

2005P - Prediction of response and identification of mechanisms of resistance to neoadjuvant chemotherapy according to molecular subtypes in muscle-invasive bladder carcinoma

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Introduction

Neoadjuvant chemotherapy (NACT) based on a platin scheme is the current standard treatment for muscle-invasive bladder carcinoma (MIBC). However, benefit of this treatment significantly differs between patients.

Material & Methods

Fifty-eight FFPE samples from MIBC patients obtained at the moment of transurethral resection (TURB) were analyzed. Also thirty cystectomy samples from patients that did not respond to NACT were analyzed. Proteins were isolated using 2% SDS and digested with trypsin. Proteins extracts were analyzed using data-independent acquisition mass-spectrometry. Proteomics data was preprocessing using Perseus software. Layer analysis based on the sparse k-means and consensus cluster to obtain independent classifications of the samples. Statistical analyses were performed in GraphPad Prism v6.

Result 1: Clinical characteristics of MIBC patients.

MIBC patients	n=58
Gender	
Male	41 (71%)
Female	17 (29%)
Response to NACT	
Yes	24 (41%)
No	32 (55%)

Result 2: Identified proteins

5.532 proteins were identified and quantified in DIA mass-spectrometry experiments. After applying quality criteria, 3.399 proteins were used for the subsequent analyses.

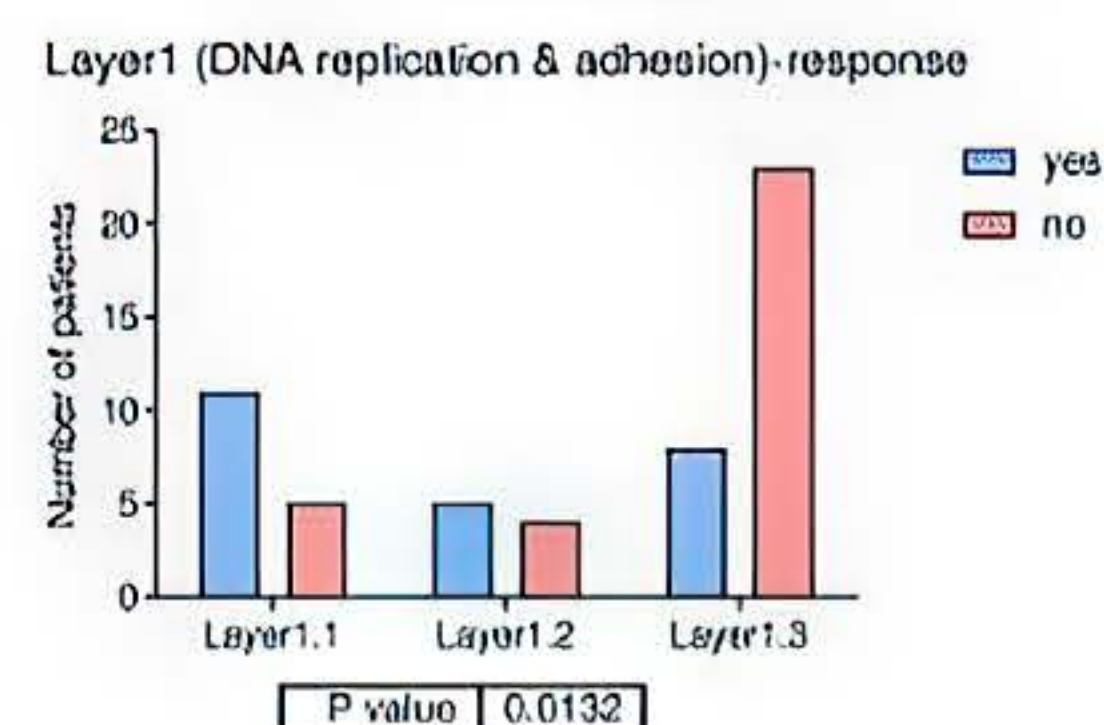
Result 3: Layer analysis identified two independent classifications

Layer 1 classification is based on proteins related to DNA replication and adhesion. Layer 3 classification is based on proteins related to immune response.

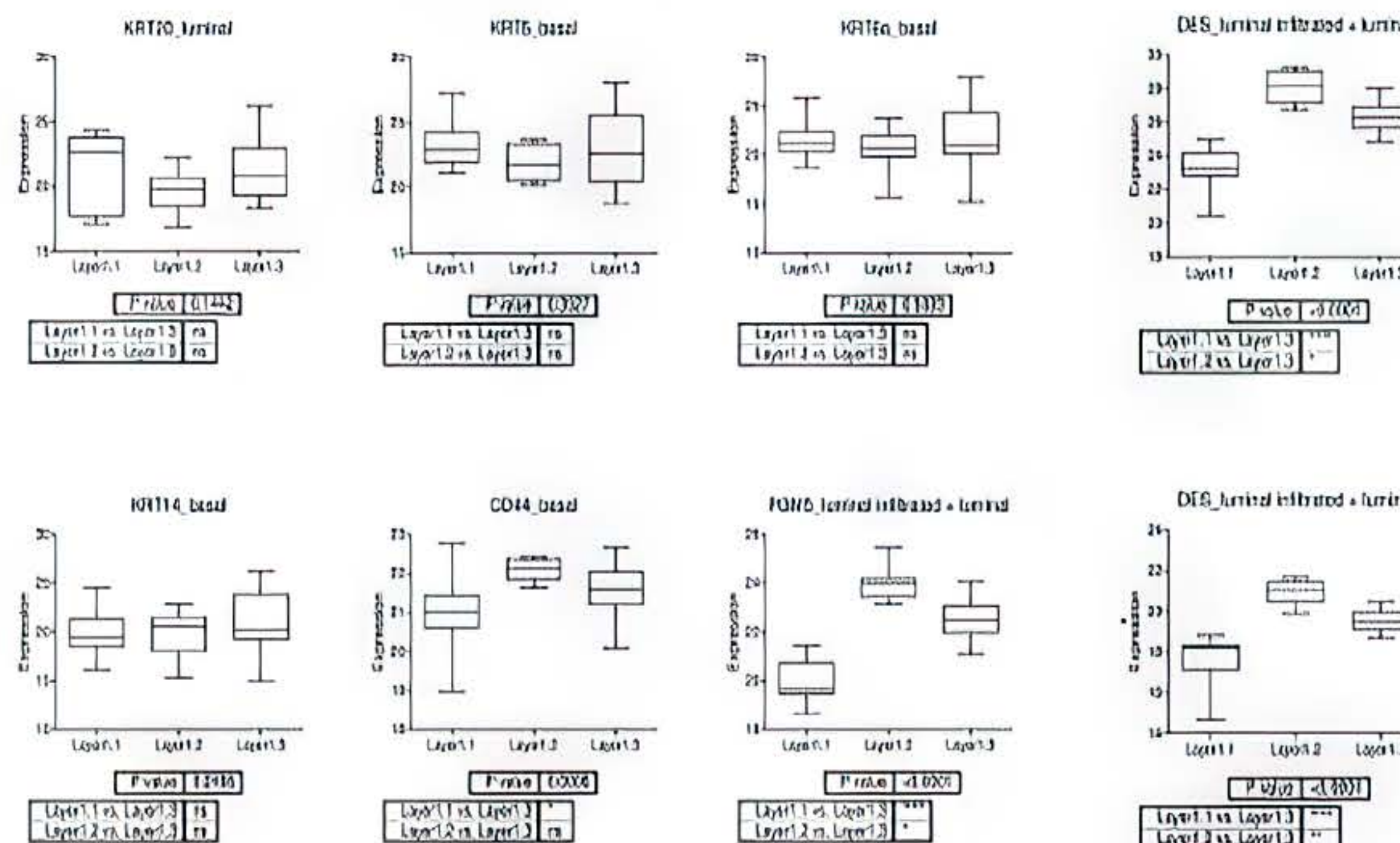
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Result 4: Layer 1 identified a group of non-responders to NACT

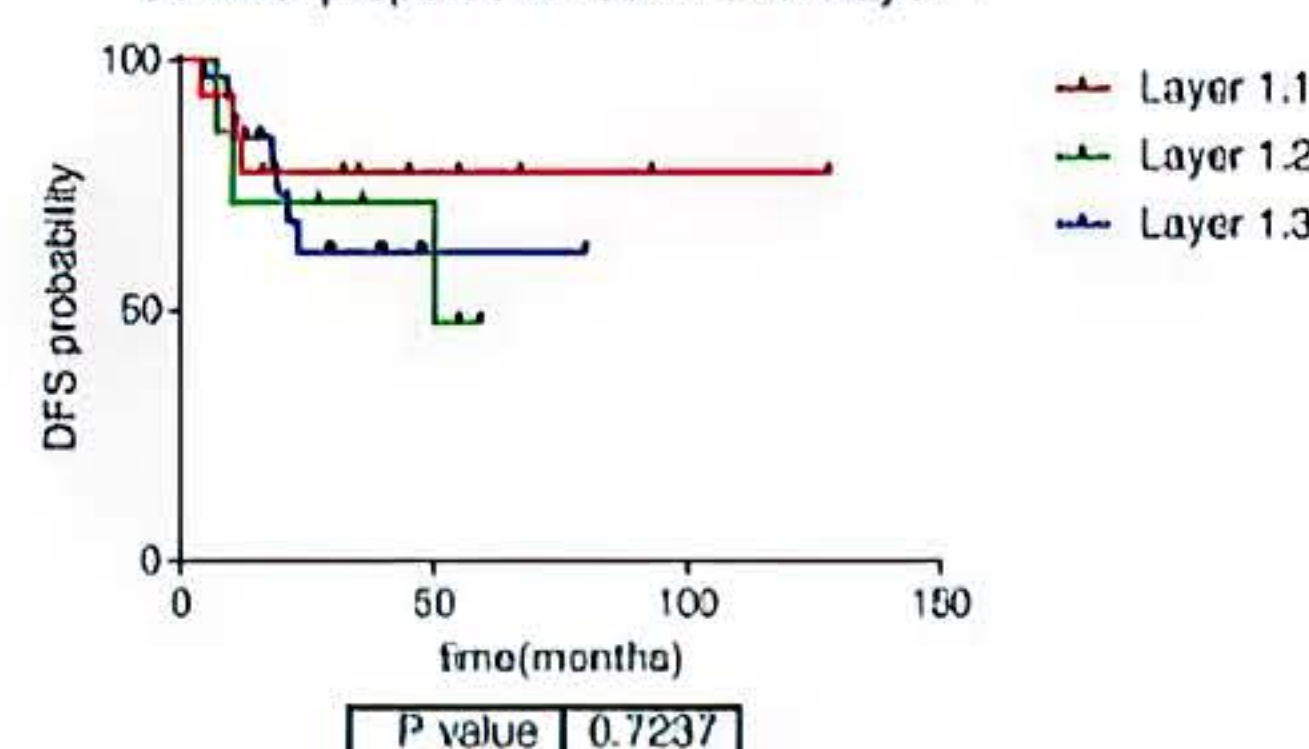
Layer 1 classification identified three groups with different response rate to NACT (Layer 1.1=69%, Layer 1.2=55%, Layer 1.3=26%). These groups are independent of Luminal and Basal groups, although Layer 1.2 presented an overexpression of Luminal-Infiltrated biomarkers. No differences in disease-free survival were found.



Layer 1 (DNA replication & adhesion)

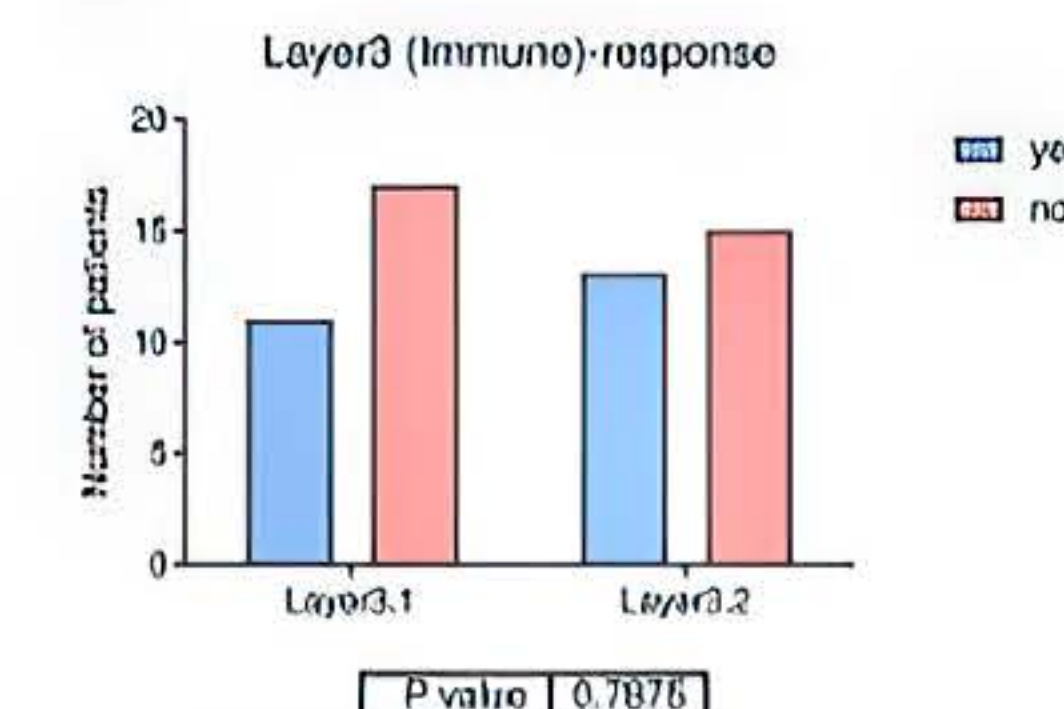


Survival proportions: Survival of Layer 1

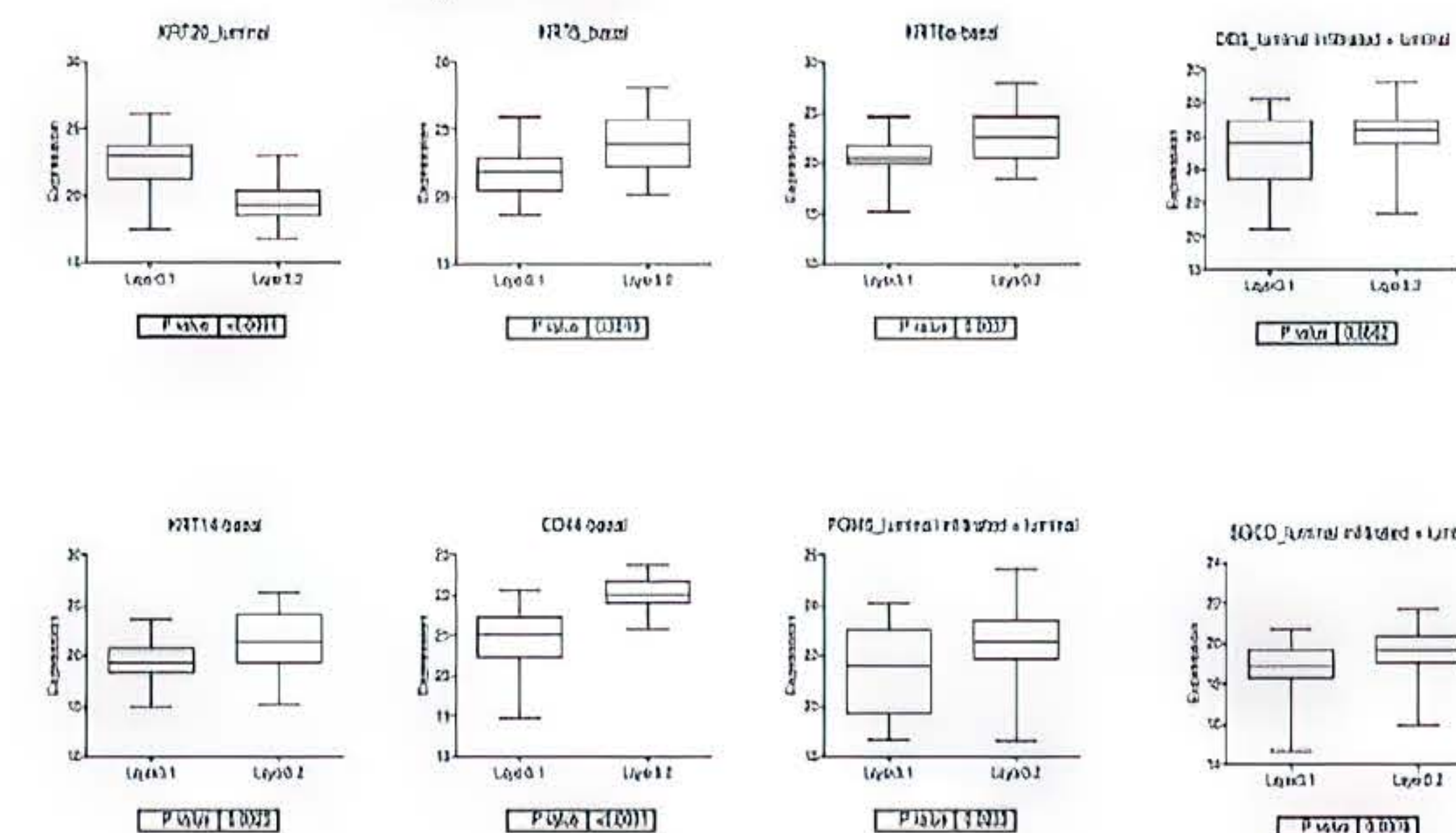


Result 5: Layer 3.2 responders had worse DFS than Layer 3.1 responders

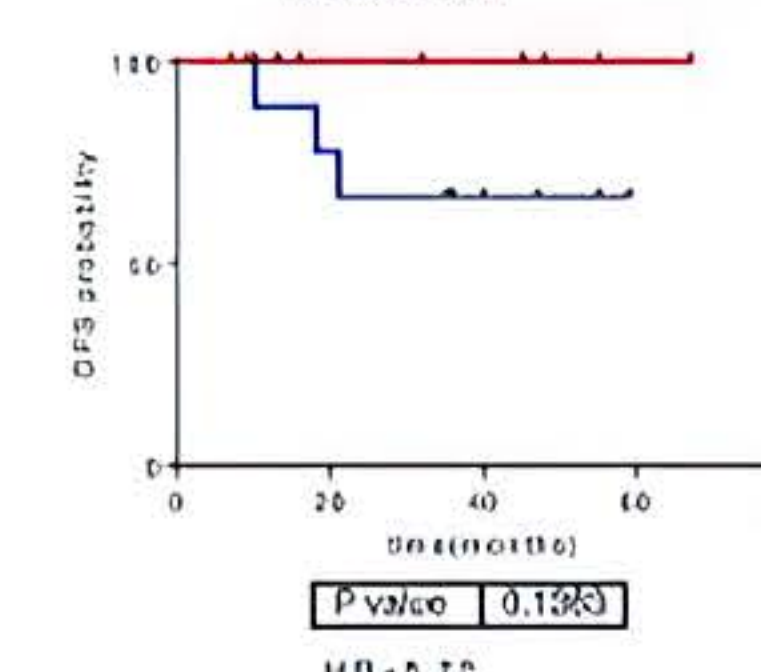
Layer 3.1 identified Luminal-papillary groups and Layer 3.2 identified Basal and Luminal-infiltrated groups. Layer 3.1 responders, i.e., Luminal-papillary tumors that had a complete response had a better DFS while Basal and Luminal-infiltrated+Luminal, despite achieving a complete response, had a worse DFS



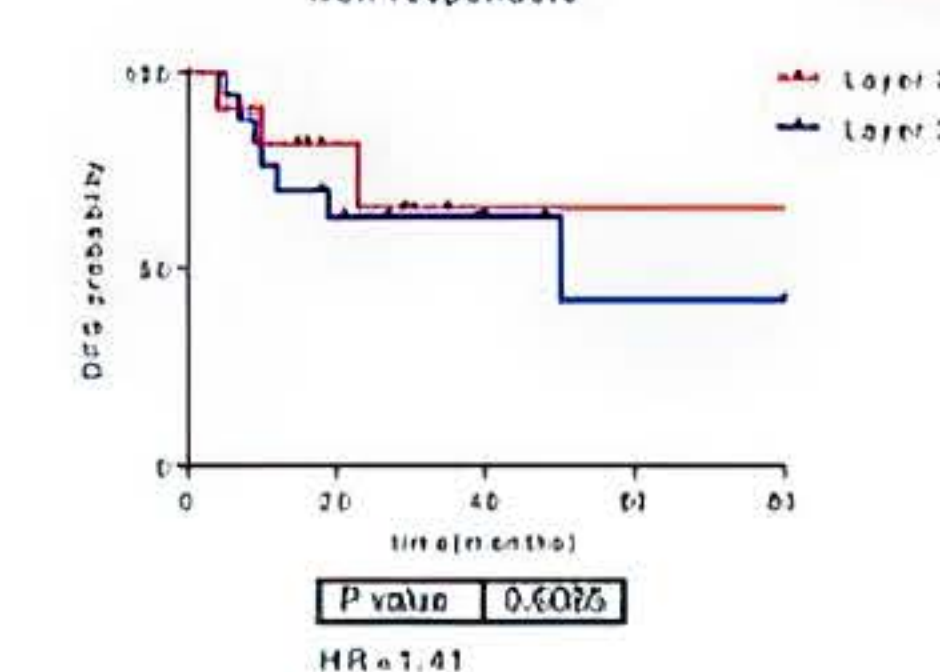
Layer 3-immune



Responders



Non-responders



Conclusions

- Two independent classifications according to proteomics profile in MIBC.
- Layer 1 identified a group of patients non-responders to NACT.
- Layer 3.2 responders had a worse DFS than Layer 3.1 responders.

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No significant COIs to be disclosed