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بسم اللّه الرحمن الرحيم

مركز الشبكات وتكنولوجيا المعلومات

قسم التوثيق الإلكتروني

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم باللّه 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

Thesis

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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
NLR	*Neutrophil-to-lymphocyte ratio*
OS	*Overall survival*
PD-1	*Programmed cell death 1*
PD-L1	*Programmed cell death ligand 1*
PD-L2	*Programmed cell death ligand 2*
PFS	*Progression free survival*
PN	*Partial nephrectomy*
pRCC	*Papillary renal cell carcinoma*
PS	*Performance status*
RCC	*Renal cell carcinoma*
RR	*Relative risk*
SDH	*Succinate dehydrogenase*
SEER	*Surveillance, epidemiology, and end results*
srRCC	*Sarcomatoid RCC*
TCR	*T cell receptor*
TILs	*Tumor infiltrating lymphocytes*
TIMCs	*Tumor-infiltrating mononuclear immune cells*
TMB	*Tumor mutational burden*
TNM	*Tumor, node and metastasis*
tRCCs	*Translocation RCCs*
UICC	*Union for International Cancer Control*
UISS	*University of California Integrated Staging System*
VHL	*Von Hippel Lindau*
WHO	*World Health Organization*
χ2	*Chi square test*

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.