Pivekimab Sunirine (PVEK, IMGN632), a CD123-Targeting Antibody-Drug Conjugate, in Combination with Azacitidine and Venetoclax in Patients with Newly Diagnosed Acute Myeloid Leukemia

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BACKGROUND

In unfit patients with newly diagnosed AML, long-term survival rates exceed 15% with standard treatment alone (1). The triplet regimens of azacitidine (AZA) and venetoclax (VEN) continue to be evaluated as a means of improving outcomes, and recent randomized studies have suggested benefit for the addition of Peterburi (PVEK) in patients with poor-risk cytogenetics. Several prognostic molecular features have been identified that are associated with treatment resistance and poor outcomes and have potential as biomarkers of susceptibility to novel agents. These include inactivating ABAT mutations, among others. In Phase II trials, median time to MRD clearance was 1.87 months (range, 0.79–6.2 months) for patients treated with PVEK + AZA + VEN. The concomitant benefits demonstrated in these studies were not observed with other AML therapies that did not involve PVEK.

PVEK Mechanism of Action:

- PVEK is a first-in-class antibody-drug conjugate (ADC) comprising a high affinity anti-CD123 antibody, chimeric V5 (67% human), and an ADC payload (targeted prodrug). The CD123 antigen is expressed on malignant hematopoietic cells, while the addition of PVEK does not appear to cause toxicity to normal marrow progenitors compared with other AML therapies targeting CD123.

RESULTS: Safety

- In efficacy evaluable patients who demonstrated a CR, CRi, CRp, or CRh, prophylactic antiemetics were used in 12% of patients, and antifungal prophylaxis was used in 1% of patients.

Table 5. Antileukemia Activity

- In patients achieving CCR cycle delay in the AZA+VEN arm as published in the VIALE trial (36%)
- Median time to onset for an edema event (all grades) was 23 days.
- Median time to resolution for all edema events was 6 days.
- Median time to resolution for grade 2 or higher edema events was 7 days.

Table 2. Overall Survival

- Median time to MRD clearance was 1.87 months (range, 0.79–6.2 months) for patients treated with PVEK + AZA + VEN. The concomitant benefits demonstrated in these studies were not observed with other AML therapies that did not involve PVEK.

Table 3. Patient and Disease Characteristics (N=50)

- Median time to MRD clearance was 1.87 months (range, 0.79–6.2 months) for patients treated with PVEK + AZA + VEN. The concomitant benefits demonstrated in these studies were not observed with other AML therapies that did not involve PVEK.

Table 4. Median time to onset of an edema event (all grades) was 23 days.

- Median time to resolution for all edema events was 6 days.
- Median time to resolution for grade 2 or higher edema events was 7 days.

Table 1. Baseline Characteristics

- Median time to onset of an edema event (all grades) was 23 days.
- Median time to resolution for all edema events was 6 days.
- Median time to resolution for grade 2 or higher edema events was 7 days.

Table 6. Baseline Characteristics

- Median time to MRD clearance was 1.87 months (range, 0.79–6.2 months) for patients treated with PVEK + AZA + VEN. The concomitant benefits demonstrated in these studies were not observed with other AML therapies that did not involve PVEK.

Table 7. Baseline Characteristics

- Median time to onset of an edema event (all grades) was 23 days.
- Median time to resolution for all edema events was 6 days.
- Median time to resolution for grade 2 or higher edema events was 7 days.

Table 8. Baseline Characteristics

- Median time to MRD clearance was 1.87 months (range, 0.79–6.2 months) for patients treated with PVEK + AZA + VEN. The concomitant benefits demonstrated in these studies were not observed with other AML therapies that did not involve PVEK.

Table 9. Baseline Characteristics

- Median time to onset of an edema event (all grades) was 23 days.
- Median time to resolution for all edema events was 6 days.
- Median time to resolution for grade 2 or higher edema events was 7 days.

Table 10. Baseline Characteristics

- Median time to MRD clearance was 1.87 months (range, 0.79–6.2 months) for patients treated with PVEK + AZA + VEN. The concomitant benefits demonstrated in these studies were not observed with other AML therapies that did not involve PVEK.

Table 11. Baseline Characteristics

- Median time to onset of an edema event (all grades) was 23 days.
- Median time to resolution for all edema events was 6 days.
- Median time to resolution for grade 2 or higher edema events was 7 days.

Table 12. Baseline Characteristics

- Median time to MRD clearance was 1.87 months (range, 0.79–6.2 months) for patients treated with PVEK + AZA + VEN. The concomitant benefits demonstrated in these studies were not observed with other AML therapies that did not involve PVEK.

Table 13. Baseline Characteristics

- Median time to onset of an edema event (all grades) was 23 days.
- Median time to resolution for all edema events was 6 days.
- Median time to resolution for grade 2 or higher edema events was 7 days.

Table 14. Baseline Characteristics

- Median time to MRD clearance was 1.87 months (range, 0.79–6.2 months) for patients treated with PVEK + AZA + VEN. The concomitant benefits demonstrated in these studies were not observed with other AML therapies that did not involve PVEK.

Table 15. Baseline Characteristics

- Median time to onset of an edema event (all grades) was 23 days.
- Median time to resolution for all edema events was 6 days.
- Median time to resolution for grade 2 or higher edema events was 7 days.

Table 16. Baseline Characteristics

- Median time to MRD clearance was 1.87 months (range, 0.79–6.2 months) for patients treated with PVEK + AZA + VEN. The concomitant benefits demonstrated in these studies were not observed with other AML therapies that did not involve PVEK.

Table 17. Baseline Characteristics

- Median time to onset of an edema event (all grades) was 23 days.
- Median time to resolution for all edema events was 6 days.
- Median time to resolution for grade 2 or higher edema events was 7 days.

Table 18. Baseline Characteristics

- Median time to MRD clearance was 1.87 months (range, 0.79–6.2 months) for patients treated with PVEK + AZA + VEN. The concomitant benefits demonstrated in these studies were not observed with other AML therapies that did not involve PVEK.

Table 19. Baseline Characteristics

- Median time to onset of an edema event (all grades) was 23 days.
- Median time to resolution for all edema events was 6 days.
- Median time to resolution for grade 2 or higher edema events was 7 days.

Table 20. Baseline Characteristics

- Median time to MRD clearance was 1.87 months (range, 0.79–6.2 months) for patients treated with PVEK + AZA + VEN. The concomitant benefits demonstrated in these studies were not observed with other AML therapies that did not involve PVEK.

Table 21. Baseline Characteristics

- Median time to onset of an edema event (all grades) was 23 days.
- Median time to resolution for all edema events was 6 days.
- Median time to resolution for grade 2 or higher edema events was 7 days.

Table 22. Baseline Characteristics

- Median time to MRD clearance was 1.87 months (range, 0.79–6.2 months) for patients treated with PVEK + AZA + VEN. The concomitant benefits demonstrated in these studies were not observed with other AML therapies that did not involve PVEK.

Table 23. Baseline Characteristics

- Median time to onset of an edema event (all grades) was 23 days.
- Median time to resolution for all edema events was 6 days.
- Median time to resolution for grade 2 or higher edema events was 7 days.

Table 24. Baseline Characteristics

- Median time to MRD clearance was 1.87 months (range, 0.79–6.2 months) for patients treated with PVEK + AZA + VEN. The concomitant benefits demonstrated in these studies were not observed with other AML therapies that did not involve PVEK.