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Gemelli

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MONOCENTRIC OBSERVATIONAL STUDY ON SECONDARY MYELOID NEOPLASIA (t-MN) SUBMITTED TO ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION.

Simona Sica

Rome, 24th September 2016

Italian Network on Secondary Leukemias (1999-2013)

Therapy-related myeloid neoplasms (t-MN) include acute myeloid leukemias (t-AML) and myelodysplastic syndromes (t-MDS) occurring in patients treated with radiotherapy (RT) and/or chemotherapy (CHT) for cancer or autoimmune diseases. s. t-MN may arise from few months to several years after the primary tumor, are associated with clinical and biologic unfavorable prognostic features.

Median **age** at t-MN diagnosis was 64 years (range, 21–87).

Most frequent **primary malignancies** (PMs) were lymphoproliferative diseases and breast cancer.

Median time between cytotoxic treatment and t-MN was 5.7 years, with t-MN following RT alone associated with significantly longer latency, compared to CHT or combined CHT/RT (mean 11.2 vs 7.1 years, $P = 0.0005$).

Allogeneic SCT was associated with the longest **survival**, compared to patients receiving other treatment types (median OS: 58.8 months vs 12.1 months, $P < 0.0001$)

Fianchi L. et al, *Am. J. Hematol.* 2015

Monocentric cases of t-MN

- **Cohort:** 27 patients submitted to HSCT between September 1999 and July 2016
- **Sex:** 15 females (55,6%) and 12 males (44,4%)
- **Median age at t-MN diagnosis:** 53 years (range 29-64)
- **Previous disease:** 13 lymphoproliferative disease (48,2%)
  2 acute leukemia (7,4%)
  9 breast (33,3%)
  2 genitourinary (7,4%)
  1 gastrointestinal (3,7%)
- **Previous treatment:** 18 CHT (70.4%)
  1 RT (3,7%)
  7 Combined (25,9%)

t-MN features

- **Median latency between primary therapy and t-MN diagnosis:** global 36 months (range 12-144)

  p=0.4 [following CHT: 32 months (range 12-144)
  following combined: CHT/RT 48 months (range 16-120)

- ✓ **Karyotype:** normal in 7 cases (30,4%)

  isolated chromosome 7 abnormalities in 7 cases (30,4%)

  complex in 2 cases (8,7%)

  balanced translocation in 2 cases (8,7%) : t(9;22) and inv16/t(9;16)

  chromosomes' number abnormalities in 5 cases (21,7%)

  not available in 4 cases

Comparison between t-AML and t-MDS

	t-AML (16)	t-MDS (11)	P value
Median age (ys)	50 (29-59)	56 (30-64)	0.1
Median latency (mo)	33 (12-120)	60 (18-144)	0.1
Previous solid	6	10	**0.005**
Previous hematological	10	1	
Previous CHT	9	10	0.1
Previous CHT+RT	6	1	
Normal Karyotype	5	2	**0.03**
Isolated chr. 7 abn	1	6	
Others	6	2	

t-MN treatment

- **Pre-transplant :** hypomethylating agents (5-AZA) in 11 pts (40,8%)
  conventional chemotherapy in 12 pts (44,4%)
  none in 4 pts (14,8%)
- **Median time to transplant:** 7 months (range 2-56)
- **Disease status at transplant:** complete remission in 10 pts (37%)
  resistant disease in 10 pts (37%)
  stable disease in 7 pts (26%)

Transplant characteristics

- **Conditioning regimens:** MAC in 15 pts (55,6%)

  RIC in 12 pts (44,4%)

- **Donor type:** Related in 13 pts (48,1%)

  MUD in 14 pts (51,9%)

- **HCT-CI*:** score 3 in 11 pts (40,8%)
  score 4 in 8 pts (29,6%)
  score 5 in 4 pts (14,8%)
  score 6 in 1 pt (3,7%)
  score 7 in 2 pts (7,4%)
  score 9 in 1 pt (3,7%)

*Sorror M.L. et al, *J. Clin. Oncol.* 2014

Post-HSCT outcomes

- **Disease response:** CR 15 pts (55,6%)
  Relapse /Refractory 7 pts (25,9%)
  NA because of early death 5 (18,5%)

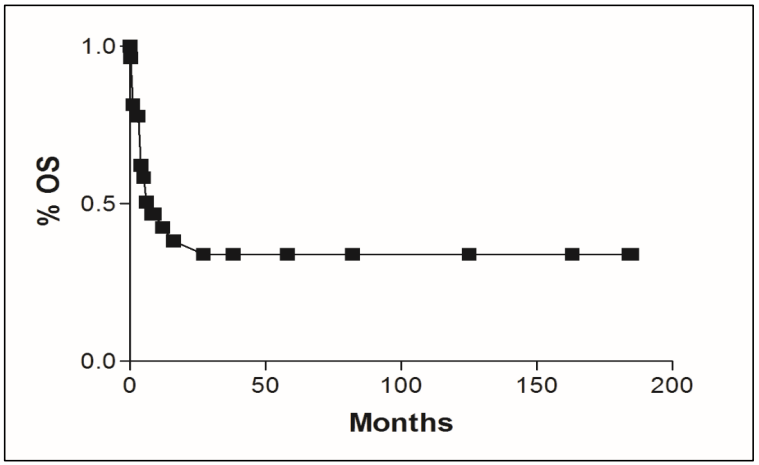
- **Overall survival rate:** 10/27 (37%)

- **Median overall survival and follow up:** global 6 months (range 0.3-185)
  alive 70 months (range 3-185)
  dead 4 months (range 0.3-27)

- **Cause of death:** TRM in 12 pts (44,4%)
  Relapse/Refractoriness 5 pts (18,6%)

* 3 **female patients during long term follow-up developed a third solid malignancies (breast cancer)**

Overall survival



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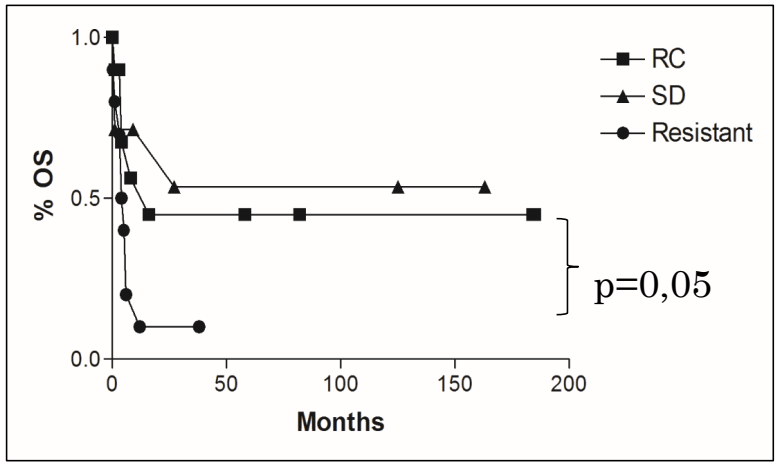

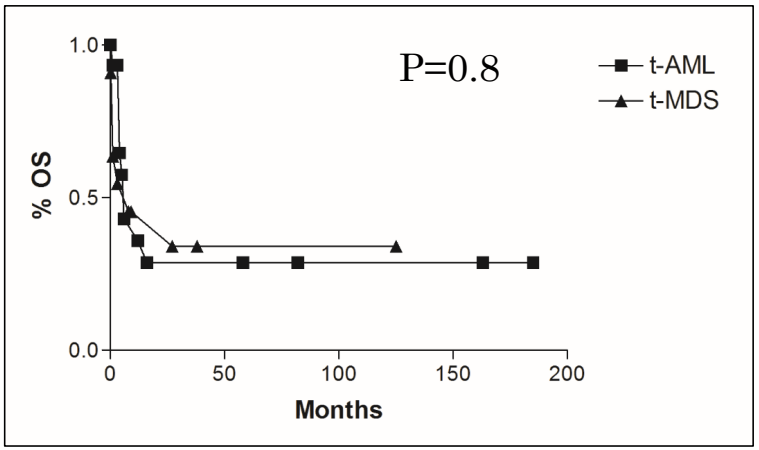

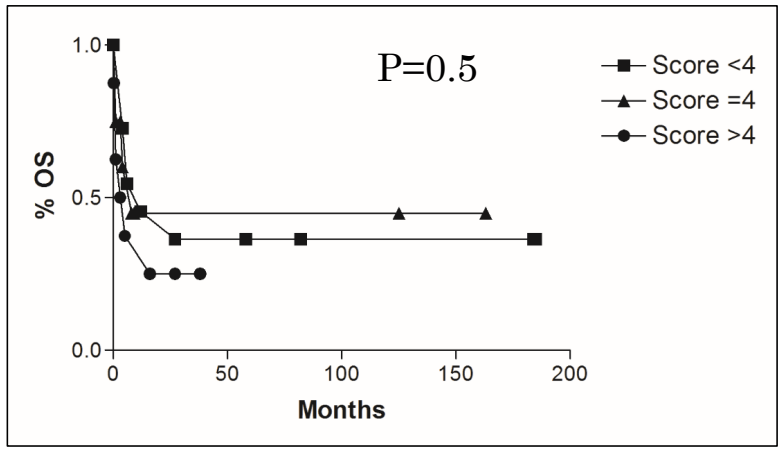

Overview (1)

- 65 patients with t-AML/MDS submitted to HSCT between 1996 and 2012
- Median **follow up** of survivors was 72 months (range 16-204)
- Global **2-ys Overall Survival** was 34%:
  - 21% for patients with abnormal adverse cytogenetics
  - 53% for patients with abnormal non-adverse cytogenetics
  - 44% for patients with normal cytogenetics

  - 23% for unrelated donor
  - 43% for related donor
- Global **2-ys non-relapse mortality**: 31%:
  - 60% for unrelated donor
  - 20% for related donor

Alam N. et al, *Bone Marrow Transplant*. 2015

Overview (2)

- 79 patients with t-AML/MDS submitted to HSCT
- **Median follow up**: 7,5 years (range 0,07-19)
- Only 19 pts (24,1%) were in **CR** before HSCT
- **NRM**: 23% at 5 years and 32% at 10 years
- **Relapse rate**: 42% at 5 years and 44% at 10 years
- **DFS:** 35% at 5 years and 24% at 10 years
- **OS:** 38% at 5 years and 24% at 10 years

Finke J. Et al, *Bone Marrow Transplant.* 2016

Conclusions

- Allo HCT is a strong indication in these patients because long term DFS is possible
- NRM is high due to comorbidity, age etc
- Follow up is necessary lifelong for the risk of new malignancies
- The question whether or not these patients should be treated (and how) before HCT remains a matter of debate

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