LymphomaHub

IACH 2018 | Treatment of adult T-cell leukemia/lymphoma

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The 1st Annual Meeting of the International Academy for Clinical Hematology (IACH) took place in Paris, France, on September 27–29, 2018. On Friday 28 September, a non-Hodgkin lymphoma session was held, with an abstract presented entitled "Therapy of HTLV-related lymphoma" by Professor Ali Bazarbachi from the American University of Beirut Medical Center, Beirut, Lebanon.

Adult T-cell leukemia/lymphoma (ATL), a rare aggressive T-cell malignancy often caused by human T-cell lymphotropic virus type-1 (HTLV-1), is associated with inferior outcomes due to resistance to chemotherapy. According to previous observations, leukemogenesis of ATL is a staged process containing several factors that result in increased proliferation of T lymphocytes. HTLV-1 is an endemic retrovirus present in certain areas of the world, its ATL virulence is around 2–4%.

To date, there is no standard of care for patients with ATL. Enrolment in clinical studies is always recommended. Administration of dose-intense multi-agent chemotherapy may improve outcomes in the lymphoma subtype. However, the most efficient survival rates were observed in patients receiving antiviral therapy using the combination of zidovudine and interferon-alpha and in patients receiving allogeneic bone marrow transplantation. A number of new therapy options are being investigated in ongoing prospective trials.

Subtypes of ATL:

- **Aggressive ATL**
  - Acute ATL: 60% of all patients
  - Lymphomatous ATL: 20% of all patients
- **Indolent ATL**
  - Smoldering ATL
  - Chronic ATL

Current treatment strategies:

- ***Chemotherapy (LSG15) with or without mogamulizumab:***
  - In this study, newly diagnosed ATL patients (acute, lymphoma, or unfavorable chronic) received LSG15 plus mogamulizumab or LSG15 alone[2]
  - Complete response (CR): 52% (95% CI, 33–71%) LSG15 with magamulizumab *vs* 33% (95% CI, 16–55%) LSG15 alone
  - No difference in median progression-free survival (PFS): 8.5 months *vs* 6.3 months in the LSG15-plus-mogamulizumab and LSG15 only groups, respectively (NS)
- ***Allogeneic hematopoietic stem cell transplantation (allo-HSCT)***

- Allo-HSCT is effective with myeloablative conditioning (MAC) or reduced intensity conditioning (RIC) increasing long-term survival in selected patients with ATL[3]
- Allo-SCT but not auto-SCT can be a feasible salvage option for ATL patients, particularly those transplanted in CR1. In this study, patients had a 3-year OS of 34.3% (95% CI, 15.5–67.2)[4]
- Allo-HSCT is an option for patients with acute and lymphoma subtypes
- Allo-HSCT in first remission yields better overall survival rates
- Potentially curative therapy option in one-third of transplanted patients
- Mogamulizumab given prior to allo-HSCT may increase morbidity and mortality

- ***Zidovudine (AZT) plus interferon-alpha (IFN)***
  - This antiviral combination therapy improves survival in smoldering-, chronic-, and *TP53* negative acute ATL with a 5-year OS of 46% as compared to 12% with chemotherapy, $P = 0.004$[5]
  - AZT/IFN should be considered as first-line therapy
  - AZT/IFN should be used alone as first line therapy in leukemic forms of ATL, not after several lines of chemotherapy
  - AZT/IFN therapy is better if it is given in higher doses because lower doses are usually not effective
- ***Chemotherapy***
  - Chemotherapy can be combined with AZT/IFN antiviral regimen
  - First-line antiviral therapy is less effective than first-line chemotherapy in ATL lymphoma[5]
  - Prevention of opportunistic pathogens is important
- ***Arsenic trioxide (As) plus IFN/AZT***
  - In a phase II study, As plus IFN/AZT showed superior response rates with a manageable toxicity profile in patients with chronic ATL, 100% response rate was observed[6]
  - Preclinical findings suggest that the addition of AS to AZT/IFN regimen as consolidation therapy may eliminate leukemia-initiating cells[7]

Professor Bazarbachi concluded that the combination of AZT and IFN has superior efficacy in leukemic subtypes of ATL and is a promising first-line therapy option in patients with adult T-cell leukemia/lymphoma. He highlighted that in order to prevent the occurrence of resistance and relapse, further clinical studies are underway to evaluate adding other targeted therapies, including arsenic/IFN combination therapy or monoclonal antibodies. He further added that allo-HSCT is effective in selected patients.

References

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