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USE OF OPIOIDS AND BURDEN OF DISEASE IN PATIENTS (PTS) WITH SICKLE CELL DISEASE (SCD) IN BRAZIL VS THE OVERALL POPULATION OF THE INTERNATIONAL SICKLE CELL WORLD ASSESSMENT SURVEY (SWAY)

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Goals: SCD is a group of inherited blood disorders associated with short- and long-term complications. Acutely painful vaso-occlusive crises (VOCs) are the hallmark of SCD and can lead to hospitalization. SWAY assessed the burden of SCD, the impact of disease on pts'lives and management of SCD. We evaluate geographical variation in pt-reported use of opioids and burden of disease among pts with SCD who participated in SWAY. **Materials and methods:** SWAY was a cross-sectional survey of pts with SCD and healthcare professionals and was developed by SCD experts, pt advocates and Novartis. Opinions were captured using a 1–7 Likert scale for some questions (a score of 5–7 indicated high satisfaction/impact/agreement). **Results:** In total, 2145 pts from 16 countries (Bahrain, Brazil, Canada, France, Germany, Ghana, India, Italy, Lebanon, Netherlands, Nigeria, Oman, Panama, Saudi Arabia, UK and USA) were surveyed (3 April–4 October 2019). Mean (SD) age of pts was 25 (13.1) years in the overall population and 23 (14.0) years in Brazil (n = 260). Globally, 53% of pts reported ever having received opioids and 34% reported use of them at the time of the survey. Substantially fewer pts in Brazil reported use of opioids (ever, 37%; at the time of the survey, 20%) than in the overall population. In Brazil, 28% of pts reported ≥ 5 days of background pain in a week (ie chronic pain) compared with 23% in the overall population. In Brazil vs the overall population, chronic pain was reported by 38% vs 32% of pts who reported having received opioids and by 22% vs 12% of pts who reported never having taken opioids. Most pts who reported ever taking pain management medication both in the overall population and in Brazil also reported a high level of concern (Likert score 5–7) over the perception of taking it (overall population, 61%; Brazil, 60%). More pts in Brazil vs the overall population reported concern over the side effects of pain management medication (75% vs 69%) and expressed a desire for alternatives to their ongoing pain management medication (78% vs 72%). **Discussion:** Results from this analysis of SWAY show that self-reported use of opioids was much lower in Brazil than in the overall population, despite the degree of self-reported chronic pain in Brazil being relatively high compared with the overall population. Chronic pain was more common in pts who reported having taken opioids than in pts who had never taken them, both in Brazil and in the overall population. The low level of opioid use in Brazil may be related to several factors, including pt concern over the side effects of pain management medication, as well as other issues, such as access, cost and levels of disease awareness among HCPs; however, these factors are beyond the scope of this analysis. The difference in sample sizes, as well as possible differences in pt demographics, between Brazil and the overall population should also be noted. **Conclusion:** Around half of pts who participated in SWAY reported taking opioids at some point during their lives. The proportion in Brazil was much lower than this and did not appear to align with the number of pts in Brazil reporting chronic pain. **Funding:** Novartis Pharmaceuticals provided sponsorship and was involved in running SWAY.

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VASO-OCCLUSIVE CRISIS IN A 12-MONTH PERIOD: PREVALENCE AMONG BRAZILIAN PATIENTS WITH DIAGNOSIS OF SICKLE CELL DISEASE

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Background and aims: Vaso-occlusive crisis (VOC) is one of the hallmark of sickle cell disease (SCD). It is defined as a multicellular adherence causing a painful vase-occlusion, driving the acute and chronic pain associated with the disease, as well as the complication by end-organ damage. In Brazil, it is estimated that about 30% of SCD patients have at least three VOCs per year. This study aims to determine VOC prevalence among SCD patients in Brazil, as well as to estimate the frequency of crises in a 12-month period. **Material and methods:** Data were obtained through a multi-country (16 countries) survey of unmatched SCD patients and HCPs developed by international SCD experts, patient advocacy groups and Novartis (The SWAY Survey). The subjects were invited to participate via their healthcare professional or patient association groups. All patients with the diagnosis of SCD were eligible for inclusion and those aged 6 to 11 years old completed the questionnaire with a caregiver/parent/legal guardian. VOC characteristics, such as mean number of crises and management strategies

in the previous 12-month period before survey, were assessed. Patients were also asked to classify which level of pain would cause them to use strong analgesics (such as opiates), to seek the assistance of a medical professional, to miss work/school and to miss important social events in a scale ranging from 0 (not severe al all) to 10 (worst imaginable). Descriptive analyses and chi-square tests were performed. **Results:** A total of 260 Brazilian patients of all genotypes (self-reported) with diagnosis SCD were included, most of them female (58.5%; n = 152) with a mean age of 23.1 (SD: 14.0) years. The prevalence of at least one VOC in the previous year was 87.7% (n = 228) for total sample, 88.3% (n = 98) among those aged 6-16 years old and 87.2% (n = 130) among those >16 years. Patients had a mean of 4.0 (SD = 4.6) crises, 12.3% (n = 32) had only one episode, 44.6% (n = 116) 2-4, 25.4% (n = 66) 5-10 and 5.4% (n = 14) ≥11 episodes. A similar percentage distribution was observed when the subjects was stratified by age. No difference in the frequency and distribution of VOC was observed in patient with or without HU (HU 87.6% *vs* without HU 87.9%; p = 1.000) and the categories of frequency of episodes during the year (p = 0.799). Considering crisis management, 32.3% (n = 84) reported to deal with it at home, most frequently due to reasons such as a poor experience at the emergency room or hospital (n = 41; 48.8%). The patients with the worst imaginable level of pain (a pain score of 10) led patients to use analgesics, to seek for assistance, to miss work/school and social events for 24.9%, 24.1%, 23.1% and 21.3% of patients, respectively. **Discussion:** Almost all patients experience at least one VOC in a 12-month period, regardless the age and HU use. Furthermore, the frequency of crisis may be greater than five for about 30% of patients in all age groups. Data is consistent with those previously reported and reinforces the importance of VOC on SCD management. **Conclusion:** The vast majority of Brazilian SCD patients reported at least one episode of VOC in a 12-month period, regardless of age. Thus, VOC is still an important issue for Brazilian SCD patients and interventions able to decrease its occurrence are still needed.

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HEMOSTASIA E PAREDE VASCULAR: DOENÇAS DA COAGULAÇÃO E FIBRINÓLISE

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A FIRST-IN-HUMAN FOUR-YEAR FOLLOW-UP STUDY OF DURABLE THERAPEUTIC EFFICACY AND SAFETY OF AAV GENE THERAPY WITH VALOCTOCOGENE ROXAPARVOVEC FOR SEVERE HEMOPHILIA A

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Background: Long-term clinical benefit has been demonstrated in people with hemophilia A following a single administration of the investigational gene therapy valoctocogene roxaparvovec (AAV5-hFVIII-SQ). Safety, clinical effectiveness, and mechanisms of episomal vector DNA persistence have been previously described, but outstanding questions pertain to the maintenance of these attributes over increasing durations of follow-up. **Aims:** The four-year safety, efficacy, and durability of valoctocogene roxaparvovec is evaluated in a Phase 1/2 clinical study for severe hemophilia A. **Methods:** Adult male study participants with severe hemophilia A were followed for up to four years after receiving a single intravenous dose of valoctocogene roxaparvovec at 6×10^{13} vg/kg (n = 7) or 4×10^{13} vg/kg (n = 6). **Results:** After four (6×10^{13} vg/kg) or three (4×10^{13} vg/kg) years, all study participants demonstrated clinically meaningful FVIII activity levels with reductions in bleeds and FVIII usage. Following withdrawal from prophylaxis, annualized bleeding rate declined from pre-treatment mean by 95% at year four in 6×10^{13} vg/kg participants, and 93% at year three in 4×10^{13} vg/kg participants. Despite FVIII activity levels continuing to decline at a shallow rate, all patients in both cohorts remained off prophylaxis. After four years, the safety profile of valoctocogene roxaparvovec remained favorable and unchanged, with no inhibitor development or treatment-related ALT elevations beyond year one. **Conclusions:** Four-year follow-up data demonstrate that gene transfer with valoctocogene roxaparvovec leads to substantial and sustained FVIII activity levels, clinically relevant reductions in self-reported bleeding episodes, and significant reductions in FVIII replacement infusions. These data from the first-in-human trial represent the most up-to-date, long term follow-up data currently available for the investigational use of AAV-mediated therapy for hemophilia A.

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