Review Article

Current management and management controversies in early- and intermediate-stage of nonseminoma germ cell tumors

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Abstract: Early stage nonseminomatous germ cell tumor (NSGCT) remains a treatable disease, with stage I cancer specific survival exceeding 95%. Using a risk-adapted approach; active surveillance (AS), adjuvant chemotherapy, and retroperitoneal lymph node dissection (RPLND) all options for treatment; with surveillance being increasingly used. With persistently elevated markers (stage IS), chemotherapy remains the hallmark of treatment. Management of stage II NSGCT varies based on status of tumor markers. With negative markers, both induction chemotherapy and upfront RPLND remain options. Management of a residual mass <1 cm after chemotherapy remains controversial, with AS and nerve-sparing RPLND considered options. The development of miR-371a-3p microRNA shows promise a novel biomarker for testicular cancer (GCT). Despite controversies in management, cures for NSGCT are achievable in 95–99% of patients.

Keywords: Testicular cancer (GCT); nonseminoma; surveillance; retroperitoneal lymph node dissection (RPLND)

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Introduction

Testicular cancer (GCT) is the most common solid organ cancer diagnosed in adult men under the age of 34. An estimated 9,000 new cases were diagnosed in 2018 in the United States, and the disease's prevalence is 5.7 per 100,000 men (based on 2011–2015). Overall survival rates are high, with 5-year survival reaching 95%; however, approximately 400 men die of GCT each year (1,2). Approximately half of GCT cases are classified as pure seminoma, and half are nonseminomatous germ cell tumors (NSGCT). The latter consists of embryonal carcinoma (11% pure and 80% mixed NSGCT cases), choriocarcinoma (0.6% pure and 33% mixed NSGCT cases), yolk sac tumors (0.6% pure and 12% mixed NSGCT), and teratoma (3.5% pure and 60% mixed NSGCT) (3). Two-thirds (68%) of patients present with stage I disease, while 19% of diagnosed cases are stage II and 12% are stage III (2).

Management of testicular care is primarily driven by clinical stage and whether the tumor is a pure seminoma or a non-seminoma. These factors hold significant prognostic value, and are directly related to recommended treatment options. Though multimodal treatment approaches combining surgery, radiation therapy, and chemotherapy are responsible for high cure rates, retroperitoneal lymph node dissection (RPLND) is therapeutic in several well-defined settings, such as in stage I NSGCT characterized by a high-risk of micrometastatic lymph node involvement and in low-volume stage II disease characterized by non-bulky retroperitoneal lymph node involvement (stage IIa/b). In

such cases, the role of RPLND includes pathologic staging, prognostic risk stratification and cancer control. In cases of non-seminomatous disease, alternatives to RPLND for high-risk stage I disease and low-risk stage II disease primarily consists of adjuvant cisplatin-based chemotherapy. NSGCT is highly sensitive to cisplatin, which when combined with surgery, contributes to cancer specific survival exceeding 95% (4). Because nuances exist between different treatment strategies, a patient with stage I NSGCT may need to decide between observation, primary RPLND or adjuvant chemotherapy while those with low-volume stage II disease may need to choose between RPLND and chemotherapy. In this review, we will discuss management options for early- and intermediate-stage nonseminomatous GCT, which we define as clinical stage (CS) I-IIb disease.

Clinical staging for GCT

GCT is staged using the Tumor-Node-Metastasis-Serum Tumor Markers (TNM-S) classification set by the American Joint Committee on Cancer (AJCC) (*Tables 1,2*). Pathologic T stage is established after orchiectomy while clinical N and M status are determined by cross sectional imaging. Staging for GCT also utilizes serum tumor markers (after radical orchiectomy) as part of TNM-S classification for GCT.

Notable changes to the 8th edition of the AJCC Staging Classification System include the new terminology of germ cell neoplasia *in situ* for pTis, subclassification of pT1 disease based on size criteria for seminoma, upstaging to pT2 based on epididymal or hilar soft tissue invasion, and M1 classification in cases characterized by discontinuous involvement of the spermatic cord (5).

Different post-orchiectomy management approaches are largely driven by the risk of retroperitoneal disease. Despite advances in imaging technology over the last several decades, clinical staging is not definitive.

Various studies, for example have reported a consistent 25–35% rate of clinical understaging of the retroperitoneum. In addition, consensus agreement regarding an absolute criteria indicating normal or abnormal retroperitoneal lymph node on CT scan does not exist. Hudolin *et al.* reviewed findings of staging RPLND on CS1 NSGCT patients and found 31.8% patients with lymph node metastasis with an average size of 1.05 cm, indicating that a >1 cm threshold for abnormal lymph nodes would miss 60% of metastatic cases (6). Some have advocated using a combination of size and location to determine if an enlarged lymph node is significant. Leibovitch *et al.* used a size cutoff of 4 mm in the primary landing zone and 10 mm outside this region and found a sensitivity of 91% and a specificity of 58% for pathologic stage II disease (7).

Management options for clinical stage I NSGCT

Determining the need for adjuvant treatments should prompt careful consideration of both the presence of high risk features as well as patient preference for or against certain adjuvant therapies given that up to 70% of clinical stage I NSGCT patients are cured by radical orchiectomy alone (8,9). Acceptable management options for CS 1 NSGCT include active surveillance (AS), RPLND, or adjuvant chemotherapy. Current National Comprehensive Cancer Network (NCCN) guidelines (Version 1.2019) recommend a risk-adapted approach that corresponds to clinical stage and histologic features found on orchiectomy pathology. For example, the absence or presence of lymphovascular invasion (LVI) stratifies stage I cases into clinical stage IA (pT1N0M0S0) and clinical stage IB disease (pT2N0M0S0), respectively (10). LVI is associated with a 40–55% relapse rate compared to 10–14% relapse risk in cases without LVI (11). Other histologic features have been investigated as predictors of relapse such as predominance of embryonal carcinoma, but the value of these features in the absence of LVI is debated (12).

While observation and AS may be appropriate for CS IA disease, adjuvant therapy (AT) is typically recommended for stage IB cases. The NCCN recommends AS (preferred), adjuvant chemotherapy with 1 cycle of bleomycin, etoposide, and cisplatin (BEP), or nerve sparing RPLND for stage IA patients. For stage IB patients, AS, 1 cycle BEP, and adjuvant RPLND are all options. The European Association of Urology (EAU) offers more definitive recommendations with surveillance being recommended as the standard option for CS IA patients. A single cycle (1) of BEP is recommended only if there are conditions against surveillance and nerve sparing RPLND only if there conditions both against surveillance AND chemotherapy. For stage IB patients the EAU recommends BEP ×1 cycle as the standard with nerve sparing RPLND or surveillance only if there are circumstances that preclude chemotherapy. The American Association of Urology (AUA) does not currently have guidelines for the management of GCT, but are currently in development. *Table 3* highlights the current recommendations of both the NCCN (10), and the EAU (13).

Table 1 American Joint Committee on Cancer (AJCC) TNM staging for Testis Cancer 8th edition, 2017

TNM	Clinical	Pathologic
Primary tumor (T)		
Tx	Cannot be assessed	Cannot be assessed
T0	No evidence of primary tumor	No evidence of primary tumor
Tis	Germ cell neoplasia *in situ*	Germ cell neoplasia *in situ*
T1	NA	Limited to testis without LVI: • pT1a: <3 cm (seminoma only); • pT1b: ≥3 cm (seminoma only)
T2	NA	• Limited to testis + LVI or • Invading hilar soft tissue or epididymis +/- LVI
T3	NA	Invades spermatic cord +/- LVI
T4	Invades scrotum +/- LVI	Invades scrotum +/- LVI
Regional lymph nodes (N)		
Nx	Cannot be assessed	Cannot be assessed
N0	No regional lymphadenopathy	No regional lymphadenopathy
N1	Lymph node mass ≤2 cm or Multiple lymph nodes, none >2 m	Lymph node mass ≤2 cm in greatest dimension AND ≤5 nodes positive (with none ≥2 cm in greatest dimension)
N2	Lymph node mass >2 but ≤5 cm or Multiple lymph nodes, any one mass ≥2 but ≤5 cm	Lymph node mass >2 but ≤5 cm in greatest dimension or >5 nodes positive (none ≥5 cm) or extranodal extension of tumor
N3	Lymph node mass >5 cm	Lymph node mass >5 cm
Distant metastasis (M)		
M0	No distant metastasis	No distant metastasis
M1a	Non-retroperitoneal nodal or pulmonary metastases or discontinuous involvement of spermatic cord	
M1b	Non-pulmonary visceral metastasis	Non-pulmonary visceral metastasis
Serum markers (S)		
Sx	Not available or performed	
S0	Makers within normal limits	
S1	LDH <1.5× normal; hCG (mIU/mL) <5,000; AFP (ng/mL) <1,000	
S2	LDH 1.5–10× normal; hCG (mIU/mL) 5,000–50,000; AFP (ng/mL) 1,000–10,000	
S3	LDH >10× normal; hCG (mIU/mL) >50,000; AFP (ng/mL) >10,000	

AS

AS is an attractive option for cases of CS I without high-risk features (e.g., LVI) as the vast majority of these cases are cured with radical orchiectomy and observation avoids the morbidity associated with more invasive treatments. One series reported patients undergoing AS had an overall relapse rate of 19%, with a 5-year cancer specific survival at 99.4% (14). NCCN guidelines recommend AS as the

Table 2 American Joint Committee on Cancer (AJCC) TNM staging for Testis Cancer 8th edition, 2017 Prognostic Stage Groups

Stage	T	N	M	S
Stage 0	pTis	N0	M0	S0
Stage I	pT1-4	N0	M0	Sx
IA	pT1	N0	M0	S0
IB	pT2-4	N0	M0	S0
IS	Any pT	N0	M0	S1-3
Stage II	Any pT	N1-3	M0	Sx
IIA	Any pT	N1	M0	S0-1
IIB	Any pT	N2	M0	S0-1
IIC	Any pT	N3	M0	S0-1
Stage III	Any pT	Any N	M1	Sx
IIIA	Any pT	Any N	M1a	S0-1
IIIB	Any pT	N1-3	M0	S2
IIIB	Any pT	Any N	M1a	S2
IIIC	Any pT	N1-3	M0	S3
IIIC	Any pT	Any N	M1a	S3
IIIC	Any pT	Any N	M1b	Any S

Table 3 NCCN and EAU recommendations for management of stage I nonseminomatous germ cell tumors

Stage	NCCN	EAU
Stage Ia (without risk factors)	Surveillance (preferred)	Surveillance (standard option)
	Nerve sparing RPLND or BEP for 1 cycle	BEP ×1 cycle (only if conditions against surveillance)
		Nerve sparing RPLND (only if conditions against surveillance and chemotherapy)
Stage Ib (with risk factors)	Surveillance or BEP for 1 cycle or nerve sparing RPLND	BEP for 1 cycle (standard option)
		Nerve sparing RPLND or surveillance (only if conditions against chemotherapy)

NCCN, national comprehensive cancer network; EAU, European Association of Urology; BEP, bleomycin, etoposide, and cisplatin; RPLND, retroperitoneal lymph node dissection.

preferred option in stage IA NSGCT, with AS being an option in stage IB NSGCT. Concerns that employing AS broadly for all patients with CS I disease subjects a significant number of patients who experience recurrence to full dose induction chemotherapy have been previously expressed and underpin the rationale for primary RPLND. However, in comparing overall number of relapses and treatment burden per 100 patients, AS results in the fewest number of total chemotherapy cycles (75–90 cycles of chemotherapy) and post chemotherapy surgeries (5–10 surgeries) compared to adjuvant BEP (110–210 cycles of chemotherapy with 3 postchemotherapy surgeries) or primary RPLND (100 surgeries and 45 cycles of chemotherapy) (15).

The use of AS has increased over time; one study reported a temporal shift in surveillance rates, with an increase in the number of patients managed with surveillance from 65% in 2004–2005 to 74% in 2012–2013

(OR 1.50; 95% CI, 1.14–1.98; P=0.004) (16). However, in a survey of panelists at the third European consensus conference on diagnosis and treatment of germ-cell cancer, the preferred strategy for stage I NSGCT varied among participants (surveillance in all patients: 28.0%; surveillance in low-risk, adjuvant 2 cycles BEP in high-risk: 30.0%; surveillance in low-risk, 1 cycle adjuvant BEP in high-risk: 36.0%; surveillance in low-risk, nerve-sparing RPLND in high-risk; nerve sparing RPLND in all patients: 6.0%) (17).

Adherence to follow-up is a key concern among patients undergoing surveillance. Yu and colleagues reported that nearly 40% of stage I cases reported through the NCDB database (including both seminoma and nonseminoma) received inadequate follow-up and testing. Despite a high rate of noncompliance to the recommended surveillance schedule, the recurrence rate was 14.3% (18).

Adjuvant chemotherapy

The evidence for adjuvant BEP for NSGCT was based on a phase II United Kingdom Medical Research Council study in which 2 cycles of adjuvant BEP resulted in a relapse-free rate at 98% at 2 years (with a median follow-up of 4 years) (19). However, because of increasing concerns regarding late term toxicities associated with chemotherapy for GCT patients, more recent studies have examined the effectiveness of a single cycle of adjuvant BEP. Long- and late-term consequences of chemotherapy include an increased risk of cardiovascular disease or secondary malignancy (1.9 fold) (20), nephrotoxicity, ototoxicity, and peripheral neuropathy (20,21). A landmark phase III RCT from Germany compared primary RPLND with 1 cycle BEP, and reported a 1.04% recurrence rate in the chemotherapy arm (median follow-up of 4.7 years) (22). The SWENOTECA group found a 3.2% risk of relapse in high-risk patients with LVI compared to 1.6% in patients without LVI at 5 years follow-up, and an overall cancer specific survival of 100% (23). A randomized controlled trial comparing 1 versus 2 cycles of adjuvant chemotherapy was abandoned, but mature results from the SWENOTECA study (median follow-up of 7.9 years) showed a total of 12 relapses in 517 patients (4). Current NCCN guidelines recommend 1 cycle of BEP if used in an adjuvant setting (10).

RPLND

Whereas surveillance is preferred modality for low-risk stage I NSGCT, both RPLND and adjuvant chemotherapy are preferred options for patients with high-risk pathologic features. Though utilized less often, advantages for RPLND include accurate pathologic staging minimizing risk of recurrence of chemoresistant NSGCT, and complete resection of teratoma. In the largest randomized controlled trial comparing RPLND and 1 course BEP, Albers *et al.* showed that there were 2 recurrences in the BEP arm and 15 recurrences in the RPLND arm (P=0.0011) with a HR of 7.937 (95% CI, 1.808–34.78) (22). An important criticism of this trial was that patients underwent a modified template RPLND so complete control of the retroperitoneum was not achieved in all cases. Prior studies have reported presence of extra-template disease in 3–23% of all cases managed with bilateral RPLND (24). The recurrence rate of the Albers study was also higher than that reported from high-volume US centers, which have been reported as less than 2% in some RPLND series (9,25). Another study demonstrated that only 15% of patients require chemotherapy after nerve-sparing bilateral RPLND (26), and de Wit *et al.* argue that chemotherapy risks are lowest following primary RPLND and should be part of counseling patients (27). Major complication rates after RPLND performed at high-volume centers are low at 2–3% (28,29). Another factor favoring RPLND is that adjuvant chemotherapy does not treat teratoma, which has been found in up to 15% of patients with occult metastases (25,30). Therefore, RPLND is a good option for carefully selected patients with early stage disease, particularly patients who are not candidates for or wish to avoid chemotherapy.

Management of CS IS

Stage IS NSGCT manifest with persistent elevation of tumor markers after radical orchiectomy without evidence of radiographic disease. Mild elevation of tumor markers after orchiectomy can be product of nonmalignant causes. Hypogonadism, marijuana use, and hepatobiliary disease should be ruled out before proposing any form of AT. If beta-hCG is elevated and stable, then testing with a different assay is recommended. Patients should not be treated based on isolated elevations of LDH as other non-cancerous conditions may cause a non-specific elevation of LDH.

Historically, RPLND was recommended in patients who had elevated tumor markers but no obvious evidence of metastatic disease on staging imaging, but subsequent reports observed high relapse rates after primary RPLND.

For example, Davis *et al.*, published a small single-institution retrospective series including 15 patients with stage IS NSGCT. All 11 patients who underwent upfront RPLND relapsed during follow-up. Of the 4 patients who received upfront chemotherapy, only 1 relapse occurred and required surgery (31).

Saxman *et al.*, suggested that patients with persistently elevated tumors markers should be treated initially with chemotherapy (32). Another small retrospective study compared cisplatin-based (16 patients) *vs.* carboplatin-based (4 patients) upfront chemotherapy. Tumor markers returned to normal in all 20 patients, though 3 patients experienced retroperitoneal relapses and 1 died due to progression of disease (33). In 2008, Dash and colleagues examined 24 patients with stage IS NSGCT, of which 17 received upfront chemotherapy and three then were treated with elective RPLND. Of the patients who received chemotherapy, 3 (of 14) had a retroperitoneal relapse. All 7 patients who were treated with RPLND relapsed. These data indicate the lack of effectiveness of RPLND alone in stage IS NSGCT (34).

The NCCN recommends that stage IS NSGCT patients with elevated AFP and/or beta-hCG in the S1 range should be treated with primary chemotherapy for good risk disease. Either 3 cycles of BEP or 4 cycles of EP are preferable treatments because the majority of these patients have disseminated disease (35,36).

Management of CS IIA NSGCT

Management for stage IIA NSGCT depends on the status of tumor markers. If markers persist, the NCCN recommends treatment with induction chemotherapy. With negative markers, patients have the option of treatment with upfront nerve-sparing RPLND or primary induction chemotherapy (10).

As noted for role of RPLND for stage I NSGCT, potential advantages include accurate pathologic staging and minimizing risk of recurrence of chemoresistant GCT and teratoma, which can be found in up to 20% of patients (37). While teratoma is histologically benign, its biologic potential is unpredictable and can undergo growth and malignant transformation (38,39). In addition, between 12–35% of patients undergoing primary RPLND for clinical stage IIA are found to have pathologically negative lymph nodes (pN0) (25,30,40,41), and such patients would be spared any additional chemotherapy. The risk of relapse after RPLND is >50% for patients with pN2 or pN3 disease (42,43), with this risk reduced to less than 1% after 2 cycles of adjuvant chemotherapy (26,44). If found to have pN1 or pN2 disease after primary RPLND, the NCCN guidelines recommends observation (which is preferred for pN1 disease) or 2 cycles of adjuvant chemotherapy (which is preferred for pN2 disease), and full induction chemotherapy for pN3 patients (10).

There are no randomized controlled trials comparing upfront RPLND to induction chemotherapy in the setting of CS II disease. A series by Stephenson *et al.* looked at patients treated CS II disease treated with primary RPLND [136] or induction chemotherapy followed by post-chemotherapy RPLND [116]. Primary chemotherapy followed by PC-RPLND was associated with significant difference in 5-year recurrence-free survival *vs.* primary RPLND (98% *vs.* 79%, P<0.001), but with no difference in 5-year cancer specific survival. Median cycles were also reduced in the upfront RPLND cohort (1.4 *vs.* 4.2, P<0.001). Furthermore, only 13% of patients in the primary RPLND group required full induction chemotherapy and 51% avoided chemotherapy altogether (41). Another study compared 109 patients who underwent RPLND followed by 2 cycles of adjuvant chemotherapy and 78 patients treated with induction chemotherapy, of which 33% required secondary RPLND. After 36-month follow-up, 7% patients in the primary RPLND group had relapsed compared to 11% in induction chemotherapy group (40). For patients wishing to minimize the lifetime risk of exposure to chemotherapy, primary RPLND remains an option for clinical stage IIA NSGCT.

Management of postchemotherapy residual masses ≤1 cm

After induction chemotherapy for CS II patients, further management depends on the size of residual masses. There is a clear consensus that for masses ≥1 cm, post-chemotherapy is recommended as there is a significant rate of both viable malignancy (11–17%) and teratoma (39–42%) (45,46). However, the management of residual masses <1 cm after induction chemotherapy is controversial as the histology of PC-RPLND masses <1 cm is 71% fibronecrosis, 24% teratoma, and 4% viable malignancy (47). Though imaging with FDG PET plays a role in the management of seminoma, a prospective trial demonstrated a false negative rate of 40% in NSGCT and furthermore, all cases of teratoma resulted in false-negative PET scans (48). Both surveillance and nerve-sparing RPLND are options for residual masses <1 cm according to

the NCCN (10).

Some groups advocate nerve-sparing bilateral RPLND regardless of size of residual mass after induction chemotherapy arguing that surgery is curative in 45–77% of patients with viable malignancy and 75–90% with teratoma (49-51). By omitting pc-RPLND, nearly all future recurrences will subject patients to salvage chemotherapy with only 25% of patients having long-term survival (52,53). Other studies note that failure to control the retroperitoneum is a risk factor for late relapse (54-56). In a large series consisting of 252 patients with CS II NSGCT, of which 116 received induction chemotherapy and underwent PC-RPLND regardless of residual mass size, Stephenson *et al.* found the histology of resected PC-RPLND specimens remained consistent over time (necrosis 50–64%, viable malignancy 6–13%, teratoma 31–50%, P=0.030) despite an increasing use of induction chemotherapy. Furthermore, in 36 patients with residual masses ≤5 mm, 6% (95% CI, 0–13%) had viable malignancy and 25% (95% CI, 10–40%) had teratoma (41). Another study examined 87 patients who underwent PC-RPLND, 62% had a residual mass ≤1 cm with 33% of cases having teratoma or vital tumor (57).

Others argue that subjecting all patients with residual masses regardless of size results in overtreatment for most patients. A large retrospective series of patients from Indiana (n=141, median follow-up 15.5 years) who underwent post chemotherapy surveillance showed 12 patients (9%) experienced relapse, 6 of whom relapsed outside the retroperitoneum. Notably, although 34% of these patients had teratoma in the orchiectomy specimen, the overall estimated 15 years RFS and CSS were 90% and 97% (58). Another series examined 161 patients who were complete responders after chemotherapy; 10 experienced relapse (6%), 8 of which were managed with PC-RPLND and an overall CSS of 100% (59). Post-chemotherapy-RPLND carries some risks that are not trivial. One series reported post-operative and late complications of 32% and 7% respectively (29). Even at tertiary care and high referral centers, reported rates of retrograde ejaculation are as high as 15–20% (60-62). One study noted a NNT (Number needed to treat) of 108 pc-RPLND to prevent 1 death in patients with a radiographically negative retroperitoneum (63).

Management of CS IIB NSGCT

Intermediate volume retroperitoneal disease (clinical stage IIB) precludes the use of AS, and AT is recommended by both the NCCN and EAU. Further management is depending on disease burden and staging. For patients with persistently elevated tumor markers; induction chemotherapy with 3 cycles of BEP or 4 cycles of EP are preferred. Furthermore, chemotherapy is recommended for patients with negative markers and multifocal metastases (10).

For patients with negative markers and lymph node metastases within the primary landing zones, both primary chemotherapy or nerve-sparing RPLND are options per NCCN guidelines (10). A prospective study by Weissbach *et al.* compared RPLND or primary chemotherapy in CS IIA/B patients and found no difference in relapse rates at 36 months. No differences in quality of life were noted between groups, and 12% of patients treated with RPLND were reclassified as pathologic stage I disease (40). Therefore, upfront RPLND remains an option for patients wishing to avoid or unable to tolerate chemotherapy. Importantly, the cure rate for CS IIB disease is high (with survival from 88–95%) (26,64,65) with either RPLND or induction chemotherapy

Surveillance after AT

Current recommendations for follow-up of NSGCT include the use of the serum tumor markers alpha feto-protein (AFP), beta-human chorionic gonadotropin hormone (B-HGG), and lactate dehydrogenase (LDH) both in AS and after AT. One limitation with current tumor markers is that up to 35% of relapsing patients have normal levels of tumor markers (66). MicroRNAS (miRNAs) are a promising novel biomarker for GCT. In a landmark study, Dieckmann *et al.* demonstrated the utility of mIR-371a-3p with a sensitivity of 88.7% and specificity of 92.5% (67). Terbuch *et al.* examined mIR-371a-3p levels in 10 patients at different periods during disease relapse and salvage chemotherapy, and found microRNA levels were 13.65 fold higher than patients without evidence of disease (P=0.014) (68). In a large, prospective multicenter study with 616 patients with GCT, miR-371a-3p levels showed a sensitivity of 90.1%, a specificity of 94.0% with a positive predictive value of 97.2%. In the same study, combined sensitivity of traditional tumor markers were under 50% for seminoma and 80% for NSGCT (69).

The mIR-371a-3p test shows remarkable promise in detecting and monitoring the recurrence for NSGCT. Possible future considerations are its use in further

stratifying/selecting and monitoring patients on AS; goal directed number of treatment cycles of chemotherapy; and management of post chemotherapy retroperitoneal masses.

Conclusions

Though GCT is the most common solid tumor in young men, it is a highly-treatable cancer for which multimodal cancer treatments provide high cure rate. For stage I NSGCT, patients have options of AS, adjuvant chemotherapy, or primary RPLND; with studies showing excellent long-term outcomes with a 99% long-term cancer-specific survival rate. The cornerstone of treatment for stage IS remains induction chemotherapy. For clinical stage II NSGCT, options are nuanced and range from nerve-sparing RPLND, primary chemotherapy (followed by surveillance or post chemotherapy surgery depending on response and size of residual mass); with cures achievable in 95–99% of patients. The discovery of microRNA as a novel biomarker for GCT may lead to future improvements in risk stratification, selection of therapies, and monitoring of treatment.

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Footnote

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