# Towards a tailored therapeutic approach for vulvar cancer patients

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## LIST OF ABBREVIATIONS

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|---|---|
| ACT | adoptive cell therapy |
| AJCC | American joint committee on cancer |
| ALA | 5-aminolevulinic acid |
| Anti-CTLA-4 | anti-cytotoxic T-lymphocyte-associated protein 4 |
| Anti-PD1 | anti-programmed cell death protein 1 |
| APC | antigen-presenting cell |
| BCC | basal cell carcinoma |
| BSA | bovine serum albumin |
| CAR T cell | chimeric antigen receptor T cells |
| CBA | cytometric bead array |
| CIN | cervical intraepithelial neoplasia |
| CSF1R | colony stimulating factor 1 receptor |
| CTLA-4 | cytotoxic T-lymphocyte-associated protein 4 |
| CxCa | cervical squamous cell carcinoma |
| DAMPs | danger-associated molecular patterns |
| DC | dendritic cell |
| DeVIL | differentiated exophytic vulvar intraepithelial lesion |
| DN | double-negative |
| DoI | depth of invasion |
| DP | double-positive |
| dVIN | differentiated type vulvar intraepithelial neoplasia |
| FCS | fetal calf serum |
| FDA | food and drug administration |
| FFPE | formalin-fixed paraffin embedded |
| FIGO | Federation of Gynecology and Obstetrics |
| Gal-3 | galactin-3 |
| GEP | gene expression profile |
| GrB | granzyme B |
| HE | haematoxylin and eosin |
| HIV | human immmunodeficiency virus |
| HLA | human leukocyte antigen |
| HLA-E | human leukocyte antigen type E |
| HPV | human papillomavirus |
| HPVneg VSCC | human papilloma virus negative VSCC |
| HPVneg/p53mut VSCC | human papilloma virus negative vulvar squamous cell carcinoma with p53 mutant expression |
| HPVneg/p53wt VSCC | human papilloma virus negative vulvar squamous cell carcinoma with p53 wildtype expression |

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|---|---|
| HPVpos VSCC | human papilloma virus positive vulvar squamous cell carcinoma |
| HR | hazard ratio |
| hrHPV | high-risk HPV |
| HVG | highly-variable genes |
| IDO | indoleamine 2,3-dioxygenase |
| IHC | immunohistochemistry |
| IFN-ɣ | interferon-gamma |
| IFN-α | interferon-alpha |
| IL-2 | interleukin-2 |
| IL-4 | interleukin-4 |
| IL-5 | interleukin-5 |
| IL-10 | interleukin-10 |
| IL-12 | interleukin-12 |
| LAG-3 | lymphocyte-activation gene 3 |
| LC | langerhans cell |
| LOH | loss of heterozygosity |
| LS | lichen sclerosus |
| LVSI | lymphovascular space invasion |
| MAGEA1 | melanoma-associated antigen 1 |
| MAGEA4 | melanoma-associated antigen 4 |
| MDSC | myeloid-derived suppressor cell |
| MHC | major histocompatibility complex |
| MoAbs | monoclonal antibodies |
| MPSM | minimal peripheral surgical margin |
| M1 macrophage | macrophage type 1 |
| M2 macrophage | macrophage type 2 |
| NeoAg | neoantigen |
| NGS | next genome sequencing |
| NK cell | natural killer cell |
| NSCLC | non-small cell lung cancer |
| OPSCC | oropharyngeal squamous cell carcinoma |
| OS | overall survival |
| PBMC | peripheral blood mononuclear cells |
| PBS | phosphate buffered saline |
| PD-1 | programmed death 1 |
| PD-L1 | programmed death ligand 1 |
| PDT | photodynamic therapy |
| PHA | phytohemagglutinin |
| p53wt | p53 wildtype |

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|---|---|
| p53mut | p53 mutant |
| RANKL | receptor activator NF-kB ligand |
| RCT | randomized controlled trial |
| RER | relative excess risk |
| RFP | recurrence-free period |
| ROC | receiver operating characteristics |
| RS | relative survival |
| SLN | sentinel lymph node |
| SN | single-negative |
| SP | single-posiitve |
| STING | stimulator of interferon genes |
| TAA | tumor-associated antigen |
| TAMs | tumor-associated macrophages |
| Tbet | T-box expressed in T cells |
| Tcm | central memory T cell |
| TCR | T cell receptor |
| Tem | effector memory T cell |
| Temra | effector memory RA+ T cells |
| TGF-β | transforming growth factor beta |
| Th1 | T helper 1 |
| Th2 | T helper 2 |
| TIL | tumor-infiltrating lymphocyte |
| TIM-3 | T cell immunoglobulin and mucin domain containing-3 |
| TLR | toll-like receptor |
| TME | tumor microenvironment |
| TNF-α | tumor necrosis factor alpha |
| TP53 | tumor protein p53 |
| Treg | regulatory T cell |
| TSA | tumor specific antigens |
| T-VEC | talimogene laherparepvec |
| uVIN | usual type vulvar intraepithelial neoplasia |
| VAAD | vulvar acanthosis with altered differentiation |
| VAF | variant allele frequency |
| VEGF | vascular endothelial growth factor |
| vHSIL | vulvar high grade squamous intraepithelial lesion |
| VISTA | V-domain Ig suppressor of T cell activation |
| VSCC | vulvar squamous cell carcinoma |
| VUS | variant of unknown significance |
| WLE | wide local excision |

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## CURRICULUM VITAE

Kim Esmée Kortekaas was born on the 24th of November 1988 in Leiderdorp, and grew up in Zoeterwoude. She graduated in 2006 from secondary school at the Stedelijk Gymnasium in Leiden, and studied Medicine at the Leiden University. During the early days of her study, she was introduced to the field of research at the department of Vascular Surgery at the Leiden University Medical Center (LUMC) under supervision of dr. J.H.N. Lindeman.

Kim decided to attend a pre-master in Biomedical Sciences, and continued her research project in vascular surgery at Stanford University, California, USA. In 2013 she obtained her medical and biomedical degree (cum laude). After one-year experience in basic research with induced pluripotent stem cells, she started working as a physician in Obstetrics and Gynecology at the Bronovo Hospital. Hereafter, Kim started her residency in Obstetrics and Gynecology at the Haaglanden Medical Center, the Hague (dr. M.J. Kagie).

Because Kim is intrigued by turning science into clinical applications, she chose to study the role of the tumor microenvironment in vulvar carcinoma. She committed to a three-year fulltime PhD project at the department of Medical Oncology (prof. dr. S.H. van der Burg), Gynecology (dr. M.I.E. van Poelgeest), and Pathology (dr. T. Bosse) at the LUMC. She presented the results of this research at several national and international conferences, and became fellow of the International Society for the study of Vulvovaginal Disease (ISSVD). During her PhD project she started her training as a registered immunologist (SMWBO) and applied for a University Teaching Qualification (BKO). Since July 2020, Kim continued her Obstetrics & Gynecology residency training at the LUMC (dr. M. Sueters).

Gratius animus est una virtus non solum maxima, sed etiam mater virtutum omnium reliquaram.

*A thankful heart is not only the greatest virtue, but the mother of all other virtues. – Marcus Tullius Cicero 106-43 B.C.*