P1503 REAL WORLD DATA ON EFFICACY OF PHARMACEUTICAL-GRADE L-GLUTAMINE IN PREVENTING SICKLE CELL DISEASE-RELATED ACUTE COMPLICATIONS AND HEMOLYSIS IN PEDIATRIC AND ADULT PATIENTS.

Topic: 26. Sickle cell disease

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Background: Oxidative stress is one of the key contributors to the pathophysiology of sickle cell disease (SCD) and related complications including acute pain (vaso-occlusive crisis or VOC), tissue ischaemia, stroke, and acute chest syndrome (ACS). L-glutamine (L-gln), a precursor of nicotinamide adenine dinucleotide (NAD), has been shown to play an important role in the regulation of oxidative stress. In the pivotal Phase 3 clinical trial, L-gln demonstrated significant reduction in VOC, hospitalizations, and ACS events compared to placebo in patients with SCD, with or without hydroxyurea (HU) use, over a 48-week period. In September 2021, a re-analysis of the Phase 3 trial data revealed that L-gln decreased the number of VOCs by 45%.

Aims: To confirm the efficacy on clinical observations and hemolysis markers of oral therapy with pharmaceutical-grade L-gln in pediatric and adult patients with SCD at follow-up time points of 24, 48 and 72 weeks.

Methods: In the observational study conducted from October 2019 through April 2021, 19 patients (4 patients from Qatar and 15 patients from French Guiana) were treated with L-gln (0.3mg/kg) twice daily. Laboratory parameters (hemoglobin (Hb) levels, hematocrit, WBC counts, reticulocyte counts, and LDH levels) were measured at baseline and follow-up time points. Clinical parameters (number of VOCs, hospitalizations, days hospitalized, ACS events, and blood transfusions) were documented for the year prior to treatment initiation as baseline values. These parameters were also collected at 24, 48, and 72 weeks from treatment initiation. Adverse events (AEs) were also collected during the treatment period. The data values at 24, 48, and 72 weeks have been annualized. Statistical analysis was performed using MedCalc 20.015.

Results: Compared to baseline, patients had significantly fewer number of VOCs at 24, 48, and 72 weeks following L-gln therapy (median change from 3.0 to 0; p<0.00001). Compared to baseline, there were fewer hospitalizations (median change from 3.0 to 0; p=0.00001) and patients spent fewer days in hospital (median change from 15.0 to 0; p<0.00001). Furthermore, at 24, 48, and 72 weeks, the number of blood transfusions was considerably lower than at baseline (median, from 3.0 to 0; p<0.00001). Following treatment with L-gln, the mean Hb level increased significantly from baseline to 72 weeks (8.2 to 8.8 g/DL; p<0.001) with peak mean increase from baseline of 11.2% at 48 weeks. A similar increasing trend was observed for hematocrit proportions from baseline to 72 weeks (24% to 27%; p=0.01) with highest mean improvement from baseline of 15.5% at 48 weeks. Conversely, mean reticulocyte counts and LDH levels were significantly reduced at follow-up time points compared to baseline (p=0.003 and p=0.001, respectively).

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Summary/Conclusion: This study demonstrated for the first time that L-gln therapy in SCD patients from Qatar and French Guiana resulted in significant improvements in clinical outcomes (number of VOCs, number and duration of hospitalizations, and number of blood transfusions) accompanied by a noteworthy increase in Hb levels and a reduction in markers of hemolysis (reticulocyte counts and LDH levels). Moreover, while 11 ACS events were reported the year before starting L-gln, only 2 ACS events occurred after 12 months of initiation of L-gln. Treatment with L-gln resulted in clinically significant outcomes combined with significant improvement of the hemolysis parameters from baseline through 72 weeks suggesting sustained long-term efficacy. Only a few number of AEs occurred and were mild. No compliance issue was reported.