PREDICTORS OF TREATMENT OUTCOME WITH THE COMBINATION OF CARFILZOMIB, LENALIDOMIDE, AND LOW-DOSE DEXAMETHASONE IN NEWLY DIAGNOSED MULTIPLE MYELOMA

INTRODUCTION

Patients with newly-diagnosed multiple myeloma (MM) treated with the triplet combination of carfilzomib (CFZ), lenalidomide (LEN), and low-dose dexamethasone (DEX) demonstrated high rates of complete response (CR, 64%) and stringent complete response (sCR, 55%) that correlated with superior progression-free survival (PFS) and overall survival (OS) rates compared with those who did not achieve sCR. Patients who achieved sCR at any time during carfilzomib, lenalidomide, and dexamethasone (CARDEL) therapy showed a trend toward longer estimated 3-year PFS and OS rates compared with those who did not achieve sCR. Among patients with high-risk cytogenetics, similar 3-year PFS rates were observed in patients with p53 mutation (69% vs 83%), and those without p53 mutation (67% vs 80%), but there was a trend toward lower 3-year PFS rates in patients with high-risk cytogenetics compared with standard-risk groups (P = .222). There was no difference in OS between standard-risk groups (91% vs 100%, log-rank P = .6). Patients had the option to receive stem cell transplantation after cycle 4.

RESULTS

Key Eligibility Criteria

- Transplant-eligible and patients
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2
- High-risk cytogenetics
- ISS stage II/III, n (%) 32 (60)
- del 13: 10/50 (20)
- t(14;16) 0/48 (0)
- Hyperploidy: 10/50 (20)
- b2m >10 (20)
- Low-risk cytogenetics
- ISS stage I, n (%) 21 (40)
- del 13 by metaphase only.
- ISS stage IV, n (%) 14 (26)
- t(14;16) 10/48 (21)
- Hyperploidy: 10/50 (20)
- b2m >10 (20)

Patient Flow and Disposition

- 53 patients initiated induction CRd
- 43 patients continued induction CRd (together, n=96)
- 10 patients proceeded to ASCT (n=7)
- 2 patients on maintenance
- 1 patient died of disease progression
- Discontinued maintenance CRd (n=8)
- Disease progression (n=3)
- Toxicity (n=1)

Treatment Schema

- For cycles 1–8, patients received 28-day cycles of CFZ 20–36 mg/m2 (phase 1; n=18/phase 2; n=18), LEN 25 mg orally (days 1–21), and DEX 40–20 mg PO weekly (cycles 1–4/5–8).
- A total of 33% of patients had high-risk disease; of these, 47% had del p53.
- Of these, 24 patients continued LEN maintenance for a median of 12 months (range, 3–15).
- Median follow-up, 31 months (range, 16–43).
- The estimated 3-year PFS and OS rates for all patients were 79% and 96%, respectively.

Patient characteristics at baseline are shown in Table 1. Of these, 24 patients continued LEN maintenance for a median of 12 months (range, 3–15).

Gene Expression Profiling

- A subset of patients enrolled with CARDEL including 7 of 10 patients with disease progression
- Based on CR, 6 of 10 patients (60%) had high-risk disease
- Multiple myeloma-specific gene expression data from high-risk patients
- Of the 15 patients with MM-ND standard-risk disease, 3 patients relapsed, out of whom had high-risk cytogenetics

Clinical Relevance

- Twenty-six patients with CRd (including 7 patients with high-risk disease) were evaluated for carfilzomib
- 3 patients who achieved CRd at any time during CRd treatment showed a trend toward longer estimated median PFS and OS compared with those who did not achieve CRd (P < .0125)
- Among patients with high-risk disease, the estimated 3-year PFS was 68% and OS was 100% (log-rank P = .05)

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Multiple Myeloma Research Consortium, under whom this multisite trial is conducted. The study is supported in part by the University of Michigan CTRAC grant, Onyx Pharmaceuticals, and the National Institutes of Health (1R01CA155797-01A1). The authors declare no potential conflicts of interest.

CONCLUSIONS

- After extended follow-up (median, 30 months), CARDEL treatment continues to show excellent outcomes, with estimated 3-year PFS of 79% and 3-year OS of 100% for patients with MM-ND, 100% of whom had high-risk cytogenetics

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