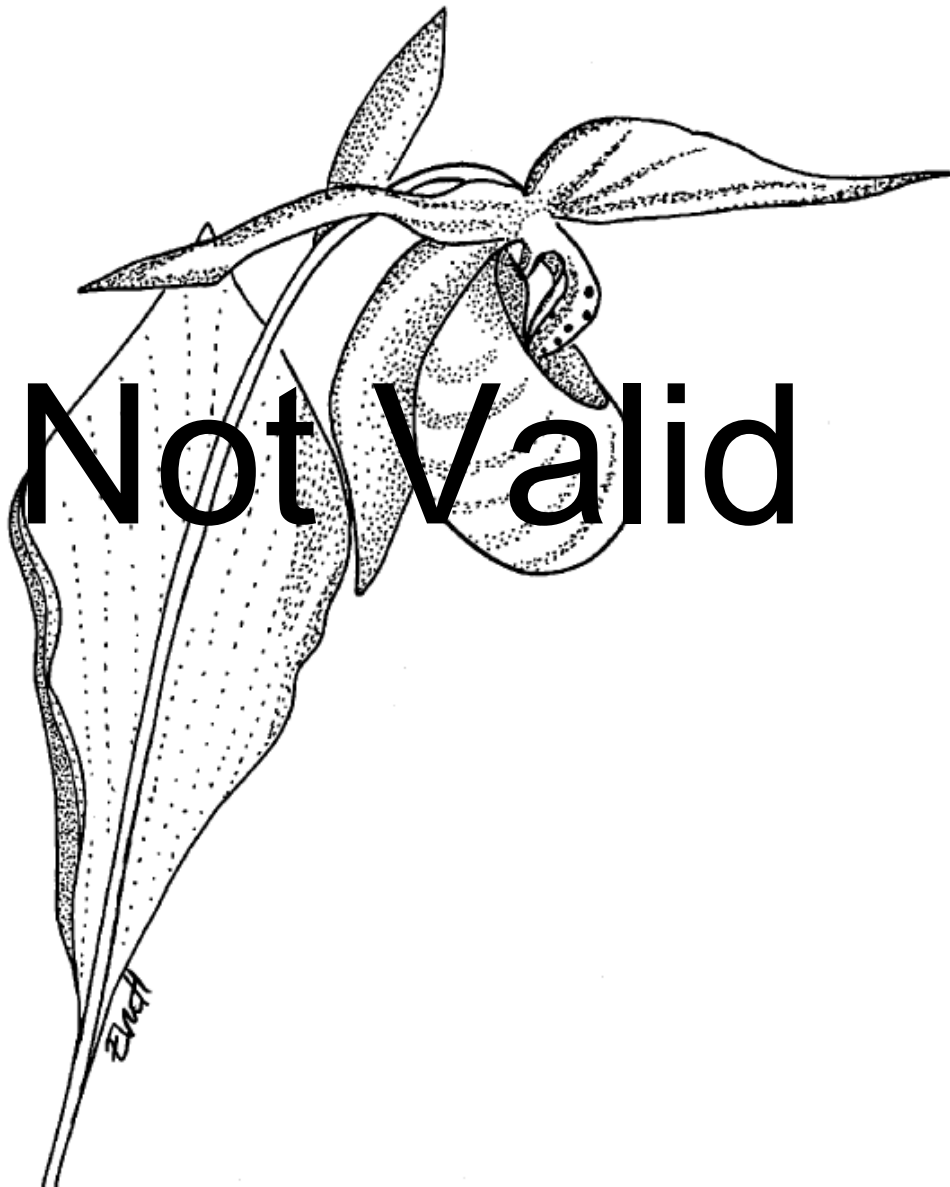


SWENOTECA IX

Revised continuation of SWENOTECA VII

A cancer care program for
Seminomatous Germ Cell Tumours
(Including testicular, retroperitoneal and mediastinal tumours)



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1 PURPOSE OF THE SWENOTECA IX CANCER CARE PROGRAM

General purposes:

- Establish a complete register including all male adolescent (≥ 16 years) and adult patients with seminomatous germ cell testicular, retroperitoneal and mediastinal cancer in Norway and Sweden
- Standardise diagnostic procedures, staging, treatment and follow-up in order to:
 - Improve patient outcome
 - Assure high quality prospective population-based clinical research
 - Reduce the radiation burden inflicted by CT in the follow-up of patients, by recommending MRI as standard abdominal-pelvic imaging modality

Specific foci in clinical stage I:

- Verify reported low relapse rate without adjuvant chemotherapy in patients with testicular tumour ≤ 4 cm and no invasion of the rete testis
- Evaluate the relapse rate with and without adjuvant chemotherapy, respectively, in patients with testicular tumour > 4 cm and/or invasion of the rete testis
- Further reduce the follow-up schedule depending on the risk and pattern of relapse
- Evaluate early and late toxicity after one course of adjuvant carboplatin

Specific foci in metastatic disease

- Evaluate therapeutic efficacy and early and late toxicity of BEP chemotherapy
- Evaluate the early and long-term side-effects of surgery for postchemotherapy residual tumour

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2 ABBREVIATIONS

AFP	Alpha fetoprotein
AUC	Area under curve
BEP	Bleomycin, etoposide, cisplatin
CIS	Carcinoma in situ
CR	Complete remission
CS	Clinical stage
CT	Computed tomography
EAU	European Association of Urology
EGCCCG	European Germ Cell Cancer Consensus Group
EP	Etoposide, cisplatin
FSH	Follicle-stimulating hormone
FU	Follow-up
β-hCG	Beta-human chorionic gonadotropin
IGCCCG	International Germ Cell Cancer Collaborative Group
LDH	Lactate dehydrogenase
LH	Luteinizing hormone
MRC	Medical Research Council
MRI	Magnetic resonance imaging
NSGCT	Non-seminoma germ cell tumour
PEI	Cisplatin, etoposide, ifosfamide
PET	Positron emission tomography
PFI	Progression free interval
PLAP	Placental alkaline phosphatase
RMH	Royal Marsden Hospital
SGCT	Seminomatous germ cell tumour
SHBG	Sex hormone-binding globulin
SWENOTECA	Swedish & Norwegian Testicular Cancer Group
TIP	Paclitaxel, ifosfamide and cisplatin
WHO	World Health Organization

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3 Flow-sheet: Diagnosis, Staging and Treatment

Testicular tumour

Ultrasound both testicles

Physical examination

History of prior testicular disorders and hereditary information



Inguinal orchiectomy and biopsy contralateral testicle, see 5.1.7



Seminomatous testicular cancer AFP normal (if slightly elevated and stable values, see protocol)

Risk factors: rete testis invasion, size of tumour > 4 cm



Clinical staging procedure

Tumour markers post-op: β -hCG, AFP, LDH (PLAP)

Hormone levels: Testosterone, LH, FSH, SHBG

Sperm count & cryopreservation, (consider if not done earlier)

CT scan of thorax, abdomen and pelvis



TNM, clinical staging* &
IGCCCG-classification



Treatment

Clinical stage I (CS I)

0 risk factor → surveillance

1-2 risk factors → carboplatin x 1 recommended, surveillance is an option

Adjuvant radiotherapy may in selected patients also be an option, see text.

Clinical stage IIA-IV, good prognosis: 3 courses of BEP-chemotherapy. If contraindications to bleomycin, 4 courses of EP-chemotherapy.

Radiotherapy 2 Gy x 15 to 30 Gy to para-aortic and ipsilateral iliac nodes is an option in CS IIA. If contraindications to chemotherapy in patients with CS IIB, treatment with radiotherapy to para-aortic and ipsilateral iliac nodes 2 Gy x 15 to 30 Gy with a boost of 2 Gy x 3 to 6 Gy to the GTV is an option.

Clinical stage IV, intermediate prognosis: 4 courses of BEP-chemotherapy. If contraindications to bleomycin, 4 courses of PEI-chemotherapy.

Tumour markers: AFP, β -hCG, LDH (PLAP optional), Hormone levels: Testosterone, LH, FSH, SHBG, Sperm count & cryopreservation. Patients should be offered a testicular prosthesis

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* If no obvious metastasis and elevated markers, tumour markers to be followed until normalization as long as declining according to half-life, see 5.2.1

* If CS IIA Mk negative, restaging after 8 weeks, see 5.2.2

4 BACKGROUND

4.1 General Information

Testicular cancer accounts for 1-2 % of all malignancies, but despite its rarity it is the most common cancer in young men. The incidence is 6.2/100 000 in Western Europe and highest in the Nordic countries except Finland. In Sweden (n=336) and Norway (n=290) approximately 600 new cases were diagnosed 2011 with an annual increase in incidence of 1.6 % the last ten year period (1, 2).

95 % of all testicular cancers are germ cells tumours of which 55 % are seminomas and 45 % are non-seminomas. The peak age incidence for seminoma is 35 years, ten years older than that for the non-seminoma patients. Despite all efforts the aetiology is still unknown, but coupled to aberrations in the development of the gonads (e.g. cryptorchidism, hypo/epispadias, hydrocele and hernia) indicating an early in utero first step oncogenesis.

Seminomas have a monomorphic pathology with one cell type derived from extra-embryonic tissue and true seminomas therefore are not compatible with elevated levels of alpha-fetoprotein (AFP). In contrast the complex non-seminomatous germ cell tumours (NSGCT) may consist of a mixture of different cell types originating from the totipotent embryonic tissue and can also include elements of seminoma.

Seminoma is biologically different from NSGCT which is reflected by the higher rate of clinical stage (CS) I disease at diagnosis, 85 % compared to 60 % in NSGCT. Seminoma is in the current prognostic classification for metastatic disease, never classified as belonging to the poor prognosis group (3, see appendix IV for prognostic groups).

Adjuvant treatment for CS I seminoma is controversial. For decades adjuvant radiotherapy was given to all stage I patients resulting in relapse rates of 1-5 %. During the last decades there has been increasing concern regarding the risk of possible late sequelae from radiotherapy. New treatment options were sought. Surveillance and treatment at relapse was shown in large observational studies to result in the same cure rate of 98 % (4, 5). In 2005 a large randomised non-inferiority study of 1447 patients with a median follow up of 4 years, comparing one course of carboplatin (AUC7) with adjuvant radiotherapy concluded that the relapse rate was 4-5 % and not significantly different (6, 7). The pattern of relapse however was different with extra-abdominal sites after radiotherapy and nodal intra-abdominal sites after carboplatin. Furthermore, two studies from the Spanish germ cell cancer group confirmed the efficacy of adjuvant carboplatin in a total of 284 patients treated with 2 courses of carboplatin (AUC7) (8, 9). In all three studies the acute toxicity was mild.

In metastatic disease the controversies regarding treatment are related to the choice of radiotherapy as opposed to chemotherapy in clinical stage II disease.

4.2 International Treatment Guidelines CS I Seminoma

In the European Germ Cell Cancer Consensus Group (EGCCCG) there is no consensus on recommended treatment to patients with CS I (10). In the EAU guidelines surveillance and carboplatin are recommended treatment options (11).

4.2.1 The SWENOTECA experience CS I seminoma 2000-2006

The SWENOTECA V protocol (2000-2006) was a Swedish-Norwegian program including patients with all stages of seminoma. Patients with CS I, had the option to choose either adjuvant radiotherapy 25.2Gy/14 fractions or surveillance. In 2004 when the results of the randomised study between adjuvant carboplatin and radiotherapy were acknowledged the options were altered to include adjuvant carboplatin. While on surveillance 65/512 (14,3%) relapsed at median time of 1.4 years, all in the abdomen, and 94% with abdominal relapse only. Only two patients died (2/512, 0,3%). Following radiotherapy 4/481 (0.8%) relapsed, one with solitary bone metastasis, one with mediastinal nodes and two within the radiotherapy field. Median time to relapse was 1.1 year. In the carboplatin group 7/188 (3.7%) relapsed after a median time of 1.8 years (12). None of these patients died. Analysis of risk factors for relapse in the surveillance group did not identify tumour size to be a prognostic factor, and invasion of the rete testis was not recorded.

4.2.2 The SWENOTECA experience CS I seminoma 2007-2010

In the SWENOTECA VII protocol 2007-2010 the treatment in CS I was adjusted to the possible prognostic risk factors, i.e. size of primary tumour and invasion in the rete testis presented by Waide et al. (13). Patients with 0-1 risk factors were recommended surveillance, but could choose the course of adjuvant carboplatin (AUC7), while patients with two risk factors were recommended one course of adjuvant carboplatin, but could choose surveillance. An analysis of CS I patients included in SWENOTECA VII until 2010 and patients from SWENOTECA V treated with adjuvant carboplatin was performed in 2014. In total 1064 patients were included in the analysis, 669 patients received adjuvant carboplatin, 339 were managed by surveillance and four patients received other adjuvant treatment. Invasion of the rete testis and tumor size > 4 cm were both confirmed as independent risk factors predicting relapse in a multivariate analysis. Patients without risk factors had a very small risk of relapse. The risk of relapse was similar in patients managed either by surveillance or adjuvant carboplatin, 2.9 % vs. 2.3 %. In patients with 1-2 risk factors the risk of relapse following surveillance was 22.8 %, compared to 9.4 % in patients receiving adjuvant carboplatin.

4.3 International Treatment Guidelines CS II-IV Seminoma

In small volume abdominal disease radiotherapy is an option besides chemotherapy. Patients with more advanced disease are recommended treatment with chemotherapy. The recommended chemotherapy is cisplatin in combination with etoposide and bleomycin (BEP), substituted with etoposide and cisplatin (EP) or with additional ifosfamide (PEI) in patients with contraindications to bleomycin, depending on prognostic risk group.

4.3.1 The SWENOTECA experience CS II-IV seminoma 2000-2006

In 102 patients with stage IIA/B seminoma three patients (2,9%) relapsed. In all three the primary treatment was radiotherapy. Median time to relapse was 2.1 year and one patient relapsed within the radiation field. In 73 patients treated with chemotherapy (EP/BEP) there were no relapses reported.

All 86 (6 %) patients with more advanced tumour spread (stage IIC/D, III and IV) were treated with chemotherapy initially.

The 5-year cancer specific survival for all patients treated for seminoma was excellent with a survival of 99.6%. According to stage, the 5-year CSS was 99.9% in CS I, 100% in CS IIA/B, 97.9% in CS IIC/D, 100% in CS III and 80% in CS IV. For patients with metastatic disease the 5-year CSS according to the IGCCCG prognostic classification was 97.2% for patients in the good prognosis group and 50% for patients in the intermediate prognosis group. The challenge will be to minimise treatment and follow up without compromising outcome for these young men and to retain fertility and quality of life. The low survival in the intermediate prognosis group is uncertain due to the low number of patients treated, but every effort should be made to improve survival in this rare group of patients.

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5 Diagnosis and Clinical Staging

5.1 Diagnosis

See flow sheet chapter 3.

5.1.1 Clinical examination of the testes

Testicular cancer usually presents as a painless, unilateral intrascrotal mass and is in the majority of cases diagnosed by palpation. Some patients will present clinical symptoms mimicking epididymitis, less than 10 %. Ultrasound of both the testicles should be performed, and exploration should be performed in all cases when clinical **or** ultrasound investigations cannot exclude a tumour. Trans-scrotal fine needle aspiration or biopsy from the tumour should not be performed.

5.1.2 Serum tumour markers

In contrast to non-seminomatous germ cell cancer, seminoma patients often lack elevated tumour markers.

Beta-human chorionic gonadotropin (β -hCG) is slightly/moderately elevated depending on tumour volume in 20–50 % of the patients. Very high levels of β -hCG should raise the suspicion of non-seminomatous germ cell components like choriocarcinoma and the specimen should be re-examined. The presence of necrosis in the primary tumour may be an explanation to why non-seminomatous elements sometimes can be found in the metastasis but not in the primary tumour.

The serum half-life of β -hCG should, as a rule, be ≤ 3 days. However, the rate of reduction in the concentration of β -hCG following chemotherapy may follow a more complex pattern, with longer apparent half-life during later stages of chemotherapy, even in patients treated successfully (14).

Cross reactivity with the beta unit of the LH might occur resulting in a false positive test. Furthermore, hypogonadism can induce LH as well as β -hCG production by the pituitary gland. Short course of testosterone replacement therapy suppresses pituitary LH and β -hCG secretion allowing for a true measure of β -hCG of germ cell origin.

β -hCG can also be produced by tumours of other origin such as liver, pancreas, stomach, kidney and bladder cancer (15).

The determination of β -hCG is used in order to:

- Identify occult spread in CSI
- Follow treatment effect
- Identify early relapse

Alpha-fetoprotein, AFP is by definition not consistent with a seminoma diagnosis. In germ cell tumours AFP is secreted by embryonic cell carcinoma and yolk sac tumour but not by pure choriocarcinoma or pure seminoma. The detection of significantly elevated levels of

AFP implies that the tumour specimen should be re-examined with respect to non-seminomatous elements. Even if these are not found, the tumour should be considered and treated as a non-seminoma! One should be aware that reparative and infectious/viral processes of the liver as well as cirrhosis and trauma also may induce an increase in AFP, sometimes as high as > 500 ng/ml. Rarely patients constitutionally may have an AFP level moderately elevated above the normal range. A modest and **stable** elevated AFP level might thus be compatible with a seminoma diagnosis.

AFP can also be elevated in hepatocellular carcinoma as well as pancreatic cancer, gastric, colorectal and bronchial cancer.

LDH (lactate dehydrogenase) is a cytoplasmic enzyme in all living cells and elevated values are seen in all kinds of tissue destruction and cell death. Total serum LDH level is elevated in about 80 % of patients with metastatic seminomatous testicular cancer. Typically it is the elevation of LDH isoenzyme number 1 that is seen. LDH elevation is taken into consideration in the classification in prognostic groups but is less specific for germ cell tumours than AFP or β -hCG. Insignificant elevated levels of LDH are commonly seen at patient visits during follow-up.

Placental alkaline phosphatase (PLAP) is elevated in 50 % of the patients with seminoma but is only analysed in a few laboratories in Sweden. The use of this marker is optional. It may be the only elevated marker in metastatic disease and can thus be useful during follow-up of such patients. PLAP may be falsely elevated in smokers.

5.1.3 Fertility measures and hormonal analyses

Cryopreservation of sperm should preferably be offered before orchiectomy. If not performed before orchiectomy it should always be offered before start of any therapy although the adjuvant chemotherapy with 1 course of carboplatin most probably has no long-lasting detrimental effect on spermatogenesis (16). Patients receiving multiple cycles of chemotherapy, radiotherapy or operated with RPLND are at risk of subfertility/ infertility. Sexual hormones (LH/FSH, testosterone and SHBG) should be analysed before and after orchiectomy and during follow up. The serum for the hormone analyses should preferentially be sampled in the morning or at least before noon (due to their circadian variations). It is important to detect and treat hormonal insufficiency both with regard to short- and long-term morbidity of hypogonadism.

5.1.4 Tests to be performed before orchiectomy

- Ultrasound examination of both testicles
- General physical examination
- Serum levels of AFP, β -hCG, LDH **Mandatory!**
- Serum levels of PLAP, optional
- Serum levels of LH, FSH, testosterone and SHBG
- All patients should be offered pre-orchiectomy sperm count with cryopreservation
- All patients should be offered a testicular prosthesis

5.1.5 Inguinal exploration and orchiectomy

An incision similar to that performed in patients with inguinal hernia is done. The anterior wall of the inguinal canal is divided, and the vas and spermatic vessels are dissected free at the internal opening of the inguinal canal. In most cases the diagnosis is certain and the spermatic vessels and the vas are divided immediately. The testis and epididymis with their surrounding tunica vaginalis are pushed out of the scrotum and dissected free from the scrotal wall. The vas and the spermatic vessels are ligated and divided separately close to the peritoneal fold. The specimen is immediately sent for definitive histology. If possible, the specimen should be sent fresh on ice to the pathology department, otherwise placed in formalin. The urologist should not incise the specimen.

It is recommended to offer every patient a testicular prosthesis before orchiectomy (17). If the patient would like to have a testicular prosthesis it is recommended to close the opening to the scrotum with an absorbable tobacco-pouch suture above the prosthesis to prevent migration to the inguinal canal.

If any doubt of the diagnosis, the spermatic cord is clamped before mobilization and inspection of the testis. In some cases the tunica albuginea of the testis is incised and a frozen section is sent for histology. If the result of the frozen section is a benign condition (for example adenomatoid tumour or epidermoid cyst) it is recommended to perform a local resection instead of an orchiectomy.

All patients should be offered cryopreservation of sperm before orchiectomy and a testicular prosthesis immediately following orchiectomy. Orchiectomy should therefore be performed in hospitals with access to these procedures.

5.1.6 Organ sparing surgery

Organ sparing surgery in testicular cancer is only indicated in a few selected cases and is not recommended in the presence of a normal contralateral testis.

Indications for organ preserving surgery are tumours in both or in a solitary testis. The aim is to preserve some endogenous endocrine function and the prerequisite is that the patient should have a normal preoperative testosterone level. Furthermore the tumour volume should be less than 30 % of the testicular volume. All patients should be offered immediate (or delayed) adjuvant local radiotherapy because of the high risk (> 85 %) of concomitant CIS. The radiation therapy may be delayed with the same precautions as mentioned in the **appendix** on CIS in the SWENOTECA VIII protocol (18-20).

5.1.7 Biopsy of the contralateral testis

Patients should be informed of the possibility of contralateral biopsy to detect possible cancer in situ (CIS), and if performed this is best done at the time of the orchiectomy. A biopsy is recommended if the patient has any of the following risk factors in addition to a contralateral testicular tumor:

- Cryptorchism
- History of infertility or sperm count ≤ 10 mill/ml
- Atrophic testicle (<12 ml)
- Heredity
- Microlithiasis

In patients over 40 years without any risk factors the risk of CIS is very low, and biopsy is not recommended.

A double-biopsy procedure yields an increase in sensitivity as compared to a single-biopsy procedure (15, 21) and is recommended. The double biopsy is best done as follows:

The testis should be held firmly, and a small scrotal incision is made at the cranial pole. Then the tunica vaginalis should be opened. Then the tunica albuginea should be incised at the cranial pole, laterally (to spare the central vessel of the testis). The first biopsy is taken at this site. Snip off a tuft of tubules cleanly with fine sharp scissors (3-4 mm specimen). The small incision of the tunica should then be closed, and the testicle should be rolled between the surgeon's fingers within the tunica vaginalis to access the lower pole. There the second incision to the tunica albuginea is performed to excise another specimen for histology.

Again, refrain from the midline to spare the main vessel. Close the incision in the tunica and skin separately with interrupted 4-0 absorbable suture.

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In an atrophic testicle a single biopsy only is required.

Place the biopsy at once into a specimen pot containing formalin. While performing the biopsy, careful handling and placement in fixative is important to prevent mechanical damage. If it is of importance to evaluate not only CIS but also spermatogenesis, the biopsy must be put in Stieve's or Bouin's solution and be analysed within 24 hours at the pathology department.

The evaluation of CIS in testicular biopsies requires experience and the pathological examination of the biopsy **should** include immunohistochemical evaluations. Orchiectomy and possible contralateral biopsy should therefore be performed in hospitals with access to pathological laboratory with experience in evaluating possible CIS or with the possibility to send the specimen to such a laboratory.

5.1.8 Pathological examination of the testis

See **appendix XXXVI**: KVASt dokument – testistumör.

Macroscopic features and sampling:

- Side, testis size, tumour size and the macroscopic features of the tumour, such as macroscopic involvement of epididymis, spermatic cord and tunica vaginalis
- Sampling: 1 cm² section for every cm of maximal tumour diameter, including normal macroscopic parenchyma (if present), tunica albuginea and epididymis selection of suspected areas. At least one proximal and one distal section of spermatic cord, plus any suspected area

Microscopic features and diagnosis:

- Histological type according to the 2004 WHO classification. Only pure seminoma tumour cells are classified as a seminoma. **Spermatocytic seminoma is not included in this protocol**
- Presence or absence of tumour vascular invasion, rete testis invasion, tunica albuginea, tunica vaginalis, epididymis or spermatic cord invasion
- Presence or absence of intratubular germ cell neoplasia in non-tumour parenchyma
- pT category according to TNM 2009

Immunohistochemical evaluation should be used in case of diagnostic difficulties.

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5.2 Staging Investigations

5.2.1 Tests to be performed after orchiectomy - Clinical staging procedure

- Serum levels of AFP, β -hCG, LDH, (PLAP optional)
- Serum levels of LH, FSH, testosterone and SHBG
- CT of thorax, abdomen and pelvis with intravenous and oral contrast should be performed as soon as possible after orchiectomy. If there is clinical indication of advanced metastatic disease the CT should be done before orchiectomy
- MRI of the brain is required in patients with clinical symptoms or signs indicating brain metastases, massive pulmonary metastases as well as in patients with non-pulmonary visceral metastases
- Other investigations may be indicated on an individual basis
- If in doubt of metastases and elevated tumour markers (not LDH) follow tumour markers weekly until nadir/normalisation, as long as the half-life is maintained

Any clear deviation from the half-life plots indicates metastatic disease, thus ending the observation period.

PLAP may also be analysed and followed, and is associated with metastatic disease

when elevated in a non-smoker.

If there is evidence of metastatic disease, the patient should be referred immediately to an oncology department for further evaluation and treatment.

Prognostic group classification in metastatic disease should be performed immediately prior to treatment.

5.2.2 Patients with slightly enlarged paraaortic lymph nodes/suspected metastases in presumed clinical stage IIA, second staging

Slightly enlarged retroperitoneal lymph nodes <2 cm in patients without elevated tumour markers offer a diagnostic problem. These lymph nodes may be benign or, on the other hand, represent metastases. An observation period of 8 weeks with a second staging is recommended unless a biopsy verifies metastatic disease.

Serum levels of β -hCG must be monitored every other week during this observation interval.

Clinical staging procedure 2 at 8 weeks from orchiectomy should include:

- CT abdomen and pelvis, with special emphasis on the retroperitoneal and iliac lymph nodes. Note that CT is the main imaging modality for the final clinical classification!
- Serum levels of AFP, β -hCG, LDH, (PLAP optional)

Positron emission tomography (PET)-CT may add information but is not reliable in small lymph nodes. If a PET-CT is positive, a biopsy should be considered if feasible.

If the stage still is equivocal after the 8 weeks observation period, further observation is warranted, or a laparoscopic lymphnode biopsy/resection can be an option.

Treatment should not be initiated unless metastatic disease is unequivocal, (e.g. growth or positive biopsy).

6 Imaging

6.1 Diagnosis and Staging

Ultrasound of the testes should be performed using high frequency (>7.5-MHz) transducers. Other imaging procedures, such as magnetic resonance imaging (MRI) or positron emission tomography/Computed tomography (PET/CT) of the testes, should not routinely be performed since the results of these examinations will not alter the clinical management of the patients.

Computed tomography (CT) of the chest, abdomen, and pelvis is required as part of the initial staging procedure. Oral and intravenous contrast media is mandatory at baseline. If solitary or multiple small (<5 mm) pulmonary nodules are found, the decision whether to biopsy or follow-up must be taken in consideration individually for each patient.

When interpreting retroperitoneal lymph nodes on CT, irrespective of size criteria for metastases used, the limited sensitivity and specificity for characterisation of lymph nodes should be considered in the clinical management. Therefore, the differentiation between clinical stages I and IIA is unreliable, if β -hCG is normal. A detailed description of the location, number, and size of lymph nodes with measures of the two perpendicular axial diameters should be provided in the radiology report(22).

MRI of the abdomen and pelvis is associated with similar limitations in sensitivity and specificity in the staging situation (23), and has not proven to provide additional information in this disease. MRI is a better option in patients in whom intravenous contrast media cannot be given.

Not Valid

On the basis of available data, PET has not demonstrated to improve sensitivity of staging of testicular cancer compared with CT scanning alone(24-27). PET scans are not recommended outside clinical trials as part of routine initial staging procedures.

Other investigations should be performed according to symptoms. Isolated skeletal involvement does occur in seminoma, although rare. MRI is the preferred method of investigation to elucidate if bone metastases are present in patients with symptoms.

Imaging of the brain, by MRI, is required in patients with clinical symptoms or signs indicating brain metastases, massive lung metastases as well as in patients with non-pulmonary visceral metastases.

6.2 Treatment Evaluation

The standard modality for response evaluation is CT. MRI should be used in patients with contraindications to CT. A detailed description of the location, number, and size of metastatic sites with measures of the two perpendicular axial diameters should be provided in the radiology report(22).

Image guided response evaluation during treatment for metastatic disease is a challenge. Response evaluation should always be performed in a hospital with a multidisciplinary team

consisting of radiologists, oncologists and surgeons all with experience in treating patients with germ cell tumours available.

PET-CT during treatment has currently no proven role outside clinical trials.

6.3 Follow-up

It is desirable to reduce the total radiation dose from repeated diagnostic imaging procedures to the patient without compromising the quality of follow-up. This is of particular concern in patients below 35 years at diagnosis.

Magnetic resonance imaging (MRI) of the abdominal and pelvic lymph node areas is the preferred method to investigate the retroperitoneum during follow-up.

Ultrasonography may also be performed if the necessary expertise is available. However, ultrasonography of the retroperitoneum is usually less sensitive in the screening situation to detect retroperitoneal lymph nodes than MRI or CT. Therefore, if there is any ambiguity, an MRI examination must be performed. Since CT is associated with undesirable total radiation dose to young patients if repeated many times during follow up it is advisable to perform MRI at least once yearly if ultrasound is used in the follow-up.

If a centre does not have access to MRI the patient should be referred to a more specialized centre. MRI should be performed according to the principles of the imaging protocol in **appendix XVLI**. A dialogue with the responsible radiologist is necessary to make sure that the principles of the protocol and the reasons for the follow up are fully understood. For the use of PET-CT with regard to handling of postchemotherapy tumour masses see chapter 8 on metastatic disease and chapter 9 on surgery other than orchiectomy.

7 Clinical Stage I Seminoma

7.1 Background

Seminoma constitutes over 50 % of patients with testicular cancer. Of these, 85 % present in clinical stage I, making CS I seminoma the most common expression of testicular cancer (28).

7.2 Surveillance

Based on large, unselected patient series on surveillance we know that 85 % of patients in CSI are cured by orchiectomy alone (12, 29, 30). The overall survival in these patient series approach 100 %, and surveillance is an attractive strategy. There have been several attempts to identify possible prognostic factor for relapse. A seminal article published in 2002, pooled 638 patients from four centres (13). This retrospective study identified tumour size > 4 cm and rete testis invasion as independent risk factors for relapse. However, an unpublished validation study from the same group could not confirm the prognostic value of these proposed risk factors (31). The results from SWENOTECA V, published in 2011, also failed to identify any prognostic factor for relapse (12). Results from a recent Spanish risk-adapted protocol give some indications that patients without any of the proposed risk factors have a very low risk of relapse (9). The newly presented results from SWENOTECA VII confirm a low risk of relapse in this group of patients, with a 2.9 % relapse rate. Both invasion of the rete testis and tumor size > 4cm were found to be risk factors predicting relapse. In SWENOTECA VII the relapse rate in patients with 1-2 risk factors and managed with surveillance was 22.8 % (32).

Not Valid

7.3 Adjuvant Carboplatin

In 2005 results from a large randomised trial of one cycle of adjuvant carboplatin versus adjuvant radiotherapy was reported (6). The long-term mature data were presented in 2011 (7). The study included 1447 patients with a median follow-up of 6.5 years. 573 patients received one cycle of carboplatin (AUC 7). The relapse rate following one course of adjuvant carboplatin was 5.3 %. Combined results from SWENOTECA V and VII, where 669 patients received one course of carboplatin, found a relapse rate of 6.2 % after a median follow-up of 5.2 years (12, 32). Invasion of rete testis or tumor size > 4 cm, result in a higher risk of relapse, 9.4 %.

Carboplatin has a steep dose response interval. Inferior outcomes, with more relapses have been reported when a lower dose than AUC 7 has been given. AUC 7 should always be calculated from uncorrected GFR, measured by iohexol- or Cr-EDTA clearance.

Several non-randomised trials have explored two courses of adjuvant carboplatin (AUC 7 or 400 mg/m²), with a reported relapse rate of about 2 % (8, 9, 33, 34).

Dosage schedule of carboplatin: **see appendix XI.**

7.4 Adjuvant Radiotherapy

Until recently, standard adjuvant treatment of CSI seminoma has been radiotherapy. Based on large randomised studies conducted by the MRC, we know that 20 Gy given to a para-aortic field results in a relapse rate of about 4 % (7). In SWENOTECA V the relapse rate following 25.2 Gy to a para-aortic and ipsilateral iliac lymph nodes was 0.8 % (12). Due to the increased risk of cardiovascular disease and secondary cancers following radiotherapy, radiotherapy is no longer recommended as a standard adjuvant treatment.

Radiotherapy may still be an option in those who by any means are not suitable for adjuvant chemotherapy or surveillance.

7.5 Treatment Recommendations Clinical Stage I Seminoma

Both invasion of the rete testis and tumor size > 4 cm predict relapse following surveillance or adjuvant carboplatin (AUC7). Patients without any of these proposed risk factors have a very low risk of relapse. SWENOTECA propose a modified risk-adapted strategy for adjuvant treatment in CSI seminoma.

- Patients with a tumour $\leq 4\text{cm}$ and no invasion of the rete testis are recommended surveillance
- Patients with a tumour $> 4\text{cm}$ and/or invasion of the rete testis are recommended one course of adjuvant carboplatin AUC 7 (calculated from unadjusted GFR, measured by iohexol- or Cr-EDTA clearance), but can choose surveillance
- Adjuvant radiotherapy is only recommended for those who by any means are not suitable for adjuvant chemotherapy or surveillance. **See chapter 12 for details.**

Not Valid

8 Metastatic Seminoma

8.1 Clinical Stage IIA Seminoma

Patients with clinical stage IIA seminoma have a limited disease with abdominal lymph node metastases < 2cm. Consequently, tumour markers are usually negative. To stage these patients properly see Chapter 5.2.2.

The standard treatment so far has been radiotherapy given to a para-aortic and ipsilateral iliac field. According to data in the literature a target dose of 25-30 Gy results in a relapse free survival of 88-95 % (12, 35).

The remaining testis receives 1-3 % of the total radiation dose. Doses less than 0.5 Gy usually cause a transient oligospermia, while higher doses cause azoospermia. If the dose is less than 1.5 Gy, a recovery is seen within 2 years (16).

Accumulating data on long-term morbidity, such as increased risk for cardiovascular events and increased risk of second malignancies following radiotherapy has lead to concerns. However, most reports refer to patients irradiated to larger target volumes and higher radiation doses, although recent studies also report on patients treated with more modern radiotherapy (36-38).

These concerns have brought forward chemotherapy as an alternative to radiotherapy also in this group of patients.

Not Valid

8.2 Treatment Recommendations Clinical Stage IIA Seminoma

There are two possible alternatives, both with excellent cure rates:

Chemotherapy

BEP x 3 is the standard chemotherapy regimen. If there are contraindications to bleomycin, EP x 4 should be chosen.

Radiotherapy

The target volume includes the para-aortic and ipsilateral iliac lymph nodes to a target dose of 30 Gy with 2.0 Gy per fraction x 15. See chapter 12. Note that the target dose is increased compared to SWENOTECA VII in order to improve local control.

8.3 Clinical stage IIB - IV seminoma

In the International Germ Cell Consensus Classification (**see appendix IV**), a prognostic factor-based classification system for metastatic germ cell cancers, metastatic seminoma is classified as good or intermediate prognosis. No seminoma patients are classified as poor prognosis. Adverse prognostic factors are non-pulmonary visceral metastases, mostly localized in liver, bone or brain.

CS IIB patients were previously treated with radiotherapy, and the reported relapse rates after radiotherapy varies between 9–24 %. All available data are based on small patient series (39-42). The relapses after radiotherapy are predominately located outside the retroperitoneum. Although there are no randomised studies on patients with stage IIB disease comparing radiotherapy and chemotherapy, SWENOTECA has recommended cisplatin-based chemotherapy to patients with CS IIB or more, because of the high reported relapse rates with radiotherapy. In the SWENOTECA patient series, 67 patients with seminoma CS IIB treated with chemotherapy had a relapse-free survival at 100 % after median 5.5 years follow-up (43).

For higher stages of seminoma, there is international consensus on treatment with 3-4 cycles of cisplatin-based combination chemotherapy (44, 45). As patients with advanced seminoma are infrequent, there are no randomised studies comparing different kinds of cisplatin-based chemotherapy for seminoma patients alone.

Good prognosis risk group

Data presented by Kondagunta et al. indicated that EP x 4 was highly effective in patients with good-risk germ cell cancers (46). However, a randomised EORTC study comparing BEP x 3 versus EP x 4, reported complete response rates at 95 % versus 87 % ($p=0.0075$), favouring 3 BEP (47). Furthermore, we believe that BEP x 3 has less acute and late toxicities than EP x 4 due to less cumulative cisplatin dose. The standard treatment of metastatic good-prognosis seminoma is therefore BEP x 3. For patients with contraindications to bleomycin, EP x 4 can be given. Although single-agent carboplatin chemotherapy in standard dosage is inferior to cisplatin-based combination chemotherapy in advanced disease (48, 49), carboplatin AUC10 may be an option in the case of severely impaired renal function (50).

Intermediate prognosis risk group

The standard treatment for intermediate prognosis metastatic seminoma is 4 x BEP (44, 45). For patients with contraindications to bleomycin, 4 x PEI can be administered (45).

Residual tumours

Seminomatous tumours are often characterised by a slow clinical regression rate after chemotherapy. Residual tumours mostly consist of fibrotic or necrotic tissue (51, 52).

Retrospective series show viable tumour in 30 % of patients with residual tumours > 3 cm (53, 54). In post-chemotherapy seminoma residual lesions, a positive PET is highly predictive for the presence of viable tumour especially when using a ≥ 3 cm cut-off. A negative PET scan is excellent for the exclusion of disease in lesions ≥ 3 cm. It should not be performed earlier than 6 weeks after day 21 of the last chemotherapy course due to the risk of false positivity

(55). PET can contribute to the management of residual seminoma lesions, especially in terms of avoiding unnecessary additional treatment for patients with non-regressing lesions ≥ 3 cm (55-57).

8.4 Treatment Recommendations Clinical Stage IIB-IV Seminoma

8.4.1 Good prognosis seminoma

- The standard treatment is BEP x 3. In case of contraindications to bleomycin, EP x 4 should be used
- There is no need to evaluate patients with good prognosis seminoma until initial treatment is completed, i.e. after full chemotherapy with BEP x 3/EP x 4
- Patients with CS IIB with contraindications to chemotherapy may be treated with radiotherapy instead. If radiotherapy is given, a dose of 2 Gy x 15 to a total dose of 30 Gy to the para-aortic and ipsilateral iliac lymph nodes plus a boost of 2 Gy x 3 to 6 Gy to the enlarged lymph nodes should be given. See chapter 12.
- Dose reductions and treatment delays should be avoided

8.4.2 Intermediate prognosis seminoma

- Patients with intermediate prognosis seminoma should always be transferred to a centre with experience in treating advanced germ cell tumours before start of treatment.
- The standard treatment is BEP x 4. In the case of contraindications to bleomycin, PEI x 4 should be used
- Patients with intermediate prognosis seminoma should be evaluated prior to the 3rd cycle
 - In case of stable disease after two courses of chemotherapy, the possibility for teratoma should be considered and a biopsy should be performed
 - In case of progressive disease, the patient should be discussed within the SWENOTECA network
- Dose reductions and treatment delays should be avoided

8.4.3 Residual masses

- Consolidating treatment after chemotherapy with either surgery or radiotherapy should not be applied routinely
- Patients with regressing or persisting radiological findings < 3 cm after primary chemotherapy should be monitored with an appropriate radiological method (MRI, CT) and serum tumour markers
- A PET scan is recommended if the residual mass is ≥ 3 cm and not regressing in order to identify viable seminoma in a residual mass. It should not be performed earlier than 6 weeks from day 21 of the last cycle of chemotherapy due to the risk of false positivity

- In case of a stable residual mass with a negative PET scan, continue the follow-up
- If clearly positive PET scan, histological verification should be performed before consolidating therapy is decided upon. In the case of weak PET positivity, a 6-8 week expectance with a supplementary PET may be an option. If viable tumour is found, surgery, if feasible, should be preferred, because of the increased risk for secondary malignancies and cardiovascular disease after combined chemotherapy and radiotherapy
- If post-chemotherapy radiotherapy is chosen in selected cases (surgery not feasible), treatment should be given to limited fields and to a total dose of 36–40 Gy given in 2 Gy fractions
- Patients with residual tumours should be checked minimum according to the general follow-up plan for patients with seminoma. Check-ups may be more intense the first 6-9 months, i.e. every third month

8.5 Chemotherapy, comments

Chemotherapy should be given without dose reductions at 21-d intervals. Dose reductions are highly discouraged. Postponing treatment, (maximum 3 days), should only rarely be done. If serious neutropenic infectious complications have occurred during one preceding chemotherapy cycle, prophylactic administration of G-CSF is recommended in subsequent cycles. Because dose reductions due to neutropenia should be avoided, prophylactic G-CSF should also be used if prolonged neutropenia occurs for maintenance of the required dose intensity. For body surface area above 2.2m² individual consideration must be undertaken (fat/muscle/length). A body surface area exceeding 2.4m² should not be used.

8.5.1 Cisplatin

To prevent cisplatin-induced nephrotoxicity saline loading alone is recommended rather than saline loading with mannitol (58). Cisplatin is not to be given if GFR < 40 (normal range 80-125 for ages 18-50). However, if GFR is reduced due to tumour obstruction cisplatin is to be given without dose-reduction. A nephrostomy or a stent should be considered.

8.5.2 Bleomycin

Bleomycin should not be given to patients with decreased lung function, lung fibrosis, diffusion capacity < 60% or if GFR < 40 ml/min (normal range 80-125 ml/min for ages 18-50). A cumulative dose > 300 000 units is associated with increased toxicity and the SWENOTECA therefore recommends a cumulative maximum dose of bleomycin of 300 000 units (59).

The risk for bleomycin-induced pneumonitis (BIP) is increased in heavy smokers, in those with decreased kidney-function and in elderly > 60 years and for these patients close observation for BIP should be undertaken during treatment.

Bleomycin and anesthesia

A negative effect of high inspired-oxygen fractions within days or weeks after bleomycin exposure has been shown in several animal studies. There is however, no unequivocal evidence that the level of oxygenation is of major importance for pulmonary complications during/after surgery in patients having been treated with bleomycin due to metastatic germ

cell cancer (60). Another possible mechanism of postoperative BIP is fluid overload. Therefore perioperative oxygen restriction in patients earlier treated with bleomycin is not necessary. However, oxygen concentration during surgery is to be maintained at the lowest level possible providing adequate oxygenation (average 40% fractional inspired oxygen) and fluid balance has to be monitored closely (61).

Bleomycin and scuba diving

Extensive clinical experience in patients resuming diving after bleomycin-containing chemotherapy, combined with the data from surgery in these patients, concludes that resuming scuba diving 6-12 months following uncomplicated therapy with 3-4 courses of bleomycin-containing chemotherapy is acceptable (62).

Not Valid

9 Surgery other than orchiectomy

9.1 Retroperitoneal Lymph Node Dissection (RPLND)

RPLND is not used as a staging procedure in seminoma.

9.2 Postchemotherapy Residual Masses

Residual postchemotherapy masses are common in advanced seminoma with bulky tumour (55-80 %) (63). In contrast to non-seminoma, residual postchemotherapy seminoma tumour masses are not generally resected. Most groups have used a cut-off of 3 cm (transverse diameter) for considering biopsy or resection (if possible) (64). Previous retrospective series have shown viable malignancy rates of 13-42 % in well-defined residual masses >3 cm compared to 0-3 % in masses <3 cm (53, 54, 64-66). Pure seminomas contain by definition no teratomatous elements.

In seminomas, surgery is technically demanding due to fibrosis and desmoplastic reaction, and it is often incomplete (26-42%) and associated with increased morbidity (54, 63-65, 67). As a consequence, RPLND is rarely used in seminomas. If surgery is needed in this situation it should be in the form of resection (if possible) or biopsy due to a positive PET-CT (53, 54, 68, 69).

Not Valid

9.2.1 PET-CT in residual masses

Today, a PET-CT is performed in residual masses >3 cm in order to discriminate between fibrosis/necrosis versus viable tumour and spare patients surgery (70).

9.2.2 Patients with normal tumour markers and residual mass ≤ 3 cm

In residual tumours <3cm, the predictive value of PET is weak (55). These patients need no further therapy and should be followed according to the follow-up schedule (53, 54, 66, 68).

9.2.3 Patients with tumour masses >3 cm and normal tumour markers

In these patients a PET scan is recommended to assess whether there is residual viable tumour (55, 69, 71). See 8.3.3.

A clearly positive PET scan is a strong indicator of residual malignant tumour and should lead to biopsy or surgical resection (69). The surgical procedure should be carried out at a centre with adequate combined competence and experience with testicular cancer treatment. If PET results are unclear, a new PET should be performed, and if the positive lesion diminishes in size, surgery should be avoided, and further follow-up is recommended.

In case of non-radical surgical margins following resection, external beam radiotherapy or chemotherapy should be considered.

In case of non-resectable tumours or patients unfit for surgery, radiotherapy (36-40 Gy/2 Gy fractions) is an option. Otherwise, second line cisplatin-based chemotherapy is the choice (72-75). Second-line chemotherapy is similar for seminoma and non-seminoma.

9.2.4 Patients with residual disease after 2nd line chemotherapy

These patients should be discussed within the SWENOTECA network. Therapy should be individualized based on tumour size, location and findings of PET imaging. Surgery, radiotherapy as well as third line chemotherapy could be considered as part of the treatment strategy.

9.2.5 Surgery at late relapse

Late relapses, defined as disease recurrence more than 2 years after successful initial treatment, are considerably less common in seminomas as compared to non-seminomas (69). The retroperitoneal space is the predominant site of relapse (65, 76, 77). Treatment has to be individualised, based on tumour size, findings on PET imaging and location.

In late relapses with poor response to chemotherapy surgical resection should be an important part of the treatment strategy. In such cases surgery increase the chance of cure (76-81).

9.2.6 Surgical techniques

RPLND is rarely used in seminoma and the indications are post chemotherapy residual masses with transverse diameter > 3 cm and a positive PET scan (PC-RPLND), late relapses and only in selected cases as desperation surgery. A PC-RPLND may be performed irrespective of tumour marker levels (i.e. hCG (PLAP)).

Historically, a complete RPLND after chemotherapy in seminoma patients has been associated with a high morbidity and even mortality (63, 82). Seminoma occurs in an older patient population compared to non-seminoma, which increases the complication risk. Recent studies, though, has reported a lower and acceptable morbidity rate because of a better patient selection and definition of the surgery (53, 63, 64, 67).

Two types of residual masses after chemotherapy have been described and should be identified before surgery (54, 63, 64, 67, 69). One is the resectable well-defined residual mass, which respects the surrounding structures and has been reported to have a higher incidence of viable cancer and lower complication rate. The other is the poorly defined “plaque” surrounding the great vessels and resembling retroperitoneal fibrosis. Since these patients have mostly negative pathological findings and a high risk of additional intraoperative procedures (including complex vascular reconstruction), they should not be candidates for surgery. In cases of non-resectable tumours, the options are radiation or chemotherapy if needle biopsies are positive. Observation is recommended if biopsies are negative.

It is recommended to make a complete resection of well-defined masses (i.e. lumpectomy) when feasible, in combination with random open biopsies to assure a complete evaluation of the retroperitoneum (53, 63, 64). Biopsies alone are not adequate to identify residual disease (83). The templates described in PC-RPLND for non-seminoma (SWENOTECA VIII) is not used for seminoma and these patients are not included in the prospective population-based study RETROP.

Extra-retroperitoneal resections in for example mediastinal seminoma should be decided on an individual basis (84).

A multidisciplinary approach is mandatory and the surgical procedure should be carried out at centres with adequate competence and experience with testicular cancer treatment.

Not Valid

10 Extragonadal seminoma

10.1 Background

Extragonadal germ cell cancers (EGCC) constitutes 5 % of all germ cell cancers (85). The histology is similar to testicular cancers and the disease occurs outside the testicles, often in midline structures from the pituitary to the sacrum and is now looked upon as a separate entity (86). It is likely that EGCC arises in primordial germ cells that have not completed the migration from the yolk sac via the hindgut to the gonadal fold during foetal organogenesis. This mirrors the typical location in the pineal body, mediastinum, retroperitoneum, bladder, sacrum, vagina and prostate. The most common localization is in the mediastinum and EGCC accounts for about 15 % of all tumours in the anterior mediastinum and 24% in children (87).

In distinction from testicular cancers, EGCC generally present with a larger tumour burden, a larger proportion are non-seminomas, and there is an association with Klinefelters syndrome, Down's syndrome and Li-Fraumenis syndrome. Mediastinal EGCC is also associated with malignant blood diseases.

Seminomas account for 16-24 % of all EGCC. They are most often localised in the mediastinum or retroperitoneum with similar distribution. The mean age of patients is 33 and 41 years for mediastinal and retroperitoneal seminoma, respectively. 40 % of patients with EGCC present with metastatic disease. According to the IGCCC criteria, no seminomas belong to the poor prognosis group.

Not Valid

10.2 Classification

The histopathological classification of seminomas is in common with testicular cancers. (87-89).

Prognostic risk group classification follows the IGCCC criteria.

10.3 Diagnostics

See Flow sheet in **appendix III**. The flow sheet is valid for both seminoma and nonseminoma.

Most patients are diagnosed due to symptoms from growing tumour masses in the mediastinum or retroperitoneum. The distinction between a primary testicular tumour and EGCC may have implications both for the treatment and prognosis, and the diagnostic staging should be thorough to reveal possible pathology in the testis. Both testicles should be assessed with ultrasound scanning to reveal possible pathology. In addition to an evident primary tumour in the testicles, a pathological ultrasound result may be sign of a burnt out tumour. Bilateral biopsy is recommended in all patients, both due to the possibility of an undetected primary tumour, and CIS which may result in the later risk of metachronous testicular cancer, which has been reported to occur in about 10% after treatment for EGCC

(90, 91). Many EGCC tumours earlier diagnosed, in particular retroperitoneal EGCC, may in fact have originated from a primary testicular cancer, in part explaining the better prognosis of retroperitoneal EGCC (92, 93). If there is clinical suspicion of Klinefelter syndrome in patients with mediastinal tumours, a chromosomal analysis may be considered.

10.4 Treatment

Patients with good prognosis should be treated with 3 courses of BEP-regimen or 4 courses according to the EP regimen. Patients belonging to the intermediate prognosis risk group should be treated with 4 courses of BEP. Radiotherapy is associated with a relatively high rate of recurrence and is not recommended as primary treatment (94). However, radiotherapy can be a good option in special situations with chemotherapy resistant disease or postoperatively.

Residual tumour < 3 cm in diameter after chemotherapy usually only consists of necrotic or fibrotic tissue that can be difficult to remove surgically (65). Positron emission tomography (PET) may help identifying viable tumour that may be treated with radiotherapy up to 40 Gy (95). In a meta-analysis, 50 % of the patients with seminoma EGCC underwent secondary surgery and only 8 % had viable tumours. Only patients in partial remission after chemotherapy were operated.

Apart from the above-mentioned treatment recommendations, treatment failures or recurrences follow the same principles as for testicular seminomas.

10.5 Follow-up

Follow-up is similar to that of testicular seminoma.

10.6 Prognosis

Primary mediastinal or retroperitoneal seminomas have the same good prognosis as primary testicular seminoma stage II and III with a 5-year survival of 88 % in a meta-analysis of 104 patients (96).

11 Treatment of Relapse

If feasible, morphological verification should be performed.

Treatment depends on site of relapse and previous treatment.

The SWENOTECA IX Follow-up form must be filled in, and sent to the regional testicular cancer registry immediately if a relapse is detected.

It is very important to detect any deviation from the postulated relapse rates and patterns as early as possible, in order to adjust the treatment and/or follow-up program, if indicated.

11.1 Relapse after Surveillance or Adjuvant Carboplatin

Relapse after initial clinical stage I, should be treated as initial metastatic disease, according to prognostic group. See chapter 8-9.

If contraindications to chemotherapy and small tumour volume (2–5 cm) in abdominal lymph nodal relapse, treatment with radiotherapy to para-aortic and ipsilateral iliac nodes 2 Gy x 15, with the addition of a boost of 2 Gy x 3 to 6 Gy to GTV might be an option.

Radiotherapy might also be an option in selected cases with small nodal relapse in other locations when chemotherapy is contraindicated.

11.2 Relapse after Radiotherapy

Relapse after initial clinical stage I or stage II treated with radiotherapy, should be treated as initial metastatic disease, according to prognostic group. See chapter 8-9.

11.3 Relapse or Progression after Standard Combination Chemotherapy

A recent publication from the International Prognostic Factors Study Group, using data from 1984 relapsing patients, identified prognostic variables in patients relapsing after conventional dose chemotherapy (97). Patients from the SWENOTECA group were included into this analysis. These variables form the IGCCCG-2 score which can help classify patients into prognostic categories with regard to PFS and OS (Table 1). Patients in the very low risk (only seminoma) or low risk prognostic groups category have a 2-year PFS > 50 %, and 3-year OS of >65 %. The intermediate-, high- and very high-risk prognostic groups have 2-year PFS of 40 %, 26 % and 6 %, respectively, and 3-year OS of 58 %, 27 % and 6 %, respectively. A retrospective study, from the same group, looking at the outcome of salvage treatment in 1594 patients has recently been published (98). The analysis indicated that high dose carboplatin based salvage treatment might benefit patients with regard to both PFS and OS. The benefit in OS was seen in the intermediate-, high- and very high-risk prognostic groups.

Not Valid

Table 1. Prognostic score for patients with relapsing vital germ-cell tumours

Parameter	Score Points				
	-1	0	1	2	3
Primary site		Gonadal	Extragonadal		Mediastinal NSGCT
Prior response		CR/PRm-	PRm+/SD	PD	
PFI, months		> 3	≤ 3		
AFP salvage		Normal	≤ 1000	> 1000	
hCG salvage (at relapse)		≤ 1000	> 1000		
LBB*		No	Yes		
Primary histology	Pure SGCT	Non SGCT			

Regroup score sum into categories: (-1) = very low-risk; (0-1) = low-risk; (2) = intermediate-risk; (3-4) = high-risk; (5) = very high-risk. *LBB = liver, bone or brain metastases

11.4 Conventional Dose Salvage Chemotherapy

The currently favoured salvage regimen is paclitaxel-based standard-dose chemotherapy (TIP). In patients with favourable prognostic features about 70% of patients can be cured by this regimen (72).

Several other regimens have curable potential in relapsing germ cell cancer. These include regimens contain platinum/etoposide/ifosfamide(99), gemcitabine/oxaliplatin (100-102), gemcitabine/paclitaxel(103), gemcitabine/oxaliplatin/paclitaxel(104, 105), oxaliplatin/irinotecan(106) and gemcitabine/cisplatin/paclitaxel(107).

11.5 HDCT Salvage Treatment

High-dose chemotherapy (HDCT) has been increasingly used as salvage treatment for patients with relapse after primary cisplatin-based chemotherapy. Several phase I/II studies and retrospective studies have evaluated the effect of HDCT in patients with relapse and/or cisplatin-refractory disease. There is considerable variation in study design, dose intensity and patient selection, and thus outcome; the reported failure-free survival range from 12% to 63%. Einhorn et al. have published the largest retrospective series, including 184 patients

treated with salvage tandem HDCT (carboplatin and etoposide) from 1996 to 2004 (108). Resection of residual masses was performed whenever technically feasible. After a median follow-up of 48 months, 63% were continuously disease-free. This is a higher proportion than previously reported in phase II studies, and may in part be explained by the exclusion of patients with primary mediastinal tumours or those with late relapse. In addition, 45% of patients refractory to cisplatin remained disease-free, confirming that HDCT can overcome cisplatin resistance in a considerable number of patients.

11.6 Treatment of Relapse

See flow sheet in **appendix II**.

All patients relapsing after initial chemotherapy for metastatic disease should immediately be referred to a centre experienced in treating metastatic germ cell tumours.

If a pathological level of β -hCG or PLAP is detected without evident metastasis on CT thorax/abdomen/pelvis, additional MRI imaging of the brain and spine should be performed. Ultrasound of the contralateral testicle should also be performed.

Repeated tumour markers should be performed to exclude false positives.

If pathological levels of the specific markers hCG-beta (but not LDH) and PLAP are confirmed, with or without clinical or radiological evidence of metastases, salvage chemotherapy should be instituted as soon as possible.

Biopsy of any evident metastatic tumour lesion is advisable, but not mandatory if there is clear and persistent serum tumour marker elevation.

11.7 Salvage Treatment Metastatic Disease

SWENOTECA uses the IGCCCG-2 score, treatment with salvage chemotherapy is determined by prognostic group and earlier treatment. Details are presented in **appendix II**. Patients with a favourable prognostic score will most likely be cured by conventional dose taxane-based regimen (TIP). However, in selected cases with small volume nodal relapses radiotherapy might be an option.

Patients with intermediate prognostic score or worse have a 2-year PFS of 40 % and hence, high-dose chemotherapy is recommended as primary salvage chemotherapy.

If there are indications of metastatic disease on imaging without elevation of serum β -hCG or PLAP, a surgery/biopsy should be performed to obtain histological verification. If a suspected lesion is relatively stable and PET is negative the lesion may be closely observed.

Further information on high-dose treatment and treatment of brain metastasis can be found in the SWENOTECA VIII protocol.

11.8 Post-Chemotherapy Surgery or Radiotherapy

In contrast to patients with non-seminoma, post-chemotherapy surgery of remaining lesions are not mandatory in seminoma. Consolidating treatment after chemotherapy in the form of surgery or radiotherapy should not be used unless remaining lesions are biopsy verified to contain vital cancer. Even PET positive lesions should be biopsied as PET can be false positive. In patients with advanced seminoma surgery after chemotherapy may be technically challenging (see chapter on surgery), but if feasible surgery should be chosen over consolidating radiotherapy.

Not Valid

12 Radiotherapy Details

The dose prescription, recording and reporting should be done according to ICRU rapport 50 and the supplementary ICRU rapports 62 and 83 (109-111).

Dose:

CSI:

Regimen 1: 1.8 Gy x 14, to a total dose of 25.2 Gy, 5 days weekly, to the para-aortic lymph nodes and the ipsilateral common iliac- and the external iliac lymph nodes.

Regimen 2: 2 Gy x 10, to a total dose of 20 Gy, 5 days weekly, to the para-aortic lymph nodes

Note: If T4 tumour or previous inguinal or scrotal surgery, the para-aortic, the ipsilateral common and external iliac and the ipsilateral inguinal lymph nodes should be treated.

CSII A: 2 Gy x 15, 5 days weekly to total dose of 30 Gy to the para-aortic and the ipsilateral common iliac- and the external iliac lymph nodes.

CSII B: 2 Gy x 15 according to CS IIA with an additional boost to enlarged lymph nodes of 2 Gy x 3 to 6 Gy.

Patient position and fixation:

The patient is placed in the supine position, fixated according to local practice for reproducible positioning of the patient during the whole treatment process. Mark the orchiectomy scar with a pewter thread. For patients in reproductive age a lead shield should be used to protect the contra lateral testis from external scattered radiation and the penis should be moved out of the treatment fields.

Radiotherapy treatment technique:

A CT-based 3-dimensional (3D) planned radiotherapy is mandatory. The standard treatment is two opposed anteroposterior-posteroanterior, AP-PA, fields. The use of intensity modulated radiotherapy, IMRT, reduces the delivered dose to active bone marrow but increases the mean dose and the dose delivered to 50% of the volume for the kidneys, liver and bowel compared to two AP-PA fields (112) which may increase the risk of secondary malignancy (113, 114) and is therefore not considered the standard approach.

The CT based plan of the fields is generated based on vascular anatomy as the lymph nodes follow the vessels (aorta, vena cava inferior, ipsilateral renal vein, the common iliac and external iliac vessels). A prospective cohort study performed by the German Testicular Cancer Study Group showed no pelvic relapses with a modified inferior border of the iliac fields to the top of the acetabulum, which now is recommended by the EGCCCG and SWENOTECA (35, 115). The upper border of the treatment volume is the top of the 12th thoracic vertebra (116).

Beam quality:

The 3D conformal RT should be delivered with a minimum of 10 MV photon quality.

Target volumes and organs-at-risk (OAR) volumes:

GTV (Gross tumour volume) should be defined as the volume of any lymph node enlarged due to metastasis (i.e., CS IIA).

Not Valid

CTV (Clinical target volume)

The CTV in the para-aortic region should include the para-aortic lymph nodes from the upper border of the 12th thoracic vertebra to the aortic division and is defined as the combined inferior vena cava and aorta volume including visible lymph nodes and any GTV with an additional symmetrical margin of 1.4 cm. Similarly for the renal vein volume except for no expansion laterally.

If the ipsilateral common iliac- and the external iliac lymph nodes are to be treated, the CTV should be extended to include the combined volume of the common iliac and external iliac vessels to the level of the top of the acetabulum, including visible lymph nodes and any GTV, with an additional margin of 1.4 cm in all directions.

In case of previous inguinal or scrotal surgery or in the rare event of a T4 tumour, the CTV should include both the ipsilateral common iliac- and the external iliac lymph nodes and the ipsilateral inguinal lymph nodes with additional margins as described in the former passage. The CTV should be trimmed to avoid bone, bowel, muscle and bladder.

ITV (internal target volume) should be identical to the CTV as organ movement can be neglected.

PTV (planning target volume) is defined according to the ICRU definition.

Organs at risk:

The volumes of both kidneys should be outlined in each CT image. No more than 25% of each kidney volume should receive more than 20 Gy.

Not Valid

13 Late effects of treatment

13.1 Long-term complications and follow-up after treatment for testicular cancer

Some side effects from testicular cancer treatment may emerge several years after treatment. Thus, regular controls at the general practitioner are recommended after the oncological follow-up has been completed. At the last oncological follow-up, all patients should receive a patient care plan that summarizes the previous treatment, the most important long-term complications and recommendations for further follow-up at the caring physician, **appendix XXI-XXIII**. In this section we will describe possible late complications after treatment for testicular cancer, with emphasis on complications that can be prevented or treated.

13.2 Cardiovascular disease (CVD)

Mortality from CVD is higher in testicular cancer survivors (TCSs) than in the general population(117, 118). Men treated with orchiectomy alone do not have an increased risk for CVD in comparison to the general population(119, 120). Thus, the risk for CVD is associated with cytotoxic treatment and not testicular cancer itself. Men previously treated with cisplatin-based chemotherapy have a 2-3 fold risk for CVD in comparison to men treated with surgery only or the general population in several studies. Two large studies indicate that the risk for CVD is increased also after infradiaphragmatic irradiation, but other results are conflicting(117, 121). The absolute risk for CVD several years after cytotoxic treatment is 6-10 %(120, 121). Combination of both chemotherapy and radiotherapy is particularly harmful, with an absolute risk for CVD at 20% several years after treatment(120). Cisplatin-based chemotherapy is associated with an increased prevalence of hypertension and the metabolic syndrome, while radiotherapy is associated with an increased prevalence of diabetes(120, 122, 123). Accordingly, the increased risk for CVD is at least partly mediated by classical cardiovascular risk factors.

Endothelial and inflammatory markers, e.g. fibrinogen and von Willebrand factor, are increased in men treated with cisplatin-based chemotherapy, while high-sensitivity C-reactive protein (hs-CRP) is increased several years after treatment with radiotherapy(120, 124, 125). These findings indicate that endothelial dysfunction might be a possible link between cytotoxic treatment and atherosclerosis. Screening for cardiovascular risk factors such as hypertension, obesity, diabetes, unfavorable lipids, smoking, physical inactivity and an unhealthy diet is important among TCSs for the prevention of CVD(126).

13.3 Subfertility and hypogonadism

Subfertility is common among men diagnosed with testicular cancer(127). Additionally, cytotoxic treatment may negatively affect both the fertility and the levels of sex hormones(128). Results from a large Norwegian follow-up study among TCSs have shown that fertility decreases with increasing treatment intensity(129). Still, nearly half of the males treated with large cumulative cisplatin doses had become fathers after testicular cancer treatment without using cryopreserved semen.

Retrograde ejaculation has been a rather frequent complication after RPLND, but the incidence has been reduced after the introduction of nerve-sparing surgery techniques(130). For men who desire to achieve fatherhood, treatment with α -sympathomimetics (Rinexin® or Tofranil® imipranin, unregistered]) should be considered as these substances may reverse the retrograde ejaculation.

Up to 20 % of TCSs are diagnosed with endocrine hypogonadism/testosterone deficiency (testosterone <8 nmol/l and/or LH >12 U/l)(131). Decreased libido, erectile dysfunction and loss of energy are common symptoms of endocrine hypogonadism, but these symptoms may also occur without accompanying testosterone deficiency. Endocrine hypogonadism is associated with hypertension, obesity, the metabolic syndrome and diabetes(132, 133) and probably also with increased mortality rates(134, 135). Thus, men with severe endocrine hypogonadism should be considered for testosterone substitution even if they lack clinical symptoms. If low levels of serum testosterone are detected, a new venipuncture should be performed in the morning to confirm the diagnosis(136). Men with considerable clinical symptoms (decreased libido, erectile dysfunction, loss of energy) but with testosterone levels within the normal range, may benefit from testosterone substitution, but there are so far no data available supporting this treatment strategy. After bilateral orchiectomy and with established testosterone deficiency after treatment for CIS, lifelong testosterone substitution is warranted.

13.4 Other long-term complications

A considerable number of TCSs suffer from other long-term complications (nephrotoxicity, neurotoxicity, ototoxicity, pulmonary toxicity and psychosocial problems)(137-139). Both treatment with large cisplatin doses (>850 mg) and smoking increase the risk for long-term ototoxicity, neurotoxicity and pulmonary toxicity. Men with treatment-induced ototoxicity (tinnitus, hearing impairment) should avoid noisy environments(140).

There is an increased risk for second malignant neoplasms after cytotoxic treatment for testicular cancer(141). After chemotherapy or radiotherapy, the relative risk of a solid second cancer is approximately doubled, while combination of both techniques is associated with a three-fold increased risk. These second cancers are often diagnosed many years after treatment. Accordingly, all doctors involved in long-term follow-up of TCSs should timely initiate necessary examinations in the case of symptomatic patients.

13.5 Controls at the general practitioner

We recommend regular examinations at the general practitioner every 2-3 years after completion of oncological follow-up, and more often in the case of pathological findings. The purpose of these controls is to prevent, identify and possibly treat risk factors that may lead to complications, e.g. cardiovascular disease. These controls should include:

- Anamnesis regarding cardiovascular risk profile and symptoms of cardiovascular disease
- Advice about lifestyle-factors such as smoking cessation, healthy diet and physical activity
- Measurement of blood pressure, height/weight (BMI) and waist circumference

- Blood samples: Fasting lipid profile (total cholesterol, HDL-and LDL cholesterol, triglycerides), glucose, testosterone and LH
- The prophylaxis (primary and secondary) of cardiovascular disease should be according to the general population recommendations
- Consider testosterone substitution in case of endocrine hypogonadism, possibly in cooperation with endocrinologist

Not Valid

14 Patient Information

The written information (see **appendix XLI**) regarding treatment options in clinical stage I must be given to the patient, with adequate time for remaining questions. The patient should always be offered a new consultation within a short time. The patient information also includes those with metastatic disease.

Furthermore, both oral and written information should be given about the registration in the SWENOTECA database.

In Sweden this is done in the Swedish Testicular Cancer Register, which is an official National Quality Register, with SWENOTECA monitoring of the case records.

In Norway the patients are registered at the University hospitals of Oslo, Bergen, Trondheim and Tromsø.

In Norway, the patient must sign the written information.

The patient should be treated and followed according to the same principles if he does not consent to be registered with full name in the database, but in such case an anonymous registration form, with only a registration number and code made by the responsible clinician must be sent to the SWENOTECA secretariat.

Immediately after the informed consent has been given, the SWENOTECA “Registreringsblankett” should be sent to:

In Norway: The respective University hospitals of Oslo, Bergen, Trondheim and Tromsø.

In Sweden: To the Regional Tumour Registry in the region where the patient is nationally registered, see www.cancercentrum.se.

Not Valid

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Not Valid

Appendix

Not Valid

Flow-sheet: Diagnosis, Staging and Treatment

Testicular tumour

Ultrasound both testicles

Physical examination

History of prior testicular disorders and hereditary information

Tumour markers: AFP, β -hCG, LDH (PLAP optional), Hormone levels: Testosterone, LH, FSH, SHBG, Sperm count & cryopreservation. Patients should be offered a testicular prosthesis



Inguinal orchiectomy and biopsy contralateral testicle, see 5.1.7



Seminomatous testicular cancer AFP normal (if slightly elevated and stable values, see protocol)

Risk factors: rete testis invasion, size of tumour > 4 cm



Clinical staging procedure

Tumour markers post-op: β -hCG, AFP, LDH (PLAP)

Hormone levels: Testosterone, LH, FSH, SHBG

Sperm count & cryopreservation, (consider if not done earlier)

CT scan of thorax, abdomen and pelvis



TNM, clinical staging* and IGCCCG-classification



Treatment

Clinical stage I (CS I)

0 risk factor → **surveillance**

1-2 risk factors → **carboplatin x 1 recommended, surveillance is an option**

Adjuvant radiotherapy may in selected patients also be an option, see text.

Clinical stage IIA-IV, good prognosis: 3 courses of BEP-chemotherapy. If contraindications to bleomycin, 4 courses of EP-chemotherapy.

Radiotherapy 2 Gy x 15 to 30 Gy to para-aortic and ipsilateral iliac nodes is an option in CS IIA. If contraindications to chemotherapy in patients with CS IIB, treatment with radiotherapy to para-aortic and ipsilateral iliac nodes 2 Gy x 15 to 30 Gy with a boost of 2 Gy x 3 to 6 Gy to the GTV is an option.

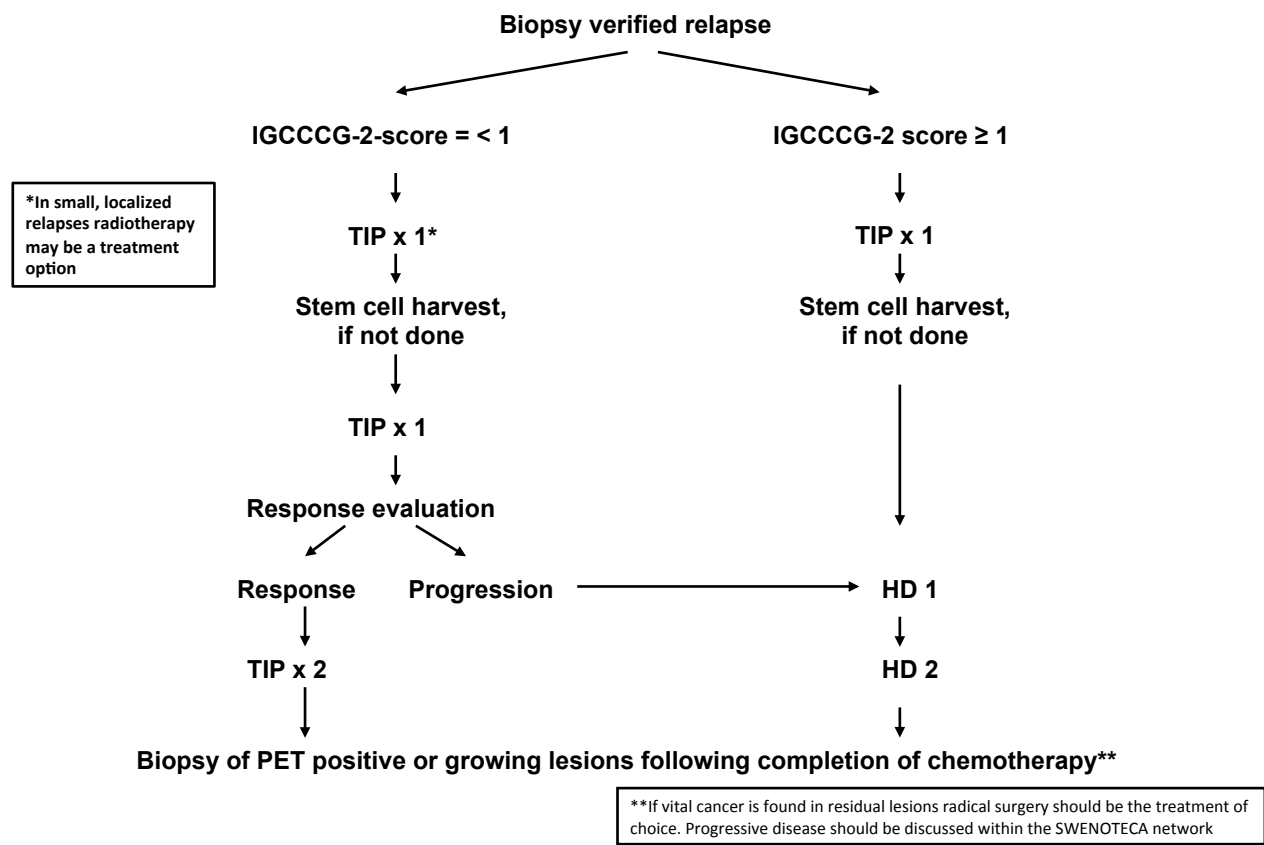
Clinical stage IV, intermediate prognosis: 4 courses of BEP-chemotherapy. If contraindications to bleomycin, 4 courses of PEI-chemotherapy.

Not Valid

If no obvious metastasis and elevated markers, tumour markers to be followed until normalization as long as declining according to half-life, see 5.2.1

* If CS I/Mk negative, restaging after 8 weeks, see 5.2.2

Salvage Treatment Germ Cell Cancers



Not Valid

IGCCCG-2 prognostic score for patients with relapsing vital germ-cell tumours

Parameter	Score Points				
	-1	0	1	2	3
Primary site		Gonadal	Extragonadal		Mediastinal NSGCT
Prior response		CR/PRm-	PRm+/SD	PD	
PFI, months		> 3	≤ 3		
AFP salvage		Normal	≤ 1000	> 1000	
hCG salvage (at relapse)		≤ 1000	> 1000		
LBB*		No	Yes		
Primary histology	Pure SGCT	Non SGCT			

Regroup score sum into categories: -1 = very low-risk; 0 = low-risk; (1-2) = intermediate- risk: (3-4) = high-risk; (5-) = very high-risk *LBB=Liver, bone or brain metastases

Extragenadal Tumours in the Mediastinum and Retroperitoneum Staging and Treatment Principles

Extratesticular tumour

Ultrasound both testicles
CT scan of thorax, abdomen and pelvis.
Additional imaging according to protocol
Physical examination
History of prior testicular disorders
Tumour markers: AFP, β -hCG, LDH (PLAP optional)
Hormone levels: Testosterone, LH, FSH, SHBG
Offer sperm count & cryopreservation

Ultrasound findings:

Normal, uni- or bilateral irregular
parenchyma, microlithiasis or atrophy

Tumour

Biopsy both testis. For the treatment of
CIS see addendum.

Flow sheet for testicular cancer

Biopsy of the extragonadal tumour should be
performed if no testicular tumour is found.
Treatment can start without histological
confirmation in case of markedly increased
tumour markers in a critically ill patient.

Not Valid

Diagnosis of Extragonadal Germ Cell Cancer (EGCC)

Marker negative disease and
teratoma only in biopsies

Marker positive disease or vital germ cell cancer
in biopsies, or at non-radical surgery

Surgery

Chemotherapy

Surgery radical
and vital germ
cell cancer

Surgery nonradical
and teratoma only

Surgery nonradical
and vital germ cell
cancer

Prognostic group classification should
be performed immediately prior to
chemotherapy

BEP x 2

Additional surgery
if possible

Treat according to histology and
prognostic group. Mediastinal
nonseminoma to be treated as poor
prognosis with non-visceral metastases

Prognostic risk group classification according to IGCCCG**GOOD-PROGNOSIS GROUP**

Any primary site

and

No non-pulmonary visceral metastases (for example liver, bone, brain)

andany β -hCG, any LDH, normal AFP**INTERMEDIATE-PROGNOSIS GROUP**

Any primary site

and

Non-pulmonary visceral metastases

andany β -hCG, any LDH, normal AFP**POOR-PROGNOSIS GROUP**

No seminoma with poor prognosis

Clinical staging according to Royal Marsden, modified

CS I	No evidence of metastases
CS Mk+	Tumour markers AFP/ β -hCG persistently elevated (not declining according to half-life), but no macroscopic metastatic disease demonstrated
CS II	Metastatic disease restricted to abdominal nodes: A Maximal transverse diameter <2 cm B Maximal transverse diameter 2–5 cm C Maximal transverse diameter >5–10 cm D Maximal transverse diameter >10 cm
CS III	Supradiaphragmatic node involvement For abdominal lymph-nodes: 0 No metastases; A-D According to CS II.
CS IV	Extra-lymphatic metastases For abdominal lymph-nodes: 0 No metastases; A-D According to CS II. H+ Liver metastases, Br+ Brain metastases, Bo+ Bone metastases

Uppföljningsschema för seminom-patienter

Namn: _____ Person-nr: _____
 Orchidectomidatum: _____ sida: hö / vä tumörstorlek: _____ inväxt i rete testis: ja / nej
 Datum definitiv stadiindelning: _____ Stadium/prognosgrupp: _____ Datum färdigbehandlad: _____

Detta är ett minimiuppföljningsschema.

Övriga undersökningar beroende på primära metastaslokaler, eventuella resttumörer.

Individuellt kontrollintervall beroende på eventuell förekomst av resttumörer och grad av recidivrisk!

Kontroll typ **Tm**: Tumörmarkörer, AFP, β -HCG och LDH, (PLAP valfritt). (Sätt upp patienten för telefonsamtal på mottagn lista)
 Kontroll typ **A**: Klinisk undersökning, AFP, β -HCG och LDH, (PLAP valfritt).
 Kontroll typ **B**: Klinisk undersökning, AFP, β -HCG, LDH, (PLAP valfritt), kreatinin, samt **MRT-retroperitoneum** (CT buk-bäcken).
 Kontroll typ **C**: Som B med tillägg av rtg pulm, testosteron, SHBG, LH, FSH.
 Kontroll typ **D**: Som C med tillägg av ultraljud testis.

Kontroll av BT, blodfetter, fasteblodsocker samt livskvalitetsenkät vid 1, 5-, och 10-årskontrollen.

	Tm	B	Tm	C	
0	3	6	9	12	Kontroller första året <i>Månader från avslutad behandling</i>
12	15	18	21	24	Kontroller andra året <i>Månader från avslutad behandling</i>
24		A		C	Kontroller tredje året <i>Månader från avslutad behandling</i>
36		A		B	Kontroller fjärde året <i>Månader från avslutad behandling</i>
48				D	Kontroller femte året <i>Månader från avslutad behandling</i>

Patienter i kliniskt stadium I och som behandlats med RT kontrolleras endast i sex år

År 6 och år 8 från avslutad behandling kontrolleras patienten med kontrolltyp A om metastatisk sjukdom, kontrolltyp B om stad I.

År 10 kontrolltyp D samt överlämnande av "Slutkontrollinfo".

Övriga undersökningar på indikation.

Follow-up schedule for seminoma patients

Name: _____ Civic registration number: _____
Orchiectomy, date: _____ side: right / left tumor size: _____ growth in rete testis: yes/no
Date definitive staging: _____ Stage/prognostic group: _____ Date end of treatment: _____

This is a minimum follow-up schedule.

Other investigations depending on site of metastasis, or residual disease.

Individualize check-up intervals with regard to residual tumors and risk of recurrence!

Control type Tm:

Tumor markers, AFP, β -HCG and LDH, (PLAP optional). (List the patient for a telephone appointment)

Control type A:

Clinical examination, AFP, β -HCG and LDH (PLAP optional).

Control type B:

Clinical examination, AFP, β -HCG, LDH, creatinin, (PLAP optional), MRI of the retroperitoneum (abdominopelvic CT).

Control type C:

Like B with addition of Chest X-ray, Tumor markers, SHBG, LH, FSH.

Control type D:

Like C with addition of scrotal ultrasound.

Metabolic screening (lipids, fasting glucose), blood pressure and quality of life questionnaire at 1, 5 and 10-year check-up.

	Tm	B	Tm	C
0	3	6	9	3
	Tm	B	Tm	B
12	15	18	21	24
		A		C
24		30		33
		A		B
36		42		48
			D	
48				60

Patients in Clinical stage I treated with med RT: only checkups for six years, only abdominal imaging at the 2 yr check-up.

Year 6 and 8 from end of treatment: check-up type A if metastatic disease, check-up type B if CS I.

Year 10 from end of treatment: check-up type D and give the patient the patient care plan/ "Slutkontrollinfo".

Other examinations on indication.

BEP**Germ cell cancer**

Preparat	Dos/ dostillfälle mg/m ²	Maxdos/ dostillfälle mg	Antal doser/ dygn	Dos interv. tim	Antal doser/ cykel	Administreringssätt	Dag
1. Bleomycin*	30 000 IE**		1		3	im/iv inf	1, 5, 15
2. Etoposid	100		1		5	iv inf	1–5
3. Cisplatin	20		1		5		

* då patienten erhållit en kumulativ dos bleomycin på 300 000 IE ges regimen utan bleomycin

** totaldos

Prep	1	2	3	4	5	15	22	
1	1					1		
2	2	2	2	2	2			
3	3	3	3	3	3			

Ny cykel
↓

Dag	1	2	3	4	5	15	22	
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Cykellängd: 21 d

Beredning och administrering v g v

Speciella åtgärder

Cisplatin: S-kreatinin inför varje cykelstart. Om patologiskt utföres iohexol-clearance. Cisplatin ges med forcerad diures.

CAVE! aminoglykosid skall ej givas under eller en månad efter cisplatinbehandling.

Bleomycin: om toxisk reaktion vid bleomycinintillförelse (feber, frossa) ges steroider exempelvis Deltison 25 mg po eller 3–4 mg Betapred. Fortsättningsvis ges steroider profylaktiskt före bleomycin.

Dosreduktionsrekommendationer**Benmärgstoxicitet**

Neutrofila × 10 ⁹ /L	TPK × 10 ⁹ /L	Preparat, % av fulldos			Åtgärd
		1	2	3	
> 0,5 och < 1,0	≥ 50	100	100	100	Ge behandling. G-CSF enligt lokala riktlinjer. OBS! – om TPK cirka 50 skall nadir ha passerats!
< 0,5	≥ 50				Behandling uppskjutes i högst 3 dagar. Behandling kan dock ges följt av G-CSF om situationen så kräver!
	< 50				Behandlingen uppskjutes till TPK ≥ 50.

Nedatt njurfunktion*

Korrigerat iohexolclearance (ml/min/1,73 m²), normalvärde 80–125 för 18–50 år.

50–59	100	100	100	Cisplatin ges endast i 4 dagar
40–49	50	100	100	Cisplatin ges endast i 3 dagar
< 40	0	100	**	Cisplatin ersätts med Karboplatin doserat efter Calverts formel AUC 7**

Korrigerat iohexolclearance (ml/min/1,73 m²), normalvärde 60–110 för 51–65 år.

40–49	50	100	100	Cisplatin ges endast i 4 dagar
< 40	0	100	**	Cisplatin ersätts med Karboplatin doserat efter Calverts formel AUC 7**

* Dock, om nedsatt njurfunktion beror på tumörobstruktion skall fulldos Cisplatin ges. Nefrostomi kan behövas.

** Totaldos Karboplatin, mg = 7 × (okorrigerat clearance ml/min + 25). Karboplatin ges endast dag 1!

Anmärkning

Bleomycin: CAVE! Risk för allvarlig pneumonit föreligger. Var observant på tecken på pneumonit. Ökad risk vid hög ackumulerad totaldos, nedsatt njurfunktion, äldre patienter, hög O₂-koncentration i inandningsluft, tidigare eller samtidig strålbehandling mot thorax.

BEP

Blandning och administrering

Preparat	Blandas i ml	Administrering sätt	Administrering tid	Sköljdropp NaCl, ml	Spoldropp NaCl, ml	Kemiskt stabil	Kommentar
Cisplatin	1000 NaCl	iv inf	2 tim	250			72 tim rumstemp
Etoposid							
Bleomycin	250 NaCl	iv inf	30 min				7 dygn, kallt

Prehydrering:
1 000 NaCl under 2 tim

Hydrering under behandlingen:
Under behandlingsdygnen gives ytterligare minst 2 000 ml vätska po el iv.

Posthydrering:
Dygnet efter sista cisplatininfusion minst 2 000 ml; om patienten ej själv kan dricka denna mängd, skall vätska givas iv.

Diuresen under behandlingsdygnet samt dygnet efter sista cisplatinbehandlingen skall vara > 400 ml/4 tim. Mätning startar samtidigt med start av prehydrering.

EP

Germ cell cancer

Preparat	Dos/ dostillfälle mg/m ²	Maxdos/ dostillfälle mg	Antal doser/ dygn	Dos interv. tim	Antal doser/ cykel	Administreringssätt	Dag
1. Etoposid	100		1		5	} iv inf 2 tim	1–5
2. Cisplatin	20		1		5		

Prep	1	2	3	4	5		
1	1	1	1	1	1		
2	2	2	2	2	2		

Dag	1	2	3	4	5	...	22

Ny cykel
↓

Cykellängd: 21 d

Beredning och administrering v g v

Speciella åtgärder

Cisplatin: S-kreatinin inför varje cykelstart. Om patologiskt utföres iohexol-clearance. Cisplatin ges med forcerad diures.

CAVE! aminoglykosid skall ej givas under eller en månad efter cisplatinbehandling.

Dosreduktionsempfehlungen

Benmärgstoxicitet

Neutrofila $\times 10^9/L$	TPK $10^9/L$	Preparat, 1	Preparat, 2	Åtgärder
$> 0,5$ och $< 1,0$	≥ 50	100	100	Ge behandling. G-CSF enligt lokala riktlinjer. OBS! – om TPK cirka 50 skall nadir ha passerats!
$< 0,5$	≥ 50			Behandling uppskjutes i högst 3 dagar. Behandling kan dock ges följt av G-CSF om situationen så kräver!
	< 50			Behandlingen uppskjutes till TPK ≥ 50 .

Nedatt njurfunktion*

Korrigerat iohexolclearance (ml/min/1,73 m²), normalvärde 80–125 för 18–50 år.

50–59	100	100	Cisplatin ges endast i 4 dagar
40–49	100	100	Cisplatin ges endast i 3 dagar
< 40	100	**	Cisplatin ersätts med Karboplatin doserat efter Calverts formel AUC 7**

Korrigerat iohexolclearance (ml/min/ 1,73 m²), normalvärde 60–110 för 51–65 år.

40–49	100	100	Cisplatin ges endast i 4 dagar
< 40	100	**	Cisplatin ersätts med Karboplatin doserat efter Calverts formel AUC 7**

*** Dock, om nedsatt njurfunktion beror på tumörobstruktion skall fulldos Cisplatin ges. Nefrostomi kan behövas.**

** Totaldos Karboplatin, mg = 7 x (okorrigerat clearance ml/min + 25). Karboplatin gives endast dag 1!

Anmärkning

EP

Blandning och administrering

Preparat	Blandas i ml	Administrering sätt	Sköljdropp NaCl, ml	Spoldropp NaCl, ml	Kemiskt stabil	Kommentar
250						
Cisplatin	1000 NaCl	iv inf	2 tim		72 tim rumstemp	
Etoposid						

Prehydrering:
1000 NaCl under 2 tim

Not Valid

Hydrering under behandlingen:
Under behandlingsdygnet ges ytterligare minst 2 000 ml vätska po el iv.

Posthydrering:
Dygnet efter sista cisplatininfusion minst 2 000 ml; om patienten ej själv kan dricka denna mängd, skall vätska givas iv.

Diuresen under behandlingsdygnet samt dygnet efter sista cisplatinbehandlingen skall vara > 400 ml/4 tim. Mätning startar samtidigt med start av prehydrering.

Karboplatin

Seminom, adjuvant behandling

Preparat	Dos/ dostillfälle mg/m ²	Maxdos/ dostillfälle mg	Antal doser/ dygn	Dos interv. tim	Antal doser/ cykel	Administreringssätt	Dag
1. Karboplatin	7×(GFR+25)*		1		1	iv inf 30 min	1

*totaldos

Calverts formel: Dos = AUC x (GFR + 25)

AUC = 7 mg/ml × min

GFR = ml/min, okorrigerat värde

Dos = mg, totaldos

Prep		
1	1	
		Ny cykel
		↓
Dag	1	22

Cykellängd: 21 d

Beredning och administrering v g v

Speciella årgårde

Iohexolclearnens hastighet vid GFR-före behandlingsstart. S-kreatinin före varje cykel.
 Om s-kreatinin stiger $\geq 20\%$ ges iohexolclearnens.

Dosreduktionsrekommendationer

Granulocyter $\times 10^9/L$ TPK $\times 10^9/L$

Vid cykelstart:

 <1.0 ≤ 100

Preparat, % av fulldos

1

Behandlingen oppskjutes

Anmärkning

Karboplatin seminom

Blandning och administrering

Preparat	Blandas i ml	Administrering		Sköljdropp NaCl, ml	Spoldropp NaCl, ml	Kemiskt stabil	Kommentar
		sätt	tid				
Karboplatin	250 5% glukos	iv inf	30 min	250		72 tim, kallt	

Not Valid

TIP

Germ cell cancer

Preparat	Dos/ dostillfälle mg/m ²	Maxdos/ dostillfälle mg	Antal doser/ dygn	Dos interv. tim	Antal doser/ cykel	Administreringssätt	Dag
1. Paclitaxel	250		1		1	iv inf 24 tim	1
2. Ifosfamid	1500		1		4	iv inf 2 tim	2–5
3. Mesna	300		1		4		
Mesna*	300		2		8	iv inj tim 4 och 8 efter avslutad ifosfamidinf	
4. Cisplatin	25		1		4	iv inf 2 tim	2–5

* **Mesna:** Kan även ges peroralt men då i **dubbel** dos (40 % av ifosfamiddosen). Första dosen gives iv tillsammans med ifosfamid, de följande perorala doserna 2 och 6 tim efter avslutad ifosfamidinf.

Prep

1	1
2	2 2 2 2
3	3 3 3 3
4	4 4 4 4

Ny cykel

↓

22

Dag

1

2

3

4

5

Cykellängd: 21 d

Beredning och administrering v g v

Speciella åtgärder

Paclitaxel premedicinering: 30 min före start av infusion gives inj. Betametason 12 mg iv, inj. Clemastin 2 mg iv, inj Ranitidin 50 mg iv.

Kontroll av puls och blodtryck före och 15 min efter start av infusion.

Akutbricka + PM för åtgärder vid akuta allergiska reaktioner skall vara tillgängliga. Läkare skall finnas nära på personsökare. Se även "Handläggning av lindrig reaktion vid Taxol infusion".

Cisplatin: S-kreatinin inför varje cyklastart. Om patologiskt uppföres överskallig. Cisplatin ges med forcerad diures.

CAVE! amino sykosis skal gives i de første måneder efter cisplatinbehandling.

G-CSF: 5 $\mu\text{g}/\text{kg}$ gives high occlusion day 7

Ifosfamid: Observerans på cystitbesvär. Hematuristicka vid behov. Om 3+ så avbryts ifosfamidbehandlingen.

Dosreduktionsrekommendationer

Benmärgstoxicitet

Neutrofila × 10 ⁹ /L	TPK × 10 ⁹ /L	Preparat, % av fulldos			Åtgärd
		1	2+3	4	
≥ 0,5	≥ 50	100	100	100	OBS! – om TPK cirka 50 skall nadir ha passerats!
< 0,5 eller	< 50				Behandling uppskjutes kortast möjliga tid.

Nedatt njurfunktion*

Korrigerat iohexolclearance (ml/min/1,73 m²), normalvärde 80–125 för 18–50 år.

50-59	100	100	80	Dag 2-5
40-49	100	100	80	Dag 2-4
< 40	100	100	**	Cisplatin ersätts med Karboplatin doserat efter Calverts formel AUC 7**

Korrigerat iohexolclearance (ml/min/ 1,73 m²), normalvärde 60–110 för 51–65 år.

40-49	100	100	80	Dag 2-5
< 40	100	100	**	Cisplatin ersätts med Karboplatin doserat efter Calverts formel AUC 7**

* Dock, om nedsatt njurfunktion beror på tumörobstruktion skall fulldos Cisplatin ges. Nefrostomi kan behövas.

**** Totaldos Karboplatin, mg = 7 x (okorrigerat clearance ml/min + 25). Karboplatin gives endast dag 1!**

Anmärkning

TIP – Testikelcancer

Blandning och administrering

Preparat	Blandas i ml	Administrering sätt	Administrering tid	Sköljdropp NaCl, ml	Spoldropp NaCl, ml	Kemiskt stabil	Kommentar
Paclitaxel	1000 NaCl	iv inf	24 tim	250			48 tim, rumstemp
Ifosfamid	1000 NaCl	iv inf	2 tim	250			72 tim, kallt
Mesna 1:a dos							
Mesna följande doser		iv inj/po					
Cisplatin	1000 NaCl	iv inf	2 tim				72 tim, rumstemp

Prehydrering:

1 000 NaCl under 2 tim

Hydrering under behandlingen:

Under behandlingsdygnet ges ytterligare minst 2 000 ml vätska po el iv.

Posthydrering:

Dygnet efter sista cisplatininfusion minst 2 000 ml; om patienten ej själv kan dricka denna mängd, skall vätska givas iv.

Diuresen under behandlingsdygnet samt dygnet efter sista cisplatinbehandlingen skall vara > 400 ml/4 tim. Mätning startar samtidigt med start av prehydrering.

2012 05 07/ES

PEI

Germ cell cancer

Preparat	Dos/ dostillfälle mg/m ²	Maxdos/ dostillfälle mg	Antal doser/ dygn	Dos interv. tim	Antal doser/ cykel	Administreringssätt	Dag
1. Etoposid	100		1		5	iv inf 2 tim	1–5
2. Cisplatin	20		1		5		
3. Ifosfamid	1200		1		5		
4. Mesna	240 (20 % av ifosf dos)		1		5	po* 2 o 6 tim efter ifosfamid	1–5
Mesna	480 (40 % av ifosf dos)		2		10		

*Om patienten inte *säkert* får i sig mesna po (kräks) gives samtliga 3 doser iv.
20 % av ifosfamiddosen gives då timme 4 och 8.

Prep

1	1	1	1	1	1
2	2	2	2	2	2
3	3	3	3	3	3
4	4	4	4	4	4

Ny cykel
↓

Dag 1 2 3 4 5 22

Cykellängd: 21 d
Beredning och administrering v g v

Speciella åtgärder

Cisplatin: S-kreatinin inför varje cykelstart. Om patologiskt utföres iohexol-clearance. Cisplatin gives med forcerad diures.

CAVE! aminoglykosid skall ej givas under eller en månad efter cisplatinbehandling.

Ifosfamid: Observera cystitbesvär. Hematuristicka vid behov. Om 3+ så avsluta ifosfamidbehandling.

Dosreduktion rekommendationer

Benmärgstoxicitet

Neutrofila $\times 10^9/L$ TPK $\times 10^9/L$

Preparat, dos	1	2	3+4	Åtgärd
> 0,5 och < 1,0	≥ 50	100	100	Ge behandling. G-CSF enligt lokala riktlinjer. OBS! – om TPK cirka 50 skall nadir ha passerats!
< 0,5	≥ 50			Behandling uppskjutes i högst 3 dagar. Behandling kan dock ges följt av G-CSF om situationen så kräver!
	< 50			Behandlingen uppskjutes till TPK ≥ 50.

Nedsatt njurfunktion*

Korrigerat iohexolclearance (ml/min/1,73 m²), normalvärde 80–125 för 18–50 år.

50–59	100	100	100	Cisplatin ges endast i 4 dagar
40–49	100	100	100	Cisplatin ges endast i 3 dagar
				Ifosfamid och Mesna ges endast i 4 dagar
< 40	100	**	100	Cisplatin ersätts med Karboplatin doserat efter Calverts formel AUC 7**
				Ifosfamid och Mesna ges endast i 4 dagar

Korrigerat iohexolclearance (ml/min/1,73 m²), normalvärde 60–110 för 51–65 år.

40–49	100	100	100	Cisplatin ges endast i 4 dagar
				Ifosfamid och Mesna ges endast i 4 dagar
< 40	100	**	100	Cisplatin ersätts med Karboplatin doserat efter Calverts formel AUC 7**
				Ifosfamid och Mesna ges endast i 4 dagar

* Dock, om nedsatt njurfunktion beror på tumörobstruktion skall fulldos Cisplatin ges. Nefrostomi kan behövas.

** Totaldos Karboplatin, mg = 7 × (okorrigerat clearance ml/min + 25). Karboplatin gives endast dag 1!

PEI

Blandning och administrering

Preparat	Blandas i ml	Administrering sätt	Administrering tid	Sköljdropp NaCl, ml	Spoldropp NaCl, ml	Kemiskt stabil	Kommentar
Cisplatin	1000 NaCl	iv inf	2 tim	250			72 tim rumstemp
Etoposid							
Ifosfamid	250 NaCl	iv inf	30 min				72 tim, kallt
Mesna 1:a dos							
Mesna dos 2 och 3 gives om möjligt po							

Prehydrering:
1 000 NaCl under 2 tim

Hydrering under behandlingen:

Under behandlingsdygnen gives ytterligare minst 2 000 ml vätska po el iv.

Posthydrering:

Dygnet efter sista cisplatininfusion minst 2 000 ml; om patienten ej själv kan dricka denna mängd, skall vätska givas iv.

Diuresen under behandlingsdygnet samt dygnet efter sista cisplatinbehandlingen skall vara > 400 ml/4 tim. Mätning startar samtidigt med start av prehydrering.

Not Valid

2012 05 07/ES

GOP**Germ cell cancer**

Preparat	Dos/ dostillfälle mg/m ²	Maxdos/ dostillfälle mg	Antal doser/ dygn	Dos interv. tim	Antal doser/ cykel	Administreringssätt	Dag
1. Gemcitabin	800		1		2	iv inf 30 min	1 + 8
2. Oxaliplatin	130		1		1	iv inf 2 tim	1
3. Paclitaxel	80		1		2	iv inf 1 tim	1 + 8

Prep							
1	1	1					
2	2						
3	3	3					

						Ny cykel	
						↓	
Dag	1	8					22

Cykellängd: 21 d
Beredning och administrering v g v

Speciella åtgärder

Oxaliplatin: Vid polyneuropati ges substitution med calcium och magnesium (se omstående sida).

Paclitaxel premedicering: 50 mg före infusion ges iv. Betametason 6 mg iv. Gives endast dag 1 och 8 i cykel 1 om inga oönskade reaktioner inträffat. Lev. Clemastin 2 mg iv inf. Ranitidin 50 mg iv gives samtliga cykler.

Kontroll av puls och blodtryck före och 15 min efter start av infusion dag 1 och 8 cykel 1.

Akutbricka + PM för åtgärder vid akuta allergiska reaktioner skall vara tillgängliga. Läkare skall finnas nåbar på personsökare. Se även "Handläggning av lindrig reaktion vid Taxolinfusion".

Dosreduktionsrekommendationer		Preparat, % av fulldos dag 1			Preparat, % av fulldos dag 8	
Granulocyter × 10⁹/L	TPK × 10⁹/L	1	2	3	1	3
≥ 1,0 och < 1,5	≥ 50 och < 75	100	100	100	75	75
≥ 0,5 och < 1,0	≥ 50	75	75	75	50	50
< 0,5	< 50	Behandlingen uppskjutes.				

G-CSF gives enligt lokala riktlinjer.

Om bestående neuropati WHO grad 2 (svåra parestesier och/eller lätt svaghet), dosreduceras oxaliplatin och paclitaxel till 75 % i följande cykler. Om grad 3–4 toxicitet gives inte denna behandling.

GOP

Blandning och administrering

Preparat	Blandas i ml	Administrering		Sköljdropp NaCl, ml	Spoldropp NaCl, ml	Kemiskt stabil	Kommentar
		sätt	tid				
500 5 % glukos							
Gemcitabin	250 NaCl	iv inf	30 min			72 tim rumstemp	
Oxaliplatin	500 5 % glukos	iv inf	1 tim			48 tim kallt	Inkompatibelt med NaCl
Paclitaxel	250 NaCl	iv inf	1 tim			48 tim rumstemp	Konc < 1,2 mg/ml ej PVC

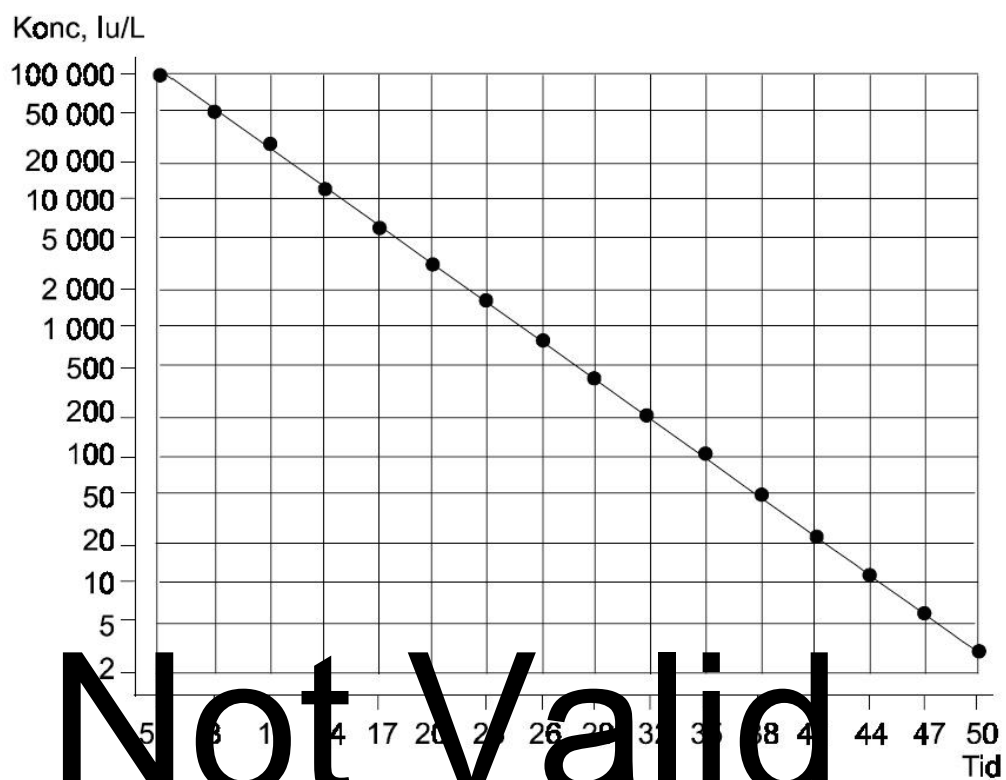
Not Valid

CE högdosregim för germinalcellscancer

Dag: T-7 (T 0: dag för återgivning av stamceller)	Inläggning. Färskt okorrigerat iohexolclearance/ Cr-EDTA-clearance av flerpunktstyp skall finnas tillgängligt! OBS försiktighetsåtgärder vid bedömning av njurfunktion– se nedan!! Om kroppsytta >2.2 måste individuell bed. av patientens konstitution göras. Insättning av Allopurinol 300 mg x1. Provtagning inkluderande tumörmarkörerna AFP och beta-HCG.
T-6	Antiemetikaprofylax Etoposid 560 mg/m² i 4000 ml NaCl 0.9% på 6 timmar (konc max 0.4 mg/ml) Maxdos 1340 mg* Karboplatin 8 x (GFR+25) mg (Obs! totaldos) i 1000 ml glukos 5% på 60 min. Maxdos 1240 mg ** GFR enligt okorrigerat iohexolclearance
T-5	Antiemetikaprofylax Etoposid 560 mg/m² i 4000 ml NaCl 0.9% på 6 timmar (konc max 0.4 mg/ml) Maxdos 1340 mg Karboplatin 8 x (GFR+25) mg (Obs! totaldos) i 1000 ml glukos 5% på 60 min. Maxdos 1240 mg GFR enligt okorrigerat iohexolclearance
T-4	Antiemetikaprofylax Etoposid 560 mg/m² i 4000 ml NaCl 0.9% på 6 timmar (konc max 0.4 mg/ml) Maxdos 1340 mg Karboplatin 8 x (GFR+25) mg (Obs! totaldos) i 1000 ml glukos 5% på 60 min. Maxdos 1240 mg GFR enligt okorrigerat iohexolclearance
T-3	Antiemetikaprofylax Etoposid 560 mg/m² i 4000 ml NaCl 0.9% på 6 timmar (konc max 0.4 mg/ml) Maxdos 1340 mg Karboplatin 8 x (GFR+25) mg (Obs! totaldos) i 1000 ml glukos 5% på 60 min. Maxdos 1240 mg GFR enligt okorrigerat iohexolclearance
T-2	
T-1	Allopurinol utsättes
T 0	Autolog stamcellsåtergivning ca 72 timmar efter avslutad cytostatikainfusion.
T+1	Insättning av G-CSF 5 µg/kg tills neutrofila >1.0 under 3 dygn
OBS angående njurfunktionsbedömning: Om absolut = okorrigerat GFR > 120 mL/min med flerpunkts-iohexolclearance/ Cr-EDTA-clearance, eller pat har avvikande kroppskonstitution (fetma eller ödem): använd även beräkningsverktyg på www.egfr.se, och om bristande överensstämmelse mellan metoderna (iohexolclearance/ Cr-EDTA-clearance, cystatin C- och kreatinin-baserat GFR-estimat) bör man vara extra uppmärksam vid dosering av karboplatin. *Maxdos etoposid beräknat på kroppsytta =2,4 m² **Maxdos karboplatin beräknat på okorrigerat GFR 130 mL/min. Övriga åtgärder: Monitorera patienten noga avseende vätskebalans. Minst 3 L vätska/m²/dygn. Vid behov diuretika! Karboplatin kan även blandas i NaCl 0.9%. Övriga åtgärder enligt egna rutiner. Varning: Aminoglykosid kontraindicerat!	

HCG, plot – halveringstid

β -HCG, halveringstid = 3 dygn



Patient care plan to be delivered to the patient and general practitioner at termination of uro-oncological follow-up

You were operated year _____ for testicular cancer, subtype:

☐ Seminoma ☐ Non-seminoma

☐ No dissemination of disease were confirmed

☐ Dissemination of disease were confirmed to _____

Additional treatment

☐ No

☐ Chemotherapy (number of cycles : _____)

☐ Radiotherapy

☐ Surgery in addition to removal of the testicle _____

Date for last follow-up: _____ Hospital: _____

Responsible doctor: _____ Telephone: _____

You have completed the last oncological follow-up after previous treatment for testicular cancer. The risk for relapse of the disease is very low, and you will be taken care of at your general practitioner in the future. This patient care plan should be shown in case of future contact with the health services.

You are at risk of a new tumor in the remaining testicle and regular self-exams are important. Further, another cancer type may develop after treatment with chemotherapy and/or radiotherapy. Some side-effects from testicular cancer treatment may emerge several years after treatment, e.g. sub-normal values of male sex hormone (testosterone). In addition, men previously treated with chemotherapy and/or radiotherapy have an increased risk for hypertension, overweight, elevated cholesterol levels and cardiovascular disease. Thus, it is advisable to keep away from smoking, avoid overweight and exercise regularly.

We recommend that the following are controlled by the general practitioner:

- 1) Blood pressure, height, weight, waist circumference
- 2) Blood samples including fasting lipids (total cholesterol, HDL and LDL-cholesterol, triglycerides), fasting glucose and hormones (testosterone, FSH and LH)
- 3) Clinical examination in case of any symptoms

The purpose of these controls is to prevent, identify and possibly treat risk factors which might lead to complications, e.g. cardiovascular disease. We recommend controls every 2.-3. years. If abnormal values are detected at these controls, further follow-up at the general practitioner is initiated.

Oppfølgingskjema som deles ut til pasient og fastlege ved avslutning av oppfølging hos onkolog

Du ble operert år _____ for testikkelkreft av typen:

☐ Seminom ☐ Non-seminom

☐ Det ble ikke påvist spredning

☐ Det ble påvist spredning til _____

Ytterligere behandling:

☐ Ingen

☐ Cellegift (Antall kurer: _____)

☐ Strålebehandling

☐ Operasjoner i tillegg til fjerning av testikkelen _____

Dato for siste kontroll: _____ Sykehus: _____

Behandlerende lege: _____ Telefon: _____

Du har vært til avsluttende sykehuskontroll etter tidligere behandling for testikkelkreft. Det er svært liten risiko for tilbakefall av sykdommen, og du skal nå følges opp videre hos fastlegen. Dette skrevet bør tas med ved senere kontakter med helsevesenet.

Det er en økt forekomst av ny skulst i gjenværende testikkel og det er viktig med regelmessig selvundersøkelse. Det er også litt økt forekomst av annen kreftsykdom. Noen bivirkninger av testikkelkreftbehandling kan vise seg mange år etter avsluttet behandling, for eksempel mangel på mannlig kjønnshormon (testosteron). I tillegg ser det ut til at de som tidligere er behandlet med cellegift og/eller strålebehandling har en økt risiko for høyt blodtrykk, overvekt, forhøyet kolesterol og hjerte-karsykdommer. Derfor er det lurt å avstå fra røyking, forsøke å unngå overvekt, og trene regelmessig.

Vi vil anbefale at følgende kontrolleres hos fastlegen:

- 1) Blodtrykk, høyde, vekt, midjemål
- 2) Blodprøver inklusive fastende lipider (totalt kolesterol, HDL og LDL-kolesterol, triglyserider), fastende blodsukker og hormonprøver (testosteron og LH)
- 3) Klinisk undersøkelse styres ut fra eventuelle symptomer

Hensikten med disse kontrollene er å forebygge, påvise og eventuelt behandle risikofaktorer for f. eks hjertesykdom, før sykdommen utvikles. Vi anbefaler kontroller hvert 2.-3. år. Ved avvikende verdier påvist ved kontrollene følges dette opp videre i regi av fastlegen.

Sammanfattning av sjukdomsförlopp och behandling

När man fått behandling för testikelcancer kan det efter lång tid dyka upp seneffekter av den givna behandlingen. Dessa seneffekter kan till exempel vara brist på manligt könshormon (testosteron), nedsatt fruktsamhet (fertilitet) samt påverkan på njurar.

Behandlingen kan även ge en liten ökad risk för hjärt-kärlsjukdom. Detta kan yttra sig som förhöjt blodtryck, kärlkramp och förhöjda blodfetter, och du bör avstå från rökning och också försöka undvika övervikt.

Det är bra att du vid kontakter med läkare i framtiden nämner att du varit behandlad för testikelcancer, och denna lapp med information om din genomgångna behandling kan vara till hjälp för dig att komma ihåg.

Namn _____ Personnummer _____

Du opererades år _____ för testikelcancer av typen:

☐ Seminom

☐ Icke-seminom

☐ Biopsiprov togs även från den friska testikeln

☐ Ingen spridning konstaterades

☐ Spridning konstaterades till _____, _____, _____

Kompletterande behandling

☐ Ingen

☐ Cytostatika (totalt antal behandlingar _____)

☐ Strålbehandling

☐ Kirurgi (förutom operation av den sjuka testikeln) _____, _____

Återfall under uppföljningsperioden:

☐ Nej

☐ Ja, år _____

Sista kontrollen gjordes: datum _____ Sjukhus _____

Behandlande läkare _____ Telefon _____

Tag gärna med denna informationslapp vid kontakt med sjukvården i framtiden.

**Nationellt kvalitetsregister
SWENOTECA Seminom testis
Registreringsblankett**

Blanketten gäller fr o m 2012 01 01 som canceranmälan

Personnummer år mån dag -

Namn

Blanketter skickas till Regionalt Onkologiskt Centrum	Tidigare cancer i andra testikeln Ar <table border="1" style="display: inline-table; vertical-align: middle;"><tr><td style="width: 15px; height: 15px;"></td><td style="width: 15px; height: 15px;"></td><td style="width: 15px; height: 15px;"></td><td style="width: 15px; height: 15px;"></td></tr></table> ☐ seminom ☐ non-seminom				
Klinik, sjukhus	Läkare				

Primärtumördata¹

Orchiektomi ☐ Nej ☐ Ja Datum <table border="1" style="display: inline-table; vertical-align: middle;"><tr><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td></tr></table> ☐ hö ☐ vä ☐ bilat. Om bilat: seminom i båda testiklar ☐ nej ☐ ja (en registreringsblankett för varje tumör) ²												
Klinik, Sjukhus (där orchiektomi utfördes)	Patolog avd	PAD nr <table border="1" style="display: inline-table; vertical-align: middle;"><tr><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td></tr></table> - <table border="1" style="display: inline-table; vertical-align: middle;"><tr><td> </td><td> </td></tr></table> Ar										
Inväxt i rete testis ☐ nej ☐ ja ☐ oklart Vaskulär invasion ☐ nej ☐ ja ☐ oklart Tumörstorlek (mm x mm) <table border="1" style="display: inline-table; vertical-align: middle;"><tr><td> </td><td> </td><td> </td></tr></table> x <table border="1" style="display: inline-table; vertical-align: middle;"><tr><td> </td><td> </td><td> </td></tr></table>								Lämnat spermieprov ☐ nej ☐ ja ☐ vet ej ☐ vill ej om ja: ☐ före orchiektomi ☐ efter orchiektomi				
"Utbränd tumör" ☐ nej ☐ ja Kontralateral testisbiopsi ☐ Cis ☐ ej Cis ☐ ej utfört												

Tumörmarkörer/utredning

Före orchiektomi		AFP		,	☐ normalt (för patienten) ³	☐ ej utfört
Datum		β-HCG		,	☐ normalt	☐ förhöjt ☐ ej utfört
		LD		,	☐ normalt	☐ förhöjt ☐ ej utfört
		PLAP		,	☐ normalt	☐ förhöjt ☐ ej utfört
Hormonstatus						
Datum		Testosteron		,	mmol/l ☐ normalt	☐ förhöjt ☐ lågt ☐ ej utfört
		SHBG	☐ normalt	☐ förhöjt	☐ lågt	☐ ej utfört
		LH	☐ normalt	☐ förhöjt	☐ lågt	☐ ej utfört
		FSH	☐ normalt	☐ förhöjt	☐ lågt	☐ ej utfört
Metastaser						
Lymfkörtelmetastaser		Största metastas (mm x mm)		Primära metastaser		
Inguinalt	☐ nej ☐ ja	☐	X ☐	Lunga	☐ nej ☐ ja	
Iliakalt	☐ nej ☐ ja	☐	X ☐	Närna	☐ nej ☐ ja	
Paraaortalt	☐ nej ☐ ja	☐	X ☐	Lever	☐ nej ☐ ja	
Mediastinalt	☐ nej ☐ ja	☐	X ☐	Skelett	☐ nej ☐ ja	
Supraklav	☐ nej ☐ ja	☐	X ☐	Annan lokal	☐ nej ☐ ja, spec.	

Definitiv klinisk stadielndelning⁴

Datum vid definitiv stadiindelning år mån dag 			☐ CSI Antal riskfaktorer ⁵ ☐ 0 ☐ 1 ☐ 2 ☐ CSMk+ ☐ CSII ☐ CSIII ☐ CSIV		
			Abdominella lymfkörtlar ☐ 0 ☐ A ☐ B ☐ C ☐ D		
Tumörmarkörer	AFP	,	☐ normalt (för patienten) ³		☐ ej utfört
(vid definitiv stadiindelning)	β-HCG	,	☐ normalt	☐ förhöjt	☐ ej utfört
	LD	,	☐ normalt	☐ förhöjt	☐ ej utfört
	PLAP	,	☐ normalt	☐ förhöjt	☐ ej utfört
Prognos enl IGCCC⁶					
☐ god ☐ intermediär					

Behandling ☐ Patient remitterad till klinik/sjukhus.

CSI	☐ ingen adj.behandling	☐ adj. karboplatin	☐ adj. strålbehandling	☐ annan, spec.....
CS MK+, II-IV	☐ BEP	☐ EP	☐ strålbehandling	☐ annan, spec.....

Kompletterande uppgifter för att gälla som canceranmälan

SNOMED-kod: 90613 Seminom			Diagnosgrund (flera alternativ kan ifyllas) ☐ Provexcision eller operation med histopatologisk undersökning ☐ Cytologisk undersökning ☐ Annan lab. undersökning (tumörmarkörer)		
TNM T-primärtumör⁷ ☐ pTX ☐ pT0 ☐ pTis ☐ pT1 ☐ pT2 ☐ pT3 ☐ pT4			N-regionala lymfkörtelmetastaser ☐ NX ☐ N0 ☐ N1 ☐ N2 ☐ N3		M-fjärrmetastaser ☐ M0 ☐ M1 ☐ M1a ☐ M1b

Registreringsblankett SWENOTECA Seminom

1. **Definition av testikulär primärtumör (ICD C 62):** A. Primärtumör belägen i testis. B. Tumör i retroperitoneala lymfkörtlar och patologiskt fynd vid ultraljudsundersökning av testis som leder till orchiectomi och histopatologisk undersökning visar ett ärr (fibrotiskt område) i testikeln "utbränd" tumör. Om dessa kriterier inte är uppfyllda räknas **retroperitoneal tumör som extragonadal (ICD C 48.0), extragonadal mediastinal (ICD C 38.3)** och skall registreras på separat blankett för extragonadala tumörer.
2. **Bilateral synkron tumör**
Om samma tumörtyp i båda testiklarna registreras båda tumörerna i samma register. Om ena tumören är ett nonseminom och andra ett seminom så registreras primärtumördata för seminom i seminomregistret men **komplett registrering** göres i nonseminomregistret. Patienten behandlas och följes som nonseminom.
3. **AFP-Nivå**
Förhöjt AFP är per definition inte förenligt med en seminomdiagnos.
Om patienten har förhöjda nivåer av AFP (pre- eller postorchiectomi) bör diagnosen omprövas med avseende på non-seminomatös testikelcancer. Man bör dock vara medveten om att smittsamma/virala processer i levern kan orsaka en liten ökning av AFP.
I sällsynta fall kan patienten konstitutionellt ha en AFP-nivå något **över** det normala. En lätt förhöjd och **stabil** AFP nivå kan således vara förenligt med en seminomdiagnos.
4. **Klinisk stadiindelning: modifierad efter RMH**
CS I Inga tecken på metastaser
CS Mk+ β -HCG kvarstående förhöjt (faller ej enl sin halveringstid) men inga metastaser påvisbara
CS II Metastaser begränsade till abdominella lymfkörtlar
A maximal diameter <2 cm
B maximal diameter 2–5 cm
C maximal diameter >5–10 cm
D maximal diameter >10 cm
CS III Metastaser i lymfkörtlar ovan diafragma
För abdominella lymfkörtlar gäller:
0 inga metastaser
A-D enl CS II
CS IV Extralymfatiska metastaser
För abdominella lymfkörtlar gäller:
0 inga metastaser
A-D enl CS II
5. **Risikfaktorer**
Primärtumör ≥ 4 cm, inbäxt i rete testis
6. **International Form CMI Consensus Classification**

Good-prognosis Any primary site and no non-pulmonary visceral metastases and normal AFP Any β -HCG Any LDH	Intermediate-prognosis Any primary site and non-pulmonary visceral metastases and normal AFP Any β -HCG Any LDH
--	---
7. **TNM Patologisk (p) och klinisk klassifikation**
Omfattningen av den primära tumören klassificeras efter radikal orkidektomi.

pT - T-stadium
pTX Primärtumören kan inte bedömas (ingen orchiectomi har utförts, TX används).
pT0 Inga tecken på primärtumör (t.ex. histologiskt påvisat ärr i testis).
pTis Intratubulär germinalcellsneoplasi (carcinoma in situ).
pT1 Tumör begränsad till testis och epididymis utan vaskulär/lymfatisk invasion; tumören kan invadera tunica albuginea men inte tunica vaginalis.
pT2 Tumör begränsad till testis och epididymis med vaskulär/lymfatisk invasion, eller tumör som sträcker sig genom tunica albuginea med engagemang av tunica vaginalis.
pT3 Tumör invaderar funikel med eller utan vaskulär/lymfatisk invasion.
pT4 Tumör invaderar scrotum med eller utan vaskulär/lymfatisk invasion.

N - Regionala Lymfkörtelmetastaser
N0 Inga lymfkörtelmetastaser påvisade
N1 Metastas i enstaka lymfkörtel med diameter högst 2 cm
N2 Metastas i enstaka 2–5 cm stor lymfkörtel, eller i multipla lymfkörtlar, högst 5 cm stora
N3 Metastas i lymfkörtel med diameter över 5 cm
NX Kriterier för diagnos av lymfkörtelmetastaser ej uppfyllda

M-fjärrmetastaser
M0 Inga fjärrmetastaser
M1 Fjärrmetastas påvisad
M1a Icke-regionala lymfkörtlar eller lungmetastaser
M1b Andra fjärrmetastaser än M1a

2012-02-27 /MRD

Behandlingsblankett–Kemoterapi Seminom

1. Gradering av toxicitet (WHO 1979)

	Grad 3	Grad 4
Hematologisk (vuxna)		
Hemoglobin g/L	65–79	< 65
Vita x 10 ⁹ /L	1,0–1,9	< 1,0
Trombocyter x 10 ⁹ /L	25–49	< 25
Urinvägar		
S-Kreatinin	5–10 x N	> 10 x N
Neurotoxicitet		
Perifer	Intolerabla parestesier och/eller uttalad svaghet	Förlamning
Obstipation*	Uppspänd buk	Uppspänd buk och kräkningar
Infektion	Svår infektion	Svår infektion med blodtrycksfall

N = Övre normalgränsen

* = Obstipation, inkluderar ej obstipation p g a morfinpreparat

Not Valid

2. Effekt av behandling. Remissionsbedömning.

Komplett remission:	Fullständigt försvinnande av samtliga tumörmanifestationer på CT/MR eller motsvarande. Normala tumörmarkörer.
Partiell remission:	Reduktion av mätbar tumör med $\geq 50\%$ ($\geq 50\%$ reduktion av produkten av de största perpendikulära diametrarna) utan samtidig progress på andra lokaler.
Stabil sjukdom:	Effekt av behandling uppfyller inte kriterier för partiell remission och inte heller för progressiv sjukdom.
Progressiv sjukdom:	Ökning av tumörmanifestationer skall vara $\geq 25\%$, eller tillkomst av nya tumörmanifestationer, eller ökning av tumörmarkörer $> 10\%$.

Nationellt kvalitetsregister SWENOTECA Seminom Behandlingsblankett – Radioterapi		Personnummer <table border="1"> <tr> <td>år</td> <td>mån</td> <td>dag</td> <td>-</td> <td></td> <td></td> <td></td> <td></td> </tr> </table>	år	mån	dag	-				
år	mån	dag	-							
Blanketten skickas till Regionalt Onkologiskt Centrum		Namn								
Klinik, sjukhus										
Läkare										

Behandling (En blankett för varje angivet target vid varje ny strålbehandlingsomgång)

Orsak till strålbehandling																			
☐ adjuvant (CS I)	☐ primärbehandling av metastatisk sjukdom	☐ konsoliderande behandling efter kemoterapi /kirurgi																	
☐ biverkningar av föregående behandling	☐ recidiv	☐ annan orsak, spec.																	
Start av behandling	Avslutad behandling	Fraktionsdos (Gy)	Targetdos (Gy)																
<table border="1"> <tr> <td>år</td> <td>mån</td> <td>dag</td> </tr> </table>	år	mån	dag	<table border="1"> <tr> <td>år</td> <td>mån</td> <td>dag</td> </tr> </table>	år	mån	dag	<table border="1"> <tr> <td></td> <td></td> <td></td> <td>.</td> <td></td> </tr> </table>				.		<table border="1"> <tr> <td></td> <td></td> <td></td> <td>.</td> <td></td> </tr> </table>				.	
år	mån	dag																	
år	mån	dag																	
			.																
			.																

Strålbehandling, lokal

☐ paraaortalt	☐ paraaortalt + iliakalt	☐ abdomen	☐ thorax	☐ CNS	☐ annat, spec.
Orsak till avslutad behandling					
☐ enligt program	☐ bristande effekt	☐ biverkningar	☐ annan, spec.		

Toxicitet¹

Grad 3–4	☐ nej	☐ ja
Om ja, specificera.....		

Effekt av behandling², anges ej om orsak till behandling = adjuvant CS I

<table border="1"> <tr> <td>år</td> <td>mån</td> <td>dag</td> </tr> </table>	år	mån	dag	☐ CR	☐ SD	☐ ej bedömbart
år	mån	dag				
	☐ PR	☐ PD				

Fortsatt behandling (ny beh blankett ifylles vid behov)

☐ ingen ytterligare behandling
☐ kemoterapi
☐ kirurgi
☐ högdoskemoterapi med rescue
☐ strålbehandling
☐ annan beh, spec:

Behandlingsblankett–Radioterapi Seminom

1. Gradering av toxicitet (WHO 1979)

	Grad 3	Grad 4
Hematologisk (vuxna)		
Hemoglobin g/L	65–79	< 65
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N = Övre normalgränsen

* = Obstipation, inkluderar ej obstipation p g a morfinpreparat

Not Valid

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Stabil sjukdom:	Effekt av behandling uppfyller inte kriterier för partiell remission och inte heller för progressiv sjukdom.
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Nationellt kvalitetsregister SWENOTECA Seminom Behandlingsblankett – Kirurgi	Personnummer år mån dag -
Blanketten skickas till Regionalt Onkologiskt Centrum	Namn
Klinik, sjukhus	
Läkare	

Denna blankett ifylles för varje typ av kirurgiskt ingrepp (förutom primär orchiectomi = registreringsblankett)

Kirurgi

Datum år mån dag 	Sjukhus där kirurgi har utförts, spec
Orsak till kirurgi ☐ postkemoterapi, som led i primärbehandling ☐ recidiv ☐ annan, spec.	
Tumörstatus vid kirurgi Markörer (ß-HCG): ☐ normalt ☐ förhöjt ☐ ej utfört Resttumör i buk: ☐ storlek ☐ <1 cm ☐ ≥1 cm Resttumör i lunga: ☐ Resttumör på annan lokal: ☐ spec. Annan tumör: ☐ spec.	
Typ av kirurgi ☐ unilat RPLND ☐ bilat RPLND ☐ excision av resttumör i: ☐ buk ☐ lunga ☐ annan lokal ☐ annan operation, spec. Operation mikroskopiskt radikal ☐ nej ☐ ja	
Patolog avd	PAD nr -
PAD ☐ nekros/fibros ☐ teratom förekomst av omogna komponenter ☐ nej ☐ ja ☐ vet ej ☐ vital cancer ☐ normala lymfkörtlar ☐ annat, spec. Fria resektionsränder ☐ nej ☐ ja ☐ ej bedömbart	
Kirurgisk livshotande komplikation ☐ nej ☐ ja, spec.	

Fortsatt behandling

☐ Ingen ytterligare behandling ☐ Kemoterapi ☐ Kirurgi ☐ Strålbehandling ☐ Högdoskemoterapi med rescue ☐ Annan, spec.
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Nationellt kvalitetsregister SWENOTECA Seminom Uppföljningsblankett		Personnummer <table border="1"> <tr> <td>år</td> <td>mån</td> <td>dag</td> <td>-</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </table>	år	mån	dag	-						
år	mån	dag	-									
Blanketter skickas till Regionalt Onkologiskt Centrum		Namn										
Klinik, sjukhus												
Läkare												

Besöksdatum <table border="1"> <tr> <td>år</td> <td>mån</td> <td>dag</td> </tr> </table>		år	mån	dag	
år	mån	dag			
Status ☐ inga tecken på sjukdom ☐ stabil eller minskande resttumör ☐ recidiv/progress					
☐ kontralateral testikelcancer ☐ annan cancer spec					
Seneffekt av behandling anges år 1, 3 och 5 efter avslutad behandling					
Retrograd ejakulation ☐ nej ☐ ja Minskad libido ☐ nej ☐ ja Impotens ☐ nej ☐ ja Annan ☐ nej ☐ ja, spec.	Testosteron <table border="1"> <tr> <td></td> <td></td> <td>,</td> <td></td> </tr> </table> SHBG LH FSH Testosteron substitution ☐ nej ☐ ja			,	
		,			
Fortsatt behandling (ny beh blankett ifylles vid behov) ☐ ingen ☐ kirurgi ☐ högdoskemoterapi med rescue ☐ kontroller avslutas ☐ kemoterapi ☐ strålbehandling ☐ annan behandling, spec					

Recidiv/Progress datum <table border="1"> <tr> <td>år</td> <td>mån</td> <td>dag</td> </tr> </table>		år	mån	dag	Progress av resttumör ☐ nej ☐ ja																																																																																											
år	mån	dag																																																																																														
Lymfkörtelmetastaser <table border="1"> <tr> <th></th> <th>nej</th> <th>ja</th> <th>evaluerbart</th> <th>Största metastas (mm x mm)</th> </tr> <tr> <td>Inguinalt</td> <td>☐</td> <td>☐</td> <td>☐</td> <td><table border="1"><tr><td></td><td></td><td></td><td></td></tr></table> x <table border="1"><tr><td></td><td></td><td></td><td></td></tr></table> </td> </tr> <tr> <td>Iliakalt</td> <td>☐</td> <td>☐</td> <td>☐</td> <td><table border="1"><tr><td></td><td></td><td></td><td></td></tr></table> x <table border="1"><tr><td></td><td></td><td></td><td></td></tr></table> </td> </tr> <tr> <td>Paraortalt</td> <td>☐</td> <td>☐</td> <td>☐</td> <td><table border="1"><tr><td></td><td></td><td></td><td></td></tr></table> x <table border="1"><tr><td></td><td></td><td></td><td></td></tr></table> </td> </tr> <tr> <td>Mediastinalt</td> <td>☐</td> <td>☐</td> <td>☐</td> <td><table border="1"><tr><td></td><td></td><td></td><td></td></tr></table> x <table border="1"><tr><td></td><td></td><td></td><td></td></tr></table> </td> </tr> <tr> <td>Supraklav</td> <td>☐</td> <td>☐</td> <td>☐</td> <td><table border="1"><tr><td></td><td></td><td></td><td></td></tr></table> x <table border="1"><tr><td></td><td></td><td></td><td></td></tr></table> </td> </tr> </table>			nej	ja	evaluerbart	Största metastas (mm x mm)	Inguinalt	☐	☐	☐	<table border="1"><tr><td></td><td></td><td></td><td></td></tr></table> x <table border="1"><tr><td></td><td></td><td></td><td></td></tr></table>									Iliakalt	☐	☐	☐	<table border="1"><tr><td></td><td></td><td></td><td></td></tr></table> x <table border="1"><tr><td></td><td></td><td></td><td></td></tr></table>									Paraortalt	☐	☐	☐	<table border="1"><tr><td></td><td></td><td></td><td></td></tr></table> x <table border="1"><tr><td></td><td></td><td></td><td></td></tr></table>									Mediastinalt	☐	☐	☐	<table border="1"><tr><td></td><td></td><td></td><td></td></tr></table> x <table border="1"><tr><td></td><td></td><td></td><td></td></tr></table>									Supraklav	☐	☐	☐	<table border="1"><tr><td></td><td></td><td></td><td></td></tr></table> x <table border="1"><tr><td></td><td></td><td></td><td></td></tr></table>									Extralympfatiska metastaser <table border="1"> <tr> <th></th> <th>nej</th> <th>ja</th> <th>evaluerbart</th> </tr> <tr> <td>Lunga</td> <td>☐</td> <td>☐</td> <td>☐</td> </tr> <tr> <td>Lever</td> <td>☐</td> <td>☐</td> <td>☐</td> </tr> <tr> <td>Hjärna</td> <td>☐</td> <td>☐</td> <td>☐</td> </tr> <tr> <td>Skelett</td> <td>☐</td> <td>☐</td> <td>☐</td> </tr> <tr> <td>Annan lokal</td> <td>☐</td> <td>☐</td> <td>spec</td> </tr> </table>		nej	ja	evaluerbart	Lunga	☐	☐	☐	Lever	☐	☐	☐	Hjärna	☐	☐	☐	Skelett	☐	☐	☐	Annan lokal	☐	☐	spec
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Tumörmarkörer Markörer förhöjda ☐ nej ☐ ja ☐ ej utfört		Enbart förhöjda tumörmarkörer som tecken på recidiv/progress ☐ nej ☐ ja																																																																																														
Symtom eller undersökning(ar) som först signalerar recidiv/progress (flera alternativ kan anges) ☐ symptom ☐ CT/MR/UL ☐ tumörmarkörer ☐ annat, spec																																																																																																
Recidiv histologiskt undersökt ☐ nej ☐ ja																																																																																																

Dödsdatum <table border="1"> <tr> <td>år</td> <td>mån</td> <td>dag</td> </tr> </table>		år	mån	dag	Obduktion utförd ☐ nej ☐ ja
år	mån	dag			
Dödsorsak ☐ testikelcancer ☐ behandlingskomplikation, spec ☐ annan cancer ☐ annan orsak, spec		Kvarvarande testikelcancer (ifylles ej om testikelcancer=dödsorsak) ☐ nej ☐ ja ☐ ej bedömbart			
Ev. kommentar					

**Nationellt kvalitetsregister
SWENOTECA
Extragonadal germinalcellscancer
Registreringsblankett**

Blanketten gäller fr o m 2012 01 01 som canceranmälan

Blanketter skickas till Regionalt Onkologiskt Centrum	Personnummer år mån dag - - -
Klinik, sjukhus	Namn Läkare

Primärtumördata¹

Lokalisation ☐ Retroperitoneal ☐ Mediastinal	Tumörtyp² ☐ Nonseminom, ☐ Seminom	Diagnosdatum år mån dag
Klinik, Sjukhus (där diagnosen faststälts)	Patolog avd	PAD/Cyt nr - år

Utredning

Testis Testisbiopsi hö ☐ Cis ☐ ej Cis ☐ ej utfört	Orchiektomi hö ☐ nej ☐ ja PAD nr - år
Testisbiopsi vä ☐ Cis ☐ ej Cis ☐ ej utfört	Orchiektomi vä ☐ nej ☐ ja PAD nr - år
Lämnat spermieprov: ☐ nej ☐ ja ☐ vet ej ☐ vill ej	

Tumörmarkörer, vid slutförd utredning

Datum år mån dag	AFP , ☐ normalt ☐ förhöjt ☐ ej utfört
	β-HCG , ☐ normalt ☐ förhöjt ☐ ej utfört
	LD , ☐ normalt ☐ förhöjt ☐ ej utfört
	PLAP , ☐ normalt ☐ förhöjt ☐ ej utfört
Hormonstatus	Testosteron mmol/l ☐ normalt ☐ förhöjt ☐ lågt ☐ ej utfört
Datum år mån dag	SHBG ☐ normalt ☐ förhöjt ☐ lågt ☐ ej utfört
	LH ☐ normalt ☐ förhöjt ☐ lågt ☐ ej utfört
	FSH ☐ normalt ☐ förhöjt ☐ lågt ☐ ej utfört

Tumörutbredning

Lymfkörtlar	Största tumör (mm x mm)	Extralymfatisk lokal
Inguinalt ☐ nej ☐ ja ☐ X ☐		Lunga ☐ nej ☐ ja
Iliakalt ☐ nej ☐ ja ☐ X ☐		Hjärna ☐ nej ☐ ja
Paraaortalt ☐ nej ☐ ja ☐ X ☐		Lever ☐ nej ☐ ja
Mediastinalt ☐ nej ☐ ja ☐ X ☐		Skelett ☐ nej ☐ ja
Supraklav ☐ nej ☐ ja ☐ X ☐		Annan lokal ☐ nej ☐ ja, spec.....

Prognosgruppering³

Datum år mån dag	Prognos enl IGCCC³ ☐ god ☐ intermediär ☐ dålig
-------------------------------	--

Behandling ☐ Patient remitterad till klinik/sjukhus.....

☐ BEP ☐ Kirurgi ☐ strålbehandling ☐ Annan spec.....

Kompletterande uppgifter för att gälla som canceranmälan

SNOMED-kod ⁴	Diagnosgrund (flera alternativ kan ifyllas) ☐ Provexcision eller operation med histopatologisk undersökning ☐ Cytologisk undersökning ☐ Annan lab undersökning
-------------------------------	---

Registreringsblankett SWENOTECA Extragonadal retroperitoneal eller mediastinal germinalcellscancer

1. **Definition av testikulär primärtumör:** A. Primärtumör belägen i testis. B. Tumör i retroperitoneala lymfkörtlar och patologiskt fynd vid ultraljudsundersökning av testis som leder till orchiectomi och histopatologisk undersökning visar ett ärr (fibrotiskt område) i testikeln "utbränd" tumör. Om dessa kriterier inte är uppfyllda räknas **retroperitoneal tumör som extragonadal (ICD C 48.0), extragonadal mediastinal (ICD C 38.3)** och skall registreras på denna blankett för extragonadala tumörer.

2. AFP-Nivå

Förhöjt AFP är per definition inte förenligt med en seminomdiagnos.

Om patienten har förhöjda nivåer av AFP (pre- eller postorchiectomi) bör diagnosen omprövas med avseende på non-seminomatös testikelcancer. Man bör dock vara medveten om att smittsamma/virala processer i levern kan orsaka en liten ökning av AFP.

I sällsynta fall kan patienten konstitutionellt ha en AFP-nivå något över det normala. En lätt förhöjd och **stabil** AFP nivå kan således vara förenligt med en seminomdiagnos.

3. International Germ Cell Consensus Classification (markörnivå vid definitiv stadiindelning)

	Good prognosis	Intermediate prognosis	Poor prognosis
Non-seminoma	Retroperitoneal primary and No non-pulmonary visceral metastases (for example liver, bone, brain) and all good markers: β-hCG < 5000 IU/L (1000 µg/L) and AFP < 1000 µg/L and LDH < 1,5 X N (upper normal limit)	Retroperitoneal primary and No non-pulmonary visceral metastases (for example liver, bone, brain) and any intermediate marker: β-hCG ≥ 5000 and ≤ 50000 IU/L or AFP ≥ 1000 and ≤ 10000 µg/L or LDH ≥ 1,5 x N and ≤ 10 x N (upper normal limit)	Mediastinal primary or Non-pulmonary visceral metastases (for example liver, bone, brain) or any poor marker: β-hCG > 50000 IU/L or AFP > 10000 µg/L or LDH > 10 x N (upper normal limit)
Seminoma	Any primary site and No non-pulmonary visceral metastases (for example liver, bone, brain) and Normal AFP, any hCG, any LDH	Any primary site and Non-pulmonary visceral metastases (for example liver, bone, brain) and Normal AFP, any hCG, any LDH	No patients classified as poor prognosis

4. Snomedkoder som ingår i malignitsregistret för Extragonadala germinalcellstumörer:

Nonseminomatös tumör

Tumörer av mer än en histologisk typ (mixed)	Snomed	Tumörer med EN histologisk typ (rena former)	Snomed	Teratom	Snomed
A. Blandad germinalcellstumör med seminom. (Innefattar koder enl cancerregistrets kodningsmanual: Germinalcellstumör, blandad teratom med seminomkomponent = 90853. Teratom med seminomkomponent = 90853).	90853	Choriocarcinom UNS	91003	Innefattar rent teratom UNS hos män ≥ 16 år = 90801	90803
		Embryonalt carcinom, UNS	90703		90843
		Endodermal sinustumör "yolk sac tumor", gulesäckstumör	90713	Teratom med malign somatisk komponent Finns ej i cancerregistrets kodningsmanual	
B. Blandad germinalcellstumör utan seminom. (Innefattar koder enl cancerregistrets kodningsmanual: Germinalcellstumör utan seminomkomponent = 90653 Teratocarcinom blandat embryonalt carcinom och teratom = 90813 Choriocarcinom komb med andra germinalcellskomponenter teratom, embryonalt carcinom = 91013).	90813	Seminom med AFP-stegring*	906130		
		* AFP-Nivå Förhöjt AFP är per definition inte förenligt med en seminomdiagnos. Om patienten har förhöjda nivåer av AFP (pre- eller postorchiectomi) bör diagnosen omprövas med avseende på non-seminomatös testikelcancer. Man bör dock vara medveten om att smittsamma/virala processer i levern kan orsaka en liten ökning av AFP. I sällsynta fall kan patienten konstitutionellt ha en AFP-nivå något över det normala. En lätt förhöjd och stabil AFP-nivå kan således vara förenligt med en seminomdiagnos.			

Seminomatösa tumörer: 90613 (bara en komponent, och utan samtidig AFP stegring)

SWENOTECA VIII & IX HÖGDOS-formulär Rapporteras när högdosterapi (HDCT) är avslutad. Ifyllt formulär skickas till Regionalt Cancercentrum.	Personnummer År Mån Dag Namn
Klinik, sjukhus	
Läkare	

Indikation för HDCT

	Nej	Ja
Fördröjd markör T1/2 AFP/ β -HCG efter första intensifiering av primärterapi	☐	☐
Som en del av recidivbehandling	☐	☐
Annan indikation, om ja specificera nedan:	☐	☐

Patienten diskuterad inom SWENOTECA:

☐ Nej ☐ Ja

Status före HDCT

Status före HDCT		Nej	Ja	Vet ej		Antal	Vet ej
Tumörmarkörer AFP/ β -HCG normala vid start av HDCT	☐	☐	☐				
Cisplatinkänslig ¹ tumör vid start av HDCT	☐	☐	☐	Givna cytostatikakurer			☐
				BEP			☐
				BEP-If/PEI			☐
Gavs Mozobil (Plerixafor) före stamcellsskörd?	☐	☐	☐	TIP			☐
				Annat _____			☐

Antal HD kurer givna ☐ 1 ☐ 2 Om endast en kur given, ange orsak:

☐ Toxicitet ☐ Bristande effekt/progressiv sjukdom ☐ Patienten vill inte ☐ Annan: _____

HDCT kur 1

Längd	Vikt	GFR okorr. värde ²	Startdatum	Stopppdatum				
cm	kg	ml/min	År Mån Dag	År Mån Dag				
Totalmängd cytosin givna g								
Karboplatin	Etoposid	Annet drog, specificera nedan						
mg	mg							
Stamceller återgivna	Antal stamceller återgivna							
År Mån Dag	x10 ⁶ /kg							
Benmärgsåterhämtning				Antal dagar på sjukhus				
ANC $\geq 1.0 \times 10^9$ /L		TRC $\geq 20 \times 10^9$ /L		dagar				
År Mån Dag		År Mån Dag						
Akut toxicitet grad 3-4 (WHO gradering, se omstående sida)								
Nej	Ja	Nej	Ja	Nej	Ja			
Lunga	☐	☐	Lever	☐	☐	Infektion	☐	☐
Njurar	☐	☐	Blödning	☐	☐	Neurotoxicitet	☐	☐
Hjärta	☐	☐	Annan toxicitet	☐	☐	Specificera annan tox:		
Avliden i samband med HDCT 1								

HDCT kur 2

Längd		Vikt		GFR okorr. värde ²		Startdatum			Stopdatum		
cm		kg		ml/min		År	Mån	Dag	År	Mån	Dag
Totalmängd cytostatika given						Annan drog ☐ Nej ☐ Ja, specificera nedan					
Karboplatin		mg		Etoposid		mg					
Stamceller återgivna		Antal stamceller återgivna									
År		Mån		Dag		*10 ⁶ /kg					
Benmärgsåterhämtning									Antal dagar på sjukhus		
ANC $\geq 1.0 \times 10^9$ /L År Mån Dag									TRC $\geq 20 \times 10^9$ /L År Mån Dag		
									dagar		
Akut toxicitet grad 3-4 (WHO gradering, se omstående sida)											
Nej		Ja		Nej		Ja		Nej		Ja	
Lunga	☐	☐	Lever	☐	☐	Neurotoxicitet	☐	☐			
Njurar	☐	☐	Blödning	☐	☐	Annan toxicitet	☐	☐	specificera nedan		
Hjärta	☐	☐	Infektion	☐	☐						
Avliden i samband med HDCT 2											

¹ Cisplatinresistens=Progress (se omstående sida för definition) ≤4 veckor efter behandling med cisplatin²iohexol- /Cr-Edta-clearance

1. Gradering av akut toxicitet (WHO 1979)

	Grad 3	Grad 4
Lunga	Vilodyspné	Komplett sängläge
Njurar		
S-Kreatinin	5–10 x N	> 10 x N
Hjärta	Symtomgivande dysfunktion som svarar på behandling	Symtomgivande dysfunktion som är terapistresistent
Lever		
Bilirubin	5–10 x N	> 10 x N
ALAT/ASAT	5–10 x N	> 10 x N
Blödning	Transfusionskrävande	Livshotande
Infektion	Svår infektion	Svår infektion med blodtrycksfall
Neurotoxicitet		
Perifer	Intolerabla parestesier och/eller uttalad svaghet	Förlamning

N = Övre normalgränsen

2. Definition av progressiv sjukdom

Progressiv sjukdom: Ökning av tumörmanifestationer skall vara ≥ 25 %, eller tillkomst av nya tumörmanifestationer, eller ökning av tumörstorlek med ≥ 10 %.

Not Valid

KVAST dokument testikeltumör

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Introduktion

Preoperativt diagnoserat av testis tumörer är huvudsakligen kliniskt och histologisk. Detta dokument behandlar hisopatologisk undersökning av orkhidektomi preparat med tumörfrågeställning i biopsi som togs från kontralateral testis vid orkhidektomi med frågeställning: Intratubulär germinalcellsneoplasi?

Den diagnostiska bedömningen som är styrande för kontroll och fortsatt behandling är huruvida tumören är malign eller benign, av könscelltyp eller stromal. Avseende tumörer av germinal typ är det helt avgörande om tumören är ett rent **seminom** eller av annan histologisk typ. Däremot är andelen av andra tumörkomponenter icke behandlingsstyrande. **Patologiskt tumörstadium** samt **tumörförekomst i rete testis** är likaledes behandlingsstyrande. Beträffande teratomen kan dessa bestå av såväl mogen, omogen som intermediärt mogen vävnad och är hos prepubertala barn en icke metastaserande tumör. Postpubertalt är teratom en potentiellt metastaserande tumör, undantaget mogen dermoidcysta.

Anvisningar för provtagarens hantering av provet

1. Operationpreparatet hanteras enligt lokala överenskommelser mellan patologavdelning och opererande klinik.
2. Som fixativ rekommenderas buffrad formalin 10% (formaldehyd 4%) som kan beställas från Apoteksbolaget. Använd minst fem gånger preparatvikten.
3. Biopsi från kontralateral testis vid orkhidektomi hanteras varsamt för att undvika klämningsartefakter och bör fixeras i formalin (rutinmässiga immunhistokemiska metoder baseras närmast uteslutande på detta fixativ).

Anamnestisk remissinformation

1. Korrekt namn och personnummer, inklusive de fyra sista siffrorna. Stämplade uppgifter skall vara läsliga och rätt placerade på remissen.

2. Adekvata och utförliga uppgifter om sjukhistoria och undersökningsfynd inkluderande kända resultat av **tumörmarköranalyser, klinisk diagnos och ultraljudsfynd**
3. Uppgifter om vad operationsmaterialet i sin helhet omfattar med sidoangivelse.
4. Antalet burkar skall anges på remiss. Numrering eller annan märkning på preparatburk skall överensstämma med remissuppgifter. (OBS! Ej märkning på locket.)

Utskärningsanvisningar

Biopsi

Efter makroskopisk bedömning inbäddas hela biopsimaterialet.

Orchidektomi

Om det intakta operationspreparatet skickas färskt till patologen kan en skiva från resektionsänden i funikel skäras ut INNAN testis delas. För optimal fixering av tumörvävnad klyv testikeln genom rete och epididymis. Fixera minst 24 timmar. Vid misstanke om engagemang av resektionsytor bör dessa färgmarkeras före utskärning.

Mät funikeln.

Beskriv parietala tunica vaginalis (notera ev hydrocele, adherenser).

Mät testikeln, beskriv ytan.

Notera tumörens (eller tumörernas) lokalisation, storlek och makroskopiska utseende på snittytan, avgränsning mot omgivande strukturer och relation till tunica, rete, epididymis och funikel.

Skiva testikelvävnaden i tunna skivor (3–4 mm)

Notera avvikelser i vävnaden såsom ärrfibros eller nekros mot normal testikelvävnad.

Bitar till mikroskopisk undersökning:

- Resektionsänden i funikel.
- Tumören – bitar representerande samtliga makroskopiskt olika områden av tumören. Tumör ≤ 3 cm paraffininbäddas i sin helhet, för större tumörer kan om tumregel anges 1 bit/cm av tumörens diameter. Gärna storsnitt genom rete och epididymis.
- Bitar omfattande övergång mellan tumör och normal testis.
- Bitar som visar tumörens relation till tunica, rete, epididymis och funikel.
- Tumörfri testisvävnad.

Analyser

1. Snitten färgas med valfri rutinfärgning.
2. Biopsi från kontralateral testis färgas med valfri rutinfärgning och vid behov immunhistokemi.

3. Förslag till immunhistokemiska undersökningar (se tabell)

	PLAP	OCT 4	AFP	HCG	CD 30	CD117	CK(Pan)	CK7	Inhibin
IGCN(Intratubular Germinal Cell Neoplasia)	+	+	-						
Seminom	+	+	-	-	-	+	-/+		-
Spermatocytiskt Seminom	-	-	-	-	-	-/+	-/+		
Embryonal cancer	+/-	+	-/+	-	+	-	+	+	-
Gulesäckstumör	-/+	-	+/-	-	?	?	+	-	
Choriocarcinom	+/-	-	-	+	-	?	+	?	+
Leydigcellstumör	-	-	-	-	?				+
Sertolicellstumör	-	-	-	-	?				+/-
Granulosacellstumör	-	-	-	-	?				+

+: >90% av tumörerna är positiva

+/- : 50-90% av tumörerna är positiva

-/+ : 10-50% av tumörerna är positiva

- : <10% av tumörerna är positiva

? : varierande uppgifter i litteraturen/uppgift saknas

4. Valfritt antal snittnivåer ska undersökas.

5. Analyser som särskilt bör kvalitetssäkras via externa kontrollprogram: relevanta immunfärgningar.

Information för klinisk användning

A. Makroskopisk beskrivning:

1. Preparatbeskrivning

2. Beskrivning av förändringar (ex lokalisation, avgränsning, relation till prepytor/resektionsytor och omgivande vävnad samt måttangivelser)

3. Övrigt (ex väsentliga bifynd, söndertrasningar och annat som begränsar möjligheterna till adekvat undersökning)

B. Mikroskopiutlåtande:

1. Tumörtyp enligt WHO med angivande av rent seminom eller annan tumörtyp (annan ren histologisk typ eller blandad histologisk typ). Samtliga förekommande tumörkomponenter anges.

2. Tumörstadium pTNM 2009. Notera att frånvaro/förekomst av kärlinvasion skall anges. Vid behov bör immunhistokemisk undersökning göras avseende kärlinvasion.

3. Andra prognosvariabler: Tumörstorlek.

Tumörinfiltration (ja/nej) i rete testis.

4. Radikalitet.

Rekommenderade klassifikationssystem

WHO Classification of Tumours: Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs 2004 (s 218)

Administrativt

SNOMED-koder

	SNOMED
Germinalcellstumörer	
Intratubular germinalcellsneoplasia, UNS	90642
Tumörer av EN histologisk typ (rena former)	
Seminom	90613
Spermatocytiskt seminoma	90633
Embryonal cancer	90703
Gulesäckstumör	90713
Trophoblastiska tumörer	91003
Teratoma	90803
Dermoidcysta	90840
Teratoma med somatisk malignitet	90843
Tumörer av mer än en histologisk typ (mixed)	
Mixed tumör MED seminom	90853
Mixed tumör UTAN seminom	90813
Sex chord/gonadala/stromala tumörer	
Leydigcell tumör	86501
Malign Leydigcell tumör	86503
Sertolicell tumör	86401
Malign Sertolicell tumör	86403
Granulosacell tumör	86201
Thecom/fibroma	
Thecoma	86000
Fibroma	88100

Not Valid

pTNM 2009

pT0	Ingen tumör
pTis	Intratubulär germinalcellsneoplasi (Cancer in situ).
pT1	Tumör inom testis och epididymis utan vaskulär/lymfatisk invasion. Tumör kan invadera tunica albuginea men inte tunica vaginalis.
pT2	Tumör inom testis och epididymis med vaskulär/lymfatisk invasion eller med tumörutbredning genom tunica albuginea med engagemang av tunica vaginalis.
pT3	Tumör infiltrerar funikel med eller utan vaskulär/lymfatisk invasion.
pT4	Tumör infiltrerar scrotum med eller utan vaskulär/lymfatisk invasion.
pNX	Regionala lymfkörtlar ej undersökta.
pN0	Ingen lymförtelmetastas
pN1	Metastas i körtel ≤ 2 cm och 5 eller färre positiva körtlar < 2 cm
pN2	Metastas i körtel $> 2 - 5$ cm eller fler än 5 metastaser ≤ 5 cm eller extranodal tumörväxt.
pN3	Metastas > 5 cm

Klinisk organisation som granskat och godkänt dokumentet:

SWENOTECA (Swedish - Norwegian Testicular Cancer Group)

Rekommenderad litteratur:

WHO Classification of Tumours. Pathology & Genetics, Tumours of the Urinary System and Male Genital Organs, Lyon 2004.

Annals of Oncology 15: 1377–1399, 2004 European consensus on diagnosis and treatment of germ cell cancer: a report of the European Germ Cell Cancer Consensus Group (EGCCCG)

Emerson R, Ulbright T: Morphological approach to tumour of the testis and paratestis, J Clin Pathol 2007;60:866-880

Emerson RE, Ulbright TM: The use of immunohistochemistry in the differential diagnosis of tumors of the testis and paratestis. Seminars in Diagnostic Pathology 2005

Krag Jacobsen G, Talerman A: Atlas of Germ Cell Tumours 1989

Raghavan D: Germ Cell Tumors: American Cancer Society Atlas of Clinical Oncology, 2003

Ulbright T: Germ cell tumors of the gonads, Mod Pathol 2005, 18, 61-79

Young RH: Testicular tumors – some new and a few perennial problems, Arch Pathol Lab Med 2008 132(4):547-564

För immunhistokemiska exempelvis

<http://www.e-immunohistochemistry.info/>

<http://www.nordiqc.org>

<http://www.ipox.org/>

<http://www.dako.com/asp/algo/default.asp?get=table&table=20>

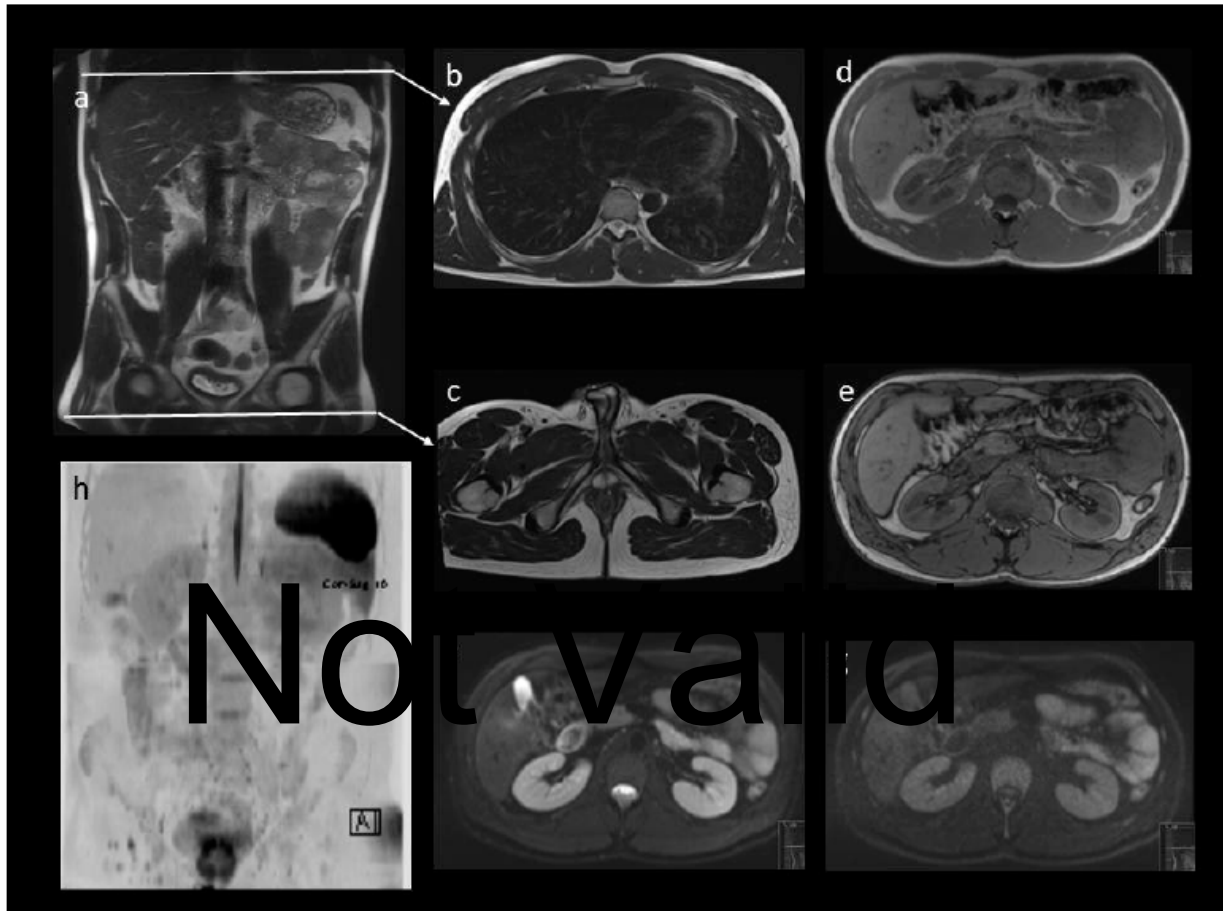
Not Valid

Abdominal Magnetic Resonance Imaging protocol for follow-up of patients operated for testicular cancer

General imaging protocol recommendations for examinations at 1.5 T or 3T

Examination is performed after at least four hours of fasting. A body phased-array coil is used.

Pulse sequences are performed with 5-6 mm section thickness with maximized feasible spatial resolution depending on the available signal with the system used.



a .Coronal Half acquisition single shot turbo-spin echo sequence with limits for upper and lower abdominal transaxial sections outlined

b and c. Transaxial T2-weighted respiratory triggered turbo spin-echo sequence

d and e. Transaxial T1-weighted breath-hold spoiled gradient-echo sequence with fat and water in- (d) and opposed (e) phase.

f and g. Transaxial T2 weighted echo planar imaging diffusion weighted sequences with $b=50$ (f) and $b=800$ (g) (optional)

h Coronal Inverted Maximum Intensity Projection (MIP) diffusion weighted image reconstructed from the volume of $b=800$ sections (optional).

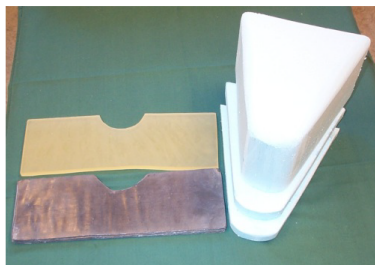
May 15, 2012

Radiotherapy of CIS

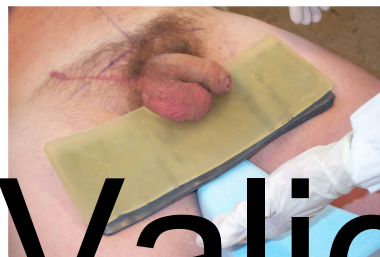
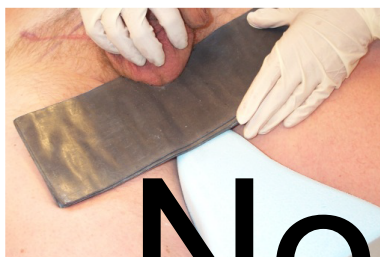
STRÅLDOS

Targetdos skall vara 18 Gy, 2 Gy*9. Detta ger en minimidos i testikeln på 17.1 Gy.

Uppläggning



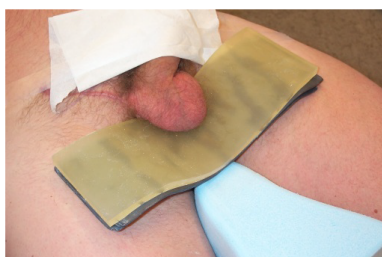
För uppläggningsen behövs ett stöd för blyskyddet (t.ex. en trekant av frigolit), 1 cm tjockt vattenekvivalent bolus, 0.8–1 cm tjockt blyskydd samt ytterligare bolus (ej med på bilden). Blyskyddet och det bolus som skall placeras under testikeln har en halvmåneformad urfasning för bättre passform mot scrotum.



Not Valid

Patienten placeras i ryggläge med benen fixerade brett isär.

Placera blystödet (trekanten av frigolit) mellan benen. Närmast under testikeln placeras 1 cm vattenekvivalent bolus följt av ett 0.8–1 cm tjockt blyskydd. Blyskyddet kan med fördel bestå av flera tunnare skivor.



Tejpa undan penis uppåt. Kring testikeln placeras vattenekvivalent bolus med en utsträckning på minst 2 cm lateralt. Det är viktigt att bolusen har en så bra passform som möjligt.

Vid användandet av ”låga” elektronenergier kan det vara aktuellt att placera bolus även ventralt om testikeln.

17. September 2014

Pasientinformasjon

September 2014

Informasjon til pasienter med testikkelkreft av typen seminom

Du er nylig blitt operert for kreft i testikkelen. Undersøkelse av svulsten har vist at det dreier seg om testikkelkreft av typen seminom. Hos 85 % av pasientene er det ingen tegn til spredning, sykdommen klassifiseres da som stadium I. Hos 15 % av pasientene er sykdommen mer utbredt og har spredt seg til andre steder i kroppen. Prognosen er utmerket med over 99 % helbredelse i stadium I og over 95 % ved spredning.

Denne pasientinformasjonen har to hoveddeler. Den første delen inneholder informasjon til pasienter uten tegn til spredning. Den andre delen inneholder informasjon til pasienter med spredning av sykdommen, samt om behandling av tilbakefall hos pasienter som primært har stadium I.

Pasienter uten tegn til spredning, stadium I

Når det gjelder den videre behandling av din sykdom (etter operasjon av testikkelen), finnes det to alternativer:

1. Kun tette kontroller
2. Forebyggende behandling med en cellegiftkur

Hos rundt 15 % av pasienter med testikkelkreft i stadium I kan det likevel foreligge mikroskopisk spredning av kreftceller som ikke vises på røntgenbilder eller blodprøver. Den vanligste plassen for spredning er i lymfeknuter i buken. Hos noen pasienter kan sykdommen også spre seg til andre organer.

Med forebyggende behandling reduseres risikoen for tilbakefall, men dette innebærer nødvendig behandling av de 80-85 % som ellers aldri ville fått tilbakefall. Vi kan i dag ikke på forhånd vite hvilke pasienter som blir helbredet etter fjerning av testikkelen alene (80-85 %), eller hvem som kommer til å få tilbakefall av sin sykdom uten forebyggende behandling.

Ved tilbakefall av testikkelkreften er behandlingen svært effektiv, og sjansen for å bli helbredet er i utgangspunktet lik uavhengig av hvilket alternativ man velger.

Risikotilpassede anbefalinger

Data tyder på at dersom svulsten er liten (≤ 4 cm) og ikke vokser inn i kanalsystemet i testikkelen så er risikoen for tilbakefall svært liten. Vi vil derfor anbefale kun kontroller til disse pasientene.

Pasienter med en eller to risikofaktorer, dvs. svulst over 4 cm og/eller innvokst i kanalsystemet har en risiko for tilbakefall på 20-25 %. Vi vil hos disse pasientene anbefale en kur forebyggende cellegift i form av karboplatin. Etter pasientens ønske kan man evt. følges med kun tette kontroller.

Behandlingsalternativer: fordeler og ulemper

Bare kontroller

Fordelen er at ingen behandles unødvendig. Man gir altså ingen etterbehandling, men blir nøye kontrollert i ti år. Ulempen er at dersom det påvises et tilbakefall, blir behandlingen mer omfattende med tre-fire cellegiftkurer, eller i sjeldne tilfeller tre uker strålebehandling.

En cellegiftkur

Dette innebærer behandling med én cellegiftkur (Karboplatin), etterfulgt av nøye kontroller i ti år. Cellegiften gis intravenøst (direkte inn i en blodåre). Dette gjøres på poliklinikken i løpet av 30 minutter, og man trenger ikke innleggelse. Den mest plagsomme bivirkningen er kvalme som i stor grad forebygges ved hjelp av kvalmestillende medisin. Antall hvite blodlegemer synker forbigående ca. en uke etter behandlingen. Dette medfører at man kan bli mer utsatt for infeksjoner. Også blodplatene kan synke noe, men sjelden så mye at dette medfører risiko for blødninger. Etter ca. 2 uker er vanligvis blodverdiene normalisert. Behandlingen gir vanligvis ikke håravfall.

Fordelene med å gi en forebyggende cellegiftkur er at 60-70 % av tilbakefall forhindres. Risikoen for senbivirkninger etter en kur med cytostatika vurderes som liten.

Ulempen med forebyggende cellegiftkur er at den kun virker hos 60-70 %, det vil si at man må følges like hyppig og like lenge som pasienter som kun følges med kontroller. I tillegg har 80-85 % ikke mikroskopisk spredning av sykdommen, og dermed ikke behov for denne behandlingen.

De ulike behandlingsalternativer har sine fordeler og ulemper. Vi ønsker derfor at du leser nøye gjennom denne informasjonen og vurderer hva du tror er det beste alternativet for deg.

Pasienter med spredning av testikkelkreft, samt pasienter i stadium I som får tilbakefall av sykdommen

Cellegiftkuren man bruker ved tilbakefall av testikkelkreft kalles BEP-kur og består av tre ulike typer cellegift. BEP-kuren gis (gjennom blodet) i form av medikamentene bleomycin, etoposid og cisplatin. Vanligvis gir man tre kurer med tre ukers mellomrom. I noen tilfeller vil vi benytte kun to typer cellegift, såkalt EP-kur. Da er 4 kurer nødvendig. Behandlingen gis vanligvis poliklinisk. Cellegiftkurer gis på fem etterfølgende dager. Ved BEP-kur gis påfyll av det ene stoffet etter to uker (melomkur).

Cellegiftbehandling gir akutte bivirkninger, som enkelte ganger kan være alvorlige. Den mest ubehagelige bivirkningen er oftest kvalme og brekninger. Dette kan forhindres og alltid reduseres ved moderne kvalmebehandling. Oftest kommer det håravfall to til fire uker etter den første cellegiftbehandlingen. Etter 3 kurer vil man miste alt hår. Håret begynner å vokse ut igjen noen uker etter siste kur.

Antall hvite blodlegemer kommer til å synke de første to ukene etter behandlingen, og man kan på grunn av dette være mer utsatt for infeksjoner. Også andre blodverdier kan påvirkes, men etter ca. tre uker er disse vanligvis normalisert. En del pasienter kan føle en plagsom tretthet som kan vedvare mellom kurene og ca. en måned etter siste kur.

Det er også kjent at 3–4 cellegiftkurer kan gi langtidsbivirkninger i form av redusert hørsel og nyrefunksjon, lett økt risiko for hjerte- og karsykdom samt noe redusert sædkvalitet.

Strålebehandling mot lymfeknuter i buken

I noen få tilfeller benyttes strålebehandling i behandlingen av seminom. Strålebehandling kan benyttes forebyggende i klinisk stadium I og som behandling ved spredning.

Strålebehandlingen gis over 2-3 uker (totalt 10-15 behandlinger med 5 behandlinger per uke. Bivirkninger av behandlingen kan være kvalme, diaré og slapphet.

Strålebehandling medfører en økt risiko for ny kreft senere i livet, dette gjelder spesielt yngre pasienter (under 35 år).

Oppfølging

Etter gjennomført behandling følges du tett med legeundersøkelse, bilder (MR/røntgen) og blodprøver. Kontrollene følger et fastsatt skjema. Kontrollene blir mindre hyppige etterhvert.

Konfidensialitet og dataregistrering

Vi ber om din tillatelse til å registrere relevant informasjon omkring utredning, behandling og oppfølging av din sykdom. Disse opplysningene lagres så ved det sykehus som har ansvar for din behandling (Helse Nord: UNN Tromsø, Helse Midt: St Olavs Hospital, Helse Vest: Haukeland, Helse Sør-Øst: Oslo Universitetssykehus). Kun leger og forskningsmedarbeidere involvert i registreringen av opplysningene omkring din sykdom vil kunne identifisere deg. Opplysninger skal brukes til forskning innen SWENOTECA, som er samarbeidsgruppen for testikkelkreft i Norge og Sverige. Opplysninger om din sykdom vil senere bli koblet sammen med informasjon fra andre sykehus i Norge og Sverige, men da vil opplysningene være aidentifisert og ingen vil kunne gjenkjenne deg i databaser eller i publikasjoner. Forskningsmedarbeidere har taushetsplikt på linje med de som behandler deg ved sykehus.

Slik registreringen og publisering av resultater i tidsskrifter er nødvendig for kontinuerlig å vurdere fordeler og ulemper ved de ulike behandlingsalternativer, og gir oss kunnskap som kan lede til best mulig behandling for pasienter med testikkelkreft. En slik registrering innebærer en ekstra trykkesikkerhet også for ditt eget etterkontroll-opplegg.

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SAMTYKKEERKLÆRING

Jeg har lest og forstått ovenstående informasjon.

Jeg gir samtykke til at medisinske opplysninger som er relevante for utredning, behandling og etterkontroll av min sykdom hentes fra min journal, og registreres med navn og personnummer i en medisinsk database ved mitt behandlende sykehus.

Sted..... Dato/..... 20.....

Navn(blokkbokstaver).....

Fødselsdato.....

Signatur.....

Behandlernde lege.....

Not Valid

Patientinformation

September 2014

Information till patienter med testikelcancer av typ seminom

Du har nyligen blivit opererad för cancer i testikeln. Mikroskopisk undersökning av tumören har visat att det rör sig om typen seminom. Hos 85% av patienterna kommer utredningen med blodprover och röntgenundersökningar inte påvisa någon spridning av tumören och då klassificeras den som stadium I. Hos 15% av patienterna är sjukdomen mer utbredd och har spridit sig till andra ställen i kroppen.

Prognosen är utmärkt, vid stadium I botas 99% och vid spridd sjukdom botas 95%.

Denna patientinformation består av två huvuddelar. Den första delen innehåller information till patienter utan tecken till spridning av tumören, stadium I. Den andra delen innehåller information till patienter med påvisad spridning av sjukdomen, samt om behandling av återfall hos patienter som från början var i stadium I.

Patienter utan tecken till spridning, stadium I

När det gäller den vidare behandlingen av din sjukdom (efter operation av testikeln) finns det två alternativ:

1. Enbart kontroller
2. Förebyggande (adjuvant) behandling med en cytostatikakur (cellgift) och därefter kontroller.

Hos ca 15–20% av patienter med testikelcancer i stadium I kan det föreligga icke påvisbar spridning av tumörceller, oftast till lymfkörtlarna längs ryggraden i buken. Hos dessa patienter kommer sjukdomen att återkomma, vilket upptäcks när tumörcellerna i lymfkörtlarna tillväxer. Hos enstaka patienter kan också sjukdomen sprida sig till andra organ.

Med adjuvant behandling minskar man risken för återfall men samtidigt behandlas de 80–85%, som ändå inte skulle fått återfall, i onödan. Idag kan man inte på förhand veta vilka patienter som utan tilläggsbehandling kommer att förbli friska (80–85%), eller vilka som kommer få återfall av sin sjukdom (15-20%).

Vid ett återfall av testikelcancer finns effektiv behandling.

De olika behandlingsalternativen har sina för- och nackdelar. Vi vill därför att du läser igenom denna information noga och värderar vad du tror är det bästa alternativet för dig. [Oavsett vilket alternativ du väljer är prognosen lika god.](#)

Risicanpassade behandlingsalternativ

Data tyder på att om tumörstorleken är liten ($\leq 4\text{cm}$) och tumören inte växer in i kanalsystemet i testikeln är risken för återfall mycket liten. Vi rekommenderar därför enbart kontroller för de patienter som saknar riskfaktorer.

Patienter med en eller två riskfaktorer har 20-25% risk för återfall och vi rekommenderar därför adjuvant cytostatikabehandling. Om man som patient efter noggrann information inte vill ha tilläggsbehandling trots förekomst av riskfaktorer kommer man att följas med enbart kontroller.

Behandlingsalternativ: för- respektive nackdelarEnbart kontroller

Fördelen är att ingen behandlas i onödan. Ingen efterbehandling ges utan du blir i stället noga kontrollerad under cirka 10 år. Nackdelen är att om du får ett återfall så blir behandlingen för detta mer omfattande med tre, ibland fyra, cytostatikakurer bestående av tre olika cytostatiska läkemedel (BEP), eller mer sällan strålbehandling i tre veckor.

En cytostatikakur

En kort förebyggande cytostatikabehandling med ett läkemedel (Karboplatin), samt därefter kontroller under cirka 10 år.

Behandlingen ges polikliniskt under ca 30 minuter i ett dropp i armens blodkärl. Den mest besvärande biverkan är illamående som dock till största delen förhindras av mediciner mot illamåendet. Antalet vita blodkroppar sjunker de första veckorna efter behandlingen vilket medför att man kan bli infektiöskänslig. Även blodplättarna kan sjunka något, men sällan så att det får några konsekvenser för blodets levringsförmåga. Efter ca 3 veckor brukar man vara återställd. Behandlingen leder i allmänhet inte till håravfall.

Fördelarna med att ge en tilläggsbehandling med cytostatika är att 60-70% av alla återfall förhindras. Risken för bestående biverkningar efter en kur cytostatika är liten.

Nackdelen med att ge tilläggsbehandling med en cytostatikakur är att eftersom den bara minskar risken för återfall med två tredjedelar så behöver kontrollerna ändå pågå i tio år. Dessutom saknar 80-85% de mikroskopiska cancer cellerna man vill behandla bort och är därmed inte i behov av behandlingen. Förenklat kan man säga att bara 15-20% av patienter kommer ha nytta av tilläggsbehandling.

Patienter med spridning av sjukdomen, samt patienter i stadium som får återfall av sjukdomen

Den cytostatikakur man vanligtvis använder vid spridning av sjukdomen eller vid ett eventuellt återfall benämns BEP-kur och vanligtvis ges tre, ibland fyra, sådana kurer. En BEP-kur (bleomycin, etoposid, platinol), ges som dropp under fem dagar (dag 1-5) samt en injektion av bleomycin dag 15. Nästa behandlingsomgång börjar dag 22, dvs tre veckor efter

att första behandlingen påbörjats. I vissa fall ges istället EP-kur (etoposid, platinol) med bara två sorters cytostatika men då måste man ge fyra sådana kurer.

De mest besvärande biverkningarna av BEP-kuren är illamående och kräkningar under och några dagar efter behandlingen. Dessa besvär kan dock i allmänhet förhindras effektivt med hjälp av mediciner mot illamående. Oftast kommer håravfall ca 2-4 veckor efter man fått sin

5-dagarsbehandling. Håret börjar växa igen ca 6 veckor efter att sista behandlingen givits. Antalet vita blodkroppar kommer att sjunka de första två veckorna efter start av behandlingen och man kan på grund av detta vara mer känslig för infektioner. Även andra blodvärden kan påverkas, men efter cirka tre veckor har de i allmänhet normaliserats. En del patienter kan känna en besvärande trötthet, som kan fortsätta under 3-4 veckor efter att all behandling avslutats. Det är också känt att biverkningar bland annat i form av hörsel och njurfunktionsskador kan uppstå efter cytostatikabehandlingen. Andra biverkningar som är relativt vanliga är tinnitus (öronsus) samt så kallat Raynauds fenomen (fingrarna blir kalla och vita/blå/röda/vid kyla), domningar och stickningar i händer och fötter, men hos de flesta är dessa besvär övergående, men dock ej hos alla. Det är även känt att 3-4 cytostatikakurer kan ge långtidsbiverkningar i form av liten ökad risk för hjärt-kärlsjukdom samt nedsatt produktion av spermier.

Strålbehandling mot lymfkörtlarna längs ryggraden i buken

I vissa fall används strålbehandling vid behandling av seminom. Strålbehandlingen pågår i två-tre veckor (totalt 10-15 behandlingar med 5 behandlingar per vecka). En av biverkningarna vid behandlingen är illamående men detta kan vanligtvis förhindras med modern behandling mot illamåendet. Andra biverkningar kan vara trötthet och diarré.

Det finns en viss risk för att denna behandling på lång sikt kan leda till en ny cancerform hos enskilda individer. Hur stor denna risk är vet man inte säkert då modern strålbehandling är olik den som man gav tidigare. Tidigare gavs en högre stråldos. Man vet därför inte säkert om de undersökningar, som har påvisat ökad förekomst av ny cancer gäller för dem som får behandling i dag med en lägre stråldos.

Uppföljning

När all behandling är avslutad sker uppföljning med kontroll av blodprover och röntgenundersökningar samt läkarbesök, tätare i början men med glesare intervall efter att några år passerat.

Vi vill be om ditt tillstånd att få registrera uppgifter som rör din sjukdom, behandlingen och förloppet av sjukdomen i det Svenska Testikelcancerregistret. Det är ett av sekretess skyddat nationellt kvalitetsregister med stöd från Sveriges Kommuner och Landsting,

Denna registrering har betydelse för att möjliggöra kontinuerlig utvärdering av behandlingen, samt för att framöver kunna dra slutsatser som skall leda till att bästa tänkbara behandling ges till patienter med testikelcancer.

Denna registrering ger oss även möjlighet att försäkra oss om att alla patienter får behandling enligt de nationella vårdprogram som gäller.

Vi kan också vid behov behöva gå igenom dina journalhandlingar och tumörpreparat, för att komplettera uppgifter i registret, om de uppgifter som skickats in på förtryckta blanketter inte varit kompletta eller varit oklara.

Om du inte samtycker till denna registrering skall du meddela detta till oss.

.....

kontaktperson

telefonnummer

Patientinformation om medverkan i kvalitetsregister

För att kunna förbättra vården registrerar vi uppgifter om klinikens patienter i kvalitetsregister. Kvalitetsregister är till för att säkra och utveckla vårdens kvalitet och detta görs genom att jämföra resultat mellan olika vårdenheter i regionen och i landet. Det övergripande syftet är att främja god vård för alla, oavsett bostadsort, kön och ålder. Uppgifterna i registret kan också användas för att framställa statistik och i forskningen för att vinna ny kunskap och bidra till en förbättrad vård för alla som drabbas av samma sjukdom.

Vad samlas in och hur hanteras uppgifterna?

I kvalitetsregistret finns uppgifter om din sjukdom och den utredning och behandling som du fått vid denna vårdenheter. Informationen sammanställs med uppgifter från andra patienter och statistik sammanställs på grupp-nivå. Det innebär att det inte går att identifiera eller spåra enskilda individer i det sammanställda materialet. Används uppgifterna för forskning måste varje forskningsprojekt godkännas av en etikprövningsnämnd.

Hur skyddas dina uppgifter?

Uppgifterna som finns om dig i kvalitetsregistret skyddas av flera lagar. Detta betyder att informationen har samma skydd som de uppgifter som finns i patientjournalen.

Sekretess

Dina uppgifter omfattas av sekretess enligt Offentlighets- och sekretesslagen. Det innebär som huvudregel att uppgifter om dig endast får lämnas ut från registret om det står klart att varken du eller någon närstående till dig lider men om uppgiften lämnas ut.

Säkerhet och åtkomst

Dina uppgifter skyddas mot obehöriga. Det finns särskilda krav som bl.a. innebär att bara den som har rätt till uppgifterna får ha tillgång till dem, att de skall kontrolleras att ingen obehörig tagit del av informationen, att uppgifterna skyddas genom kryptering samt att inloggning för att få tillgång till dina uppgifter bara får ske på ett säkert sätt. Endast sjukvårdspersonal och registerpersonal med tystnadsplikt har tillgång till dina uppgifter.

Gallring

Dina uppgifter tas bort när de inte längre behövs för att utveckla och säkra kvaliteten i vården.

Vem är ansvarig för uppgifterna som registreras i kvalitetsregister?

För varje kvalitetsregister finns en centralt personuppgiftsansvarig myndighet, oftast ett landsting.

Dina rättigheter som patient

Din medverkan i registret är frivillig och påverkar inte den vård du får. Om du inte vill att dina uppgifter registreras, vänd dig till den vårdgivare du besökt

Du har när som helst rätt att få dina uppgifter utplånade ur registret

Du har rätt att få information om vid vilken vårdenheter och tidpunkt någon tagit del av dina uppgifter

Du har en gång per år, kostnadsfritt, rätt att få veta vilka uppgifter som har registrerats om dig (registerutdrag).

En sådan ansökan skall vara skriftlig, undertecknad och skickas till centralt personuppgiftsansvarig (se nedan)

Du bidrar till en bättre vård

Genom registrering av dina uppgifter i kvalitetsregistret är du med och förbättrar vården. Ju fler som är med desto statistiskt säkrare blir resultaten.

För att få ett utdrag på vilka uppgifter som registrerats i kvalitetsregistret eller om du vill ha dina uppgifter borttagna kontakta Centralt Personuppgiftsansvarig. Vårdenheten eller Regionalt cancer centrum i din region kan lämna besked om vilken myndighet som är Centralt Personuppgiftsansvarig för det kvalitetsregister som är aktuellt för din del.

Vill du ha mer information om kvalitetsregister- se hemsidan för Regionalt cancercentrum www.cancercentrum.se

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