

Hanaa Mohammed



بسم الله الرحمن الرحيم

مركز الشبكات وتكنولوجيا المعلومات

قسم التوثيق الإلكتروني



Safaa Mahmoud



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قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات





Clinicopathological and Prognostic Value of PD-L1 in Renal Cell Carcinoma

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By

Hoda Sayed Abdel Moneam Elkhodary

Assistant Lecturer of Clinical Oncology, Ain Shams University

Under Supervision of

Prof. Khalid El Hussein Nasr

*Professor of Clinical Oncology and Nuclear Medicine
Faculty of Medicine, Ain Shams University*

Assist. Prof. Amr Lotfy Farag (R.I.P)

*Assistant Professor of Clinical Oncology and Nuclear Medicine
Faculty of Medicine, Ain Shams University*

Assist. Prof. Mai Mohamed Ali Ezz El Din

*Assistant Professor of Clinical Oncology and Nuclear Medicine
Faculty of Medicine, Ain Shams University*

Dr. Sherif Hassanien Ahmed

*Lecturer of Clinical Oncology and Nuclear Medicine
Faculty of Medicine, Ain Shams University*

Faculty of Medicine, Ain Shams University

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سُبْحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

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List of Abbreviations

Abb.	Full term
AJCC	American Joint Committee on Cancer
APC.....	Antigen presenting cell
ASR	Age-standardized rate
BMI	Body mass index
ccRCC	Clear cell renal carcinoma
CDC	Collecting duct carcinoma
ChRCC	Chromophobe RCC
CRP	C-reactive protein
CTLA4	Cytotoxic T-lymphocyte-associated protein 4
DFS	Disease free survival
EGFR	Epidermal growth factor receptor
FDA	Food and Drug Administration
FDG-PET	Fluorodeoxyglucose positron emission tomography
FGFR1.....	Fibroblast growth factor receptor-1
FH	Fumarate hydratase
GISTs	Gastrointestinal stromal tumors
HLRCC	Hereditary leiomyomatosis and renal cell carcinoma
IFNa	Interferon alpha
IHC	Immunohistochemistry
IL-2	Interleukin 2
IMDC	International Metastatic Renal Cell Carcinoma Database Consortium
LDH.....	Lactate dehydrogenase
MHC1	Major histocompatibility complex 1
MiT	Microphthalmia-associated transcription
MRI	Magnetic resonance imaging
MSKCC	Memorial Sloan Kettering Cancer Center
MVI	Microvascular invasion
nccRCC	Non-clear cell RCC
NK	Natural killer

List of Abbreviations *cont...*

Abb.	Full term
<i>NLR</i>	<i>Neutrophil-to-lymphocyte ratio</i>
<i>OS</i>	<i>Overall survival</i>
<i>PD-1</i>	<i>Programmed cell death 1</i>
<i>PD-L1</i>	<i>Programmed cell death ligand 1</i>
<i>PD-L2</i>	<i>Programmed cell death ligand 2</i>
<i>PFS</i>	<i>Progression free survival</i>
<i>PN</i>	<i>Partial nephrectomy</i>
<i>pRCC</i>	<i>Papillary renal cell carcinoma</i>
<i>PS</i>	<i>Performance status</i>
<i>RCC</i>	<i>Renal cell carcinoma</i>
<i>RR</i>	<i>Relative risk</i>
<i>SDH</i>	<i>Succinate dehydrogenase</i>
<i>SEER</i>	<i>Surveillance, epidemiology, and end results</i>
<i>srRCC</i>	<i>Sarcomatoid RCC</i>
<i>TCR</i>	<i>T cell receptor</i>
<i>TILs</i>	<i>Tumor infiltrating lymphocytes</i>
<i>TIMCs</i>	<i>Tumor-infiltrating mononuclear immune cells</i>
<i>TMB</i>	<i>Tumor mutational burden</i>
<i>TNM</i>	<i>Tumor, node and metastasis</i>
<i>tRCCs</i>	<i>Translocation RCCs</i>
<i>UICC</i>	<i>Union for International Cancer Control</i>
<i>UISS</i>	<i>University of California Integrated Staging System</i>
<i>VHL</i>	<i>Von Hippel Lindau</i>
<i>WHO</i>	<i>World Health Organization</i>
χ^2	<i>Chi square test</i>

INTRODUCTION

Renal cell carcinoma (RCC) accounts for about 2% of cancer diagnoses and deaths globally.¹

It is considered the seventh most common form of neoplasm in the developed world. In the US, The surveillance, epidemiology, and end results (SEER) statistics report that RCC accounts for 4.2% of all cancer diagnoses (almost double the global average).²

Renal cell tumors represent a group of histologically and molecularly heterogeneous diseases. The histologic classification of renal cell carcinoma (RCC) has significantly changed in the last few decades, many new entities were added based on either characteristic pathologic features or distinctive molecular alterations.³

The major subtypes are clear cell RCC (CCRCC) representing 65–70% of all RCC, papillary RCC (PRCC) 15–20%, and chromophobe RCC (ChRCC) 5–7%.³

RCC is considered an immunogenic cancer, with pathologic specimens harboring a high number of tumor-infiltrating lymphocytes (TILs) which are considered manifestations of host immune reactions against cancers.^{4,5}

PD-1 is a cell surface glycoprotein within the B7 family of T cell costimulatory molecules; it was first described by

Ishida et al in 1992.⁶ PDL1, when bound to PD1 protein, leads to downregulation of activated T cells.⁷

It was suggested that approximately 30% of malignant tumor cells, including RCC among other tumors, express PD-L1 and closely associate with the prognosis of the patients.⁸⁻¹⁰

PD-1 protein is mainly expressed on TILs, whereas PD-L1 is expressed on both immune cells and tumor cells.¹¹

The expression of PDL-1 is currently being investigated as an important prognostic and predictive biomarker; however, it is still not validated alone determining which patients should be offered PD-1/L1 blockade therapy.^{12,13}

AIM OF THE WORK

Primary end point:

Correlation of PD-L1 expression both in tumor cells and tumor infiltrating lymphocytes (TILs) with disease free survival (DFS) and Overall survival (OS) for patients with non-metastatic RCC and with Progression free survival (PFS) and Overall survival (OS) for metastatic patients.

Secondary end point:

Correlation of PD-L1 expression in tumor cells and TILs with clinical and pathological features.