North of Scotland Clinical Management Guideline (CMG): Testicular Cancer Last Updated 20/10/2020

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For symptoms of suspected urological cancers, please refer to the Scottish Referral Guidelines for Suspected Cancer

General Principles

- All patients referred with a suspicion of testicular cancer need to be treated equally whether referred as USC, Urgent or Routine by referral GP / HCP / other speciality.
- All patients must be discussed at MDT meeting throughout their patient journey as required.
- Patients with symptoms potentially indicative of testicular cancer should have an urgent testicular ultrasound and if malignancy suspected, urgent review by urology team.
- Patients should be vetted in accordance with the Scottish Referral Guidelines for Suspected Cancer.
- Where available, clinical trials should always be considered as an option for all eligible patients and consideration given to referral to other Scottish boards.
- Patients must be involved in decision-making relating to their care with informed consent required for patients undergoing treatment.
- All patients should be referred to or made aware of the Clinical Nurse Specialist services available in the North of Scotland, for assessment and ongoing advice, education, support and coordination.
- The wishes of the patients must influence decision-making with respect to treatment choices within this CMG.
- A list of SACT regimens is provided (page 10).
- Full regional SACT Protocols will be developed and linked to from this document.

Contents

North Cancer Alliance

Initial Evaluation

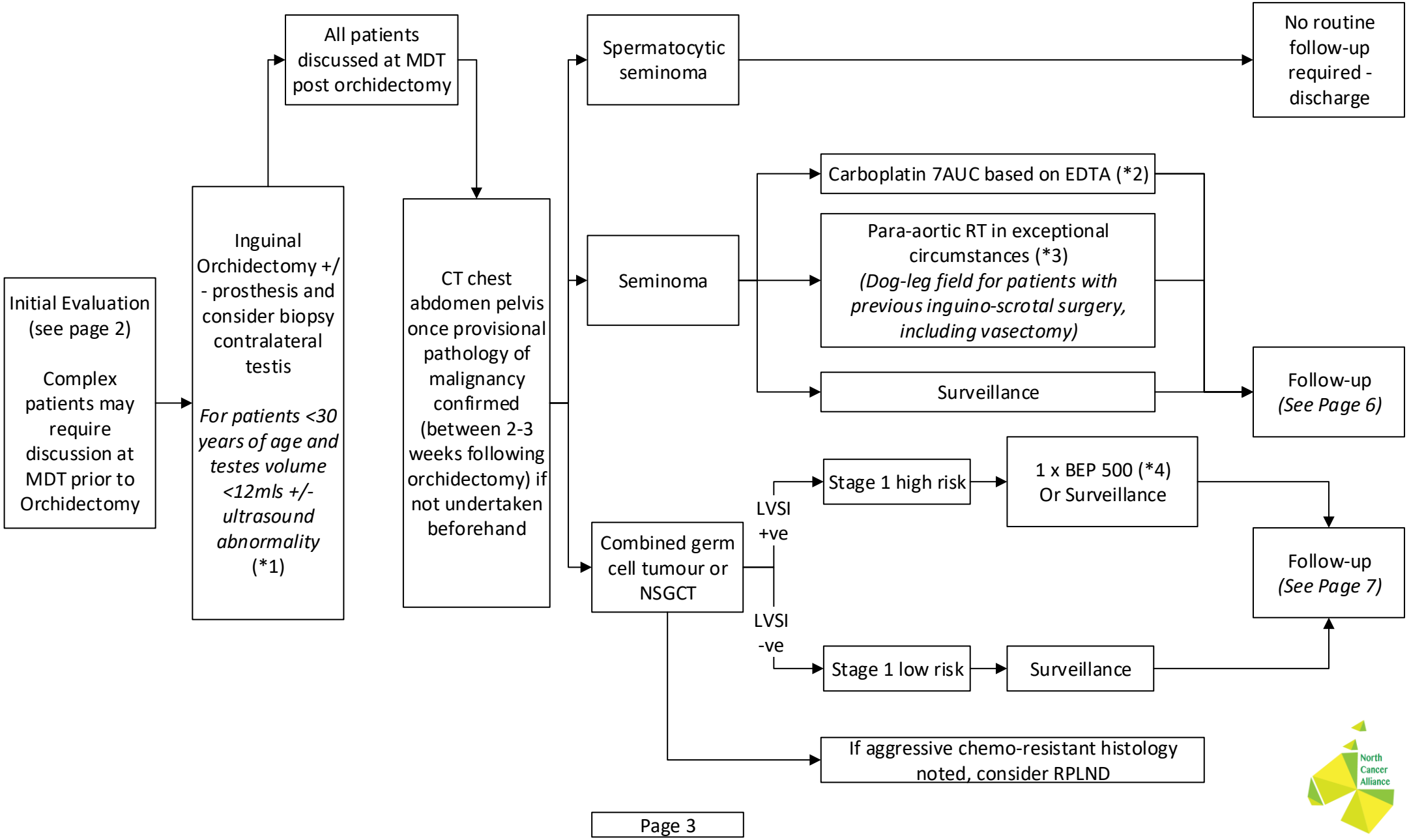
- Patient history and clinical examination
- Full Blood Count, Liver Function Test, Urea & Electrolytes
- Tumour Markers (AFP, HCG, LDH)
- Biopsy of extra-gonadal site if relevant
- Testicular ultrasound
- Chest X-Ray
- CT chest abdomen and pelvis (prior to histology if grossly elevated markers, or suspicion of metastatic disease from CXR / US)

For relevant patients:

- Semen cryopreservation after HIV and Hepatitis B & C testing.
- Brain MRI for those with HCG > 10,000 or >20 pulmonary metastases, or poor prognosis non-seminomas

North of Scotland Clinical Management Guideline (CMG): Testicular Stage 1 Seminoma or NSGCT Last Updated 20/10/2020

Evaluation	Primary Treatment	Adjuvant Treatment	Follow-up



North of Scotland Clinical Management Guideline (CMG): Testicular Metastatic Germ Cell Cancer Prognosis

Last Updated 20/10/2020

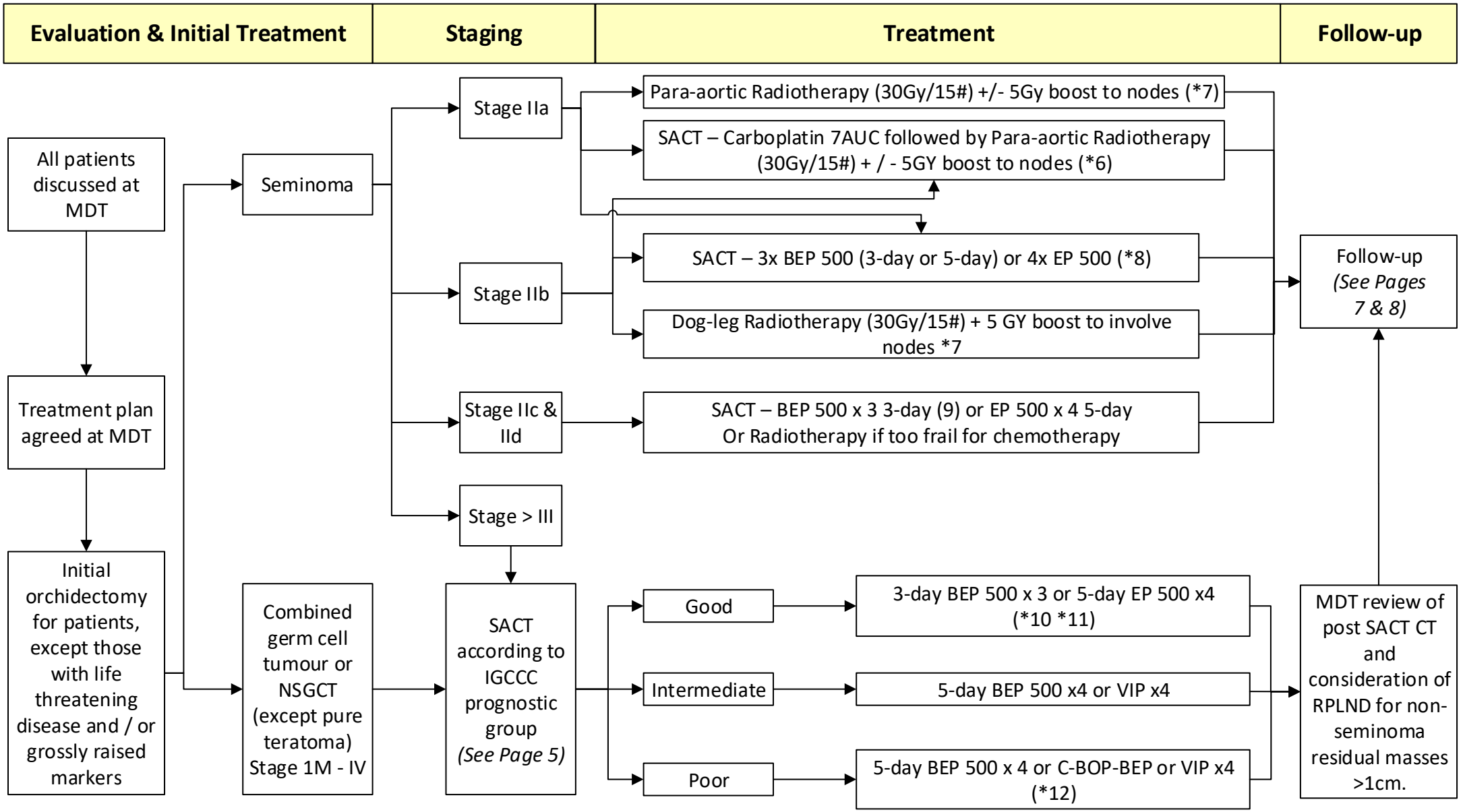
Metastatic Germ Cell Cancer IGCCCG International Prognostic Classification (*9)

Non-Seminoma	Seminoma
GOOD PROGNOSIS	
Testis/Retroperitoneal primary **And** No non-pulmonary visceral metastases **And** Good markers-*all of:* AFP<1000ng/ml and hCG <5000iu/L and LDH<1.5 xULN **56% of non-seminomas** **5yr PFS 89%** **5yr OS 92%**	Any primary site **And** No non-pulmonary visceral metastases **And** Normal AFP, any hCG, any LDH **90% of seminomas** **5 yr PFS 82%** **5 yr OS 86%**
INTERMEDIATE PROGNOSIS	
Testis/Retroperitoneal Primary **And** No non-pulmonary visceral metastases **And** Intermediate markers – ***any of****:* 10 000 ng/mL > AFP > 1 000 ng/mL or 50 000 iU/l > hCG >5 000iu/l or 10 x ULN > LDH >1.5 x ULN **28% non-seminoma** **5yr PFS 75%** **5 yr OS 80%**	Any primary site, **And** Non-pulmonary visceral metastases **And** Normal AFP, any hCG, any LDH **10% seminomas** **5 yr PFS 67%** **5 yr OS 72%**
POOR PROGNOSIS	
Mediastinal Primary, **Or** Non-pulmonary visceral metastases **Or** Poor markers – ***any of:*** AFP > 10 000 ng/mL or hCG>50 000 iU/L or LDH > 10 x ULN **16% of non-seminoma** **5 yr PFS 41%** **5yr OS 48%**	No patients classified as poor prognosis

NB: Refers to nadir markers post orchidectomy (where appropriate)

North of Scotland Clinical Management Guideline (CMG): Testicular Seminoma or NSGCT, Advanced Stage

Last Updated 20/10/2020



Follow up schedule for Stage 1 Seminoma

STRATEGY	Year 1	Year 2	Year 3	Year 4	Year 5
Surveillance Clinic visits* CXR	3-4 monthly No CXR	3-4 monthly No CXR	6 monthly No CXR	6-12 monthly No CXR	6-12 monthly No CXR
Surveillance Imaging of abdomen§	6 monthly (CT/MRI)	6 monthly (CT/MRI)	36 month (CT/MRI)	nil	60 month (CT/MRI)
Adjuvant Carboplatin Clinic visits* CXR	4-6 monthly No CXR	4-6 monthly No CXR	6-monthly No CXR	6-12 monthly No CXR	6-12 monthly No CXR
Adjuvant Carboplatin Imaging of abdomen§	12 month (CT/MRI)	24 month (CT/MRI)	36 month (CT/MRI)	nil	60 month (CT/MRI)

- *each clinic visit involves an assessment of symptoms, clinical examination & tumour markers (AFP and HCG); LDH has not been shown to be helpful in the follow up in patients with germ cell tumours
- § may include CT of pelvis as well (if prior inguinoscrotal surgery)
- Beyond 5 years discharge with note for GP indicating symptoms for prompt referral
- If clinical of symptoms of androgen deficiency check testosterone SHBG, FSH, LH on early morning sample
- BP, fasting lipids and glucose years 1,3 & 5

Follow up schedule for Metastatic Seminoma (Post Radiotherapy for Stage IIA/B, Post-Chemotherapy for Stage II-IV)

STRATEGY	Year 1	Year 2	Year 3	Year 4	Year 5!!
After radical radiotherapy or chemotherapy.	3-monthly clinic visit*	4-monthly clinic visit*	6-monthly clinic visit*	6-monthly clinic visit*	6-monthly clinic visit*
	If post treatment CT abdomen and pelvis scan is normal, no further routine CT scans. If post treatment CT scan abnormal, repeat the CT scan every six months for 18 months but stop as soon as CT scan is normal or appearance is stable				

- *each clinic visit involves an assessment of symptoms, clinical examination, chest X-ray & tumour markers (AFP and HCG); LDH has not been shown to be helpful in the follow up in patients with germ cell tumours
- Beyond 5 years discharge with note for GP indicating symptoms for prompt referral
- If clinical of symptoms of androgen deficiency check testosterone SHBG, FSH, LH on early morning sample
- BP, fasting lipids and glucose years 1,3 & 5
- ‼ **No discharge for those second line treated (after 3 or 4 cycles of platinum based chemotherapy) patients**

Follow up schedule for Stage 1 Non-seminomatous/Mixed Germ Cell Cancer

STRATEGY	Year 1		Year 2	Year 3	Year 4	Year 5!!
T1 Low Risk Surveillance Clinic visits* CXR	0-3 months	4 weekly*	™8-12 weekly*	™3-4 monthly*	6 -12 monthly*	6 -12 monthly*
	3-12 months	™4-8 weekly*				
	CXR alternate visits		6 monthly CXR	No CXR	No CXR	No CXR
T1 Low Risk Surveillance Imaging§	CT (chest) abdomen at 3 & 12 months§		Nil	Nil	Nil	CT CAP @ 60 months if TD\YST
T2≥ High Risk Surveillance Clinic visits* CXR	monthly* No CXR (due to CT frequency)		2-monthly* alternating with CT 3 monthly	3-monthly* 36 months	4-monthly* No CXR	6-monthly* 60 months
T2≥ High Risk Surveillance Imaging§	CT CAP 3, 6, 12		CT CAP 18, 24	Nil	Nil	CT CAP @ 60 months if TD\YST
T2≥ High Risk *Post 1 cycle* of Adjuvant $BE_{500}P$ Clinic visits* CXR	0-6 months	8 weekly*	3-monthly*	4-monthly*	6-monthly*	6-monthly*
	7-12 months	12 weekly*				
	CXR alternate visits		CXR alternate visits	36 months	No CXR	No CXR
Imaging§	CT CAP	6 &12 months	CT CAP 24 months	Nil	Nil	CT CAP 60 months

- *each clinic visit involves an assessment of symptoms, clinical examination, chest x-ray (**as per above schedule**) & tumour markers (AFP and HCG); LDH has not been shown to be helpful in the follow up in patients with germ cell tumours.
- ™ those with raised pre-operative markers should be considered for the follow up with the minimum of interval between visits
- § may include CT of pelvis as well (if prior inguinoscrotal surgery)
- ‼ **No discharge for those with differentiated elements in initial orchidectomy specimen**
- Beyond 5 years discharge with note for GP indicating symptoms for prompt referral
- If clinical of symptoms of androgen deficiency check testosterone SHBG, FSH, LH on early morning sample
- BP, fasting lipids and glucose years 1,3 & 5

Follow up schedule for Non-seminomatous/Mixed Germ Cell Cancer
Mixed Germ Cell Cancer (Stage IM-IV)

STRATEGY	Year 1	Year 2	Year 3	Year 4	Year 5!!
After chemotherapy (+/- resection of residual masses) Clinic visits*	1-3 monthly for 6 months then 2-3 monthly for 6 months	3 monthly	6 monthly	6 monthly	6 monthly
CXR	6 -12 monthly CXR	12 monthly CXR	12 monthly CXR	12 monthly CXR	12 monthly CXR
Imaging§	NO CT/MRI	NO CT/MRI	NO CT/MRI	NO CT/MRI	CT CAP @ 60 months if TD\YST
	CT of CAP after treatment and if CT normal, no further routine CT scans. If post-treatment CT is abnormal, then ongoing imaging of the area of abnormality is required, this will be bespoke for each such patient and MRI (Abdomen ±pelvis) can be considered to reduce radiation exposure.				

- *each clinic visit involves an assessment of symptoms, clinical examination, chest x-ray (**as per above schedule**) & tumour markers (AFP and HCG); LDH has not been shown to be helpful in the follow up in patients with germ cell tumours
- ‼ **No discharge for those with differentiated elements in initial orchidectomy or subsequent resection specimens or for poor prognosis or second line treated (after 3 or 4 cycles of platinum based chemotherapy) patients**
- Beyond 5 years discharge with note for GP indicating symptoms for prompt referral
- If clinical of symptoms of androgen deficiency check testosterone, SHBG, FSH, LH on early morning sample
- BP, fasting lipids and glucose years 1,3 & 5

North of Scotland Clinical Management Guideline (CMG): Testicular Stage 1 Seminoma or NSGCT relapse

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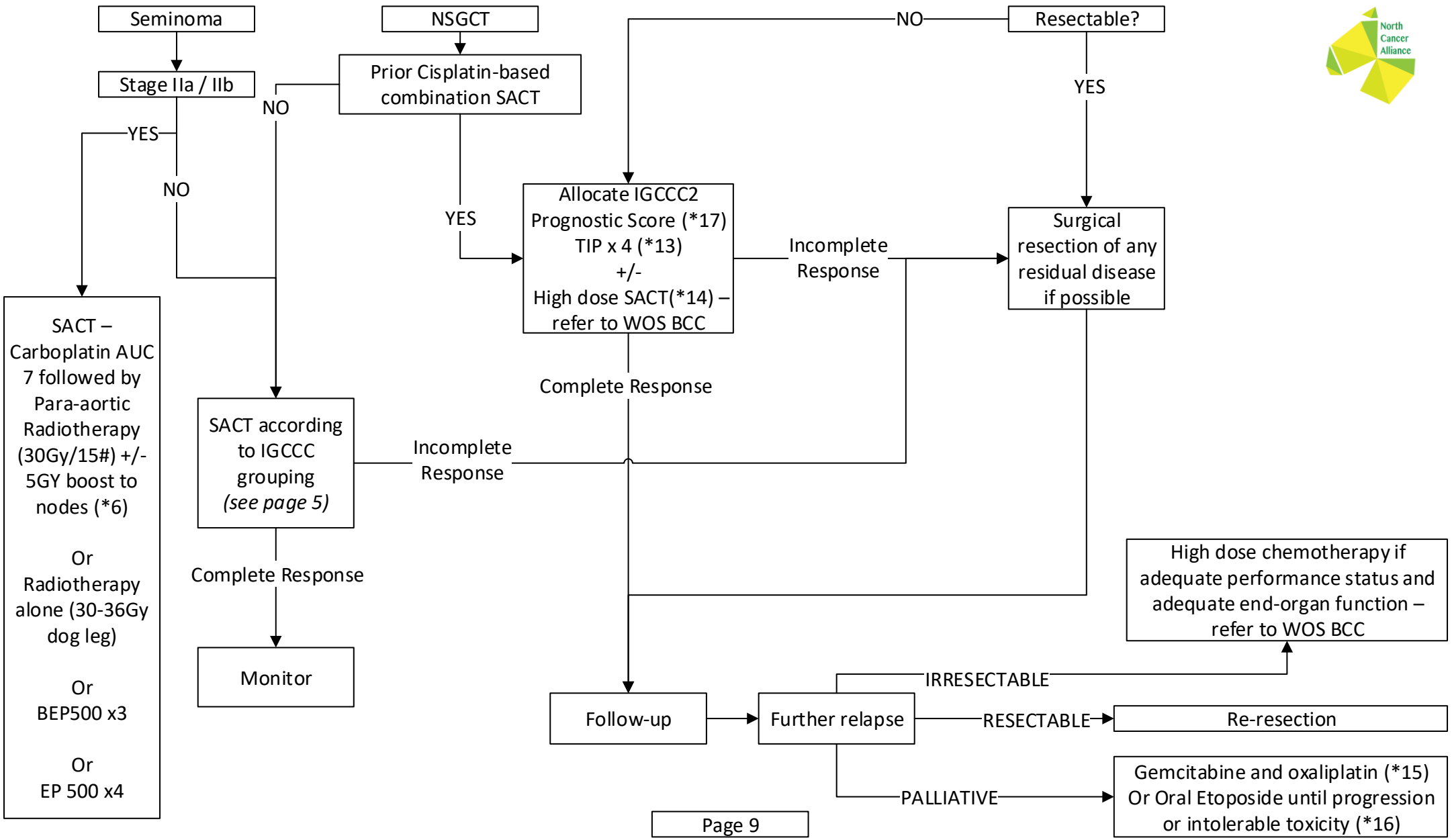
Early	Late
<2 years from primary treatment	>2 years from primary treatment



SACT Regimens*	Treatment Intent
BEP500 (5 day)	Curative
BEP500 (3 day)	Curative
TIP	Curative
Carboplatin AUC 7	Curative
Carboplatin AUC 10	Curative
EP500 (5 day)	Curative
CBOP/BEP	Curative
VIP	Curative
JEB #	Curative
BEP 500 (3 day)	Adjuvant
Etoposide (oral)	Palliative
Gemox	Palliative

* add regimen names as hyperlinks to Regional SACT Protocols

Notes
JEB – where cisplatin is contraindicated and where would otherwise receive BEP, JEB can be considered.

TNM Staging for Testis (ICD-O-3 C62) Union for International Cancer Control (8th Edition; 2017)

The classification applies only to germ cell tumours of the testis. There should be histological confirmation of the disease and division of cases by histological type. Histopathological grading is not applicable. The presence of elevated serum tumour markers, including alpha fetoprotein (AFP), human chorionic gonadotropin (hCG), and lactate dehydrogenase (LDH), is frequent in this disease. Staging is based on the determination of the anatomic extent of disease and assessment of serum tumour markers.

Primary Tumour (T) - Except for pTis and pT4, where radical orchiectomy is not always necessary for classification purposes, the extent of the primary tumour is classified after radical orchiectomy. In other circumstances, TX is used if no radical orchiectomy has been performed.

pTx	Primary tumour cannot be assessed
pT0	No evidence of primary tumour (e.g., histological scar in testis)
pTis	Intratubular germ cell neoplasia (carcinoma in situ)
pT1	Tumour limited to testis and epididymis without vascular/lymphatic invasion; tumour may invade tunica albuginea but not tunica vaginalis*
pT2	Tumour limited to testis and epididymis with vascular/lymphatic invasion, or tumour extending through tunica albuginea with involvement of tunica vaginalis
pT3	Tumour invades spermatic cord with or without vascular/lymphatic invasion
pT4	Tumour invades scrotum with or without vascular/lymphatic invasion
Note	*AJCC subdivides T1 by T1a and T1b depending on size no greater than 3 cm or greater than 3 cm in greatest dimension.
Regional Lymph Nodes (N)	
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis with a lymph node mass 2 cm or less in greatest dimension with 5 or fewer positive nodes, none more than 2 cm in greatest dimension
N2	Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension, or more than 5 positive nodes, any one mass more than 2 cm but not more than 5 cm in greatest dimension
N3	Metastasis with a lymph node mass more than 5 cm in greatest dimension
Distant Metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis
M1a	Non regional lymph node(s) or lung metastasis
M1b	Distant metastasis other than non regional lymph nodes and lung
Serum Tumour Markers (S)	
SX	Serum marker studies not available or not performed
So	Serum marker study levels within normal limits

	LDH (N indicates the upper limit of normal for the IDH assay)	**hCG (mIU/ML)**	**AFP (ng/ml)**
S1	<1.5 x N	And <5,000	And <1,000
S2	1.5-10 x N	Or 5,000-50,000	Or 1000-10,000
S3	>10 x N	Or >50,000	Or >10,000

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Definitions	
BCC	Beatson Cancer Centre
CXR	Chest X-Ray
IGCCC	International Germ Cell Consensus Classification
LVSI	Lymphovascular space invasion
MDT	Multi-disciplinary Team
NSGCT	Non-seminomatous germ cell tumours
RPLND	Retroperitoneal lymph node dissection
SACT	Systemic Anti-Cancer Therapy
RT	Radiotherapy
WOS	West of Scotland