**Alkaline Phosphatase Decline and Pain Response as Markers for Overall Survival in Patients with Metastatic Castration-Resistant Prostate Cancer Treated with Radium-223 in the REASURE Study**

**BACKGROUND**

- Radium-223 (Ra) is an established targeted alpha therapy that prolongs overall survival (OS) in patients with bone-predominant metastatic castration-resistant prostate cancer (mCRPC).
- During the development of bone metastases, prostate cancer cells and cancer-associated osteoblasts secrete elevated levels of alkaline phosphatase (ALP).
- In the phase 3 ALPHANAPA study, pts treated with Ra as compared to placebo had a significantly increased OS and normalization of ALP levels.
- A population-based analysis of pts with mCRPC showed that meaningful pain responses were associated with "Ra therapy."

**OBJECTIVE**

- To evaluate potential associations of ALP decline and pain response with OS during Ra treatment.
- To define pt subgroups with different survival outcomes, which may help improve disease management strategies.

**METHODS**

- **REASURE** is an ongoing, prospective, non-interventional study assessing the long-term safety of "Ra in pts with mCRPC.
- The closest ALP value to week 12 between weeks 8 and 16 was selected for all pts. Pts treated with "Ra" were grouped by "any ALP decline" vs "no decline" from baseline at that time.
- Pain levels were assessed with the Brief Pain Inventory-Short Form (BPI-SF), describing the worst pain in the last 24 hours. The cut-off point for bl/col baseline BPI-SF <1.0.
- Pts with baseline BPI-SF >1.0 were grouped by "pain response" (decrease in >3 points from BL-BPI SF) or "no pain response." (decrease or decrease of >3 points in BPI SF score during treatment.
- Median OS is provided with a hazard ratio (HR) 95% confidence interval (CI).

**RESULTS**

- 779 pts with ALP measurements at both baseline and week 12 were included in the analysis.
- 624 (80%) pts had a decline in ALP and 155 (20%) had no decline.
- While best outcomes were achieved when pts had at least one of ALP decline, no pain at baseline or pain response, less ALP decline without pain response was the worst prognostic indicator for OS.
- These results may help physicians and pts to monitor markers of pain and ALP decline during "Ra" treatment that may be associated with survival, and therefore may help to support clinical decisions.

**REFERENCES**


**ACKNOWLEDGMENTS**

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**DISCLOSURES**

- All presenters and authors have no financial and personal relationships with other people or organizations that could influence their work.

**Table 1. Summary of baseline and characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All pts (N=785)</th>
<th>No ALP decline (N=624)</th>
<th>Any ALP decline (N=155)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>72 (65–79)</td>
<td>72 (65–79)</td>
<td>72 (65–79)</td>
</tr>
<tr>
<td>EOD</td>
<td>72 (65–79)</td>
<td>72 (65–79)</td>
<td>72 (65–79)</td>
</tr>
<tr>
<td>PSA (ng/mL)</td>
<td>26 (19–39)</td>
<td>26 (19–39)</td>
<td>26 (19–39)</td>
</tr>
<tr>
<td>ALP (U/L)</td>
<td>147 (133–167)</td>
<td>147 (133–167)</td>
<td>147 (133–167)</td>
</tr>
</tbody>
</table>

**Table 2. Adjusted hazard ratios for overall survival**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EOD</td>
<td>1.00 (0.86–1.16)</td>
</tr>
<tr>
<td>PSA</td>
<td>1.00 (0.86–1.16)</td>
</tr>
<tr>
<td>ALP decrease</td>
<td>0.63 (0.42–0.95)</td>
</tr>
</tbody>
</table>

**Figure 2. Kaplan-Meier curves of overall survival**

**Figure 1. Design for post hoc analysis of REASURE**

**Figure 3. Associations of ALP decline at Week 12, no baseline pain or pain response with OS**

**Summary of Outcomes**

- Pts with ALP decline at week 12 had longer OS than pts with no ALP decline.
- Pts with pain at baseline and ALP decline at week 12 had similar results of pain response.
- For pts with no pain at baseline, OS trended longer in pts who had ALP decline.

**Figure 2. Kaplan-Meier curves of overall survival**

**Figure 3. Associations of ALP decline at Week 12, no baseline pain or pain response with OS**

**Summary of Outcomes**

- The markers ALP decline and pain response have the potential to be considered jointly when assessing survival outcomes for "Ra therapy.
- ALP decline is a marker for improved outcomes.
- Pain response was associated with longer OS in pts with no ALP decline.
- While best outcomes were achieved when pts had at least one of ALP decline, no pain at baseline or pain response, lack of ALP decline without pain response was the worst prognostic indicator for OS.
- These results may help physicians and pts to monitor markers of pain and ALP decline during "Ra" treatment that may be associated with survival, and therefore may help to support clinical decisions.

**References**


**Acknowledgements**

- Supported by Bayer