Optimal Management of Clinical Stage I Nonseminoma: New Data for Patients to Consider

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The optimal management of clinical stage I (CSI) nonseminomatous germ cell tumors (NSGCT) is still controversial. The obvious explanation is that either early definitive treatment or watchful waiting and chemotherapy at the time of disease recurrence cures nearly 100% of patients. There are no trial data that provide robust evidence for the superiority of one approach over the other. As a result, treatment choices have been guided by institutional or national consensus rather than based on evidence. In 2006, in a special Urologic Oncology issue in *Journal of Clinical Oncology* (JCO), a review article was dedicated to this topic.1 In the setting of CSIA NSGCT (lymphovascular invasion [LVI] absent in the primary tumor), the risk for occult metastatic spread is less than 20%, and there seems to be universal agreement to opt for watchful waiting and to treat only if metastatic disease becomes apparent. In the setting of high-risk CSIB NSGCT (LVI present), associated with as high as a 40% to 50% risk of recurrence, there is an equal split in preferences for either the use of one or two cycles of adjuvant chemotherapy or for watchful waiting, which in view of the ultimate identical outcome, are both valid options. In a recent article in *JCO*, Nichols et al2 aimed to end the debate as to whether adjuvant chemotherapy still has a place in NSGCT, given that the authors concluded that surveillance can be safely applied in all patients, including those with high-risk NSGCT.

However, the most striking observation in this study4 was the unexpected high frequency of postchemotherapy surgery. No less than 26% of relapsing patients needed surgery for residual tumor masses after three to four cycles of chemotherapy with bleomycin, etoposide, and cisplatin. Of these, viable cancer was found in 8%, 50% had mature teratoma (MT), 32% had fibrosis/necrosis only, and in 10% of patients, the histology was reported as unknown. The high incidence of MT in postchemotherapy/postsurgery residuals in low-volume disease has been reported previously.1,5-7 Notably, the majority of patients with MT in resected postchemotherapy specimens have no MT in the primary tumor.4-7 These findings lend support to preclinical data that suggest that metastatic immature teratoma may transform into MT, or that MT is preferentially selected for, under the influence of chemotherapy.5

The frequent need for additional surgery to resect residual masses sheds important new light on the balance between the choice of early definitive treatment versus chemotherapy at the time of disease recurrence. Today, the equation is no longer a simple computation of the number of cycles needed (one to two immediate cycles in 100% of patients with CSIB NSGCT1-3 three to four cycles at the time of recur-

ence in 40% to 50% of patients with CSIB NSGCT); we have to take into account that a sizeable percentage of relapsing patients (one of every four in this study4) will need additional surgery. Moreover, postchemotherapy retroperitoneal lymph node surgery is a technically demanding procedure, causing immediate as well as late morbidities, quite often including retrograde ejaculation.9,11

For some physicians this new information may shift their preference toward early definitive treatment, or they may be more inclined...
to convey the pros and cons of the options to their patients with CSIB disease. For those who maintain that surveillance is the preferred option, it becomes more critical than ever to detect recurrent disease at the earliest possible time, to reduce the morbidity of the treatment that is needed for rendering patients disease free. In that regard, the goal of surveillance should no longer simply be to detect recurrences that are highly curable with chemotherapy, but also to reduce the need for postchemotherapy surgery by detecting small-volume relapses. Thus, more than ever, it is critical that watchful waiting continue to involve monthly follow-up visits and repeat CT scans every 3 or 4 months during the first 2 years. Studies that have investigated a reduction in the number of CT scans have neither been powered to allow noninferiority conclusions nor addressed the size of recurrences and the procedures that are needed to eventually achieve cure.12,13

Informed decision making is especially relevant, given that a Dutch study has shown that in the setting of CSIB NSGCT, the threshold for preferring definitive treatment over surveillance is precisely at the actual 50% risk-for-recurrence cutoff point.14 In this investigation the assumption, in 1990, was that chemotherapy would be the single treatment modality, and the ultimate outcome would be identical.14 With the current evidence that additional surgery is required in 25% of patients despite full-dose chemotherapy at disease recurrence, a new patient preference study is warranted, because it is possible that a substantial number of well-informed patients with CSIB NSGCT might find that early definitive treatment is preferable to surveillance.

AUTHOR’S DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST
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REFERENCES

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