Pivekimab sunirine (PVEK) triplet with azacitidine and venetoclax shows broad activity in adverse genetic subsets of relapsed/refractory AML and reduced infusion-related AML

**INTRODUCTION**

**PVEK Background**

- PVEK, also known as IMGN632, is a CD123-targeting antibody-drug conjugate (ADC) comprised of a high-affinity antibody coupled to a DNA-alkylating pseudodimer (IGN) class payload, demonstrating less toxicity to normal marrow progenitors than other DNA-targeting payloads.
- Hypomethylating agents (HMA) and venetoclax (VEN) demonstrate improved outcomes in frontline older/unfit patients with AML but long-term survival remains poor.
- Preclinical data have demonstrated synergy of PVEK when combined with AZA and/or VEN, including in AZA/VEN resistant murine AML models.
- PVEK demonstrated single-agent CR/CRi rates of 22-40% in subgroups of patients with relapsed/refractory AML.

**Methods**

- IMGN632-0802 is an open-label, multicenter, Phase 1b/2 study of PVEK in combination with AZA + VEN in patients with relapsed/refractory AML.
- PVEK triplet with azacitidine and venetoclax shows broad activity in adverse genetic subsets of relapsed/refractory AML and reduced infusion-related AML.

**Safety**

- No bona fide syndrome, veno-occlusive disease, capillary leak, or cytokine release syndrome observed.
- Prior to change in steroid prophylaxis, IRRs primarily consisted of grade 3 rash, chills/rigors; one patient with grade 5 pneumonia observed was grade 1-2 and resolved with limited intervention.
- New IRR prophylaxis: 2 doses of dexamethasone (8 mg) on the day of PVEK administration.

**Efficacy**

- Prior to change in steroid prophylaxis, IRRs primarily consisted of grade 3 rash, chills/rigors; one patient with grade 5 pneumonia observed was grade 1-2 and resolved with limited intervention.
- New IRR prophylaxis: 2 doses of dexamethasone (8 mg) on the day of PVEK administration.

**Subgroup Analysis Overall Response Rate**

<table>
<thead>
<tr>
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<th>CCR</th>
<th>MPLS</th>
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<tbody>
<tr>
<td>FLT3-ITD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IDH2</td>
<td>60%</td>
<td>57%</td>
</tr>
<tr>
<td>ASXL1</td>
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<td>57%</td>
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<tr>
<td>TP53</td>
<td>43%</td>
<td>25%</td>
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<tr>
<td>MPLS</td>
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**CONCLUSIONS**

- **PVEK triplet with AZA+VEN demonstrates anti-leukemic activity across multiple high-risk genetic subsets of patients with relapsed/refractory AML.**
- **Prophylactic steroids added on day 1 have significantly reduced IRRs. After change in prophylaxis, all IRRs observed were grade 1-2 and resolved with limited intervention.**
- **PVEK triplet with AZA+VEN is a promising anti-leukemic combination with a manageable safety profile that warrants further investigation.**
- **Expansion cohorts are now enrolling for patients with newly diagnosed AML (NCT04082664).**