New Trends in Management of Advanced Stages of Renal Cell Carcinoma

Essay

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Mary Tharwat


Dedication
To the soul of my beloved Dad
To my wonderful Mom
To my amazing Brother and Sister
The most sincere and most beloved

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List of Abbreviations

5-FU	5-fluorouracil
5-HT3	5- hydroxytryptamine receptor 3
ACE	Angiotensin converting enzyme
AEs	Adverse events
BEV	Bevacizumab
BHD	Birt-Hogg-Dube
CA IX	Carbonic anhydrase IX
CCBs	Calcium channel blockers
ccRCC	Clear cell renal cell carcinoma
CEUS	Contrast enhanced ultrasound
chRCC	Chromophobe renal cell carcinoma
CR	Complete remission
CSF-1R	Colony stimulating factor
CT	Computerized tomography
CWG	Cytokine Working Group
CXR	Chest X Ray
CYP 450	Cytochrome P450
DFS	Disease free survival
DOX	Doxorubicin
EGFR	Epidermal growth factor receptor
EORTC	European Organization for Research and Treatment of Cancer
EPIC	European prospective investigation into cancer and nutrition
FDA	Food and Drug Administration
FDG-PET/CT	Fluoro-D-glucose positron emission Tomography/Computerized tomography

FGFR	Fibroblast growth factor receptors
FH	Fumarate hydratase
FKBP-12	FK506-binding protein 12
FLK/KDR	Fetal liver kinase/ Kinase insert domain receptor
FLT-3	Fms-like tyrosine kinase receptor-3
GEM	Gemzar
GLUT-1	Glucose transporter 1
HD	High dose
HFSR	Hand foot skin reaction
HGM-CoA reductase	3-hydroxy-3-methyl-glutaryl-CoA reductase
HIF-1a	Hypoxia inducible factor-1 alpha
HLRCC	Hereditary leiomyomata and renal cell carcinoma
HR	Hazard ratio
Hs	Hours
HU	Hounsfield units
I.V.	Intravenous
INF-a	Interferone-alpha
IU	International Unit
Kg	Kilogram
KPS	Karnofsky Performance status
LC	Local control
LDH	Lactate dehydrogenase
LND	Lymph node dissection
LRF	Locoregional failure
MRI	Magnetic resonance imaging
MSKCC	Memorial Sloan-Kettering Cancer Center
mTOR	Mammalian target of rapamycin
mTORC1	Mammalian target of rapamycin complex 1

MTSC	Mucinous tubular and spindle cell carcinoma
NCCN	National Comprehensive cancer network
NWLCN	North west London Cancer Network
ORR	Overall response rate
OS	Overall survival
P53	protein 53
P70 S6K	Phospho-p70 S6 Kinase
PDGF	Platelet derived growth factor
PHD	prolyl hydroxylase domain
PI3K	Phosphoinositide 3- kinase
PIP3	Phosphatidylinositol-triphosphate
PR	Partial remission
pRCC	Papillary renal cell carcinoma
PTEN	Phosphatase and tensin enzyme
pVHL	Von Hippel-Lindau product
RCC	Renal cell carcinoma
RECIST	Response Evaluation Criteria in Solid Tumor
RN	Radical nephrectomy
RR	Relative risk
RT	Radiation therapy
S.C.	Subcutaneous
SD	Stable disease
SEER	Surveillance, Epidemiology and End Results
STAT1	Signal transducer of activated T 1
SUV	Standardized uptake value
SWOG	Southwest Oncology Group
TARGET	Treatment Approaches in Renal Cancer Global Evaluation
TFE3	Translation elongation factor 3

TGF-a	Transforming growth factor-alpha
TKIs	Tyrosin kinase inhibitors
TSH	Thyroid stimulating hormone
TTP	Time to progression
UCAs	Ultrasonographic contrast agents
US	Ultrasound
VEGF	Vascular endothelial growth factor
VEGFR-1	Vascular endothelial growth factor-1
VHL	Von Hippel-Lindau
Vs.	Versus
WHO	World health organization

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Introduction

Each year In Europe, approximately 40,000 patients are diagnosed with Renal cell carcinoma (RCC), leading to 20,000 deaths ***(Patard et al., 2011).*** Although it is the tenth most common malignancy in Europe it accounts for only 2–3% of cancers ***(Escudier et al., 2012).*** With newer therapies, the median survival period of patients with advanced RCC is about 26 months ***(Banumathy and Cairns, 2010).***

The incidence of RCC is increasing at around 2% per year, this had been attributed to increased detection due to the wide spread of imaging modalities ***(Wood and Brown, 2012).***

Renal cell carcinoma accounts for approximately 90% of renal malignancies. According to the World Health Organization, there are three major histological RCC types; clear cell renal cell carcinoma (ccRCC) (75%), papillary renal cell carcinoma (pRCC) (10–15%), and chromophobe renal cell carcinoma (chRCC) (5%). pRCC can further be divided into two different subtypes, type 1 and type 2 ***(Ljungberg et al., 2010).***

Immunohistologic and ultrastructural analysis have suggested that the proximal renal tubular epithelium is the tissue of origin of most renal tumors. Renal tumors tend to be spherical, but may vary widely in size. The average diameter is