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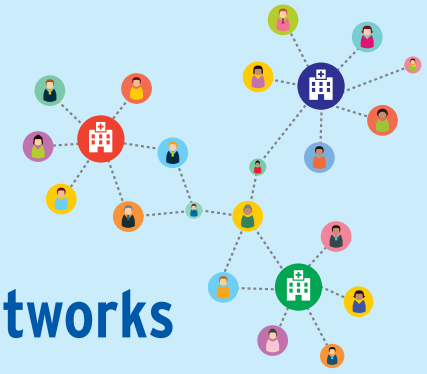
Building Effective Amyloidosis Care Networks



AL Amyloidosis: Management and Treatment

Goals of Treatment[1]

- Amyloid light chain amyloidosis (AL) is caused by overproduction of misfolded immunoglobulin light chain and subsequent deposition of the amyloid protein in various organs such as the heart, kidney, and nervous system
- The goals of treatment are to:
  - Improve organ function—stabilize and recover from dysfunction
  - Prolong patient survival
- Better hematological responses correlate with better organ responses and overall survival. However,
  - Organ response lags behind hematological response and can take months to years
  - Hematological response is necessary but not a guarantee for organ response

Treatment

Initial Treatment[2,3,4,5]

- Daratumumab + bortezomib, cyclophosphamide, dexamethasone (Dara-VCd) is the only treatment specifically approved for AL amyloidosis
- The ANDROMEDA trial demonstrated that daratumumab + VCd:
  - Tripled complete response (CR)
  - Doubled organ response
  - Extended survival free from major organ deterioration or hematological progression
- Phase 3 trials are evaluating the role of stem cell transplant (SCT) and Dara-VCd in relation to each other

After Initial Treatment[1]

- There is no standard-of-care therapy after initial treatment
- Various proteasome inhibitors, alkylating agents, immunomodulatory imide drugs (IMIDs), and antibodies are used per clinical guidelines or because they are approved for multiple myeloma

Treatments in Development[6]

Several therapies are in development, some of which have been previously approved for multiple myeloma.
The therapies in clinical trials include:

- Targeted therapies: BCL-2 inhibitors, nuclear export protein blockers
- Novel immunotherapies: anti-BCMA antibody drug conjugates, bispecific antibodies
- CAR T cells: anti-BCMA CAR T cells, anti-GPRC5D CAR T cells, CAR-macrophage
- Amyloid-directed therapy: anti-IgG antibody, anti-SAP antibody

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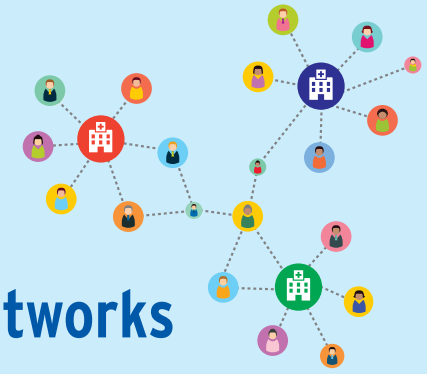

AL Amyloidosis: Management and Treatment

Multidisciplinary Supportive Care and Monitoring[1]

- Given that AL amyloidosis affects multiple organs, coordinated care across specialties is essential. Additionally, organ dysfunction may persist despite hematological remission
- Treatment modification is often necessary
- Consult and coordinate with AL specialists
- Cardiologists and neurologists can manage cardiomyopathy
- Supportive care includes:
  - Fluid and salt restriction for fluid overload
  - Diuretics for heart and renal failure, used with caution
  - Blood pressure and neuropathy management with pharmacologic and behavioral interventions
- Monitoring requires regular measurements of the following to determine hematologic and organ response:
  - FLC, SPEP/IF, UPEP/IF
  - Cardiac biomarkers
  - Urine proteinuria

Key Takeaways

- The goal of treatment is to achieve hematological response that can delay or prevent further organ dysfunction and thus prolong survival
- Dara-VCd is the standard of care for newly diagnosed AL amyloidosis
- The role of SCT is evolving since Dara-VCd became available
- Newer therapies such as CAR T cells and bispecific antibodies are in development, with promising results
- Multidisciplinary care from the time of diagnosis and proactive supportive care are needed throughout the course of the disease to improve patient outcomes

References

1. Sanchorawala V. *N Engl J Med*. 2024;390(24):2295-2307.
2. Kastritis E, et al. *N Engl J Med*. 2021;385(1):46-58.
3. Landau H. *ASN Kidney News*. 2021;13(10/11):18.
4. Hagen P, et al. *J Clin Oncol*. 2024; 42 (Suppl 16): Abstract TPS7575.
5. Locke M, et al. *Adv Hematol*. 2025;2025:7280805.
6. Sammartano V, et al. *Cancer Drug Resist*. 2023;6(1):169-181.

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