

Supplementary

Table S1 Changes in T-lymphocyte subsets before and during immunotherapy

No.	Project	Prior to immunotherapy, 2020-8-21 (%)	2 cycles, 2020-9-14 (%)	3 cycles, 2020-10-13 (%)
1	T-helper/inducer lymphocytes	60.4	56.9	30.6
2	Pure T-helper/inducer lymphocytes	11.2	9.1	0.8
3	Central memory T-helper/inducer lymphocytes	59.7	53.5	7.2
4	Effector T-helper/inducer lymphocytes	0.3	0.6	2.3
5	Effector memory T-helper/inducer lymphocytes	28.8	36.8	89.7
6	T-inhibitory/cytotoxic lymphocytes	34.3	34.7	59.1
7	Pure T-inhibitory/cytotoxic lymphocytes	5.4	5.3	0.7
8	Central memory T-inhibitory/cytotoxic lymphocytes	7.4	15.5	1.6
9	Effector T-inhibitory/cytotoxic lymphocytes	43.5	38.9	36.7
10	Effector memory T-inhibitory/cytotoxic lymphocytes	17.6	14.1	26.4
11	Cytotoxic T cells (Tc)	10.3	11.1	11.1
12	Inhibitory T cells (Ts)	23.8	23.5	47.8
13	CD4/CD8 ratio (Th/Ts)	1.76	1.64	0.52
14	Activated T-helper/inducer lymphocytes	9.7	9.3	16.8
15	Activated T-inhibitory/cytotoxic lymphocytes	12.1	46.8	29.5
16	Th1 cells	17.7	17.6	17.0
17	Th2 cells	15.8	21.8	8.4
18	Th17 cells	22.6	25.1	20.6
19	Th9 cells	4.6	3.7	4.0
20	Regulatory T cells (Tregs)	3.2	3.1	6.6

Table S2 Treatment overview and changes in tumor markers

Date	Months between diagnosis	PSA (ng/mL)	NSE (ng/mL)	Pro-GRP (pg/mL)	Treatment
2018/8/24	0	1,302	–	–	Confirmed; biopsy pathology: adenocarcinoma, GS4+5
2018/12/1	3	2.68	–	–	LHRHa + bicalutamide
2019/3/1	6	0.33	–	–	LHRHa + bicalutamide
2019/6/1	9	0.188	–	–	LHRHa + bicalutamide
2019/9/9	12	0.087	–	–	LHRHa + abiraterone
2020/1/13	16	0.098	–	–	Progression of prostate and bladder lesions; 2nd biopsy pathology: small-cell carcinoma; LHRHa + docetaxel + cisplatin
2020/6/8	21	0.089	–	–	6 cycles of chemotherapy ended, LHRHa
2020/8/21	23	0.263	17.27	52.74	Progression of prostate and bladder lesions; LHRHa + RT + PD-L1
2020/10/9	25	0.397	12.48	58.18	Radiotherapy ended, LHRHa + PD-L1
2020/11/26	27	0.727	12.3	–	LHRHa + etoposide + carboplatin + PD-1
2021/3/1	30	1.38	–	–	Concurrent. PR, metastatic lymph nodes reduced
2021/9/1	36	10.03	–	–	After 6 cycles of intravenous chemotherapy, continued maintenance therapy, LHRHa + oral etoposide + PD-1
2021/11/4	38	15.71	–	–	Concurrent
2022/1/7	40	18.50	–	–	Progression of left sacroiliac joint bone metastasis LHRHa + oral etoposide + PD-1 + enzalutamide

PSA, prostate-specific antigen; NSE, neuron-specific enolase; GRP, gastrin-releasing peptide; GS, Gleason score; LHRHa, luteinizing hormone-releasing hormone agonist; PD-1, programmed cell death 1; PD-L1, programmed cell death 1 ligand 1; PR, partial response; RT, radiotherapy.

Table S3 Recommendations for NEPC-related markers

No.	Gene/marker name
Gene up-regulation	
1	Synaptophysin/major synaptic vesicle protein p38 (<i>SYP</i>)
2	Chromogranin A and B (<i>CHGA/CHGB</i>)
3	Aurora kinase A (<i>AURKA</i>)
4	Neuroblastoma-derived v-myc avian myelocytomatosis viral-related oncogene (<i>N-MYC</i>)
5	Enhancer of zeste 2 polycomb repressive complex 2 subunit (<i>EZH2</i>)
6	Neuron-specific enolase (<i>NSE/ENO2</i>)
7	Calcitonin (<i>CALC1</i>)
8	Secretogranin II (<i>SCG2</i>) and III (<i>SCG3</i>)
9	Vasoactive intestinal peptide (<i>VIP</i>)
10	Gastrin-releasing peptide (<i>GRP</i>)
11	NK2 homeobox 1 (<i>NKX2.1</i>)/thyroid transcription factor 1 (<i>TTF-1</i>) and <i>NKX2.2</i>
12	Neural cell adhesion molecule (<i>NCAM1/CD56</i>)
13	Forkhead Box A2 (<i>FOXA2</i>)
14	<i>WNT11</i>
15	POU class 3 homeobox 2 (<i>POU3F2/BRN2</i>)
16	Serine/arginine repetitive matrix 4 (<i>SRRM4</i>) (RNA splicing factor)
17	Sex determining region Y (SRY)-Box 2 (<i>SOX2</i>) and <i>SOX11</i>
18	Carcinoembryonic antigen-related cell adhesion molecule 5 (<i>CEACAM5</i>) or <i>CD63E</i>
19	Human achaete-scute homolog 1 (<i>ASH1/ASCL1</i>)
20	Paternally expressed gene 10 (<i>PEG10</i>)
21	<i>TMPPRSS2-ERG</i> gene rearrangement
22	P16 or cyclin-dependent kinase inhibitor 2A
23	Delta-like protein 3 (<i>DLL3</i>)
Gene deletion/down-regulation	
1	Androgen receptor (<i>AR</i>)
2	Prostate-specific antigen/kallikrein-3 (<i>PSA/KLK3</i>)
3	Retinoblastoma tumor-suppressor gene (<i>RB1</i>) and <i>TP53</i>
4	Forkhead Box A1 (<i>FOXA1</i>)
5	<i>PTEN/AKT1</i>
6	RE1 silencing transcription factor (<i>REST</i>)
7	Tumor suppressor <i>CYLD</i>
8	SAM pointed domain-containing ETS transcription factor (<i>SPDEF</i>)
9	<i>Cyclin D1</i>

NEPC, neuroendocrine prostate cancer.