EAU Guidelines on Testicular Cancer

Disease Management

DISEASE MANAGEMENT

Cis-platin based chemotherapy, to which testicular cancer (TC) is exquisitely sensitive, in combination with surgery and in highly selected cases, radiotherapy, has resulted in the high cure rates seen with this disease. Careful staging at diagnosis, adequate early treatment based on a multidisciplinary approach, rigorous follow-up and adequate initiation of salvage therapies are critical to successful outcomes.

Stage I germ cell tumours:

GERM CELL NEOPLASIA "IN SITU": If the contralateral testis is normal, management options include orchidectomy or close observation, as the five-year risk of developing TC is 50% . In a patient with a solitary testis, local radiotherapy (18-20 Gy in fractions of 2 Gy) should be considered.

SEMINOMA GERM CELL TUMOUR CLINICAL STAGE I:

Approximately 15% patients have subclinical metastatic disease, usually in the retroperitoneum, and will relapse after orchidectomy alone. Adjuvant treatment decisions should be based on thorough discussions with the patient, incorporating potential advantages and disadvantages, as well as individual patient circumstances.

Recommendations	Strength rating
Fully inform the patient about all available management options, including surveillance or adjuvant therapy after orchidectomy, as well as treatment-specific recurrence rates and acute and long-term side effects.	Strong
Offer surveillance as the preferred management option if resources are available and the patient is compliant.	Strong
Offer one dose of carboplatin at area under curve (AUC) 7 if adjuvant chemotherapy is considered.	Strong
Do not perform adjuvant treatment in patients at very low-risk of recurrence (no risk factors).	Strong
Do not routinely perform adjuvant radiotherapy.	Strong
Adjuvant radiotherapy should be reserved only for highly selected patients not suitable for surveillance and with contraindication for chemotherapy.	Strong

NON-SEMINOMATOUS GERM CELL TUMOURS CLINICAL STAGE I:

Management options comprise surveillance, adjuvant chemotherapy or retroperitoneal lymph node dissection. Overall, approximately 70% are cured with orchiectomy alone. In those with the high-risk feature lymphovascular invasion (LVI), relapse occurs in 50% vs 15% in those without LVI.

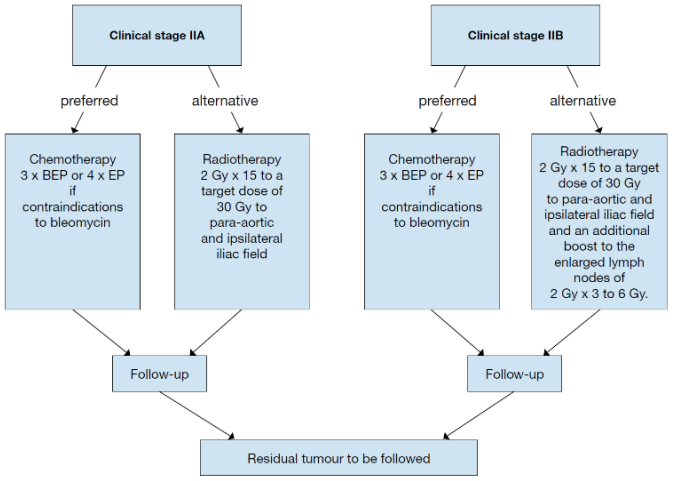
Recommendations	Strength rating
Stage IA (pT1, no vascular invasion): low-risk	
Offer surveillance if the patient is willing and able to comply.	Strong
Offer adjuvant chemotherapy with one course of cisplatin, etoposide, bleomycin (BEP) in low-risk patients not willing (or unsuitable) to undergo surveillance.	Strong
Stage IB (pT2-pT4): high-risk	
Offer adjuvant chemotherapy with one course of BEP, or surveillance and discuss the advantages and disadvantages.	Strong
Offer surveillance to patients not willing to undergo adjuvant chemotherapy.	Strong
Offer nerve-sparing retroperitoneal lymph node dissection to highly selected patients only; those with contraindication to adjuvant chemotherapy and unwilling to accept surveillance.	Strong
Primary retroperitoneal lymph node dissection should be advised in men with post-pubertal teratoma with somatic malignant component.	Weak

Metastatic germ cell tumours:

The first-line treatment of metastatic GCTs depends on:

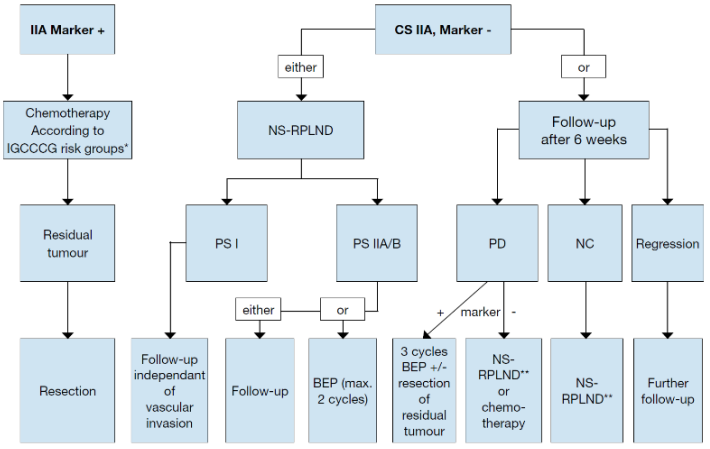
- **The histology of the primary tumour**
- **Prognostic groups**
- **Serum tumour marker decline during the first cycle of chemotherapy in poor-prognosis patients.**

Seminoma clinical stage IIA and B



* When enlarged retroperitoneal lymph nodes are < 2 cm and with normal markers, treatment should not be initiated unless metastatic disease is unequivocal based on biopsy, increasing nodal size/number, or subsequent marker rise.
BEP = cisplatin, etoposide, bleomycin; EP = etoposide, cisplatin.

Stage II A non-seminoma



* Most of the patients will be good prognostic group (BEP x3 or PE x4). ** In case of PS II A/B patient can be followed-up or receive adjuvant chemotherapy (maximum of 2 cycles). BEP = cisplatin, etoposide, bleomycin; NS = nerve-sparing; RPLND = retroperitoneal lymph node dissection; PS = pathological stage; PD = progressive disease; NC = no change.

Metastatic disease (stage II C and III)

In cases of life-threatening disseminated disease, chemotherapy should commence immediately, particularly when the clinical picture supports TC. Orchidectomy can be delayed until clinical stabilisation occurs or subsequently be performed in combination with resection of residual lesions.

Cisplatin, etoposide, bleomycin (BEP) regimen (interval 21 days)

Drug	Dosage	Duration of cycles
Cisplatin	20 mg/m^2	Days 1-5*
Etoposide	100 mg/m^2	Days 1-5
Bleomycin	30 mg	Days 1, 8, 15

Plus, hydration.

Recommendations	Strength rating
Balance the individual patients' potential benefits and risks of thromboprophylaxis during first-line chemotherapy in men with metastatic germ cell tumours.	Weak
Avoid use of central venous-access devices during first-line chemotherapy whenever possible.	Weak

Recommendations	Strength rating
Treat low-volume non-seminomatous germ cell tumour (NSGCT) stage IIA/B with elevated markers like metastatic good- or intermediate-prognosis risk group IGCCCG with three or four cycles of cisplatin, etoposide, bleomycin (BEP).	Strong
Nerve-sparing retroperitoneal lymph node dissection when performed by an experienced surgeon in a specialised centre is the recommended initial treatment in clinical stage (CS) IIA NSGCT disease without elevated tumour markers.	Weak
Repeat staging after six weeks before making a final decision on further management should be considered in patients with small volume (CS IIA < 2 cm) marker-negative NSGCT.	Weak
Treat metastatic NSGCT (stage ≥ IIC) with an intermediate prognosis with four cycles of standard BEP	Strong
In metastatic NSGCT with a poor-prognosis, treat with one cycle of BEP, (or cisplatin, etoposide and ifosfamide [PEI], in cases with pulmonary dysfunction), followed by tumour marker assessment after three weeks. Continue the same schedule up to a total of four cycles with favourable marker decline. With unfavourable decline, initiate chemotherapy intensification.	Weak
Perform surgical resection of visible (> 1 cm) residual masses after chemotherapy for NSGCT when serum levels of tumour markers are normal or normalising.	Strong
Initially offer cisplatin-based chemotherapy according to IGCCCG prognosis groups, or alternatively radiotherapy to seminoma patients with stage II A/B and, inform the patient of potential long-term side effects of both treatment options.	Weak
Treat seminoma stage IIC and higher, with primary chemotherapy according to IGCCCG classification (BEP x 3 in good-prognosis and BEP x 4 in intermediate prognosis).	Strong