

Fibroblast Activation Protein (FAP) generates a specific type III collagen fragment detectable in serum, which is associated with survival outcomes in patients with PDAC

Nicholas Willumsen¹, Dora Chrysoulidou¹, Rasmus S. Pedersen¹, Julia S. Johansen^{2,3,4}, Astrid Johansen^{2,3,4}, Inna M. Chen², Morten A. Karsdal¹

1. Nordic Bioscience, Herlev, Denmark; 2. Department of Oncology, Copenhagen University Hospital – Herlev and Gentofte, Herlev, Denmark; 3. Department of Medicine, Copenhagen University Hospital – Herlev and Gentofte, Herlev, Denmark; 4. Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark

BACKGROUND & AIM

FAP expression is very low in healthy tissues, and highly upregulated in tumors

Fibroblast activation protein (FAP) has unique proteolytic activity.

The disease specific expression and unique proteolytic activity have made FAP an interesting protein to be utilized for drug targeting purposes.

Therefore, it is important to identify the patients with FAP activity.

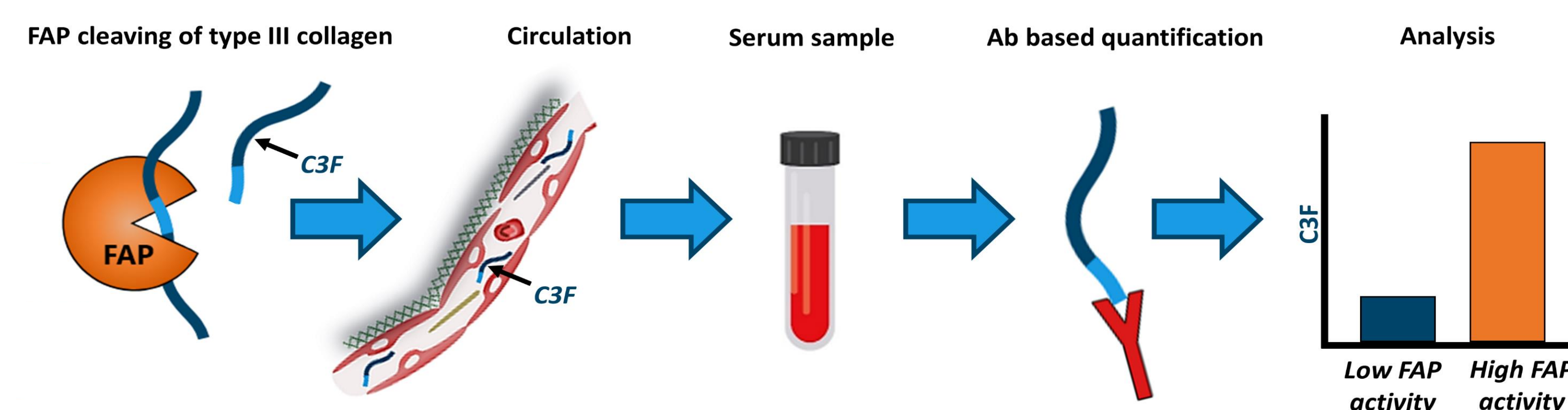
The aim of this study was to measure FAP activity indirectly through its proteolytic degradation of type III collagen in serum from patients with PDAC and evaluate its prognostic value..

METHODS

FAP activity was assessed indirectly by quantifying FAP-cleaved type III collagen using the nordicC3F ELISA, as previously described by Pedersen RS, et al., Biomedicines. 2024

Assay principle:

FAP-mediated cleavage of type III collagen results in release of a peptide fragment into circulation (C3F)



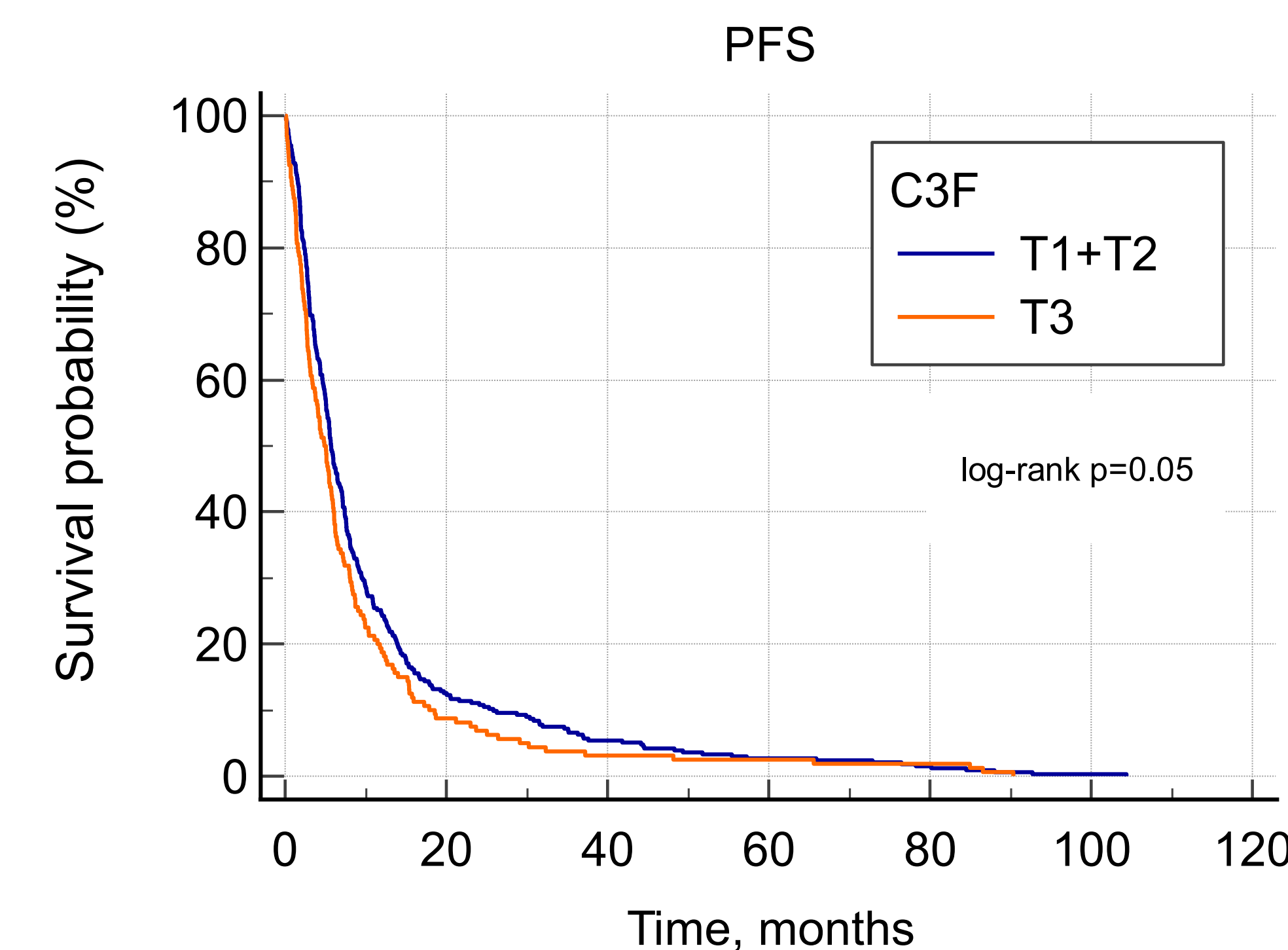
Samples & Patients:

Pre-treatment serum samples were obtained from 525 patients with PDAC (stage II-IV) from the BIOPAC cohort (NCT03311776). Patients were treated with standard of care chemotherapy.

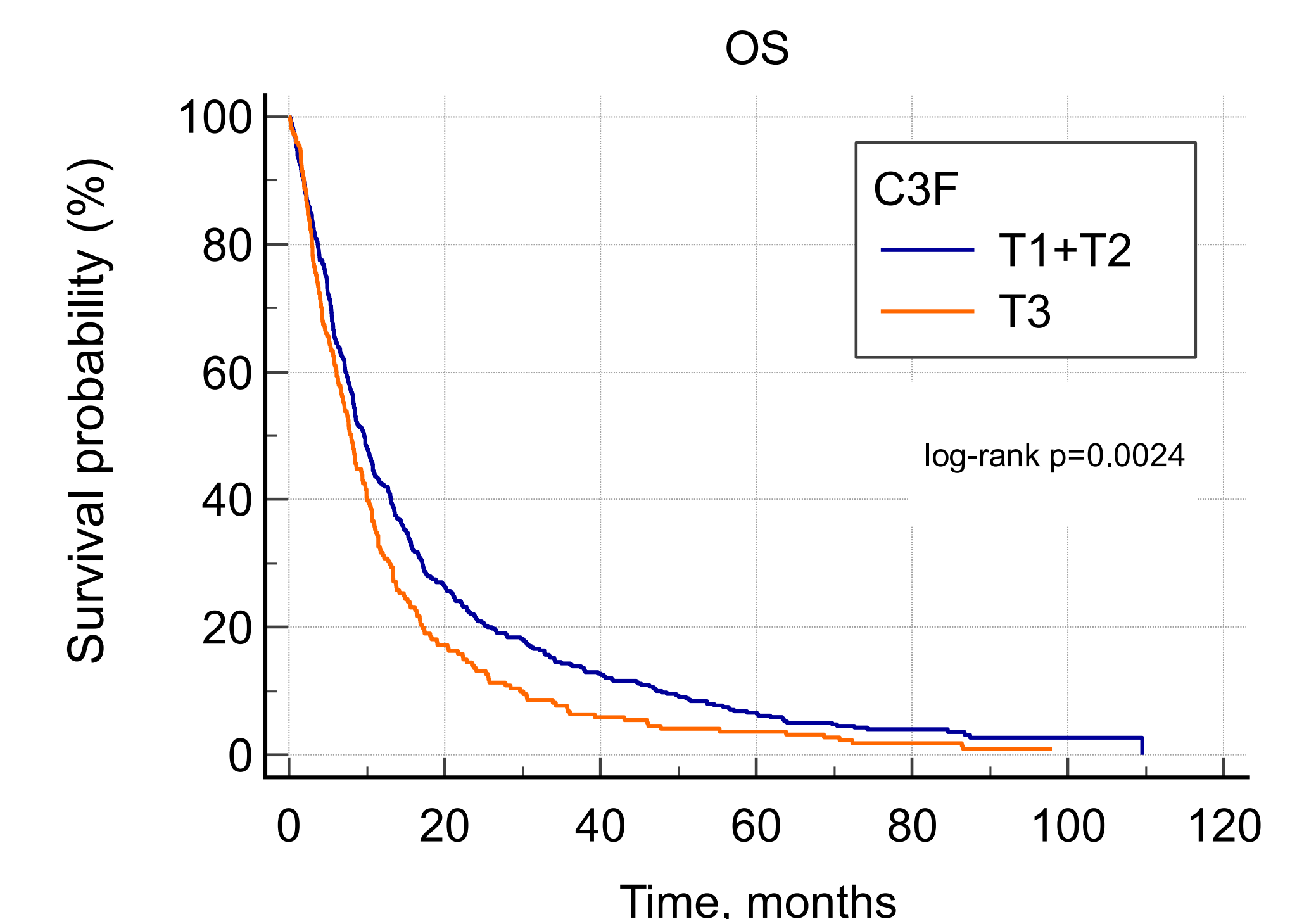
The patients were grouped based on the measured C3F levels, and the prognostic potential of the biomarker was assessed by investigating associations with progression free survival (PFS) and overall survival (OS) by Kaplan-Meier analysis and cox proportional hazard ratios..

Pharmacodynamic changes were assessed in a subgroup of patients (n=72)

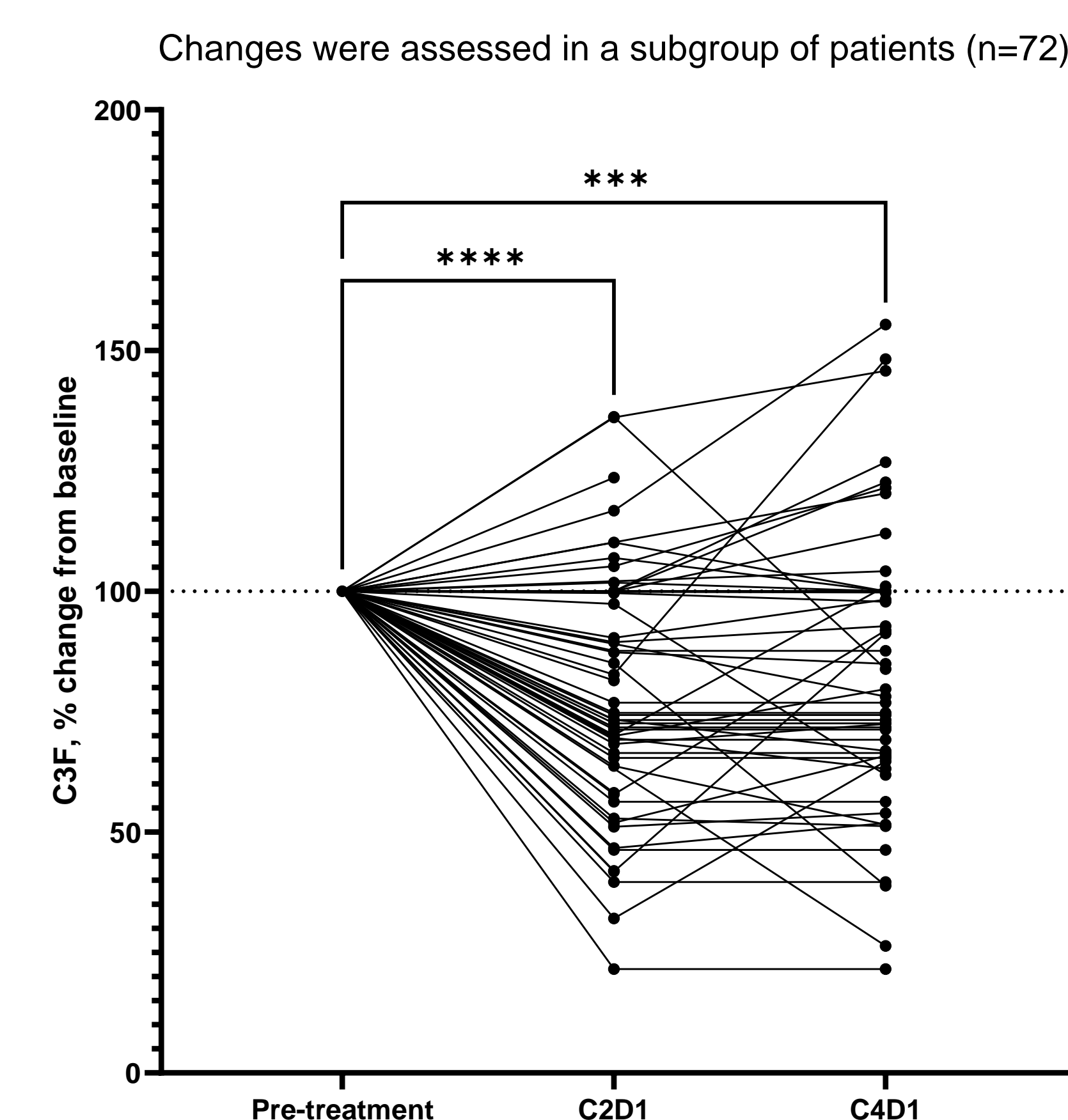
RESULTS



HR: 1.22, 95%CI: 1.00-1.48, p=0.05
Multivariate Cox regression analysis
Adjusted for age, gender, BMI, diabetes and CA19-9



HR: 1.36, 95%CI: 1.45-1.62, p=0.0004
Multivariate Cox regression analysis
Adjusted for age, gender, BMI, diabetes and CA19-9



Conclusion:
FAP-activity can be assessed non-invasively through quantification of FAP-cleaved type III collagen and is associated with survival outcome in patients with PDAC