4. STUDY POPULATION

4.1 Population (base)

Research subjects with primary SCC of the vulva will be asked to participate in this study when they have undergone the SN procedure according to the inclusion criteria for this procedure and have been diagnosed with a macrometastasis in their SN (metastasis > 2mm and/or extracapsular extension). Research subjects with > 1 micrometastasis can also be included.

Research subjects will be asked to participate in GROINSS-V III, which means they will be treated with chemoradiation instead of an inguinofemoral lymphadenectomy.

Vulvar cancer has an incidence of 2-3/100 000 women per year. In the Netherlands approximately 375 patients are diagnosed with vulvar cancer each year. The incidence is increasing. Approximately 50% of them will have an indication for a SN procedure, and 10% of them will have macrometastasis. Based on data from GROINSS-V II, we expect to include approximately 25 patients per year.

4.2 Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

- Histological confirmed primary SCC of the vulva
- T1 tumor, not encroaching urethra/vagina/anus
- Depth of invasion > 1mm
- Tumor diameter < 4cm
- Unifocal tumor
- No enlarged (>1.5cm) or suspicious inguinofemoral lymph nodes at imaging (CT/MRI/ultrasound)
- Possibility to obtain informed consent
- Metastatic sentinel lymph node; size of metastasis > 2mm and / or extracapsular extension, or
- Metastatic sentinel lymph node: more than 1 SN with metastasis ≤ 2mm
- Patients are able to understand requirements of study, provide written informed consent and comply with the study and follow-up procedures
- Adequate bone marrow, renal and liver function:
    - Absolute neutrophil count ≥ 1.5 x 109 /L
    - Platelet count ≥ 100 x 109 /L
    - Creatinine clearance ≥ 40 ml/min measured by the Cockroft Gault formula
    - Total bilirubin < 1.25 x ULN

- Aspartate transaminase (AST) and alanine transaminase (ALT) ≤ 2.5 x ULN

- Performance status of 0, 1 or 2 on the Eastern Cooperative Oncology Group (ECOG) Scale (Appendix A)
- Age 18 years or older
- Life expectancy of ≥ 12 weeks
- Written informed consent

4.3 Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Inoperable tumors and tumors > 4cm
- Multifocal tumors
- Tumors with other pathology than squamous cell carcinoma
- Patients with enlarged / suspicious lymph nodes which are proven metastatic after fine needle aspiration cytology
- No other carcinomas, other than basal cell carcinomas, within last 5 years
- History of pelvic radiotherapy
- History of any infection requiring hospitalization or antibiotics within 2 weeks before enrollment
- Pregnant female or nursing mother
- Desire to become pregnant
- Known brain or spinal cord metastases unless adequately treated (surgery or radiotherapy) with no evidence of progression and neurologically stable off anticonvulsants and steroids
- Unstable angina, myocardial infarction, cerebrovascular accident, > Class II congestive heart failure according to the New York Heart Association Classification for Congestive Heart Failure (see Appendix B) within 6 months before enrollment

4.4 Sample size calculation

In GROINSS-V I the percentage of groin recurrences was 8.1% in patients with a positive SN, for all sizes of SN metastases [8]. Sample size for GROINSS-V III is calculated based on a conservatively estimated groin recurrence rate of 7%, with a maximum increase in groin recurrences of 7%. The sample size, considering an alpha of 0.05 and a beta of 0.20, is then calculated to be 157 patients with macrometastases in their SN.