Exosomes profiling reveals prognostic markers of response to Cabazitaxel in metastatic castration resistant prostate cancer

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Background: Prostate cancer is the second most common cancer type and the second most common cancer-related cause of death in men. Cabazitaxel, a next generation taxane, chemically similar to docetaxel, shows different toxicity levels and is efficient in tumors with resistance to docetaxel and to next generation AR targeted treatments. Unfortunately, although initial response, in most cases, prostate cancer will acquire resistance. It is essential to identify molecular markers that predict treatment response. Exosomes are a valuable source of biomarkers in different type of cancers. They contain RNA, proteins and lipids and are found in higher amounts in plasma from cancer patients.

Methods: We performed transcriptional exosome profiling (Human Transcriptome Array-HTA 2.0) from the plasma of 19 castration resistant prostate cancer patients at baseline and in 23 patients after the first cycle (C1) of Cabazitaxel. The patients were stratified in two groups according to their clinical response to Cabazitaxel. Gene Set Enrichment Analysis (GSEA) and Ingenuity Pathway analysis (IPA) platforms were used for pathway analysis.

Conclusions: Transcriptional profiling of plasma-derived exosomes reveals differential expression of genes that may reflect therapy response and acquisition of resistance.

Patient No	Cycles of	treatment	Response to Cabazitaxel
2101	BL	C1	Yes
2102	BL	C1	Yes
2103	BL	C1	Yes
2105	BL	C1	No
2107	BL	C1	No
2109	BL	C1	No
2110	BL	C1	Yes
2111	BL	C1	No
2114	BL	C1	No
2116	BL	C1	No
2118	BL	C1	Yes
2119	BL	C1	Yes
2120	BL	C1	No
2121	BL	C1	No
2122	BL	C1	Yes
1101	BL	-	No
1103	BL	-	No
1104	BL	C1	Yes
1105	-	C1	No
1106	-	C1	No
1107	BL	C1	No
1108	-	C1	No
1109	-	C1	No
1111	-	C1	Yes
1121	-	C1	Yes
1130	-	C1	No
1131	-	C1	No

Table: Patient characteristics.

RESULTS

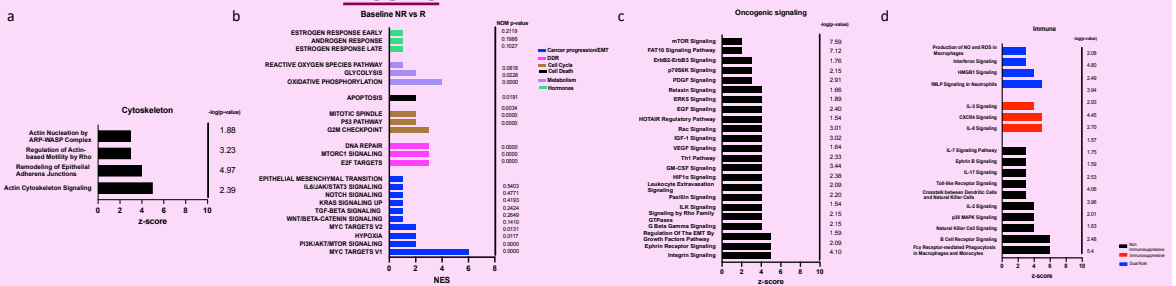

Figure 1: Bioinformatic analysis at Baseline in Non responders vs Responders. **a** Ingenuity Pathway Analysis (IPA) for pathways related to cytoskeleton (z-score ≥ 2, and –log2(p-value) ≥ 2) **b** Gene set enrichment analysis (GSEA) of pathways categorized in domains of interest. **c** IPA analysis for pathways related to oncogenic signaling (z-score ≥ 2, and -log(p-value) ≥ 1.5). **d** IPA analysis for immunological related pathways -log(p-value) ≥ 1.5).

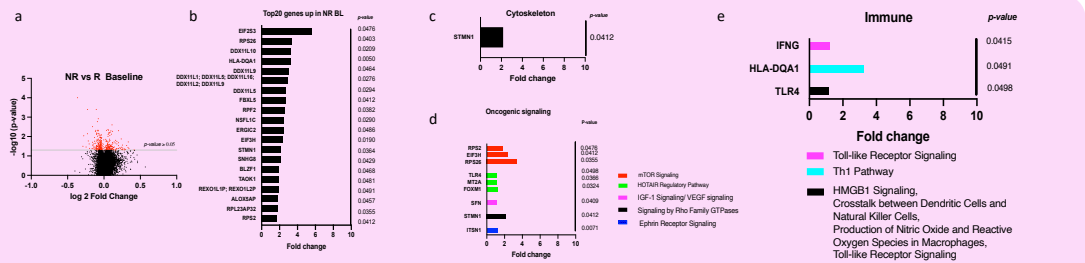

Figure 2: Genes' bioinformatic analysis at Baseline in Non responders vs Responders. **a** Volcano plot of upregulated and downregulated genes in Non responders compared to responders. **b** Top 20 upregulated genes in Non Responders compared to Responders. **c,d and e** significant upregulated genes in Non Responders in and the corresponding pathways they belong to.

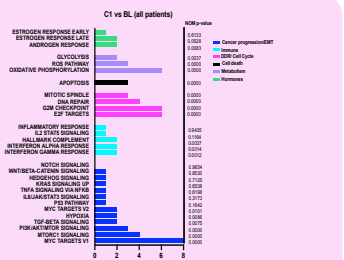

Figure 3: Pathways' bioinformatic analysis at C1 in all patients. GSEA analysis of pathways upregulated upon treatment.

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I have NO financial disclosure or conflicts of interest with the presented material in this presentation.