Canadian Urological Association guideline: Management of testicular germ cell cancer

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Disclosures

Speaker	Advisory boards	Payment/honoraria	Grants/research support	Clinical trials	Investments
Robert Hamilton	Janssen, Astellas, Bayer, Tolmar, Knight, Tersera, Advanced Accelerator Applications			Janssen (GURC) Bayer (ARASENS)	
Maria (Di) Jiang	EMD Serono, Pfizer	Amgen, Bayer, EMD Serono, Ipsen, Janssen			
Peter Chung		Abbvie, Boston Scientific, TerSera, Verity		CTG, ICON, Medivation, Mount Sinai Health Systems, NRG, and Princess Margaret Cancer Centre	

Disclosures cont'd

Speaker	Advisory boards	Payment/honoraria	Grants/research support	Clinical trials	Investments
Sebastien Hotte	AAA/Novartis, Astellas, Bayer, BMS, Eisai, Ipsen, Janssen, Merck, Pfizer, Seagen	Astellas, Bayer, BMS, Janssen		AAA/Novartis, Astellas, BMS, CCTG, Eisai, Merck, Pfizer, SeaGen, SignalChem	
Eric Winquist	Amgen, Bayer, Eisai, Merck, Roche		Eiasi	Ayala, Eisai, Merck, Roche	
Armen Aprikian	Abbvie, Astellas, Bayer	Abbvie, Astellas, Bayer, Sanofi, TerSera			
Denis Soulières	Adlai-Nortye, BMS, Eisai, Ipsen, Merck, Pfizer		BMS, Eisai, Ipsen, Merck, Pfizer		

Disclosures cont'd

Speaker	Advisory boards	Payment/honoraria	Grants/research support	Clinical trials	Investments
Scott Tyldesley		Bayer, Janssen, and TerSera		Janssen	
Alan I. So	Abbvie, Astellas, Bayer, Janssen, Merck, TerSera				
Ricardo A. Rendon	Abbvie, Astellas, Bayer, Ferring, Janssen, Sanofi, TerSera, Tolmar	Abbvie, Astellas, Bayer, Ferring, Janssen, Sanofi, TerSera, Tolmar		Abbvie, Astellas, Bavarian Nordic, Bayer, Ferring, Janssen, Myovant, Sanofi	Myovant
Lori Wood	AstraZeneca BMS, Ipsen, Merck, and Pfizer			AstraZeneca, BMS, and Merck	

Methods

- Multidisciplinary group:
  - 9 medical oncologists
  - 5 uro-oncologists
  - 2 radiation oncologists
  - 1 GU pathologist
  - 1 GU radiologist
- Each section had a lead with a working group
- Series of large group and small group zoom meetings
  - Develop and update content, propose recommendation statements

Methods cont'd

- Modified methods from EAU and ESMO Guidelines Committees
- Whole group rated each recommendation on 5-point Likert scale:

Completely disagree	Somewhat disagree	Undecided	Somewhat agree	Completely agree

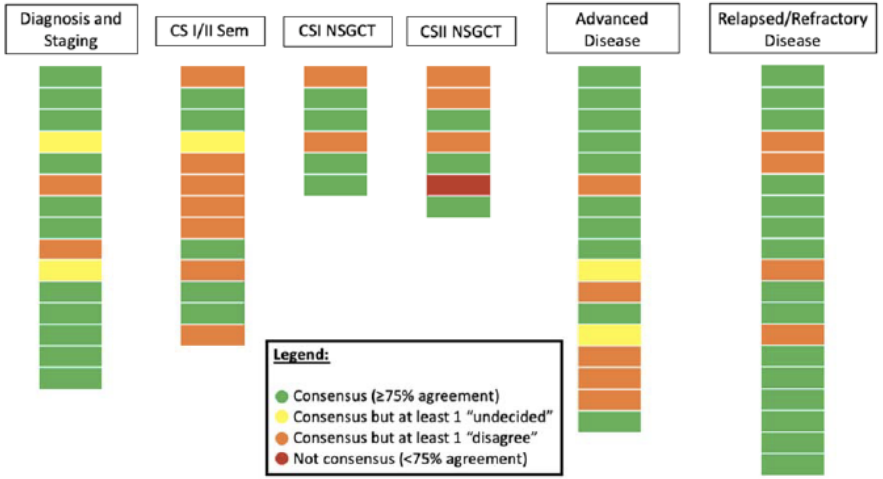
*Abstain (out of scope for practice)

- Agreement: ≥75% of experts voting somewhat or completely agree

Methods cont'd

- June 2021: Full group virtual meeting
  - 1 recommendation didn't reach agreement
  - 22 others at least one person disagreed
  - Recommendations revised accordingly
- July 2021: Second and final vote
  - 100% of recommendations reached agreement

Supplementary Figure 1. Overview of initial survey results for each stage-specific topic.



Overarching themes

- Whenever possible refer or discuss with centers with experience
  - Pathological expertise
  - Radiological expertise
  - Med-onc, surg-onc, rad-onc expertise
- Don’t be afraid to re-image in a few weeks to confirm the stage/re-stage
- Minimize overtreatment, prioritize survivorship

Diagnosis & staging

Table 1. Mandatory investigations

Complete history and physical exam, including scrotal exam

Laboratory
- Alpha-fetoprotein (AFP)
- ß-human chorionic gonadotrophin (ß-HCG)
- Lactate dehydrogenase (LDH)

Baseline imaging*
- Scrotal ultrasound
- CT abdomen and pelvis
- CT thorax

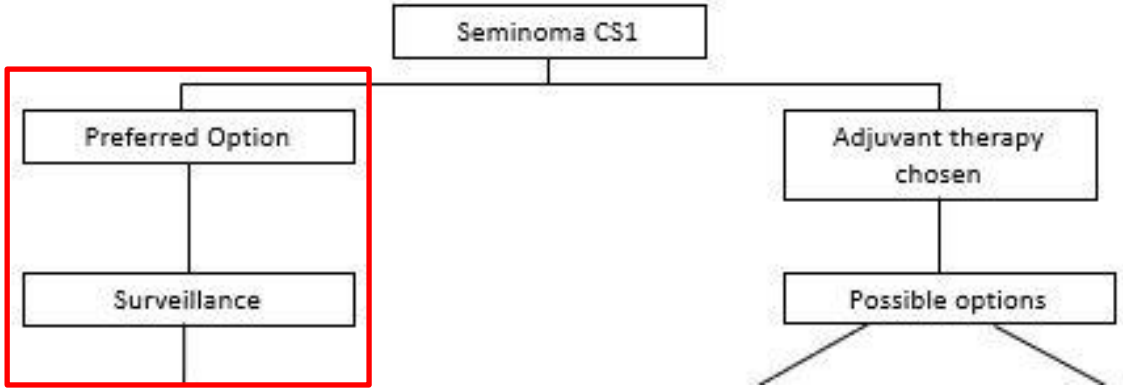
Other imaging procedures, such as body MRI and positron emission tomography (PET), should not be routinely used for staging *(agreement: 94%)*.

Insertion of a testicular prosthesis at the time of orchiectomy should be discussed with patients prior *(agreement: 83%)*.

Orchiectomy may be deferred in patients with life-threatening metastatic disease when a confirmed diagnosis of NSGCT (e.g., an unequivocally elevated AFP and/or HCG >5000 IU/L) or seminoma (e.g., biopsy of metastatic site) is made so as not to delay the start of chemotherapy. In such cases, orchiectomy should be performed after chemotherapy[14,15] *(agreement: 100%)*.

A full discussion on semen cryo-preservation for all patients undergoing therapy (surgery, chemotherapy, and/or radiation) for GCT should take place *(agreement: 100%)*.

CSI and CSII seminoma

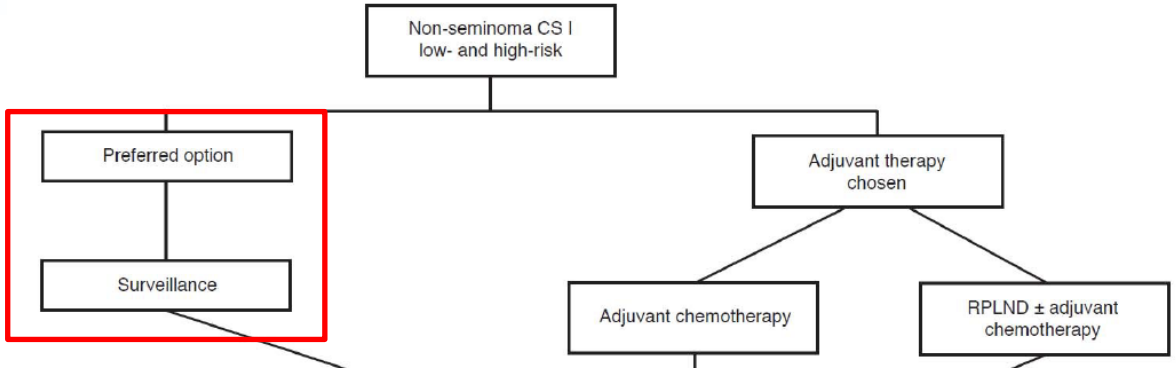


In patients with CSIIA seminoma without marker elevation, an initial period of surveillance with repeat imaging in 6–8 weeks is recommended *(agreement: 94%)*.

In CSIIA seminoma, radiation therapy or chemotherapy are standard treatment options and should be discussed *(agreement: 100%)*.

In CSIIB seminoma, radiation therapy or chemotherapy are treatment options. Chemotherapy is the preferred option in most cases (*agreement: 94%*).
In CSIIC seminoma, chemotherapy is the standard treatment approach *(agreement: 100%)*.

CSI NSGCT

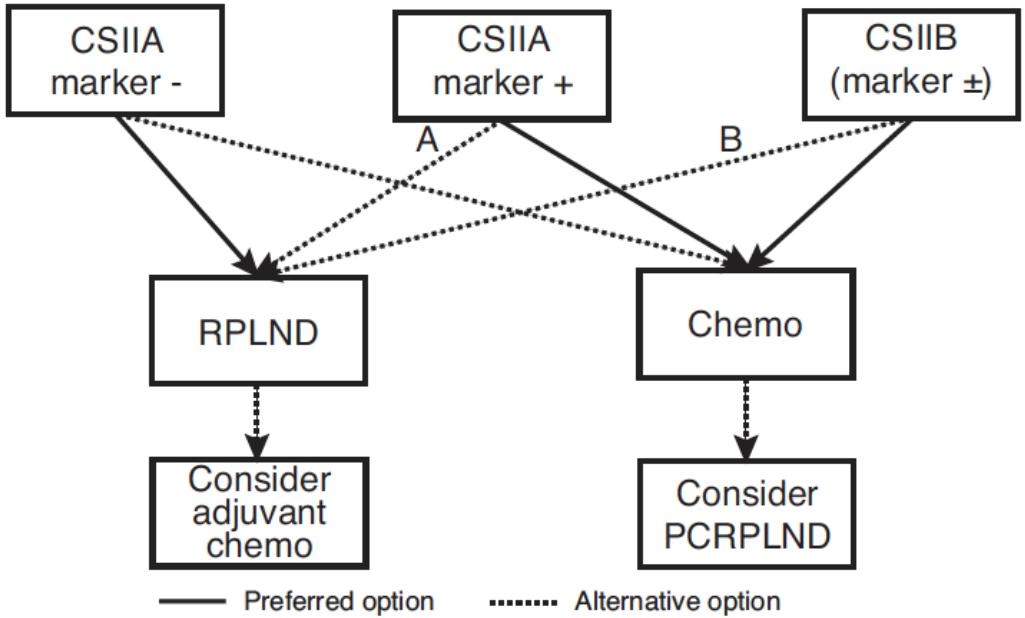


In a patient willing and able to adhere to a surveillance program, for all stage I risk groups, surveillance should be the preferred option *(agreement: 100%)*

For patients who prefer immediate treatment or who are unsuitable for primary surveillance, adjuvant chemotherapy or RPLND are both options *(agreement: 93%)*.

If RPLND is chosen, surgery should be performed by surgeons who are experienced with the procedure. Full bilateral templates and nerve-sparing techniques should be employed *(agreement: 100%)*.

CSIIA/B NSGCT



A: RPLND remains an option in select patients with low-level and slowly rising markers who wish to avoid chemotherapy, though a higher relapse risk is acknowledged.
B: RPLND may be an option in highly select patients, though a higher relapse risk is acknowledged.

Advanced/metastatic disease

All patients with advanced GCT should be treated for cure and referral to (or consultation with) experienced centers should be strongly considered *(agreement: 100%)*.

. In NSGCT, post-chemotherapy residual masses ≥1 cm and normal tumor markers should be resected *(agreement: 100%)*.

In NSGCT, post-chemotherapy residual masses <1 cm and normal tumor markers can be safely surveyed *(agreement: 100%)*.

Post-chemotherapy residual masses in seminoma are common.

a. If they are ≤3 cm, PET scans are not recommended and the patient should be surveyed *(agreement: 100%)*.
b. If they are >3 cm, a PET may be considered:
    1. If the PET scan is negative, patients can be surveyed *(agreement: 100%)*.
    2. If the PET scan is positive, continued close observation is the preferred option *(agreement: 100%)*.
    3. If the PET scan remains strongly positive over time, surgical resection or biopsy of the residual mass is the preferred option *(agreement: 100%)*.
c. If the post-chemotherapy residual mass is growing on radiological imaging, surgical resection of the mass should be performed if technically feasible *(agreement: 94%)*.

Relapsed/refractory disease

Table 5. Prognostic score for patients who relapse after cisplatin-based first-line chemotherapy

	Score points			
Parameter	**0**	**1**	**2**	**3**
Primary site	Testis	Extragonadal		Mediastinal non-seminoma
Prior response	CR or PR marker -	PR marker + or SD	PD	
Progression-free interval, months	>3	≤3		
AFP at relapse	Normal	≤1000 ug/L	>1000 ug/L	
β-HCG at relapse	≤1000 IU/L	>1000 IU/L		
Mets to liver, brain, bone	No	Yes		
Score sum (values from 0–10)				
Regroup score sum into categories: (0)=0; (1 or 2)=1; (3 or 4)=2; (5 or more)=3				
Add histology score points: pure seminoma=-1; non-seminoma or mixed tumors=0				
Final prognostic score (-1=very low risk; 0=low risk; 1=intermediate risk; 2=high risk; 3=very high risk)				

CR: complete remission; PD: progressive disease; PRm-: partial remission, negative markers; PRm+: partial remission, positive markers; SD: stable disease.[149]

Relapsed/refractory disease cont'd

IPFSG Group	Recommended Rx
Very Low	Conventional chemo (TIP x 4) HDCT with ASCT
Low	Conventional chemo (TIP x 4) HDCT with ASCT
Intermediate	HDCT with ASCT
High	HDCT with ASCT
Very high	HDCT with ASCT

Conclusions

- Successful update of Canadian testicular germ cell tumor guidelines
- Can serve as ready-reference for your next patient in clinic
- Major take-home messages:
  - Strongly encourage discussion with or referral to an experienced center
  - Minimize overtreatment
  - Prioritize survivorship
  - Don’t be afraid to phone a friend