ANZUP SURVEILLANCE RECOMMENDATIONS FOR METASTATIC TESTICULAR CANCER POST-CHEMOTHERAPY

Note: These surveillance recommendations are provided as recommendations only. Clinicians should take into account individual circumstances and adaptations may be appropriate. These recommendations do not apply following radiotherapy. The recommendations have been developed by a working group and are provided for use within Australia and New Zealand. Neither the Germ Cell Subcommittee nor ANZUP shall be liable for any inaccuracies, or adverse outcomes that may occur as a consequence of following these recommendations.

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METASTATIC SEMINOMA - IGCCCG GOOD / INTERMEDIATE RISK

SEMINOMA: GOOD / INTERMEDIATE RISK – POST-CHEMOTHERAPY - NO RESIDUAL MASS*						
Year	Physical Examination	Tumour Markers[A]	CT Abdo/Pelvis[B]	Chest Imaging[B]	Testosterone Assessment, Lipids[C]	FBC, UEC, LFT, Mg[D]
1	3, 6, 9, 12	3, 6, 9, 12	6, 12	6, 12	12	3, 6, 12
2	18, 24	18, 24	24	24	24	24
3	36	36	36	36	-	36
4	48	48	-	-	-	48
5	60	60	60	60	60	60
6+	Clinician Preference - Some patients require follow-up beyond 5 years[E]					

***Management of a Residual Mass:**

A residual mass following chemotherapy is common in patients with bulky SII/III seminoma. Residual masses are more often fibrotic tissue or inflammatory change. Any residual mass > 3cm in maximum trans-axial diameter should be discussed in a multidisciplinary meeting at a high volume centre due to the possible requirement for a PET scan or biopsy, and the technical difficulty of surgery in this setting [1].

For patients with brain or bone metastases as a previous site of disease, surveillance imaging of these additional sites (such as MRI or bone scan) is required during follow-up.

A. Tumour markers – AFP, BHCG, LDH

B. The majority of all relapses of seminoma will occur in the retroperitoneum, however a proportion will occur in the mediastinum and rarely in the lungs [2]. Chest imaging with CXR is therefore recommended at the same time as CT abdo/pelvis. If the chest was previously the site of disease, a CT Chest is recommended.

C. Patients are at risk of hypogonadism after chemotherapy and orchidectomy – approximately 20% of patients will develop hypogonadism [3, 4]. Assessment of testicular function with an *early morning* fasting testosterone, LH, and FSH are advised at 3 time points over five years with more frequent monitoring if there is borderline low levels of testosterone or isolated elevations of LH/FSH. This is best done first thing in the morning to ensure accuracy of the assessment of the testosterone [5]. Notably the risk of hypogonadism does increase after five years, and a further test should ideally be performed at 10 years in conjunction with assessment for metabolic syndrome [4,6]. Testosterone replacement therapy should be supervised by an endocrinologist given fertility implications and potential long duration of administration.

D. Long term sequelae of cisplatin includes a significant risk of developing renal impairment or bone marrow dysfunction. Patients should receive a FBC and UECr during follow-up to assess for marrow disorders or platinum nephropathy [7]. Patients also carry a lifetime elevated risk of cardiovascular toxicity and the metabolic syndrome. Primary risk factor reduction counselling for cardiovascular disease should form a regular part of follow-up and fasting lipids assessed to identify dyslipidemia as a modifiable risk factor [8].

E. Relapses in patients treated for SII/III seminoma are rare after 2 years but occur in approximately 2% of patients [9]. While the value of follow up beyond 5 years and interval imaging beyond this point is uncertain, some patients require follow up beyond 5 years including those with intermediate risk seminoma and large bulky residual masses [2]. These patients should be managed at a high volume centre.

METASTATIC NON-SEMINOMA - IGCCCG GOOD / INTERMEDIATE RISK

NON-SEMINOMA: GOOD / INTERMEDIATE RISK – POST-CHEMOTHERAPY - NO RESIDUAL MASS*						
Year	Physical Examination	Tumour Markers[A]	CT Abdo/Pelvis[B]	Chest Imaging[B]	Testosterone Assessment, Lipids[C]	FBC, UEC, LFT, Mg[D]
1	3, 6, 9, 12	3, 6, 9, 12	6, 12	6, 12	12	3, 6, 12
2	15, 18, 21, 24	15, 18, 21, 24	18, 24	18, 24	24	24
3	30, 36	30, 36	36	36	-	36
4	48	48	-	-	-	48
5	60	60	60	60	60	60
6+	Some patients require more intense monitoring and follow-up beyond 5 years[E]					

***Management of a Residual Mass:**

The retroperitoneal lymph nodes should regress to <1cm in maximal trans-axial diameter following chemotherapy to be classified as a complete response (no residual mass). All sites of significant residual masses should be resected as soon as is feasible after completing chemotherapy and may require multi-level surgery (ie RPLND and lung nodule removal) best performed at high volume centres. Any uncertainty over the need for possible resection should be discussed in a multidisciplinary meeting at a high volume centre.

A. Tumour markers – AFP, BHCG, LDH

B. A CXR is appropriate for chest imaging only if there were no prior pulmonary or mediastinal sites of disease. Otherwise patients should have CT or MRI surveillance imaging of chest and any other sites (eg. neck) that were present at the time of initial diagnosis.

C. Patients are at risk of hypogonadism after chemotherapy and orchidectomy – approximately 20% of patients will develop hypogonadism [3,4]. Assessment of testicular function with *early morning* fasting testosterone, LH, and FSH are advised at 3 time points over five years with more frequent monitoring if there is borderline low levels of testosterone or isolated elevations of LH/FSH. This is best done first thing in the morning to ensure accuracy of the assessment of the testosterone [5]. Notably the risk of hypogonadism does increase after five years, and a further test should ideally be performed at 10 years in conjunction with assessment of the metabolic syndrome [4,6]. Testosterone replacement therapy should be supervised by an endocrinologist given fertility implications and potential long duration of administration.

D. Long term sequelae of cisplatin includes a significant risk of developing renal impairment or bone marrow dysfunction. Patients should receive a FBC, UECr, Mg, LFT during follow-up to assess for marrow disorders or platinum nephropathy [7]. Patients also carry a lifetime elevated risk of cardiovascular toxicity and the metabolic syndrome. Primary risk factor reduction counselling for cardiovascular disease should form a regular part of follow-up and fasting lipids assessed to identify dyslipidemia as a modifiable risk factor [8].

E. Relapses in patients treated for SII/III non-seminoma are uncommon after 2 years but occur in approximately 3% of patients [9]. Patients with intermediate disease and those who had resection of teratoma or viable malignancy in a residual mass require follow up beyond 5 years [2].

METASTATIC NON-SEMINOMA – IGCCCG POOR RISK DISEASE

Patients with poor risk disease should be treated and followed-up in a high volume centre. Surgery should be aggressively pursued for any residual mass following chemotherapy as soon as is feasible. These patients should be referred early to minimise the gap between systemic treatment and surgery. Follow-up is more intensive than in good or intermediate risk patients and should be individualized to primary site and surgical outcome. Beyond 3 years they are not at a greater risk of recurrence compared to good / intermediate risk disease. Attention should be paid to testosterone, lipids, FBC and biochemistry in follow-up (discussed in other sections).

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