SUPPLEMENTARY APPENDIX

The toxicity of very prolonged courses of PEGasparaginase or *Erwinia* asparaginase in relation to asparaginase activity, with a special focus on dyslipidemia

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Supplemental file accompanying the paper

Toxicity of very prolonged PEGasparaginase and *Erwinia* asparaginase courses in relation to asparaginase activity levels with a special focus on dyslipidemia

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Supplemental results

Toxicities (pancreatitis, thrombosis, central neurotoxicity)

To evaluate the relation between the parameters; asparaginase activity levels, triglyceride and ammonia levels after log-transformation and the incidence of toxicities (pancreatitis, thrombosis, central neurotoxicity), Cox-regression with time-dependent variables was used. Treatment with either PEGasparaginase or *Erwinia* asparaginase in case of an allergy to or silent inactivation of PEGasparaginase was taken into account by stratification in this analysis. No significant relations were found using time-dependent Cox-regression.

Legends to Supplemental Figures

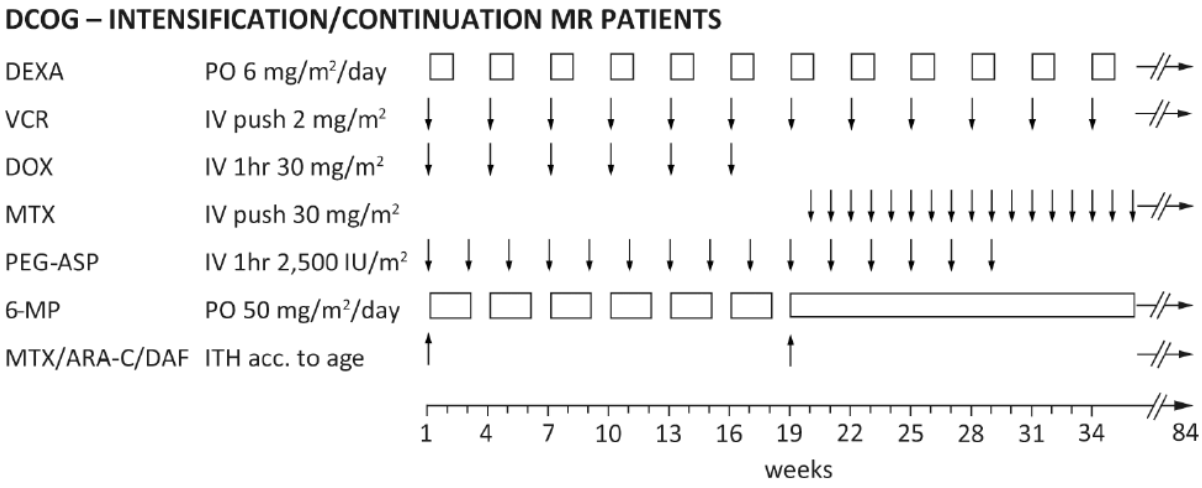
Supplemental Figure 1

The intensification/continuation phase of the Dutch Childhood Oncology Group ALL-10 protocol (medium risk group, MRG).

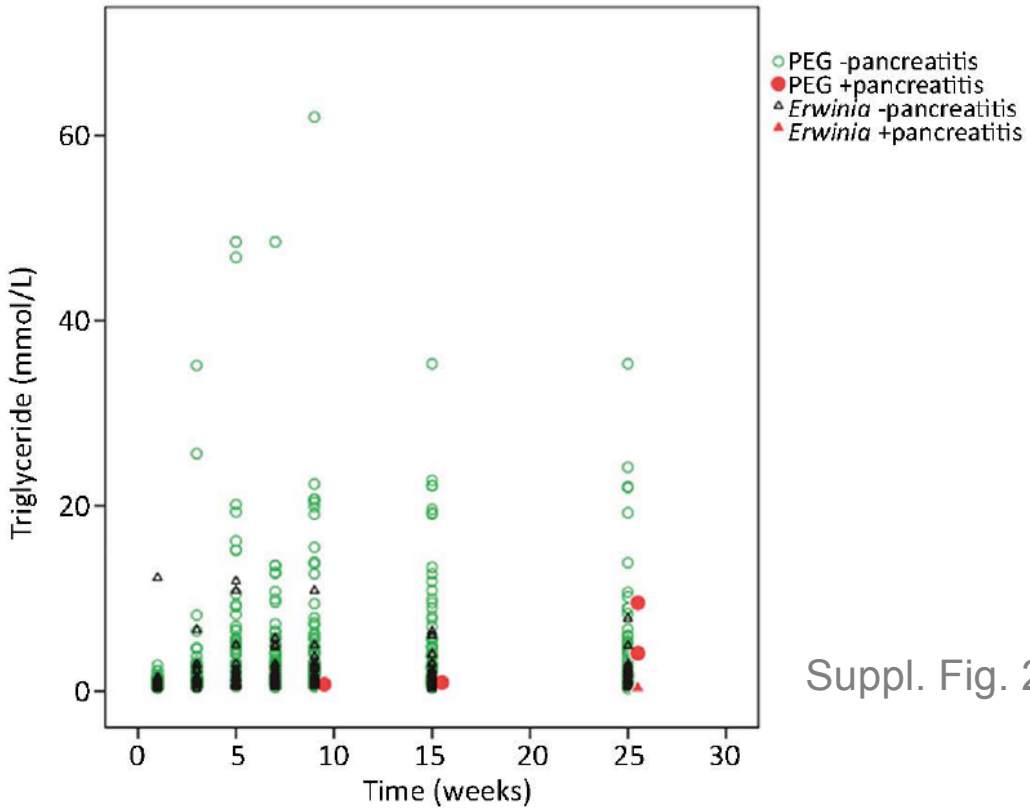
Supplemental Figure 2

Incidence of toxicities (pancreatitis, thrombosis, central neurotoxicity) in relation to longitudinal parameters (asparaginase activity levels, triglyceride and ammonia levels).
Panels A-B: pancreatitis; panels C-D: thrombosis; panels E-F: central neurotoxicity.
The red dots and red triangles indicate the occurrence of toxicities using very prolonged PEGasparaginase or *Erwinia* asparaginase courses.
Please note that in Panels A-B one patient on *Erwinia* asparaginase with pancreatitis is not shown as this patient had not subsequent asparaginase activity level and/or triglyceride level at the moment of pancreatitis occurrence.

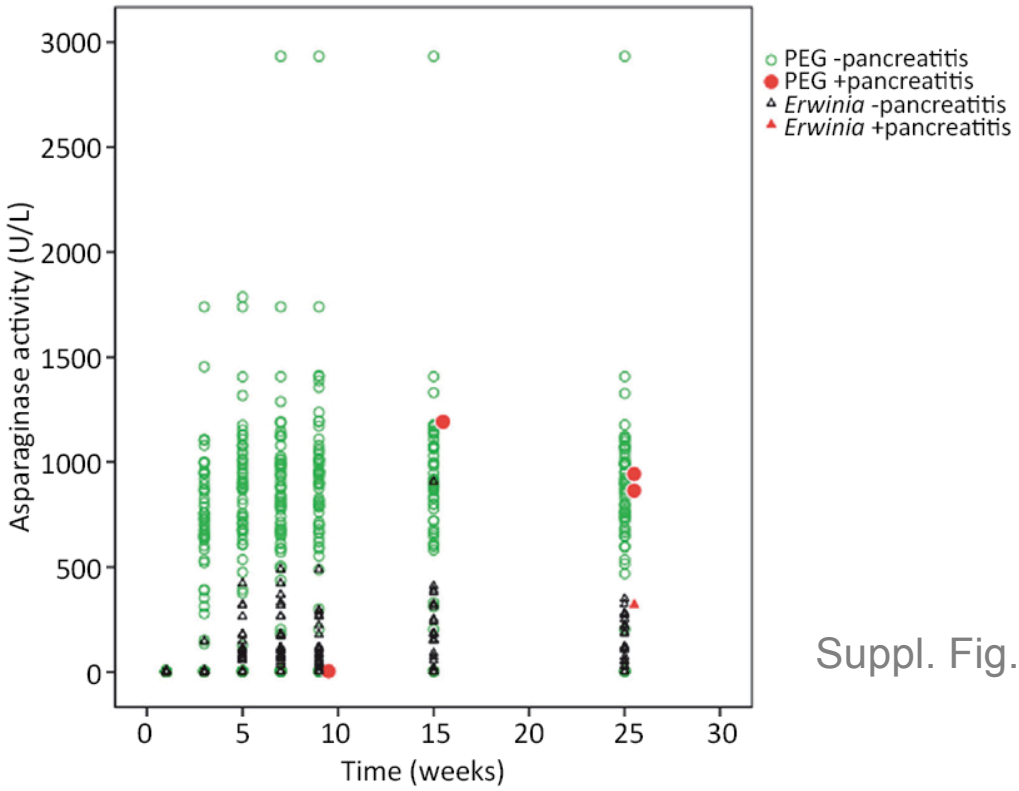
Supplemental Figure 1: DCOG ALL-10 medium risk intensification protocol.



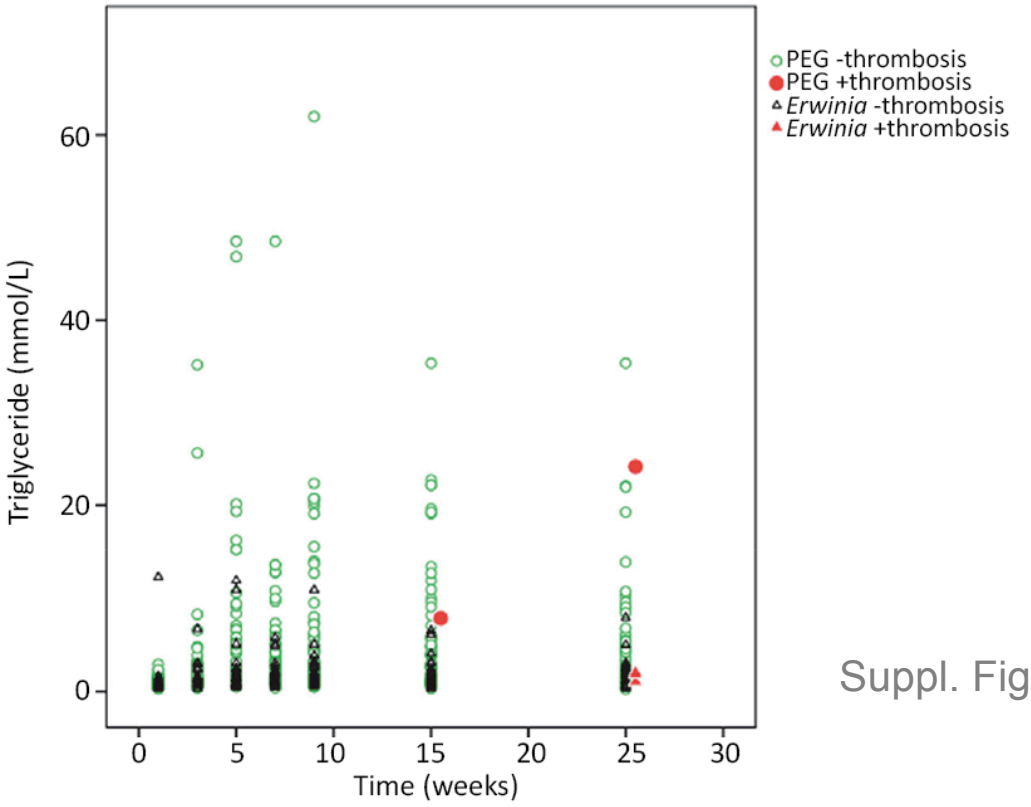
Supplemental Figure 2: Incidence of toxicities (pancreatitis, thrombosis, central neurotoxicty) in relation to longitudinal parameters (asparaginase activity levels, triglyceride and ammonia levels).



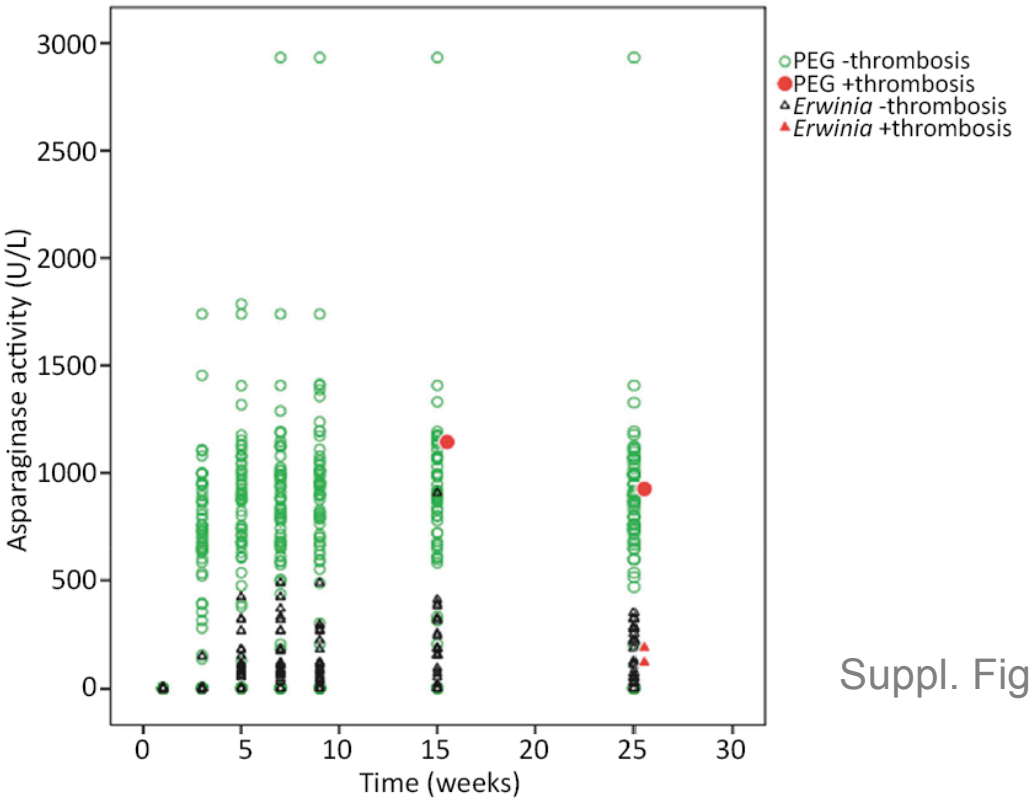
Suppl. Fig. 2A



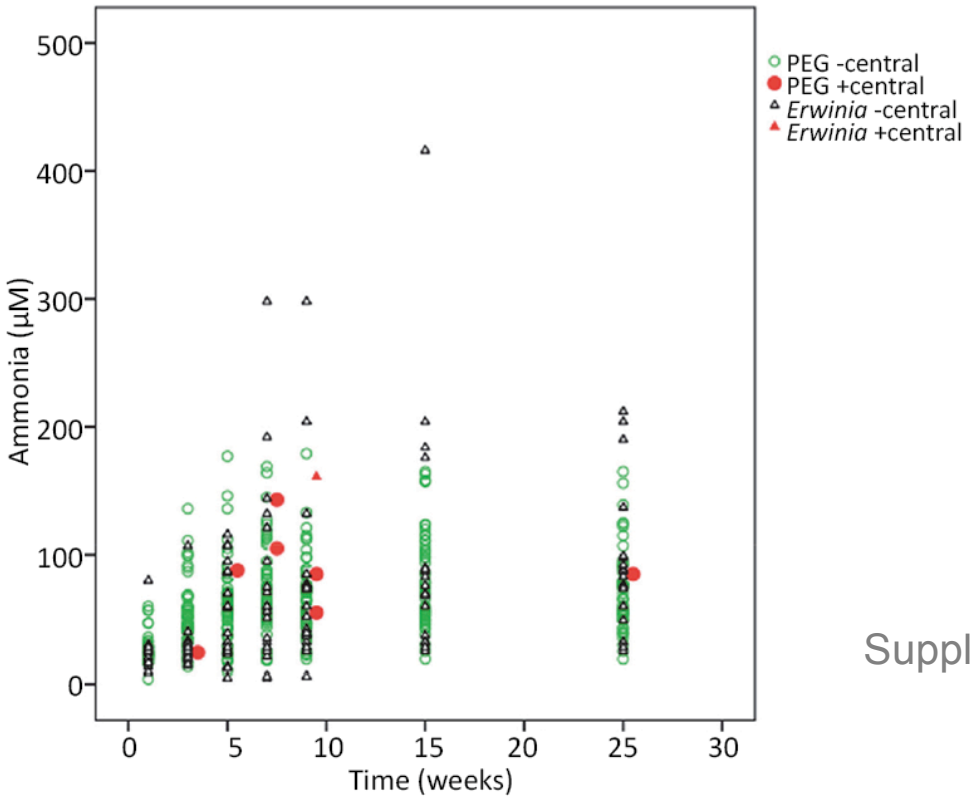
Suppl. Fig. 2B



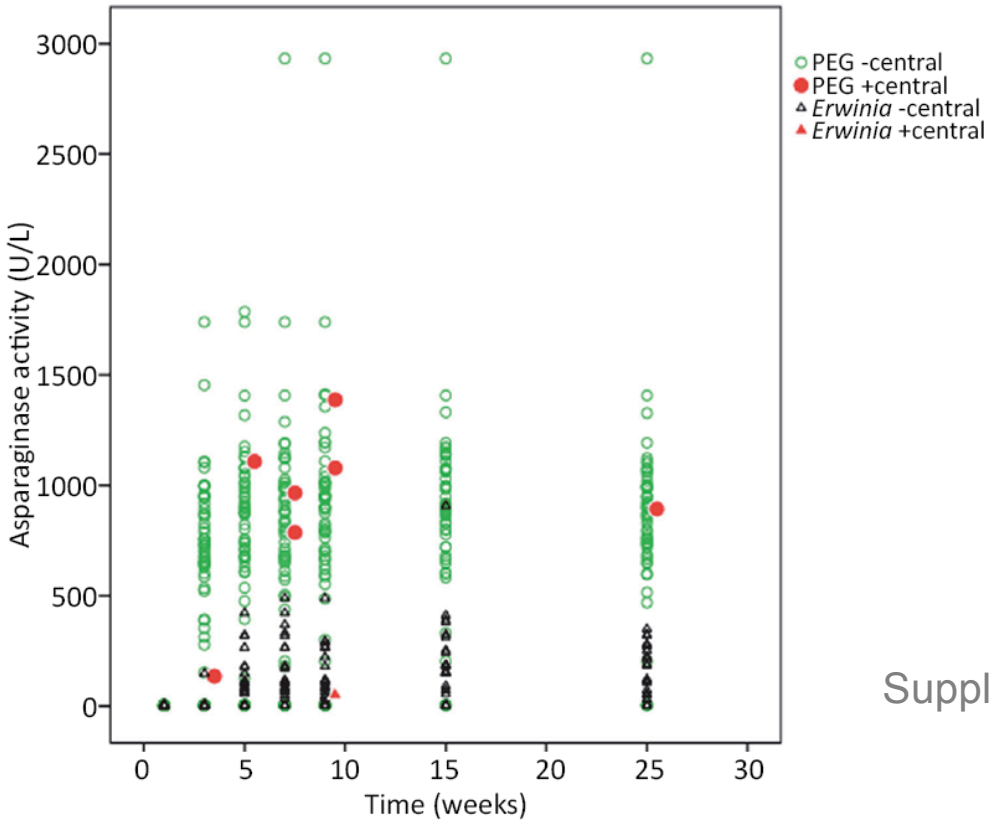
Suppl. Fig. 2C



Suppl. Fig. 2D



Suppl. Fig. 2E



Suppl. Fig. 2F