A WT-1 and PRAME "Fast-DC" Immunotherapy as a Potential post-Remission Strategy for AML

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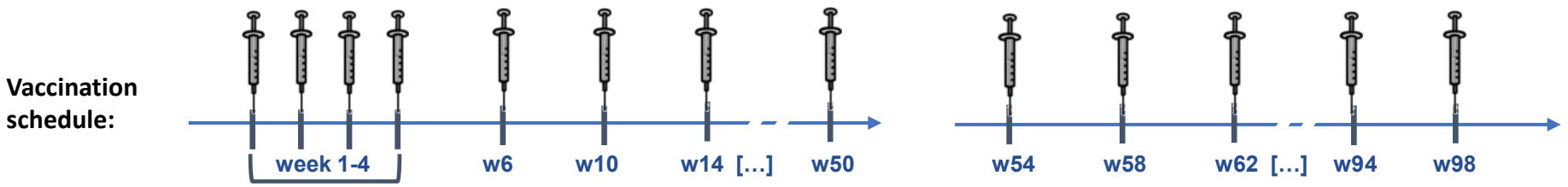
Introduction

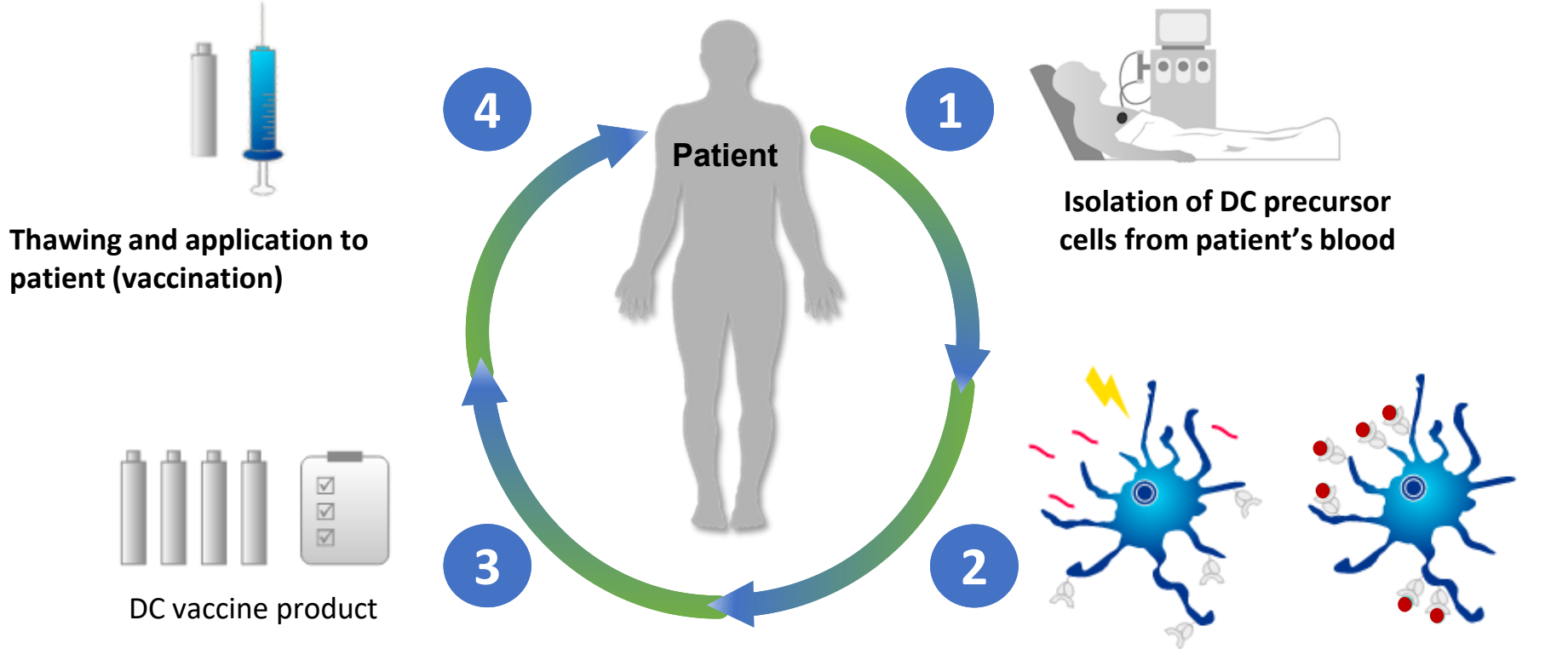
- The medical need for patients with AML, not eligible for allogeneic HSCT, remains high
- Vaccination against leukemia-associated antigens could provide a possibility for disease control
- A post-remission vaccination strategy was carried out in a Phase I/II clinical trial against the antigens:
  - WT-1, a leukemia-associated antigen
  - PRAME, a cancer-testis antigen

Study overview

- Single center, open-label Phase I/II trial (ClinicalTrials.gov Identifier: NCT02405338)
- Key inclusion criteria:
  - AML in CR or CR_i after induction/consolidation chemotherapy
  - Not eligible for allogeneic hematopoietic stem cell transplantation
  - Expression of antigen WT-1 with or without the antigen PRAME
- Continuous vaccination for 2 years or until progression/death
- Primary objectives
  - Safety and feasibility
- Secondary objectives (among others):
  - Overall survival (OS)
  - Progression free survival (PFS)



Personalized cancer treatment using a mature DC vaccine



- Patients received 2.5 or 5.0 million mature DCs per antigen (WT-1 or PRAME) per vaccination
- DC vaccines were applied by intradermal injection (200 µl per antigen)

Baseline demographics and parameters

Number of subjects	20	
Sex	Female: 5 Male: 15	
Median age	59 (Range 24-73)	years
ECOG	0 (100%)	
Prognostic Risk classification (HOVON/SAKK 102)	Poor: 2 Intermediate: 5 Good: 13	
Mean time from diagnosis to first vaccination (±StDev)	10.1 ± 3.7 (Range 4.5-17.5)	months
Mean time from last chemotherapy of last regimen to first vaccination (±StDev)	7.2 ± 3.4	months

Safety and tolerability of DC vaccines

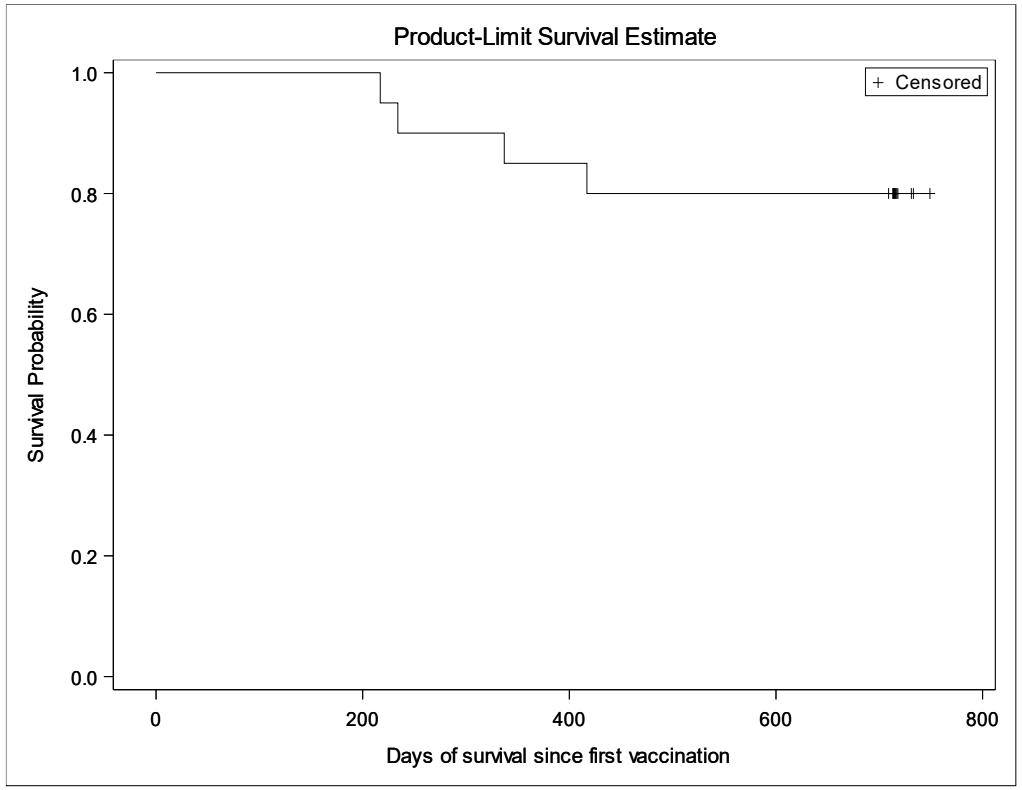
- No vaccine related SAE or SUSAR was reported
- No patient was withdrawn due to toxicity or intolerability
- Grade I/II toxicity was experienced by 18 (90%) of the 20 patients
  - Most common AEs were grade I injection site related, accounting for 28% (22 out of 80) of all AEs
- Grade III toxicity was experienced by (25%) patients and all unrelated to the vaccine:
  - 3 patients with thrombocytopenia grade III due to an imminent relapse
  - 2 other grade III AEs (1 upper respiratory tract infection; 1 herpes zoster)

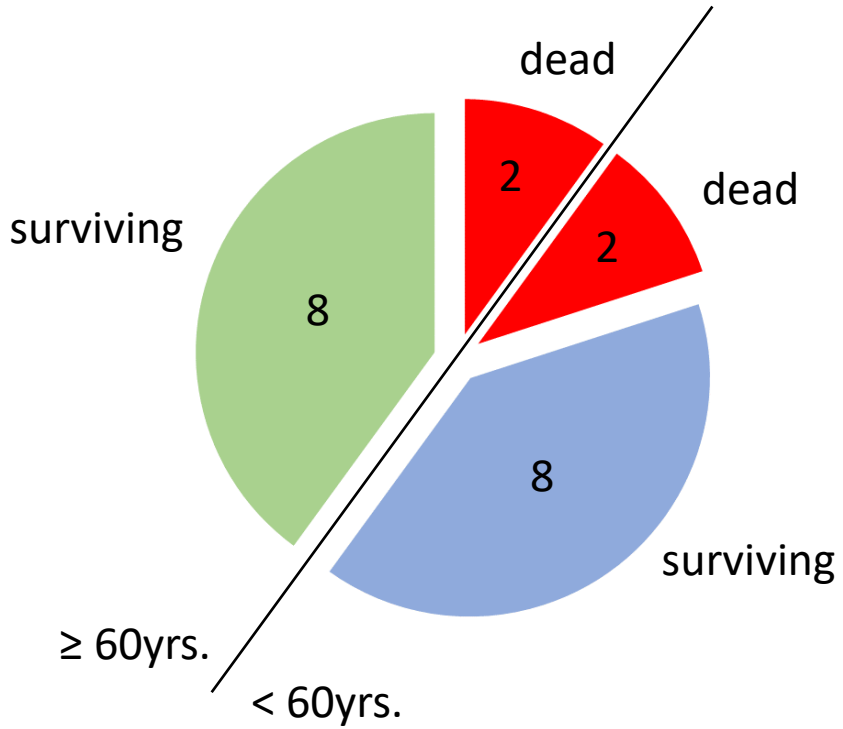
Feasibility of DC vaccine production

- DC vaccines could be produced for all 20 patients included in the clinical trial
- 17 out of 24 DC productions yielded 20 or more vaccine doses
- 5 patients needed apheresis twice for vaccine production, the remaining patients received all vaccines produced from one apheresis.

Overall survival (OS) rate

- The 2-year OS rate was estimated at 80% (95%CI:55-92%)
- 80% OS rate was identical in patients < 60 years as well as ≥ 60 years (10 patients per age group)

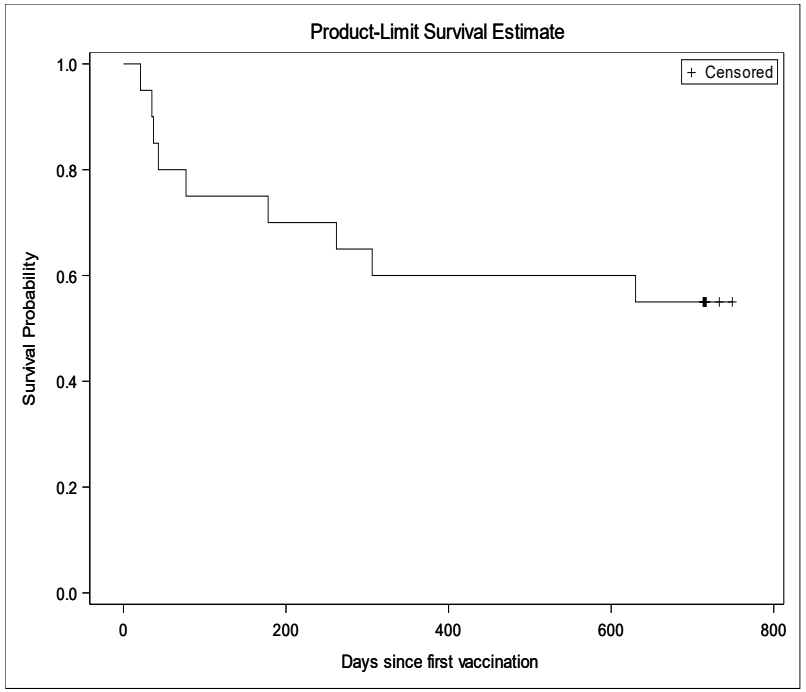




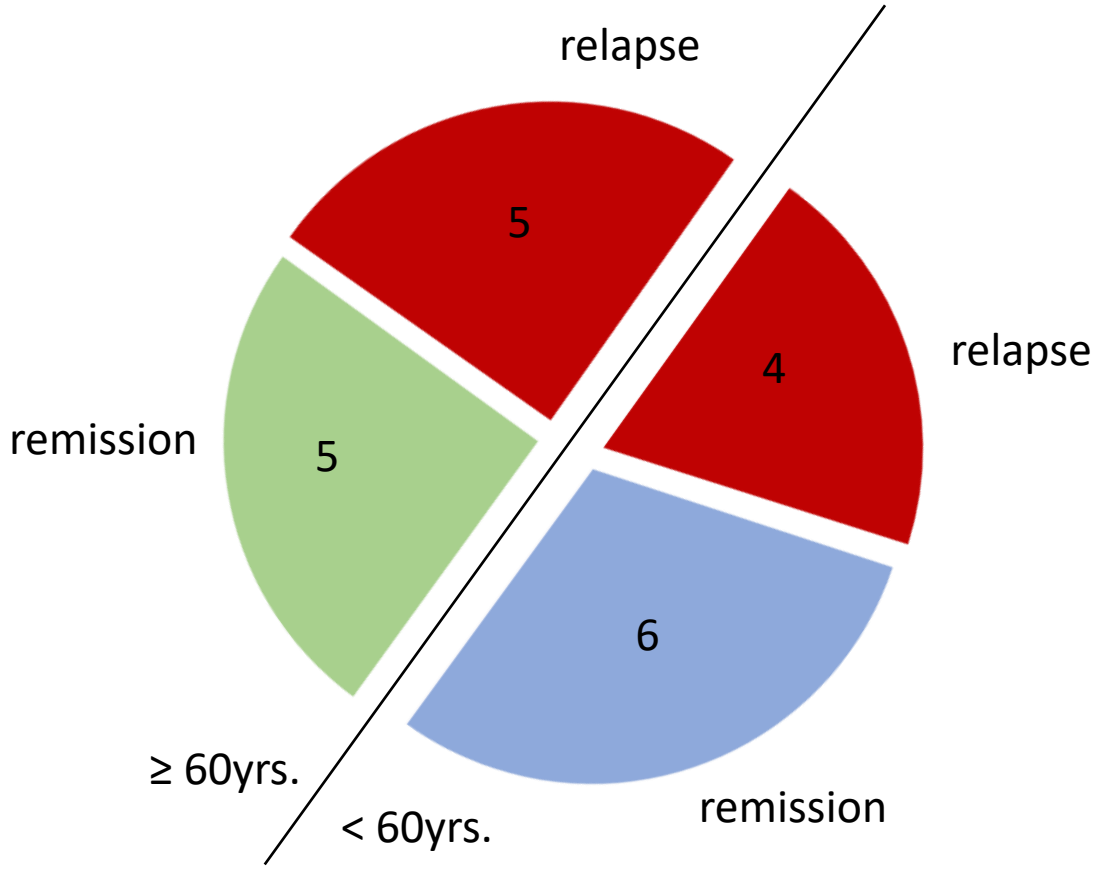
Overall survival from first IMP vaccination, Kaplan-Meier curve

Progression free survival (PFS) rate

- The 2-year PFS rate was estimated at 55% (95%CI:31-74%)
- A total of 9 patients progressed, 5 of which were within 80 days after 1st vaccination
- 2-year PFS rate:
  - patients < 60 years 60% (95%CI:25-83%)
  - patients ≥ 60 years 50% (95%CI:18-75%)

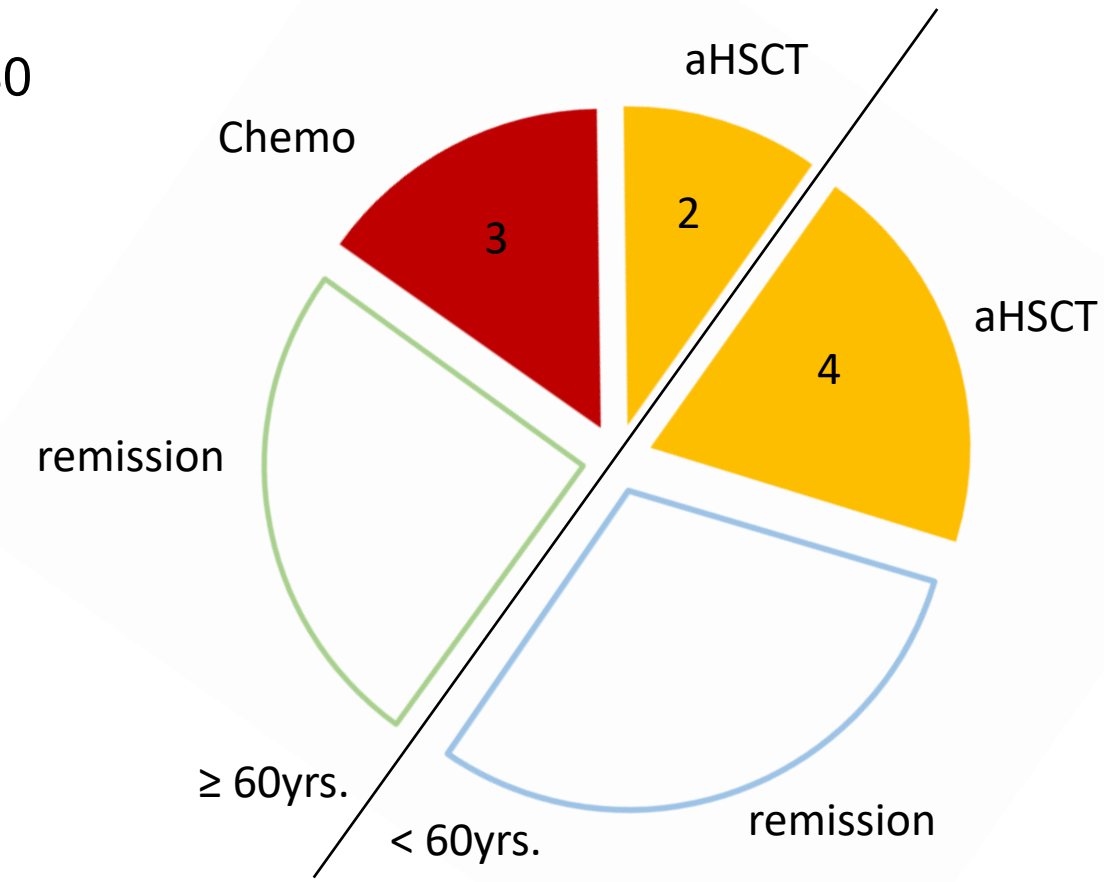


Kaplan-Meier curve, Progression free survival from first IMP vaccination



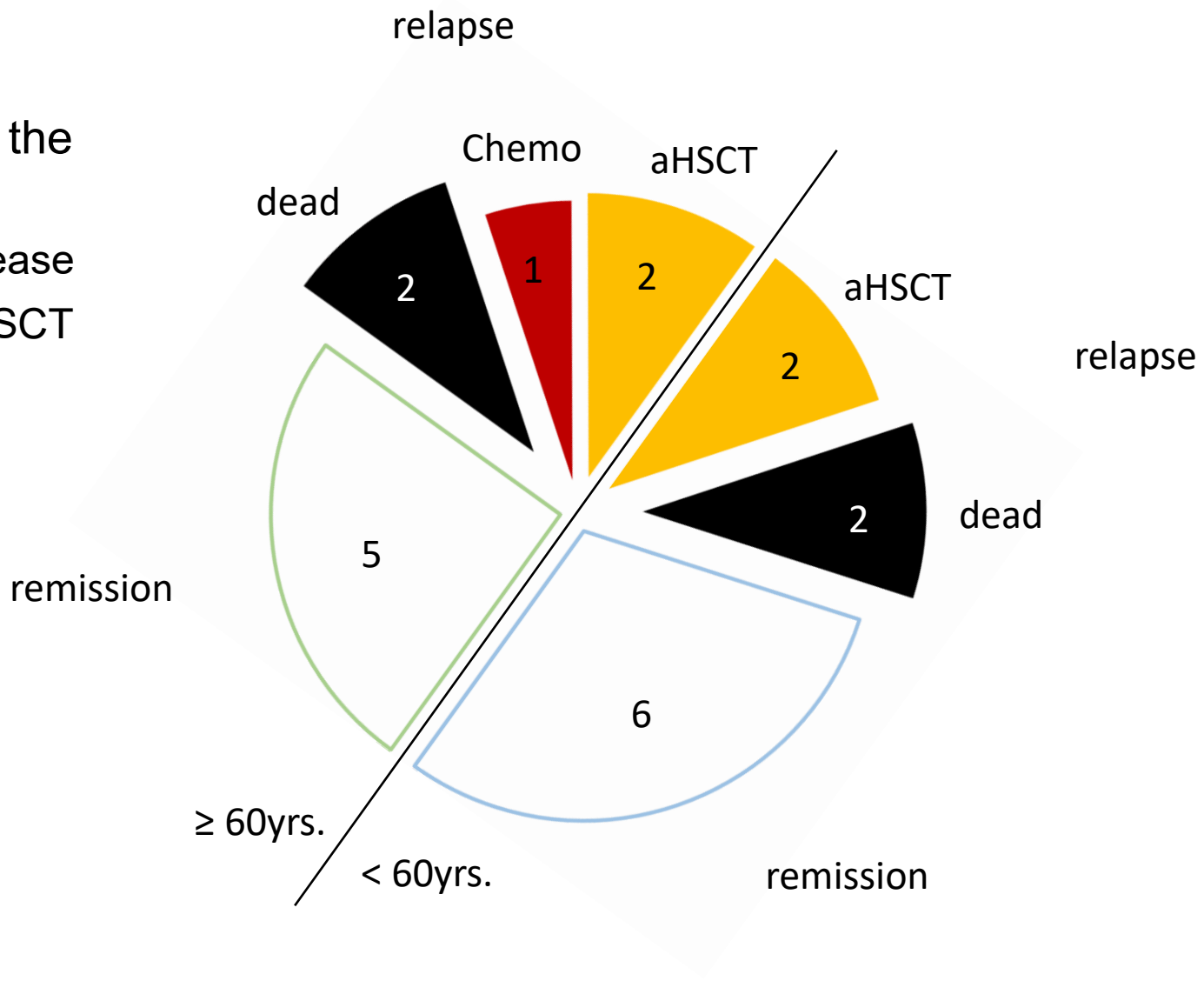
Disease course after progression

- Among the 9 progressing patients:
  - 6 could undergo allogeneic HSCT
  - Allogeneic HSCT was performed 104-380 days after first vaccination
  - Risk categories: 4 good, 2 poor risk

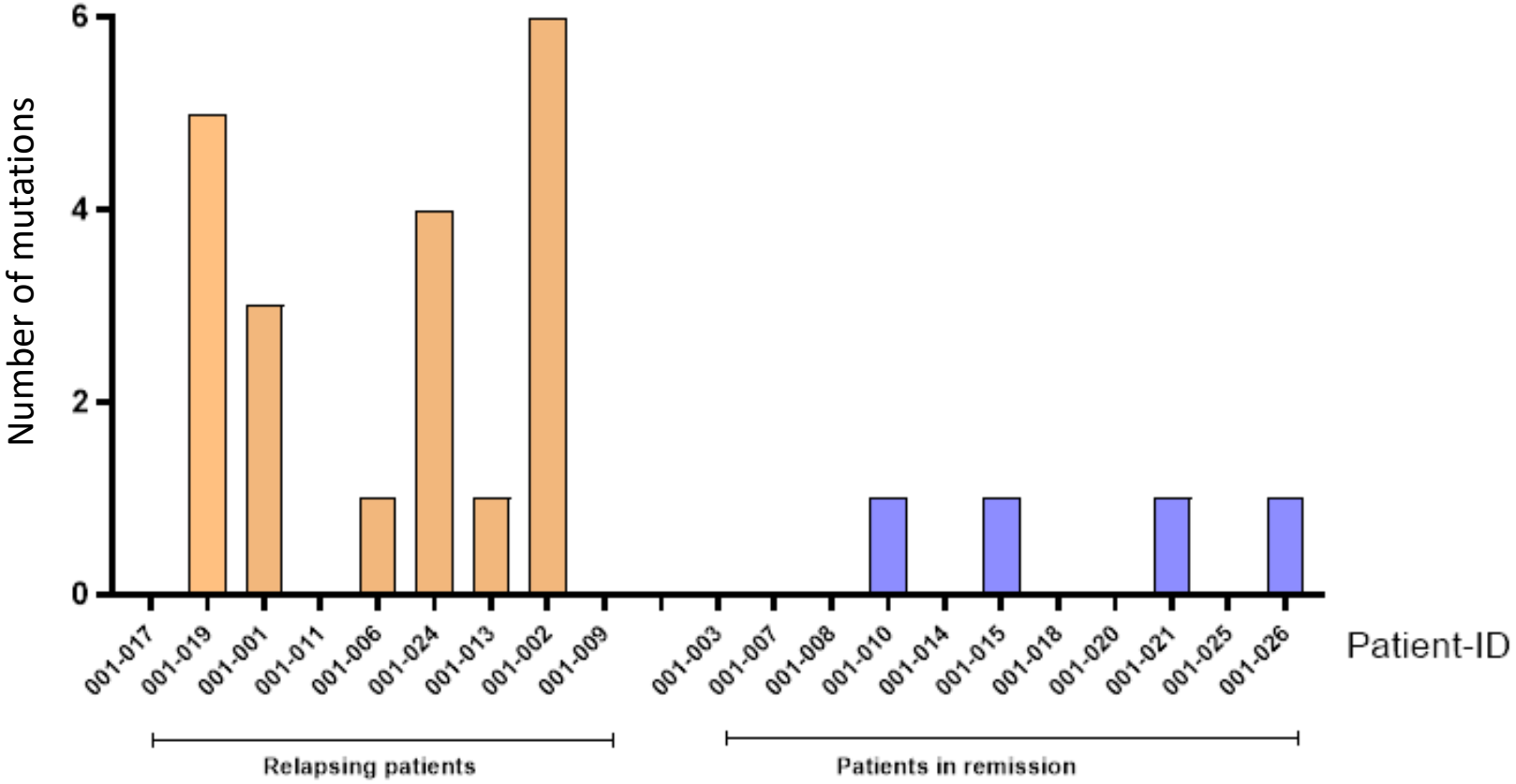


Disease course after progression

- Among the 9 progressing patients:
  - 4 patients in total died (including 2 of the transplanted patients)
    - 3 patients died to the underlying disease
    - 1 patient died due to GvHD after aHSCT



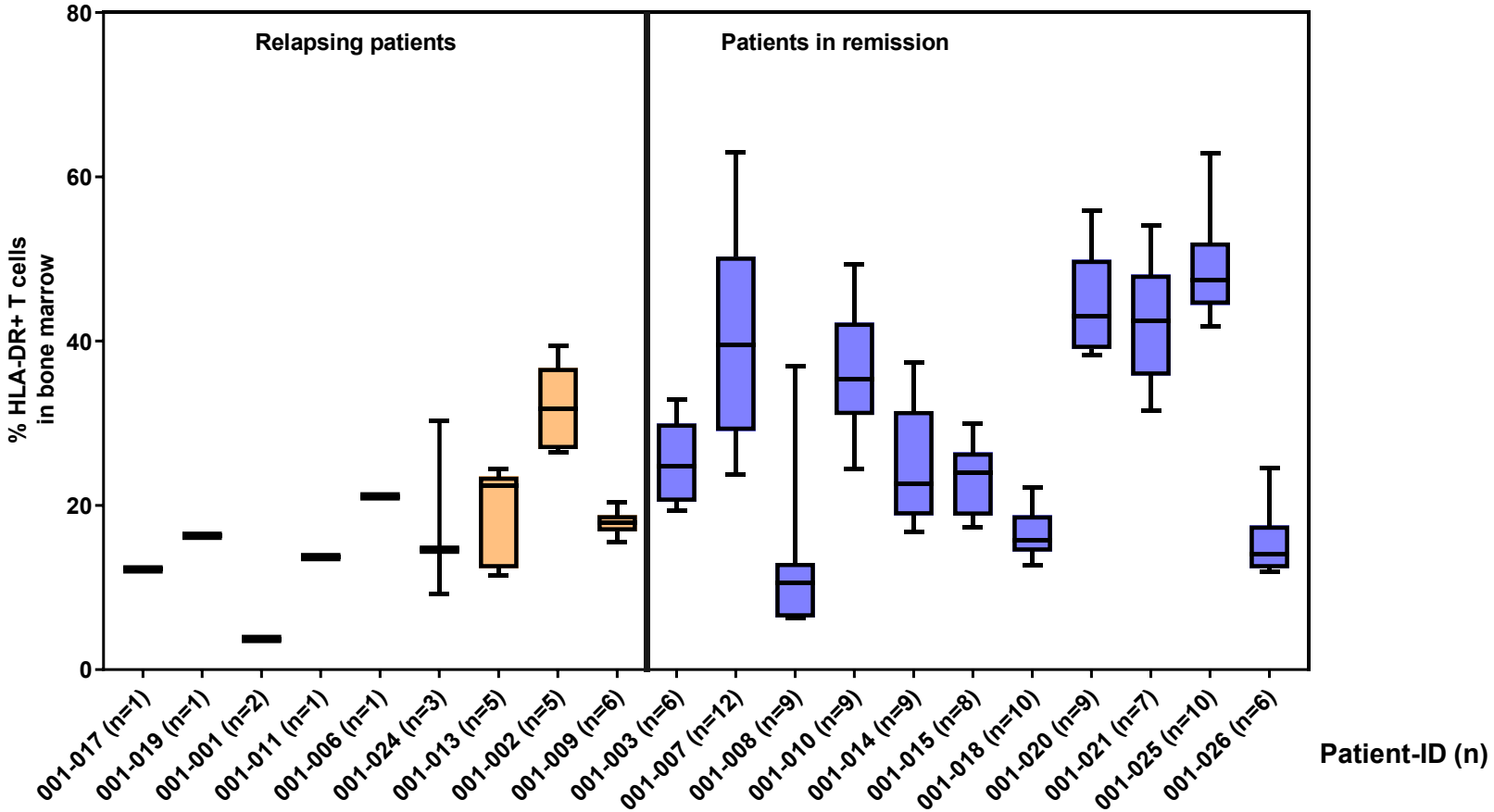
Mutational load in relation to relapse



- 23 common mutations were analysed: ASXL1, BCOR, CALR, CBL, CEBPA, DNMT3A, ETV6, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MPL, NPM1, NRAS, RUNX1, SF3B1, SRSF2, TET2, TP53, U2AF1
- As expected, higher mutational load correlated with relapse

Activation of T-cells in the bone marrow

- The number of activated, HLA-DR+/CD3+ T cells is increased in bone marrow and peripheral blood (not shown) of patients that stay in remission



Summary

- A fast DC immunotherapy against WT-1 and PRAME in post-remission AML patients is safe and well tolerated, which is particularly important for elderly patients
- The vaccines could be manufactured in all patients, despite chemotherapy pretreatment
- PFS and OS showed encouraging results at 2 years in this first in human clinical trial in 20 patients
- Specifically the OS in patients ≥ 60 years of 80% at 2 years is worth highlighting and warrants further studies to assess efficacy