MultipleMyelomaHub

General MM, Patients eligible for transplant, Patients non-eligible for transplant

Translocation t(11;14) confers an inferior prognosis to other standard-risk patients with MM

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Following diagnosis, patients with Multiple Myeloma (MM) are subjected to FISH analysis of the bone marrow plasma cells (PCs) to check for chromosomal deletions or translocations. This allows classification as either standard-risk or high-risk and helps to determine prognosis as well as steer treatment choices. Translocation t(11:14), which occurs on the immunoglobulin heavy chain region, occurs in 16–24% of MM patients and is currently classified as standard-risk. However, this classification was made before the introduction of newer agents, which have hugely improved overall prognosis. Observations from more recent assessments using novel agents suggest that patients with t(11:14) translocation have a worse outcome than standard-risk patients.

In order to further assess the prognostic impact of the t(11:14) translocation in light of current therapies, a retrospective study was conducted by Arjun Lakshman from the Division of Hematology, Mayo Clinic, Rochester, NY, USA and Muhamad Alhaj Moustafa from the Department of Internal Medicine, MedStar Washington Hospital Center, WA, USA, and led by Shaji Kumar, also from The Mayo Clinic, Rochester and a member of the MM Hub Steering Committee. Primary endpoints were progression-free survival (PFS), time to next treatment (TTNT) and overall survival (OS).

Key Highlights:

- Patients (pts), 365 diagnosed with MM between January 2004 and November 2014 with t(11;14) detected on FISH qualified for assessment in this study
- Matched controls (two control pts without the translocation were matched for age and year of diagnosis) = 730; pts with non-(11;14) translocations = 132 and pts with no chromosomal translocations = 598

All data is given in the following order: t(11;14) cohort, non-(11;14) translocation cohort and no translocation cohort

- Median duration of follow-up: 70.7 (95% CI, 63.6–77.3), 54.9 (95% CI, 47.0–71.5) and 65.9 (95% CI, 63.0–70.6) months; $P = 0.225$
- Deaths at data cut-off = 170 (46.6%), 76 (57.6) and 220 (36.8%) pts
- Response to induction therapy: partial response or better (overall response rate) = 71.4%, 82.2% and 85.4%, $P = 0.001$; very good partial response (VGPR) = 42.6, 40.6, 39.8% and $P = 0.720$
- Median PFS = 23.0 (95% confidence interval (CI), 20.8–27.6), 19.0 (95% CI, 15.8–22.7) and 28.3 (95% CI, 25.7–30.6) months, ($P < 0.01$)
- Estimated median TTNT = 20.8 (95% CI, 17.0–24.0), 18.2 (95% CI, 15.1–22.0) and 27.0 (95% CI, 23.6–29.5) months; $P = 0.064$ for t(11;14) *vs* non-(11;14) translocation and $P = 0.01$ for t(11;14) vs no-translocation

- Estimated median OS = 74.4 (95% CI, 64.8–89.3), 49.8 (95% CI, 40.0–60.6) and 103.6 (95% CI, 85.2–112.3) months; *P* = 0.001 for t(11;14) *vs* non-(11;14) translocation and *P* = 0.003 for t(11;14) *vs* no- translocation
- Estimated 5-year survival = 57.8%, 41.7% and 68.1%
- Median OS in pts receiving early *vs* delayed SCT = 88.4 (95% CI, 68.8–124.7) *vs* 58.1 (95% CI, 50.0–81.7) months, 51.9 (95% CI, 45.2–not reached) *vs* 40.0 (95% CI, 30.1–60.6) months and 112.3 (95% CI, 103.6–not reached) *vs* 73.7 (95% CI, 66.9–97.0) months, (*P* = 0.002, *P* = 0.022 and *P* = 0.001
- Median OS (with 17p abnormality excluded) = 81.7 (95% CI, 67.0-90.7), 58.2 (95% CI, 47.0-76.4) and 108.3 (95% CI, 92.4-140.1) months, (*P* <0.01)
- Additional predictors of poor OS in t(11;14) patients include age ≥ 65 years, International Staging System (ISS) III, and presence of 17p abnormality

Conclusion:

This study followed the outcome of a large cohort of patients with the t(11;14) translocation and identified this subset as having a poorer prognosis than patients currently classified as standard-risk. The study found that such patients have a lower PFS and OS, as well as a reduced response to induction therapy of all kinds. Previous studies followed patients in clinical trials for outdated regimens, or included small patient sets, or did not follow-up for as long. In addition, FISH was carried out either prior to, or within 12 months, of starting therapy, although the retrospective nature of the study is a limitation. The authors suggest that a new classification for patients with the t(11;14) translocation is warranted, so that tailored treatments such as single agent venetoclax, can be considered.

References

1. Lakshman A., Moustafa M.A. *et al.* Natural history of t(11;14) multiple myeloma. Leukemia. 2017 Jun 27. DOI: 10.1038/leu.2017.204 [Epub ahead of print]