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Safety Profile and Adverse Drug Reactions of Radium-223 in the EudraVigilance Database: A Retrospective Descriptive Analysis

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INTRODUCTION & AIM

Radium-223 dichloride (Ra-223) is an alpha-emitter radiopharmaceutical approved for the treatment of metastatic castration-resistant prostate cancer with symptomatic bone metastases. Ra-223 preferentially targets regions of elevated bone turnover, delivering high-linear energy transfer radiation that induces double-strand DNA breaks while minimizing harm to adjacent tissues.

Although its proven survival advantage and positive tolerability profile in clinical studies, concerns persist regarding hematological toxicity and underreporting of adverse drug reactions (ADRs) in the real-world.

Post-marketing pharmacovigilance databases are essential for detecting unusual, delayed, or severe adverse reactions that may not be well recorded in pre-approval trials.

AIM

This study aimed to characterise the safety profile of Ra-223 based on spontaneous ADR reports submitted to the EudraVigilance database.

METHOD

The data extraction was conducted through the publicly accessible EudraVigilance Data Analysis System. A retrospective descriptive analysis was conducted using EudraVigilance data covering all ADR reports associated with Ra-223 from 2013-2023.

The analysis was structured based on the following variables available in the exported EudraVigilance files:

- Year and notification's country
- Sex and Age Group
- Type of Reporter (Healthcare Professional/Non-Healthcare Professional)
- Seriousness Criteria (e.g., hospitalization, death, disability)
- Outcome
- System Organ Class (SOC) classification of the reaction
- Reaction counts per SOC and per age group

The events were classified according to MedDRA® terminology (version available at the time of data export) and grouped by SOC and Preferred Term (PT) where applicable.

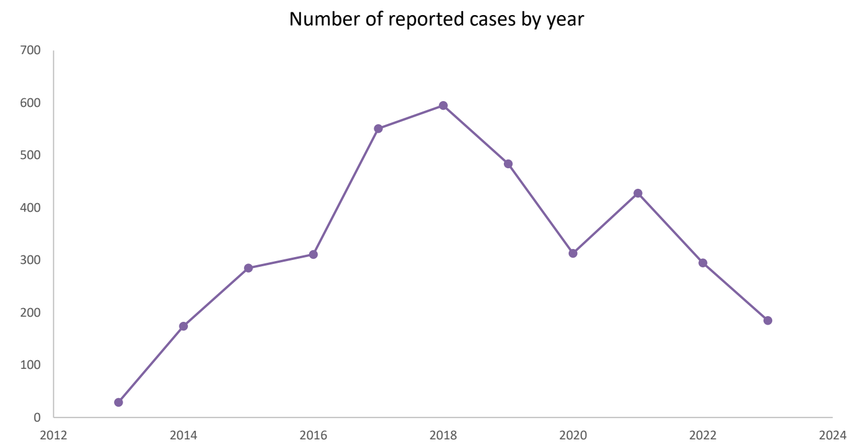
The seriousness and outcome fields were coded following EudraVigilance classification standards.

RESULTS & DISCUSSION

A total of 3650 notifications were analyzed, corresponding to 8919 individual adverse reactions. Healthcare professionals were responsible for most reported cases, which is expected, since Ra-223 is administered in a hospital under medical supervision.

RESULTS & DISCUSSION

A progressive increase in notifications is observed until 2018, the peak's year of reported cases occurred.



EudraVigilance, 2013-2023

As expected, most cases occurred in male patients (approximately 87%), since Radium-223 is indicated for the treatment of metastatic prostate cancer to the bone. Notifications in women are residual, and in about 13% of cases the sex was not specified, reflecting common gaps in pharmacovigilance databases. Regarding age distribution, it was observed that more than half of the patients (53%) were over 85 years old, and about 35% were between 65 and 85 years old. This predominance of elderly patients is consistent with the epidemiological profile of prostate cancer, which mainly affects older men. The most frequent classes of adverse reactions (SOCs) were general disorders and administration site conditions; benign, malignant and unspecified neoplasms and blood and lymphatic system disorders. This is consistent with the pharmacological profile of Ra-223, whose action is centered on bone tissue, also affecting the bone marrow and justifying the hematological changes observed. Among the analyzed notifications, 559 cases had a fatal outcome, another 539 cases did not show recovery, and only 127 patients recovered completely. In 181 cases, the patient was in the process of recovery at the time of notification, and in 2236 notifications the outcome was unknown, reflecting the lack of clinical follow-up in spontaneous reports.

CONCLUSION

Ra-223 exhibits a generally acceptable safety profile, though haematological toxicities remain the most recurrent and clinically significant adverse effects. The findings reinforce the need for continuous pharmacovigilance, structured reporting, and clinician awareness to mitigate risks and ensure patient safety in radionuclide therapy.

FUTURE WORK / REFERENCES

Future research should focus on comparative pharmacovigilance analyses between alpha- and beta-emitter radiopharmaceuticals and development of structured reporting tools adapted to radiopharmaceuticals.

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