

# Circulating tumor DNA (ctDNA) analysis from the prospective pT0 study of systematic endoscopic evaluation (SEE) in patients undergoing radical cystectomy (RC) for bladder cancer

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Abstract number: 837  
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## BACKGROUND/METHODS

- Accurately predicting the absence of residual tumor in the bladder after neoadjuvant treatment can facilitate bladder preservation options
- Prior investigator-initiated trial of SEE prior to RC to predict pT0 showed high specificity/low sensitivity<sup>1</sup>
- NPV in original cohort was 48.4% with SEE alone; 26% of SEE-negative pts were pT<sub>≥</sub>2 (NCT02968732)<sup>1</sup>
- Samples were retrospectively analyzed using the GRAIL research use only tumor-agnostic ctDNA platform<sup>2</sup> to improve NPV and predictive capacity
- ctDNA +/- SEE findings were evaluated as predictors of pT stage using Bayesian logistic regression and a grid search was used to identify a ctDNA cut-off that maximized the AUROC for pT=0
- RFS/OS by Kaplan-Meier (KM) method and Cox proportional hazards regression using ctDNA were calculated

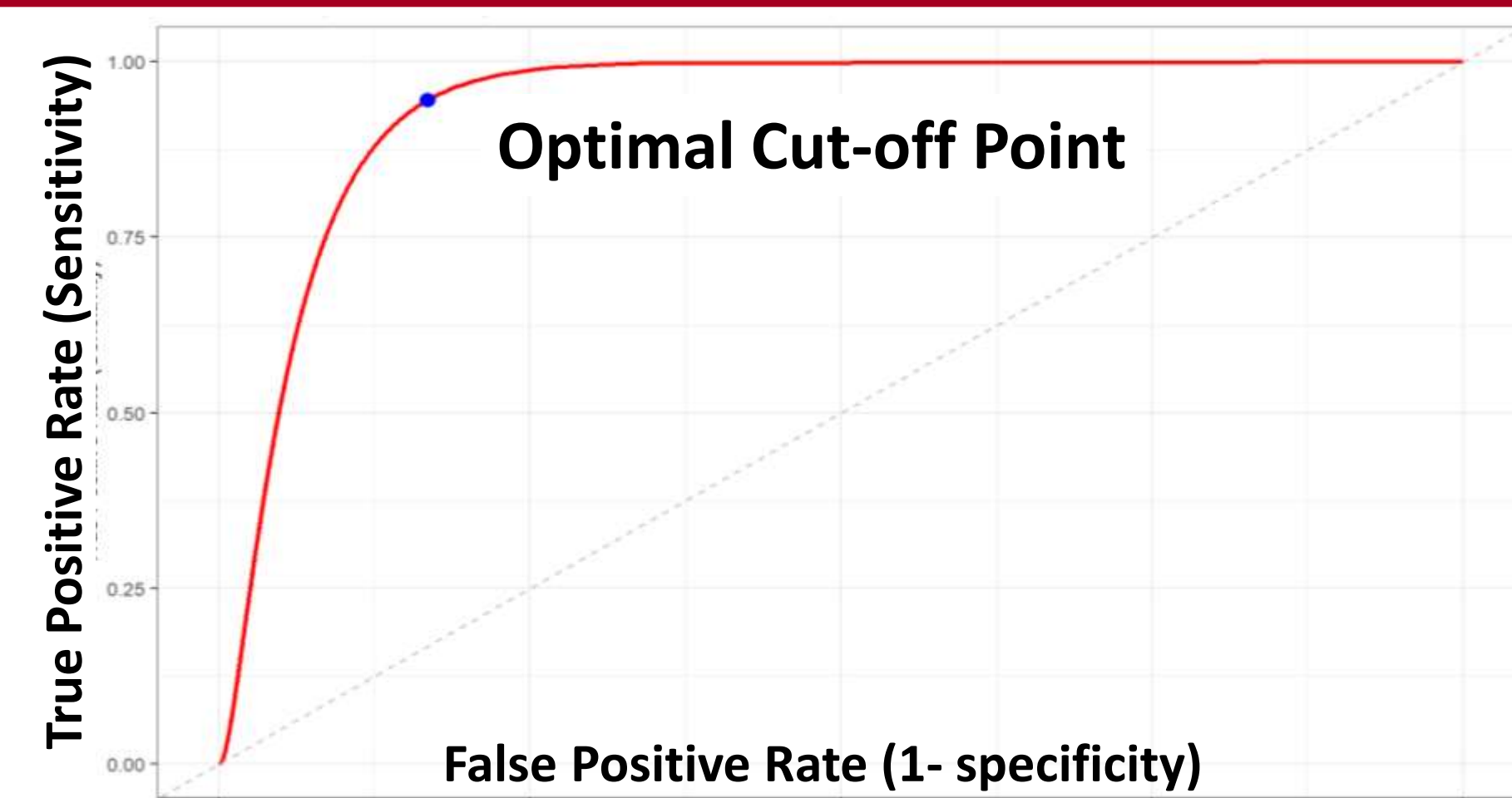
## DEMOGRAPHICS

Characteristic	pT>0, N (%)	pT=0 (N, %)
<b>Final (y)pT Stage</b>	40 (74.1%)	14 (25.9%)
<b>Sex</b>		
Male	31 (77.5%)	13 (92.9%)
<b>Race</b>		
White	38 (95.0%)	12 (85.7%)
<b>Initial Clinical Stage</b>		
NMIBC	14 (35.0%)	2 (14.3%)
MIBC	26 (65.0%)	12 (85.7%)
<b>Neoadj Chemo</b>		
Yes	22 (55.0%)	12 (85.7%)
<b>Median Age, yrs</b>	68.4	69.9
<b>Median F/up, yrs</b>	7.24	

## CONCLUSIONS

- Combining SEE with ctDNA improved prediction of pathologic complete response (pT0) at surgery
- Prognostic value of neg ctDNA at cystectomy compares favorably to pathologic complete response (pT0) as a prognostic marker for OS and RFS
- Analysis requires validation in additional datasets, but the high NPV is encouraging and warrants further prospective study using ctDNA with SEE to identify patients able to forgo RC

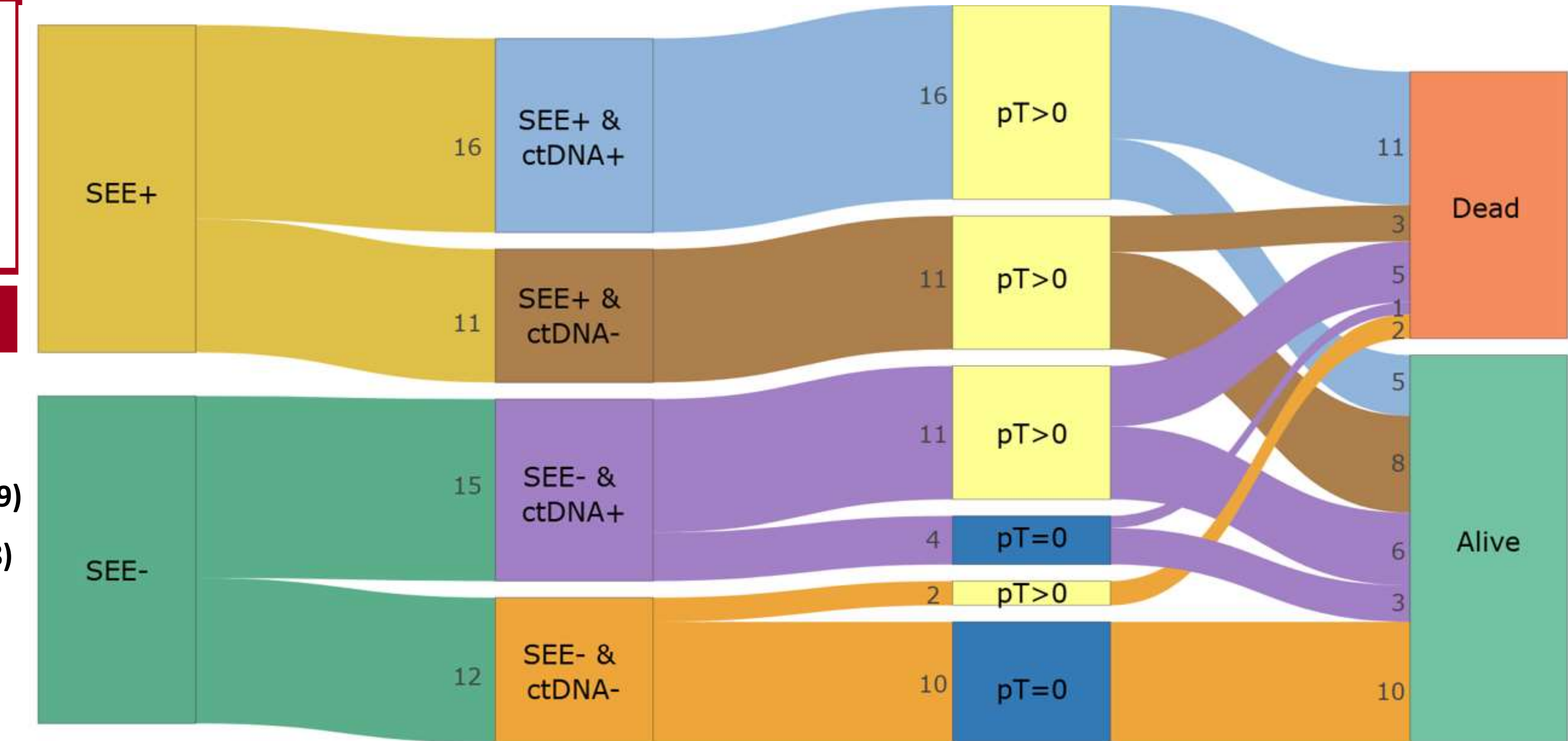
### Smoothed ROC Curve for ctDNA Cut-off



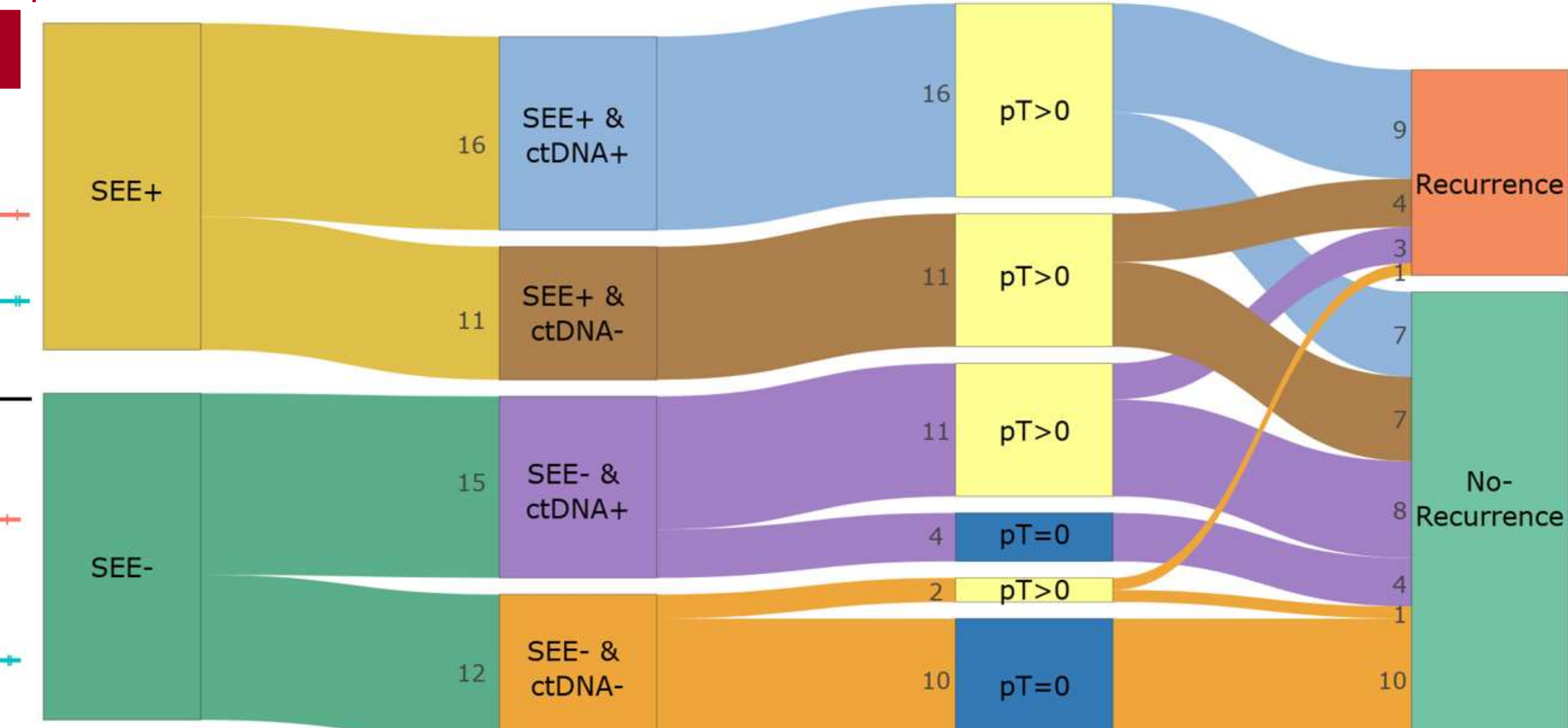
### Accuracy of ctDNA & SEE to Predict pT=0

	SEE OR ctDNA +	BOTH SEE & ctDNA -	Metric: % (95% CI)
>pT0	38	2	<b>SENSITIVITY: 95%</b> (0.83, 0.99)
pT=0	4	10	<b>SPECIFICITY: 71%</b> (0.45, 0.88)
			<b>PPV: 90%</b> (0.78, 0.96)
			<b>NPV: 83%</b> (0.55, 0.95)
			*NPVs Alone: <b>SEE: 52%; ctDNA: 43%</b>

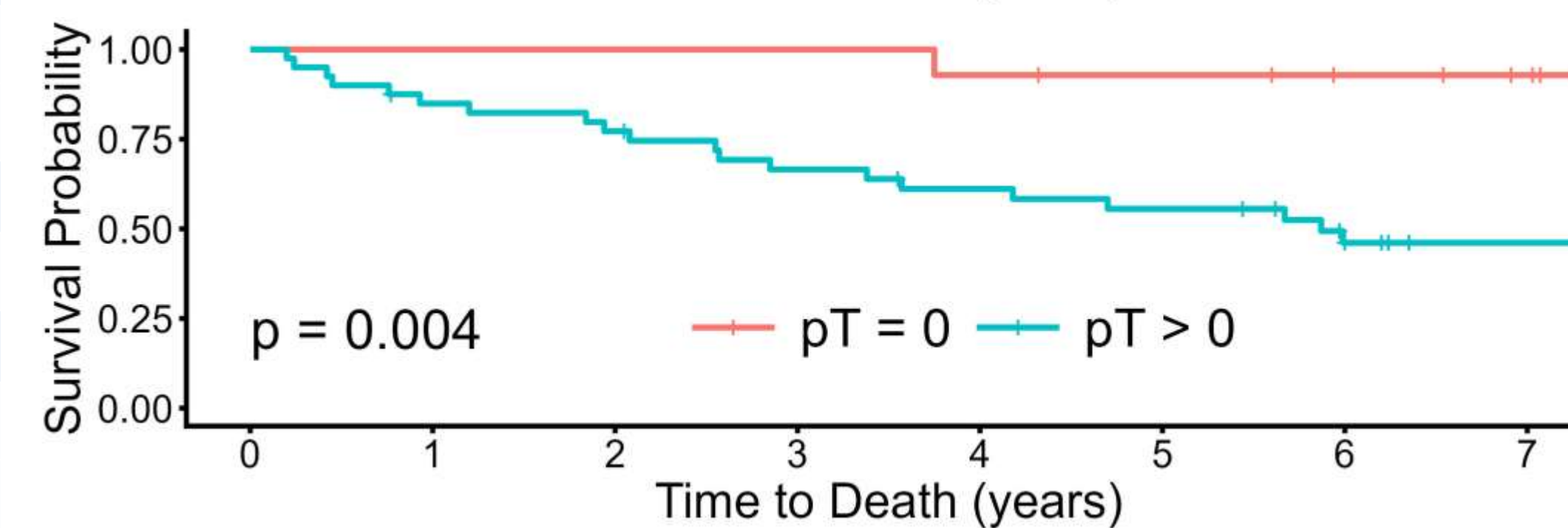
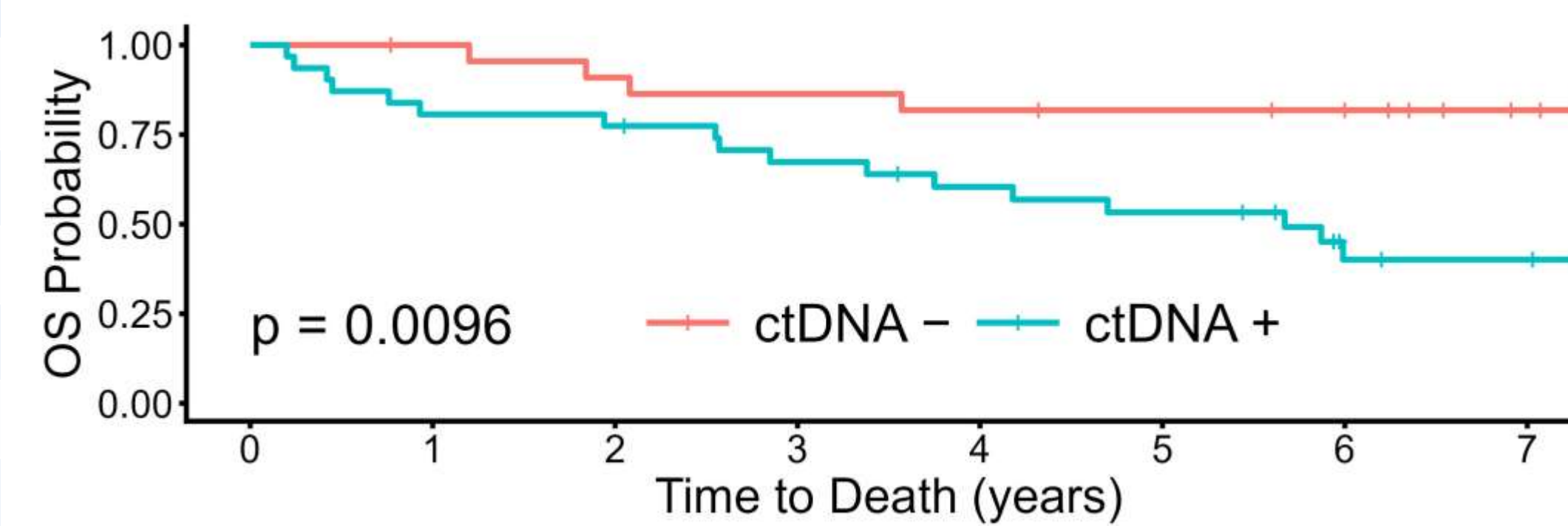
## Sankey Plot for Overall Survival



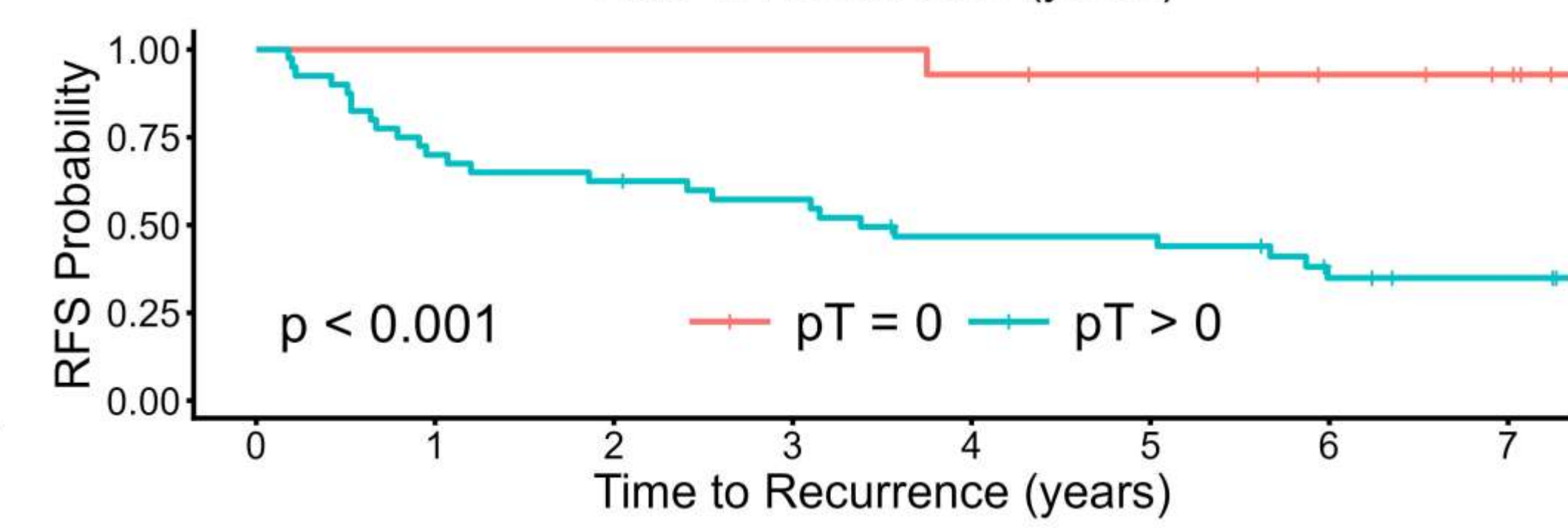
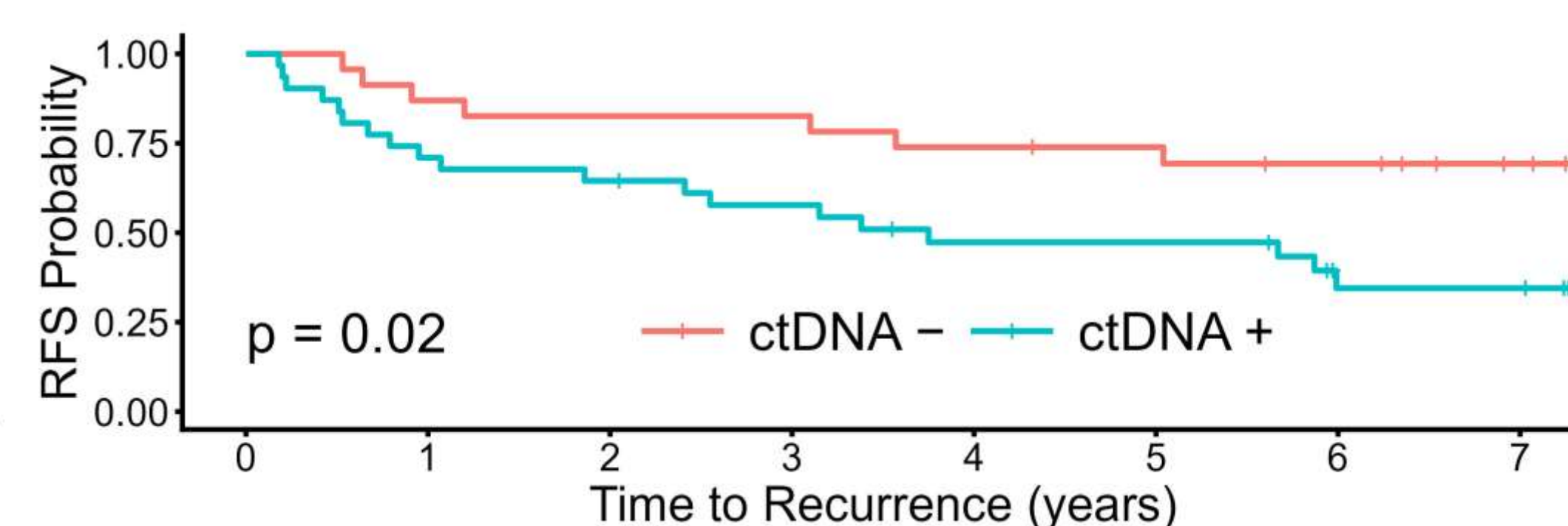
## Sankey Plot for Recurrence



### KM Curves: Overall Survival (ctDNA, pT0)



### KM Curves: Recurrence Free Survival (ctDNA, pT0)



References: 1) Zibelman et al. *Journal of Urology*. 2021; 2) Desai et al. AACR Annual Meeting. 2023