Real-world validation of the PurIST classifier demonstrates enhanced therapy selection for Pancreatic Ductal Adenocarcinoma (PDAC) patients.

TEMPUS

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INTRODUCTION

PDAC is a particularly fatal condition lacking established biomarkers for the choice of first-line treatment (1L). The **PurIST** algorithm is a gene signature that categorizes PDAC tumors into **basal** or **classical** molecular subtypes and has been previously validated in a patient cohort of advanced PDAC (N=258).

In this post-hoc analysis study, we examine whether the PurIST subtypes can distinguish patients likely to respond to **FOLFIRINOX** (FFX) versus **Gemcitabine + nab-Paclitaxel** (GnP).
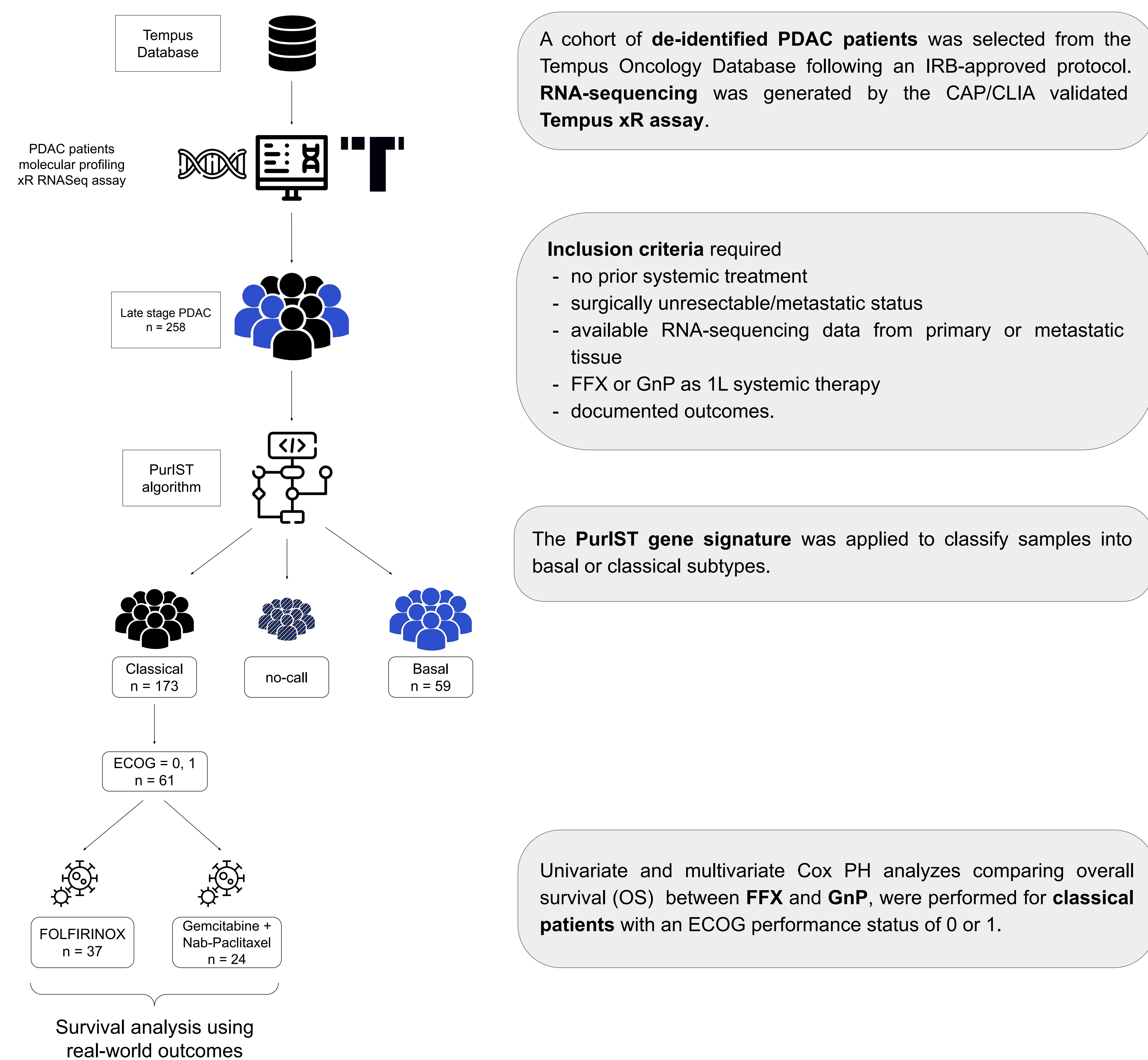
METHODS

Figure 1. Study workflow.

A cohort of **de-identified PDAC patients** was selected from the Tempus Oncology Database following an IRB-approved protocol. **RNA-sequencing** was generated by the CAP/CLIA validated **Tempus xR assay**.

Inclusion criteria required
- no prior systemic treatment
- surgically unresectable/metastatic status
- available RNA-sequencing data from primary or metastatic tissue
- FFX or GnP as 1L systemic therapy
- documented outcomes.

The **PurIST gene signature** was applied to classify samples into basal or classical subtypes.

Univariate and multivariate Cox PH analyzes comparing overall survival (OS) between **FFX** and **GnP**, were performed for **classical patients** with an ECOG performance status of 0 or 1.

SUMMARY

- Post-hoc analysis of real-world cohort of advanced PDAC patients.

- **Classical** patients with low ECOG scores have longer survival on 1L **FFX** compared to 1L GnP.

- Demonstrated potential for **PurIST** to be used in **treatment selection.**

RESULTS
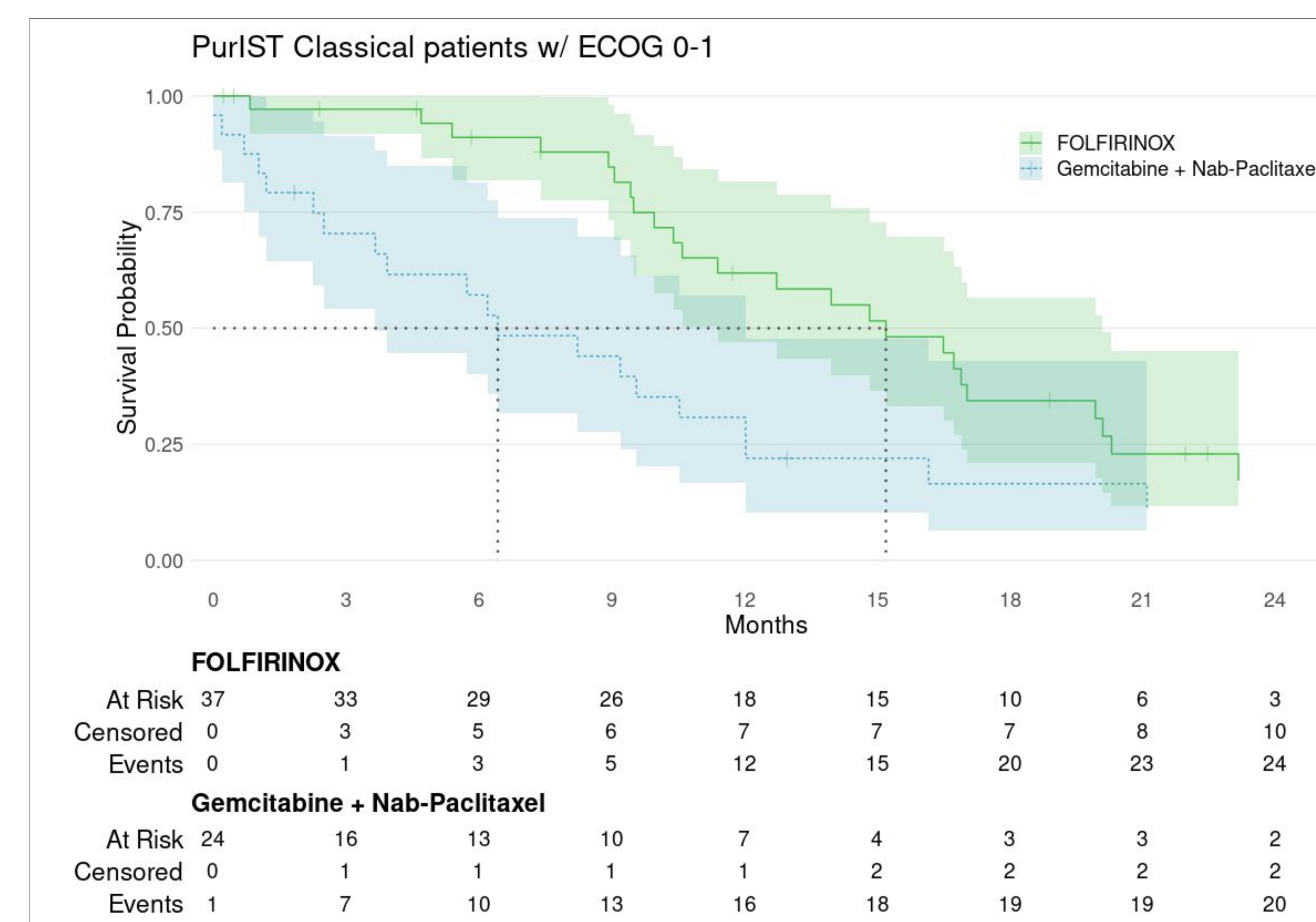
FOLFIRINOX benefit for classical patients

A univariate Cox PH analysis showed that classical patients with an ECOG score of 0 or 1 treated with FOLFIRINOX (N = 37) had a significantly longer OS time then classical patients with an ECOG score of 0 or 1 treated with Gemcitabine + nab-Paclitaxel (HR (95% CI) = 2.32 (1.29-4.17)).

This result remained significant in a multivariate Cox PH, adjusting for age and ECOG, (HR=2.5 (1.15-5.44)).

Figure 2. A. Kaplan-Meier curves showing differential survival in a univariate Cox PH model for classical patients. **B.** Forest plot representation of the multivariate Cox PH model with adjustment for age and ECOG status.
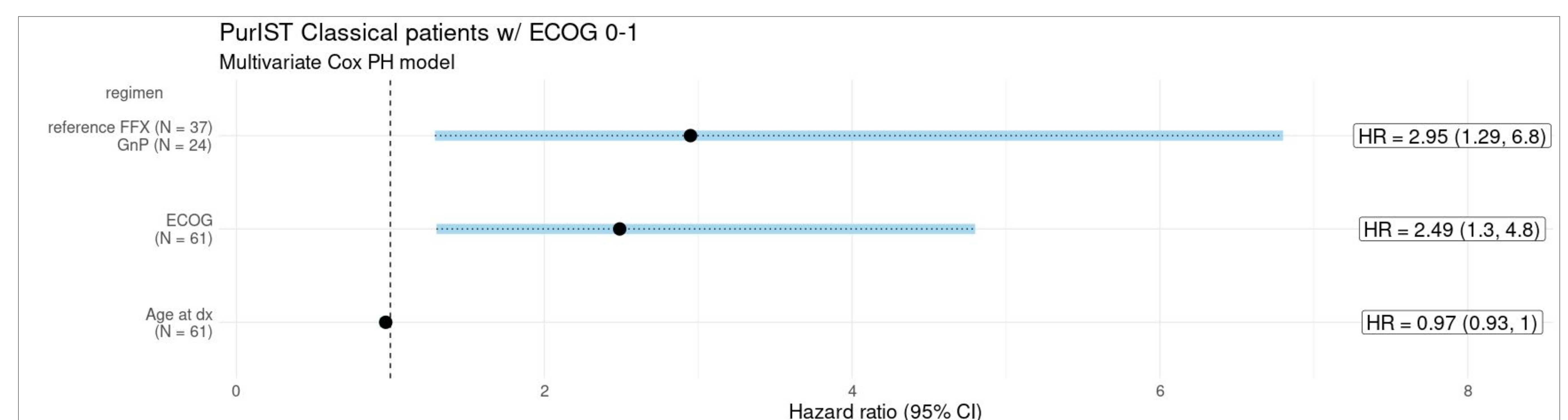
CONCLUSION

In this real-world cohort of advanced PDAC patients, we showed that classical patients with low ECOG scores had superior OS with 1L FFX treatment compared to 1L GnP. These findings demonstrate the potential for PurIST to aid in optimal treatment selection for patients with advanced PDAC.

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