# Evaluating the clinical impact and feasibility of therapeutic drug monitoring of pazopanib in a real-world soft tissue sarcoma cohort

Marinda Meertens[#1], Eline L. Giraud[#2], Maud BA van der Kleij[3,4], Kim Westerdijk[5], Niels AD Guchelaar[4], Roos F Bleckman[6], Amy Rieborn[7], Alex LT Imholz[8], Hans-Martin Otten[9], Annelie Vulink[10], Maartje Los[11], Paul Hamberg[12], Winette TA van der Graaf[3], Hans Gelderblom[13], Dirk Jan AR Moes[7], K. Esther Broekman[6], Daan J Touw[14], Stijn LW Koolen[4,15], Ron HJ Mathijssen[4], Alwin DR Huitema[1,16,17], Nielka P van Erp[2], Ingrid ME Desar[5], Neeltje Steeghs[3]*, On behalf of the Dutch Pharmacology Oncology Group (DPOG)

[#]Both authors contributed equally to this work.

[1]Department of Pharmacy & Pharmacology, The Netherlands Cancer Institute, Antoni van Leeuwenhoek, Amsterdam, The Netherlands

[2]Department of Pharmacy, Radboud University Medical Centre, Nijmegen, The Netherlands

[3]Department of Medical Oncology, The Netherlands Cancer Institute, Antoni van Leeuwenhoek, Amsterdam, The Netherlands

[4]Department of Medical Oncology, Erasmus MC Cancer Institute, Rotterdam, The Netherlands

[5]Department of Medical Oncology, Radboud University Medical Centre, Nijmegen, The Netherlands

[6]Department of Medical Oncology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

[7]Department of Clinical Pharmacy and Toxicology, Leiden University Medical Center, Leiden, Netherlands

[8]Department of Medical Oncology, Deventer Hospital, Deventer, The Netherlands

[9]Department of Medical Oncology, Meander Medical Centre, Amersfoort, The Netherlands

[10]Department of Medical Oncology, Reinier de Graaf Hospital, Delft, The Netherlands

University of Groningen, Groningen, The Netherlands

[11]Department of Medical Oncology, St. Antonius Hospital, Nieuwegein, The Netherlands

[12]Department of Medical Oncology, Franciscus Gasthuis & Vlietland, Schiedam, The Netherlands

[13]Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

[14]Department of Clinical Pharmacy and Pharmacology, University Medical Center Groningen, The Netherlands

[15]Department of Pharmacy, Erasmus University Medical Center, Rotterdam, The Netherlands

[16]Department of Clinical Pharmacy, Utrecht University Medical Centre, Utrecht, The Netherlands

[17]Department of Pharmacology, Princess Máxima Centre for Pediatric Oncology, Utrecht, The Netherlands

*Corresponding author: n.steeghs@nki.nl

## Supplemental Material

***Table S1.*** *univariate and multivariate cox-regression on progression-free survival.*

| **Variable** | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | HR (95%CI) | P-value | HR (95%CI) | P-value |
| Performance status ≥ 2 vs. 0-1 | 1.76 (0.80 – 3.85) | 0.157 | 1.95 (0.85 – 4.46) | 0.113 |
| Subtype Soft-Tissue Sarcoma: | | | | |
| Leiomyosarcoma vs. all other subtypes | 1.16 (0.75 – 1.80) | 0.497 | 1.17 (0.75 – 1.84) | 0.478 |
| Synovial sarcoma vs. all other subtypes | 1.02 (0.52 – 2.00) | 0.945 | 1.09 (0.55 – 2.15) | 0.806 |
| Previous lines of systemic treatment ≥ 2 vs. 0-1 | 1.17 (0.71 – 1.92) | 0.546 | 1.00 (0.59 – 1.72) | 0.988 |
| TDM-guided dosing vs. no-TDM guided dosing | 0.79 (0.50 – 1.26) | 0.327 | 0.77 (0.47 – 1.25) | 0.287 |

*CI* confidence interval, *TDM* therapeutic drug monitoring

***Table S2.*** *univariate and multivariate cox-regression on overall survival.*

| **Variable** | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | HR (95%CI) | P-value | HR (95%CI) | P-value |
| Performance status ≥ 2 vs. 0-1 | 3.12 (1.48 – 6.57) | 0.003* | 2.99 (1.38 – 6.50) | 0.005* |
| Subtype Soft-Tissue Sarcoma: | | | | |
| Leiomyosarcoma vs. all other subtypes | 0.58 (0.37 – 0.90) | 0.016* | 0.58 (0.37 – 0.91) | 0.018* |
| Synovial sarcoma vs. all other subtypes | 0.57 (0.27 – 1.22) | 0.148 | 0.62 (0.29 – 1.32) | 0.214 |
| Previous lines of systemic treatment ≥ 2 vs. 0-1 | 1.12 (0.69 – 1.81) | 0.641 | 1.08 (0.65 – 1.79) | 0.780 |
| TDM-guided dosing vs. no-TDM guided dosing | 0.94 (0.58 – 1.51) | 0.786 | 0.95 (0.57 – 1.60) | 0.858 |

*CI* confidence interval, *TDM* therapeutic drug monitoring

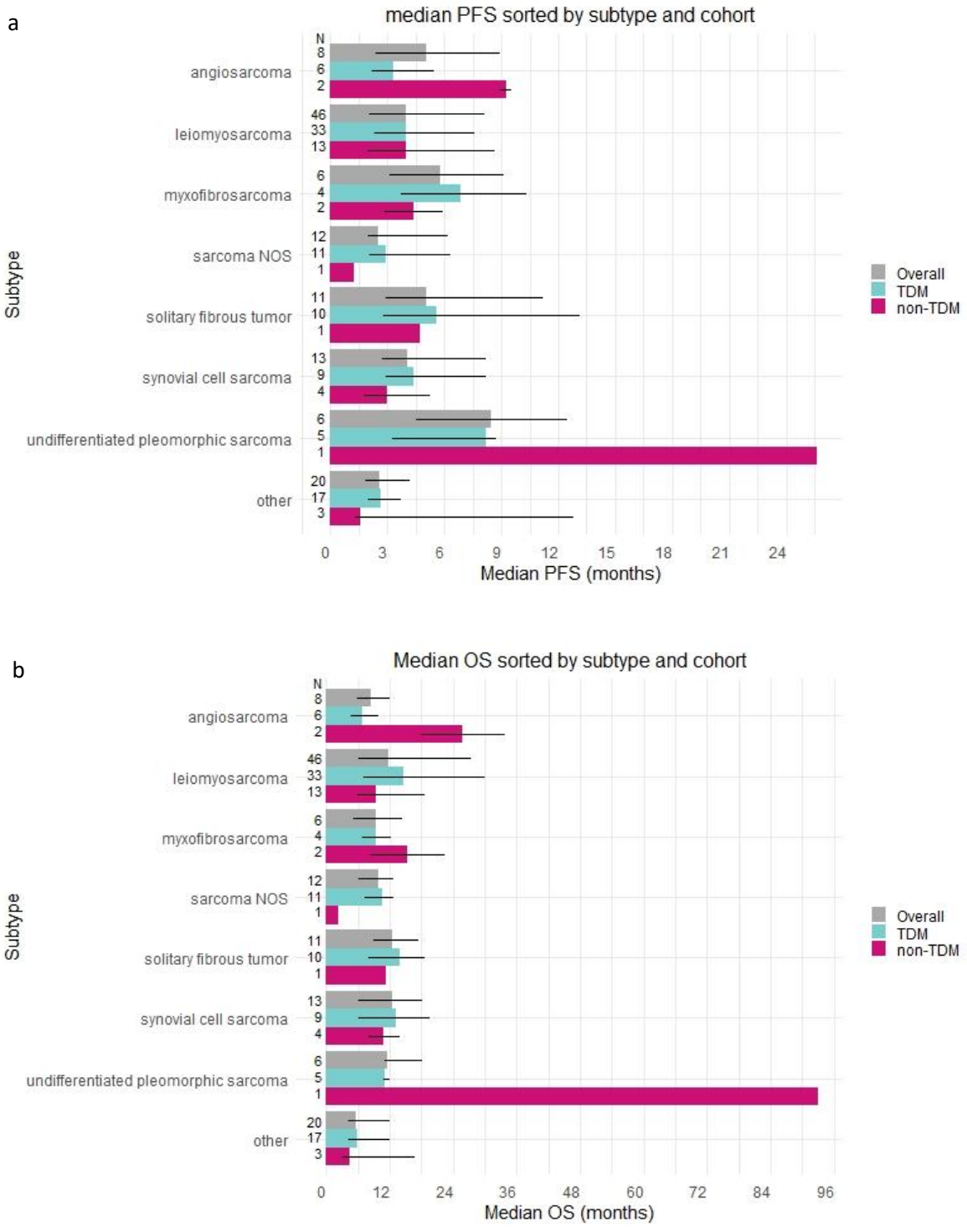
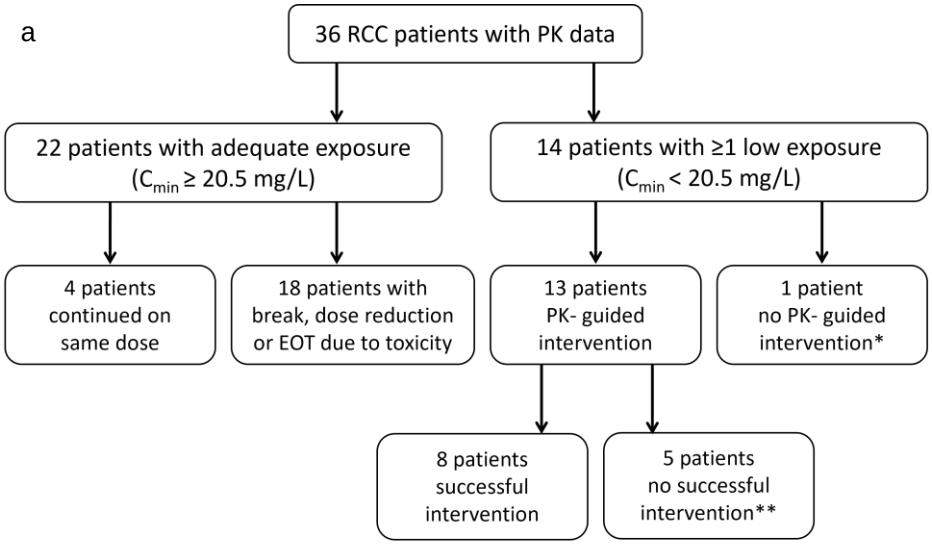



***Fig. S1*** *Median progression-free survival (a) and median overall survival (b) sorted by subtype and cohort. N* number, *NOS* not otherwise specified, *OS* overall survival, *PFS* progression-free survival, *TDM* therapeutic drug monitoring. Other is a sum of all patients with subtypes including <5 patients. These include among others malignant peripheral nerve sheath tumor (n=4), liposarcoma (n=3), epithelioid hemangioendothelioma (n=2), rhabdomyosarcoma (n=2) and intima sarcoma (n=2).



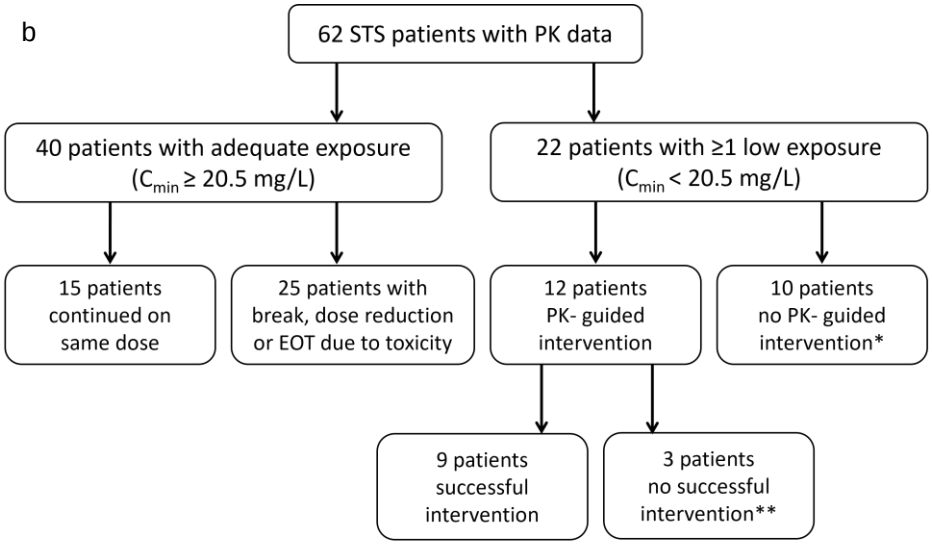




***Fig. S2*** *Feasibility analysis for metastatic renal cell cancer (a) and soft-tissue sarcoma (b).* $C_{min}$ trough concentration, *EOT* end of treatment, *PK* pharmacokinetic, *RCC* renal cell carcinoma