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Pain and arthralgia adverse events associated with crizanlizumab and voxelotor: Disproportionality analysis of US FDA Adverse Events Reporting System (FAERS)

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Background

- Sickle cell disease (SCD) is a genetic erythrocyte disorder with limited treatment options. According to the Centers for Disease Control and Prevention (CDC), SCD has about 100,000 prevalent cases in the United States (1).
- Annually, over 300,000 babies are born with SCD worldwide, and approximately 1 out of 365 Black/African American babies are born with SCD in the United States (1). About 3.5 million individuals in the United States are heterozygous carriers of sickle hemoglobin (HbS; HbAS genotype) (2).
- In 2019, the FDA approved a monoclonal antibody, crizanlizumab (Nov 15, 2019), and an HbS polymerization inhibitor, voxelotor (Nov 25, 2019), for the treatment of SCD (3, 4).
- As newly approved medications become more widely used in real-world clinical practice, it is important to monitor their safety.

Objective

- This study aimed to assess adverse event reports for arthralgia and pain associated with crizanlizumab and voxelotor.

Methods

- FAERS data were analyzed from January 2020 through September 2021. Adverse events reports of arthralgia and pain were assessed separately for voxelotor or crizanlizumab, and each was compared with all other drugs.
- Search terms were used for Crizanlizumab: “crizanlizumab” and “adakveo”.

Methods

- Search terms were used for voxelotor: “oxbryta” and “voxelotor”.
- Medical Dictionary for regulatory activities (MedDRA) search terms: “arthralgia”, “pain”.
- Reporting odds ratios (RORs), proportional reporting ratios (PRRs), and corresponding 95% confidence intervals (CIs) were calculated using SAS OnDemand for academics.

Results

- With 16,231 reports of arthralgia, reporting rates for crizanlizumab were significantly higher than with other medications (ROR 6.77, 95% CI 3.34-13.71; PRR 6.58, 95% CI 3.33-13.00).
- Alternatively, voxelotor was not associated with arthralgia (ROR 0.75, 95% CI 0.50-1.09; PRR 0.76, 95% CI 0.51-1.11).
- With 85,266 reports of adverse pain events, reporting rates for crizanlizumab were significantly higher than other medications (ROR 15.79, 95% CI 11.97-20.83; PRR 11.28, 95% CI 9.3, 13.67).
- Reporting rates of adverse pain events for voxelotor were also significantly higher than with other medications (ROR 1.38, 95% CI 1.22-1.57; PRR 1.37, 95% CI 1.21- 1.55), though at a lower magnitude compared to crizanlizumab.

Results

	Arthralgia			Pain		
	Present	Absent	Total	Present	Absent	Total
Voxelotor	26	6648	6674	454	6220	6674
Other drugs	16,205	3,126,054	3,142,259	116,978	3,025,281	3,142,259
Total	16,231	3,132,702	3,148,933	117,432	3,031,501	3,148,933
Crizanlizumab	10	226	236	67	169	236
Other drugs	16,221	3,132,476	3,148,697	117,365	3,031,332	3,148,697
Total	16,231	3,132,702	3,148,933	117,432	3,031,501	3,148,933

		ROR	95% CI	PRR	95% CI
Voxelotor	Arthralgia	0.75	0.51, 1.11	0.76	0.52, 1.11
	Pain	1.89	1.72, 2.08	1.83	1.67, 2.00
Crizanlizumab	Arthralgia	8.55	4.54, 16.1	8.23	4.48, 15.09
	Pain	10.24	7.72, 13.59	7.62	6.22, 9.33

Conclusion

- Our disproportionality analysis identified an association between crizanlizumab and arthralgia, and pain. Alternatively, voxelotor was not associated with arthralgia and was weakly associated with pain.
- Further studies are needed to confirm these findings and to quantify the real-world safety profiles of these newer medications for SCD.

References

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