Frontline Systemic Therapeutic Patterns and Outcomes in Rosai-Dorfman Disease: A Multicenter Retrospective Analysis

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Background

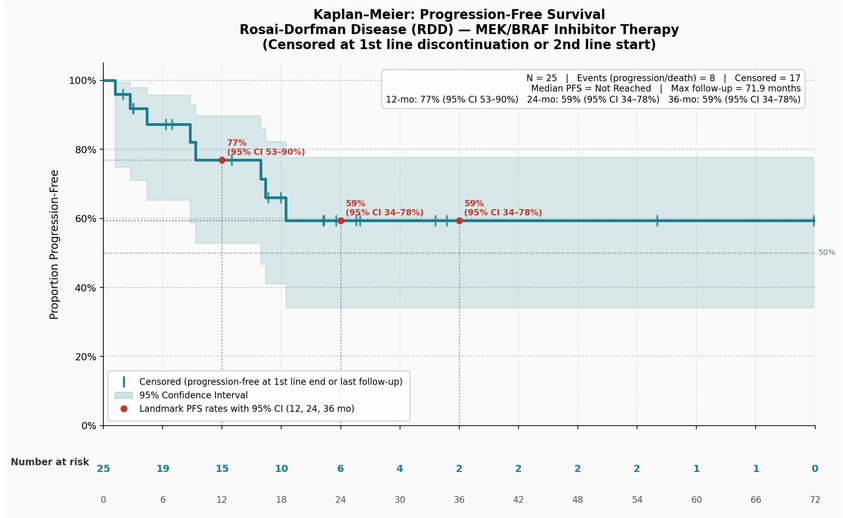
- Rosai-Dorfman disease (RDD) is a rare histiocytic neoplasm often characterized by MAPK pathway alterations in 30% to 50% of cases. MEK inhibitors have shown efficacy, but real-world treatment patterns remain insufficiently characterized.

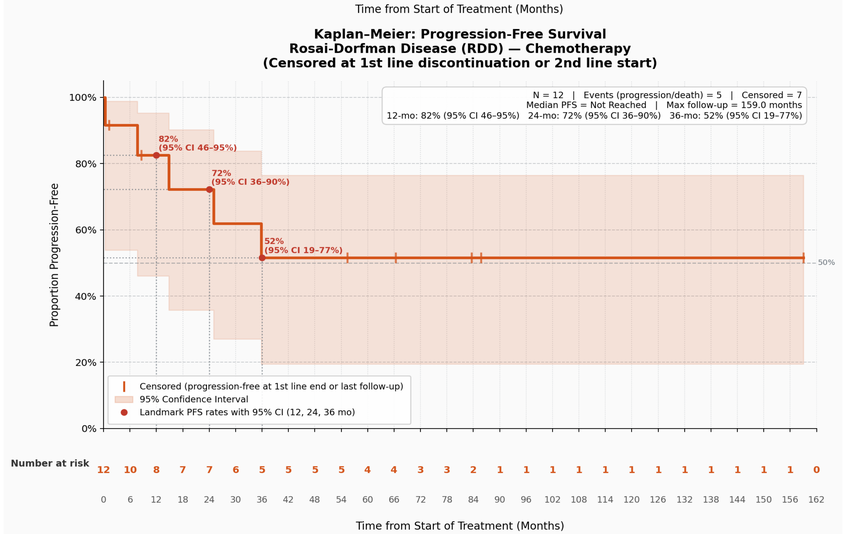
Objective

- To describe real-world treatment patterns and clinical outcomes in patients receiving targeted therapy and chemotherapy for RDD.

Methods

- This was a multicenter retrospective cohort analysis of adults with RDD receiving frontline targeted therapy with MEK inhibitors or fixed-duration chemotherapy as frontline treatment.
- Disease-specific genetic alterations were assessed through next-generation sequencing and response by PET-CT criteria.
- Patients were included from routine clinical settings at large academic institutions and were diagnosed with RDD between 1998 and 2024.





Results

- Median follow-up for cohort was 62.0 months (IQR, 25.5–83.9).
- Nineteen patients (43.2%) had tumor-specific gene alterations. Cohort-wide ORR was 65% (PR, 50%; CR, 15%).

Targeted Therapy (TT) Cohort (n = 25)

- ORR was 60% (CR, 20%; PR, 40%), 3-year PFS was 59% (95% CI, 34%–78%), median PFS was not reached, and 3-year OS was 92%. Median TTNT was 30.3 months; 50% (95% CI, 24%–72%) required next-line therapy at 3 years.
- AEs from first-line therapy occurred in 40.7%; 37.0% required dose modification. Among 14 targeted therapy patients with MAPK mutations, ORR was 50% (PR/CR, 7; SD, 5; PD, 2 [BRAF V459A, 1; MAP2K2, 1]).

Chemotherapy (CT) Cohort (n = 12)

- ORR was 73.3% (CR, 6.7%; PR, 66.7%), 3-year PFS was 52% (95% CI, 19%–77%), OS was 100%, and 36% (95% CI, 30%–85%) required next-line therapy. Median PFS and TTNT were not reached. AEs occurred in 70%, with 10% switching therapy.

Discussion

Both chemotherapy and targeted therapy demonstrated clinically meaningful ORR and PFS. Although small sample size prevented statistical comparison, a greater proportion of targeted therapy patients required next-line therapy, reflecting higher discontinuation rates from AEs. While preliminary data suggest both treatment approaches may be effective, larger studies would provide more definitive insights.