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CIRCULATING ENDOTHELIAL AND PROGENITOR
CELLS DURING ANTI-ANGIOGENIC TREATMENT IN
CANCER PATIENTS

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VRIJE UNIVERSITEIT

CIRCULATING ENDOTHELIAL AND PROGENITOR CELLS
DURING ANTI-ANGIOGENIC TREATMENT
IN CANCER PATIENTS

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad Doctor aan
de Vrije Universiteit Amsterdam,
op gezag van de rector magnificus
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in het openbaar te verdedigen
ten overstaan van de promotiecommissie
van de faculteit der Geneeskunde
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in de aula van de universiteit,
De Boelelaan 1105

Door
Laura Vroling
geboren te Hoorn

promotoren: prof.dr. V.W.M. van Hinsbergh
prof.dr. H.M.W. Verheul
copromotor: dr. H.J. Broxterman

*Voor mijn ouders
Aan mijn mannen*

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LIST OF ABBREVIATIONS

7-AAD	7-aminoactinomycin
acLDL	acetylated Low Density Lipoprotein
APC	Allophycocyanin
ATP	Adenosine-5'-triphosphate
bFGF	basic fibroblast growth factor
BM	Bone marrow
BMD	Bone marrow derived
BMDC	Bone marrow-derived cells
BOECs	Blood outgrowth endothelial cells
BV	Bevacizumab
CB	Clinical benefit
CB-MNCs	Cord-blood mononuclear cells
CD	Cluster of differentiation
CEC	Circulating endothelial cell
CEP	Circulating endothelial progenitor
CFU	Colony Forming Unit
CM	Conditioned medium
CPCs	Circulating progenitor cells
CR	Complete response
CT	Computed tomography
CTX	Cyclophosphamide
CXCR	C-X-C chemokine receptor
DAPI	4'-6-Diamidino-2-phenylindole
DC	Dendritic cells
DNA	Deoxyribo Nucleic Acid
dssiRNA	double stranded small interfering RNA
EBM	Endothelial basal medium
EC	Endothelial cell
ECFCs	Endothelial colony forming cells
EDTA	Ethylenediaminetetraacetic acid
EGFR	Epidermal growth factor receptor
EGM	Endothelial growth medium
ELISA	Enzyme-linked immunosorbent assay
EOCs	Endothelial outgrowth cells
EPC	Endothelial progenitor cell
EPO	Erythropoietin
ER	Erlotinib
FACS	Fluorescence-Activated cell sorting
FC	Flow cytometry
FDA	Food and drug administration
FGF	Fibroblast growth factor
FITC	Fluorescein isothiocyanate
Flk-2	Fetal liver kinase-2
FSC	Forward scatter
GIST	Gastrointestinal stromal tumors
HCC	Hepatocellular carcinoma
HIF	Hypoxia-inducible factor
HMVEC	Human microvascular endothelial cells
HPC	Hematopoietic progenitor cells
HRE	IF responsible element
HUVECs	Human umbilical cord vein endothelial cells

IL-8	Interleukin-8
IMS	Immunomagnetic separation
KDR	Kinase insert domain receptor
MAP	Mean arterial pressure
MCH	Mean cellular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
mCRC	metastatic colorectal cancer
MCV	Mean corpuscular volume
MFI	Mean fluorescence intensity
MNC	Mononuclear cell
MoAb	Monoclonal antibody
MRI	Magnetic resonance imaging
MSKCC	Memorial Sloan-Kettering Cancer Center
MTD	Maximum tolerated doses
ND	Not Detected
NF-kB	Nuclear factor-kappa B
NOS	Nitric oxide synthase
NSCLC	Non-small cell lung cancer
OR	Overall Response
OS	Overall survival
PB	Peripheral blood
PBS	Phosphate buffered saline
PD	Progressive disease
PDGFR	Platelet-derived growth factor
PE	Phycoerythrin
PET	Positron emission tomography
PFS	Progression free survival
PGF	Placental growth factor
PR	Partial response
RCC	Renal cell cancer
RECIST	Response Evaluation Criteria in Solid Tumors
RNA	Ribonucleic acid
SD	Stable disease
SD	Standard deviation
SDF	Stromal cell-derived factor
SEM	Standard Error of Mean
SO	Sorafenib
SPECT	Single photon emission computed tomography
SSC	Side scatter
SU	Sunitinib
TKI	Tyrosine kinase inhibitor
TNF- α	Tumor necrosis factor
TTP	Time To Progression
UEA-1	Ulex europaeus lectin-1
VEGF	Vascular endothelial growth factor
vWF	von Willebrand factor
WBC	White blood cells
WBRT	Whole brain radiotherapy

