

# The case of an orphan disease:



**Observational study on T-PLL transplants based on EBMT/ERIC recommendations for allogeneic and autologous stem cell transplantation in T-prolymphocytic leukaemia**

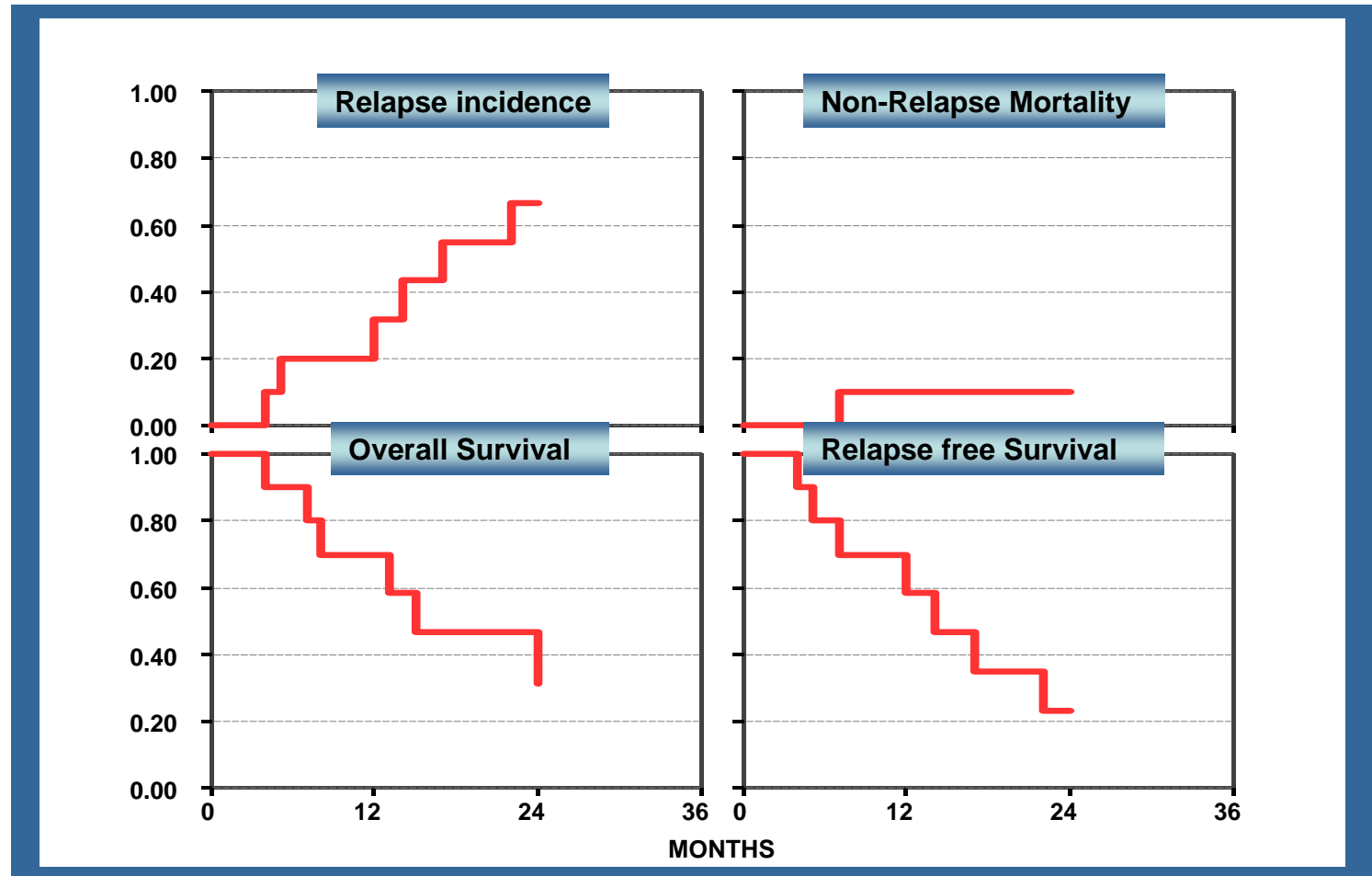
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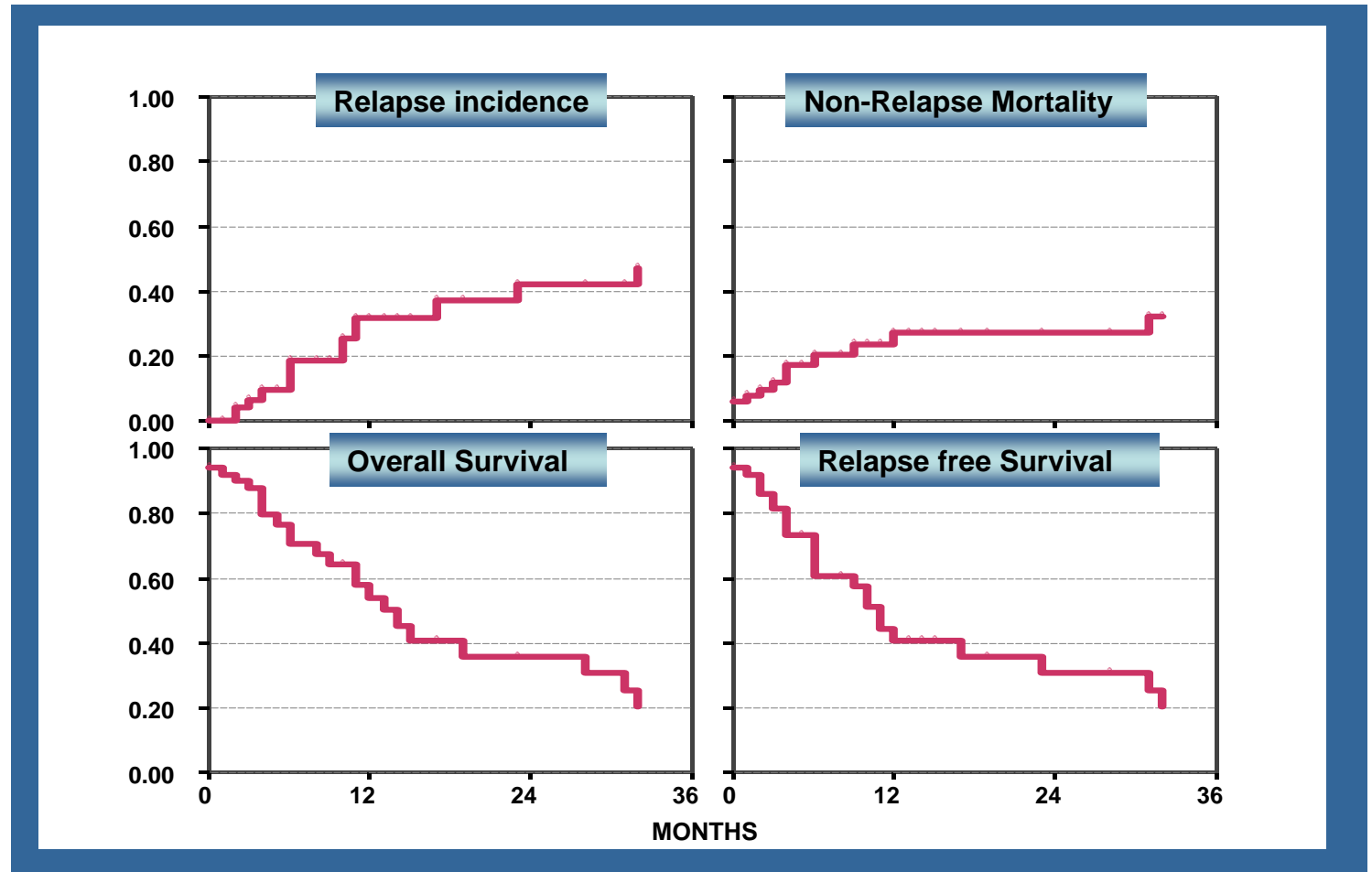
# Prospective Observational Audit on T-PLL

- T prolymphocytic leukemia (T-PLL) is a rare, aggressive neoplasia of T lymphoid lineage which is characterized by poor survival of less than one year.
- Incidental reports suggest that both autologous and allogeneic hematopoietic stem cell transplantation (HSCT) might be effective in this disease.
- This is also supported by a retrospective analysis of 65 patients registered in the EBMT database (presented last year) but more formal proof of this concept is lacking.

# Relapse, NRM, OS and RFS in autoSCT for T-PLL (N=13)



# Relapse, NRM, OS and RFS in alloSCT for T-PLL (N=52)



# Prospective Observational Study on T-PLL

- Originally, we have planned prospective trial on T-PLL. However, during CLWP discussion in Lyon it became clear that it is impossible to perform such an international formal prospective trial under the current regulatory framework. Then, our answer to the criticism was that it is possible to prospectively register patients and then to retrospectively analyze the results. This way, we developed a new concept of two complementary projects:

# Prospective Observational Study on T-PLL

- The first is called "**EBMT prospective observational audit on allogeneic and autologous transplantation in T-PLL**" and means that transplant centers are encouraged to register their patients with T-PLL very timely with the EBMT, followed by **mandatory** submission of EBMT MedB and follow-up forms.



# EBMT/ERIC recommendations for allogeneic and autologous transplantation in T-PLL



- The second is the "**EBMT/ERIC recommendations for allogeneic and autologous transplantation in T-PLL**".
- These are expert opinion-based recommendations that cover criteria for the diagnosis of T-PLL, transplant eligibility, pre-transplant remission induction strategies, remission requirements, timing of HSCT, donor compatibility criteria, conditioning, GVHD prophylaxis, and MRD monitoring.

# The inclusion of T-PLL patients will be based on uniform criteria

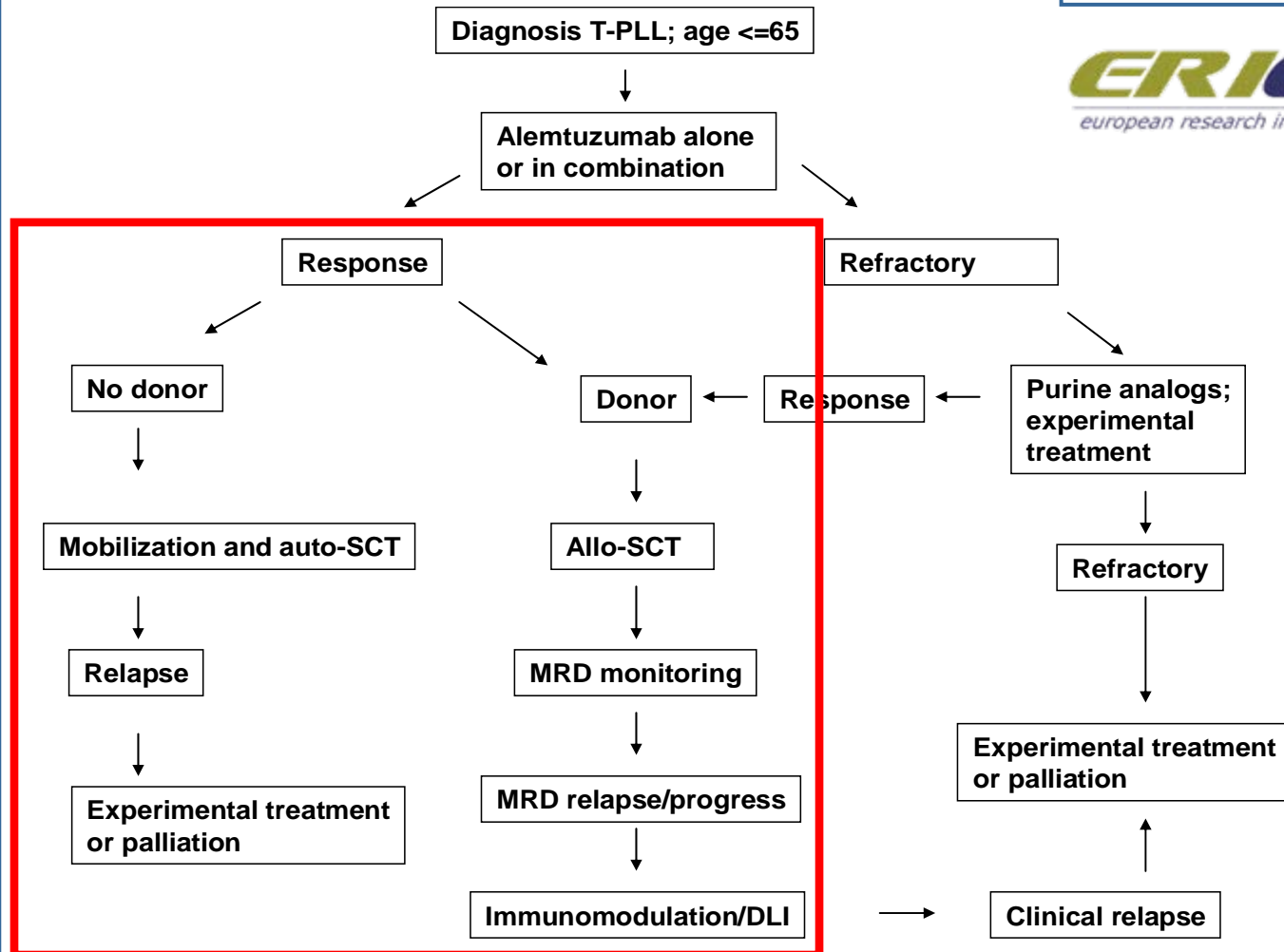
## Major criteria

- lymphocytosis above  $5 \times 10^9/L$  composed of either CD4+, CD8-, or CD4+, CD8+ or CD8+, CD4- cells, that are usually TdT negative and positive for CD2, CD3 (that could only be in cytoplasm), and CD7 combined with characteristic cytogenetic abnormalities [inv(14)(q11q32), t(14:14)(q11q32), del(14)(q12), t(11:14)(q23;q11), t(7:14)(q35;q32.1), t(X:14)(q35;q11) and/or idic(8) (p11)] detected in either marrow and peripheral blood cells or TCL1 expression [determined by Western blotting with anti TCL1 antibody]. Presence of more than 10% marrow infiltration with cells of the same phenotype and/or cytogenetics.
- lymphocytosis above  $50 \times 10^9/L$  composed of either CD4+, CD8-, or CD4+, CD8+ or CD8+, CD4- cells at diagnosis with aforementioned cytogenetic abnormalities but also with other abnormalities and with unavailable result of cytogenetic analysis. Presence of more than 10% marrow infiltration with cells of the same phenotype and/or cytogenetics.

## Minor criteria

- presence of effusions with cells of aforementioned appearance and phenotype
- enlarged spleen and/or lymph nodes at diagnosis.
- presence of B symptoms at diagnosis.
- progressive course of disease (doubling time of less than 6 months)

**One major and one minor criterion would be required for diagnosis.**



# Reporting and analysis

- **Initial registration** of T-PLL patients scheduled for the transplantation with the EBMT
- **Mandatory** submission of EBMT MedB and follow-up forms including also patients who were finally not transplanted.
- **Outcome analysis.**

# Conclusion

- With these two complementary components (prospective registration and recommendations) it should be possible to largely improve the usual quality of registry-based data and to generate scientifically sound knowledge on HSCT in an orphan disease such as T-PLL.

# Participation

- 23 centers agreed to participate
- 14 centers said no
- 27 patients in 12 centers included so far (expectation 50, interim analysis 25 pending)
- 18 MedB forms entered
- Information is available on EBMT website.
- Data registration and data collection is done by the Leiden Data Office.
- **Join this audit, please!**