Plenary Paper # 2001

EFFECTS OF THE CDC'S 2016 OPIOID GUIDELINES ON PEDIATRIC AND ADULT PATIENTS WITH SICKLE CELL DISEASE

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Background: New guidelines were instituted by the Centers for Disease Control and Prevention (CDC) in 2016 for the prescription of opioid analgesics. Despite acknowledgement that it was not intended to restrict opioid therapy to individuals with sickle cell disease (SCD), the patients stated that it decreased access to opioid analgesics. The CDC is seeking evaluations of the intended and unintended impact of the guideline on patient outcomes.

Objectives: To evaluate the effect of the *CDC Guidelines for Prescribing Opioids for Chronic Pain* on prescribing practices and health outcomes among pediatric and adult patients with SCD.

Design/Method: This retrospective cohort study employed an interrupted time series analysis using the IBM® MarketScan® Commercial Database (1/1/2011-12/31/2019). Individuals who were ≥1 year old, had ≥3 SCD diagnoses documented within 5 years, and no cancer diagnosis were included. Prescription opioid use outcomes (opioid prescription rate, mean total morphine milligram equivalents [MME] per patient, mean daily MME per opioid prescription, mean number of days supplied per opioid prescription) and health outcomes (rates of vaso-occlusive crisis [VOC]-related emergency department [ED] visits and hospitalizations) were measured on a monthly basis. Segmented regressions (breakpoint: March 2016) were conducted for all outcomes to compare their trends before and after the guideline release.

Results: Among 14 979 patients (1-65 years old, 56.9% female) included, 5 459 were pediatric patients (age<18; mean[SD] age=8.3[5.3]) and they experienced significant decreases in the total MME per patient (–7 MME/month, P=0.016) and the number of days' supplied per prescription (-0.03 days/month, P<0.001), but a significant increase in the VOC-related hospitalization rate (+0.10 hospitalizations/100person-month, p=0.022) after the guideline release vs. pre-guideline period. There was no significant change in the opioid prescription rate, daily MME per prescription, or the rate of VOC-related ED visits. Among 9 520 adult patients (age≥18; mean[SD] age=36.1[12.2]), there were significant decreases in the opioid prescription rate (-0.41 prescription/100person-month, p<0.001), total MME per patient (–221 MME/month, P=0.001), daily MME per prescription (–11 MME/month, P<0.001), and days' supplied per prescription (-0.05 days/month, P<0.001), but significant increases in the rates of VOC-related ED visits (+0.07 visits/100person-month, p=0.045) and hospitalizations (+0.20 hospitalizations/100person-month, p<0.001) in the post-guideline vs. pre-guideline period.

Conclusion: The CDC guideline release timing corresponded with decreases in opioid prescribing practices and unfavorable health outcomes among patients with SCD. The guideline may have an unintended negative impact on this population, with greater impact in adults

compared to pediatric patients.

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Plenary Paper # 2002

BETIBEGLOGENE AUTOTEMCEL IN PEDIATRIC PTS WITH TRANSFUSION-DEPENDENT β-THALASSEMIA IN PHASE 3 TRIALS

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Background: Phase 3 studies evaluating betibeglogene autotemcel (beti-cel) gene therapy in patients with transfusion-dependent β-thalassemia (TDT), HGB-207 (non-β^0/β^0 genotypes; NCT02906202) and HGB-212 (β^0/β^0, $\beta^0/\beta^{+IVS\text{-}I\text{-}110}$, $\beta^{+IVS\text{-}I\text{-}110}/\beta^{+IVS\text{-}I\text{-}110}$ genotypes; NCT03207009), demonstrated positive outcomes in adults.

Objectives: We describe interim efficacy and safety of beti-cel in pediatric patients treated in HGB-207 and HGB-212.

Design/Method: Autologous CD34+ cells were transduced ex vivo with BB305 lentiviral vector to produce beti-cel. Patients underwent pharmacokinetic-adjusted busulfan-based myeloablation followed by beti-cel infusion. Transfusion independence (TI; weighted average hemoglobin [Hb] ≥9 g/dL without red blood cell transfusions for ≥12 months) was the primary endpoint. Data are presented as median (min–max).

Results: As of 9 March 2021, 27 pediatric patients were treated and followed for 25.5 (4.1–41.5) months: 16 patients <12 years (HGB-207: n=8; HGB-212: n=8) and 11 patients ≥12–<18 years at assent (HGB-207: n=6; HGB-212: n=5). The youngest patients were 4 years of age (n=3). Neutrophil and platelet engraftment occurred at Day 26 (16–39) and 50 (20–94), respectively. TI was achieved in 10/12 evaluable patients <12 years and 10/10 evaluable patients ≥12–<18 years. The duration of ongoing TI was 23.2 (12.5–37.9) months in pediatric patients (n=20), with TI rates (90.9% [20/22]) similar to adults (85.7% [12/14]).

Weighted average Hb during TI in patients <12 years and ≥12–<18 years was 10.0 (9.7–11.5) g/dL (n=10) and 11.7 (9.6–13.2) g/dL (n=10), respectively. At last visit, beti-cel-derived adult Hb (HbA^{T87Q}) was 8.6 (6.0–10.2) g/dL (n=10) and 9.4 (4.4–11.8) g/dL (n=10), respectively. In adults, the weighted average Hb during TI was 12.6 (9.3–13.7) g/dL and HbA^{T87Q} at last visit was 9.6 (7.9–12.7) g/dL (n=12). Markers of ineffective erythropoiesis and iron overload improved in pediatric patients who achieved TI.

Non-hematologic ≥Grade 3 adverse events (AEs) in ≥3 patients <18 years were stomatitis (n=15), febrile neutropenia (n=15), epistaxis (n=6), decreased appetite (n=5), increased alanine aminotransferase (n=3), hypoxia (n=3), pharyngeal inflammation (n=3) and pyrexia (n=3). Veno-occlusive liver disease occurred in 3 patients <18 years (Grade 4 [n=2], Grade 2 [n=1]); events resolved with defibrotide. Drug-product related AEs were reported in 4 patients (thrombocytopenia and tachycardia [n=1 each]; abdominal pain [n=2]). No replication-competent lentivirus, clonal predominance or insertional oncogenesis was reported.

Conclusion: Pediatric patients with diverse TDT genotypes achieved TI rates comparable to adults. The safety profile of the treatment regimen was reflective of busulfan myeloablation. beti-cel is a potentially curative gene therapy for pediatric patients with TDT through the ability to achieve TI with near-normal to normal Hb levels.

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