmann-La Roche Ltd. Schaefer F has received consulting and speaker honoraria from F Hoffmann-La Roche Ltd. Meyer Reigner S is employee of F Hoffmann-La Roche Ltd. Reigner B is employee and holds stocks in F Hoffmann-La Roche Ltd. Frey N is employee of F Hoffmann-La Roche Ltd.

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APPROPRIATENESS OF ANTIBIOTIC PRESCRIPTIONS FOR CHILDREN AND ADOLESCENTS ATTENDING EMERGENCY DEPARTMENTS FOR PHARYNGOTONSILLITIS

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Background Qualitative and quantitative differences in the antibiotic prescription profiles for paediatric outpatients have been found between and within countries, and Italy has a high prevalence of prescriptions and frequent use of cephalosporins and macrolides. Scant data, on small samples, are available concerning the prescription profiles in emergency departments (ED), also in Italy.

Methods The data sources were administrative healthcare databases of the Lombardy region (16% of the national paediatric population).

Children and adolescents between 1 and 13 years old with an ED access and an antibiotic prescription in the first semester of 2012 represented the target population. Subjects with ED access, hospital admissions, or antibiotic prescriptions in the previous two months were excluded, and the analyses were focused on children visited for pharyngotonsillitis.

The percentage of subjects receiving amoxicillin (first-choice antibiotic) and the percentages receiving macrolides or cephalosporins (second-choice therapies) were estimated.

Results During the observation period 23,216 children attended the ED for upper respiratory tract infections, 9,611 of which were visited for pharyngotonsillitis. In all, 5,427 (56%) children with pharyngotonsillitis received an antibiotic prescription: 24% were given amoxicillin and 18% received macrolides or cephalosporins. The percentage of children treated with amoxicillin decreased with increasing age (from 31% in 1–2 year olds to 15% in 10–13 year olds). On the contrary, the prescription of second choice treatments increased with age, reaching 23% in children 10–13 years old. Only in 5 out of 56 EDs more than half of children with pharyngotonsillitis received amoxicillin, while in 5 other EDs the first-choice antibiotic was never prescribed.