Prognostic classification of endometrial cancer according to transcriptomic-based immunophenotype

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Background

The Cancer Genome Atlas (TCGA) Project defined four prognostic subgroups of Endometrial Cancer (EC): POLE (favorable prognosis), MSI and Copy Number Low (CNL) the intermediate prognosis; and Copy Number High (CNH) unfavorable prognosis.

Objectives

The aim of the study is to perform a characterization at immune level of the prognostic EC-TCGA groups to identify those cases that could be benefited of immunotherapy.

Methods

A total of 48 FFPE EC were retrospectively selected (Ref): POLE (n=6); MSI (n=9); CNL (n=16) and CNH (n=17). Transcriptomic profiling was performed with HTG EdgeSeq Precision Immuno-Oncology Panel (PIO), which interrogates 1392 genes involved in tumor/immune interaction. The estimation of the relative abundance of immune and stromal cellular content and cell types was assigned to the 23 HTG EdgeSeq Reveal software immunophenotyping signatures. DESeq2 R package was used for differential expression analysis. Statistical analysis and data visualization was performed in R version 4.1.2. Clinicopathological information is collected in Table 1.

Results

Figure 1 Unsupervised analysis showed 2 clusters

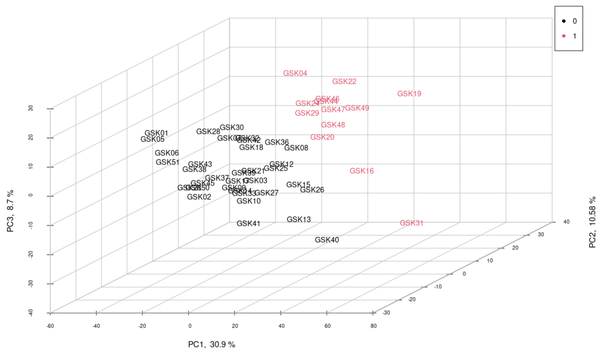


Table 1 Baseline characteristics

		Cluster 1	Cluster 2	Total
Nº of patients (%)		35 (73)	13 (27)	48 (100)
Histological type (%)	Endometrial	31 (65)	9 (19)	40 (84)
	Serous	4 (8)	4 (8)	8 (16)
Grade (%)	1	17 (35)	6 (13)	23 (48)
	2	11 (23)	3 (6)	14 (29)
	3	7 (15)	4 (8)	11 (23)
Stage (%)	I	25 (52)	10 (21)	35 (73)
	II	1 (2)	0 (0)	1 (2)
	III	9 (19)	3 (6)	12 (25)
TCGA Group (%)	POLE	6 (12.5)	0 (0)	6 (12.5)
	MSI	8 (16.7)	1 (2.1)	9 (18.8)
	CNL	14 (29.2)	2 (4.2)	16 (33.3)
	CNH	7 (14.6)	7 (14.6)	14 (29.2)
Median follow-up [range] months		89,9 [5 -152]		
Median OS		101,1 [26-152]	85,33 [6 - 143]	92,02 [6 – 152]
Median DFS		101,1 [10-152]	81,17[5 – 105]	89,87 [5 - 152]
Relapse (%)		4/35 (11,4)	7/13 (53,8)	11/48 (22,9)
Éxitus (%)		1/35 (2,9)	4/13 (30,8)	5/48 (10,4)

Figure 2 Overall Survival

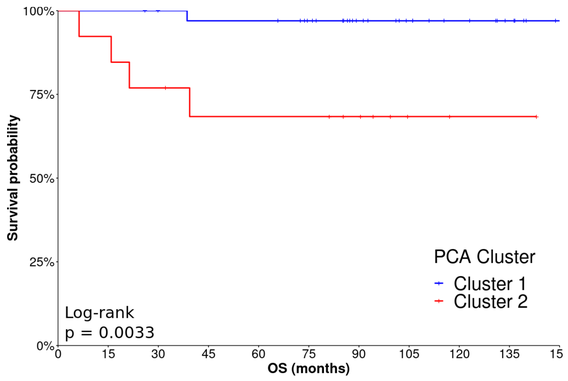


Table 2 Differential expression analysis, the most significant genes

	pvalue	padj	Significant
TGFBI	9,80E-17	1,37E-13	Significant
BEX1	2,71E-16	1,90E-13	Significant
CDK4	4,48E-14	1,57E-11	Significant
TUBB	3,62E-14	1,57E-11	Significant
RFC4	6,20E-13	1,46E-10	Significant
TRIP13	6,24E-13	1,46E-10	Significant
NCL	9,38E-13	1,88E-10	Significant
RPS7	1,47E-12	2,57E-10	Significant
AURKA	6,94E-12	8,89E-10	Significant
IL15	6,98E-12	8,89E-10	Significant
MSH6	6,13E-12	8,89E-10	Significant

Differential expression analysis resulted in 897 genes between clusters, 400 overexpressed and 497 under expressed in Cluster 1.

Figure 3 Immune related scores

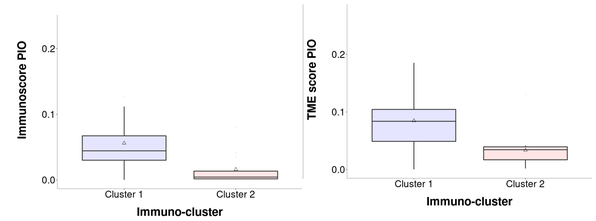
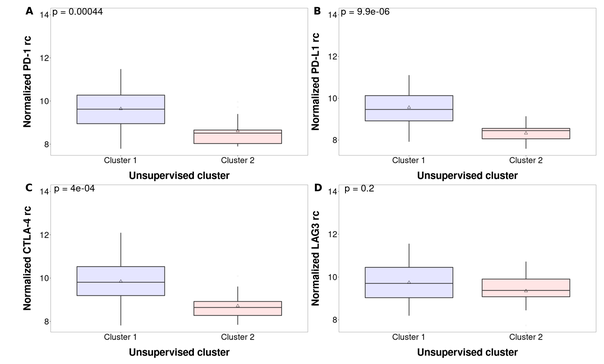


Figure 4 The cluster 1 was related with higher PD-1 (A), PD-L1 (B), CTLA-4 (C) expression



Conclusions

Cluster stratification suggests implication of immune-related features in classification of EC-patients beyond TCGA subgroups. These findings could be useful in the clinical management of the disease, constituting an open window in the selection of EC patients for immunotherapy

References:

1. López-Reig R, Fernández-Serra A, Romero I, Zorrero C, Illueca C, García-Casado Z, et al. Prognostic classification of endometrial cancer using a molecular approach based on a twelve-gene NGS panel. Sci Rep. 2 de diciembre de 2019;9(1):18093.
2. Levine DA. Integrated genomic characterization of endometrial carcinoma. Nature. mayo de 2013;497(7447):67-73.

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Presented at the 2023 European Society of Medical Oncology Gynecological Cancer; Barcelona, Spain; February 23-24, 2023