Venetoclax in patients with AL Amyloidosis: A Meta-Analysis of Clinical Outcomes

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Introduction

AL amyloidosis is a rare plasma cell disorder characterized by misfolded light chains leading to progressive multi-organ dysfunction. Treatment options for relapsed/refractory (R/R) cases are limited[1]. Venetoclax has demonstrated efficacy in multiple myeloma. Its role in AL amyloidosis, however, remains underexplored.

Aim

To evaluate the safety and efficacy of Venetoclax in relapsed/refractory amyloidosis through a systematic review and meta-analysis

Objectives

- Assess pooled overall response rate (ORR) to Venetoclax
- Evaluate mortality outcomes (disease-related, treatment-related, infection-related)
- Examine organ involvement and cytogenetic characteristics

Methods

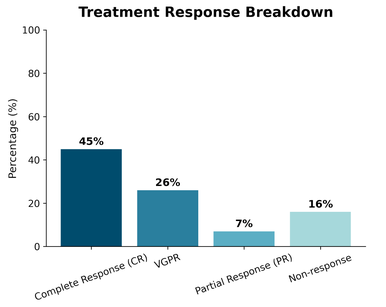
- A systematic search of PubMed Central, Embase, and Cochrane was conducted using PRISMA 2020 guidelines
- 13 studies included with a total of 285 patients
- Meta-analysis was conducted using R version 4.4.0 with the “meta” and “metasens” packages.
- Pooled proportions and 95% confidence intervals were calculated using the inverse variance method with Freeman-Tukey double arcsine transformation
- Confidence intervals estimated using Hartung-Knapp adjustment
- Tau^2 was derived using the restricted maximum likelihood (REML) method.

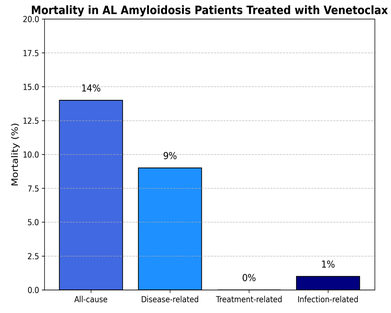
Results

- Median age: 64.9 years (27-89)
- 67.3% were male
- 83.2% had R/R disease; 89.6% had t(11;14)
- 15.2% had concurrent multiple myeloma
- Organ involvement: Cardiac (97%), Renal (66.4%), Neurologic (27.6%), GI (19,6%), soft tissues (12%), Hepatic (10.9%).

Results

- **Overall Response Rate(ORR):** 84%
  - Complete response (CR): 45 %
  - Very good partial response (VGPR): 26%
  - Partial response (PR): 7%
- Non-responders: 16%
- **Mortality outcomes:**
  - All-cause mortality: 14%
  - Disease-related mortality: 9%
  - Treatment-related: 0%
  - Infection-related: 1%
- **Overall survival (OS):**
  - 1-year OS: 79%
  - 2-year OS: 74%





Summary

Venetoclax is associated with **high response rates (ORR 84%)** and minimal treatment-related mortality in patients with R/R AL amyloidosis.

Discussion

- Venetoclax shows significant potential in AL amyloidosis, with high response rates and a favorable toxicity profile.
- High response rates may translate into survival benefit, but prospective trials are needed to validate its safety and long-term benefit.

References

1. Locke, M., & Nieto, M. (2025). AL Amyloidosis: Current Treatment and Outcomes. *Advances in hematology*, *2025*, 7280805. https://doi.org/10.1155/ah/7280805

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