Surgery in Metastatic Seminoma: Negative Trial Should Be Treated as Negative

TO THE EDITOR:

With great interest, we have read an article by Daneshmand et al[1] describing outcomes after retroperitoneal lymph node dissection (RPLND) for testicular seminoma with limited retroperitoneal lymphadenopathy. The idea of surgical treatment is to avoid cytotoxic cisplatin-based chemotherapy and decrease the risk of late toxicities to maintain quality of life. The authors enrolled 55 patients with either nonbulky stage IIA-IIB diseases (n = 19; 35%) or metachronous retroperitoneal metastases after regional recurrence of stage I seminoma (n = 36; 65%).[1]

With a median follow-up of 33 months, 12 patients eventually experienced disease recurrence. The primary end point of the trial was not reached, and the authors assumed to achieve a 2-year recurrence-free rate (RFS) of ≥90% with 90% power and 10% one-sided type I error to reject the null hypothesis of RFS ≤ 75%, whereas the trial has shown a 2-year RFS of 81% and overall recurrence rate (RR) of 22%. Short follow-up time for relapsed patients in the trial does not allow adequately assessing the long-term oncological safety of this approach.

Long-term complications were detected in four patients (7%), including three patients (5%) with anejaculation. In conclusion, the authors claimed that RPLND is a treatment option for patients with testicular seminoma with low long-term morbidity.

According to the primary end point, this is a negative trial, and we think the achieved results should be approached in this way. The reported RR appears to be unacceptably high and far exceeding the RR with standard approaches. Furthermore, nine operated patients (16%) did not have tumor in the resected retroperitoneal lymphatic nodes, clearly representing pitfalls in the preoperative diagnosis. Excluding these patients, we have 26% RR in the population with retroperitoneal lymph nodes. Similar high relapse rate (30%) was reported in the PRIMETEST trial with RPLND as a single treatment option.[2]

For comparison, Tandstad et al[3] reported zero recurrences (0%) in patients with clinical stage II seminoma treated with modern cisplatin-based chemotherapy. One should also note short follow-up time for relapsed patients in the trial by Daneshmand et al,[1] which does not allow us to establish long-term oncological safety of this approach. Complications, as noted by the authors, including anejaculation, may affect quality of life of the patients. We agree that immediate and late toxicity related to chemotherapy may be troublesome for patients receiving treatment with curative intent; however, benefits of surgery are arguable in this setting.

If there are contraindications for this kind of treatment, other less aggressive approaches are emerging. The SAKK 01/10 trial (n = 120) demonstrated a 3-year RFS of 93.7% in patients with stage IIA or IIB classic seminoma (either at primary diagnosis or equivalent clinical finding at relapse during active surveillance for stage I seminoma).[4] Interestingly, this trial also failed to achieve the primary end point of 3-year RFS ≥ 95%; however, this estimate exceeds the expectations of the authors of the current trial.

In conclusion, we think it is quite early to recommend primary RPLND for stage II seminoma as a possible treatment option outside the clinical trials, and the patients have to be informed about the potential survival harms of this intervention. Further trials should focus on opportunities for treatment de-escalation for these patients.

Alexey A. Rumyantsev, MD, PhD
N.N. Blokhin National Medical Research Center of Oncology, Moscow, Russia

Alexandra S. Tyulyandina, MD, PhD
N.N. Blokhin National Medical Research Center of Oncology, Moscow, Russia
Sechenov First Moscow Medical University (Sechenov University), Moscow, Russia

Alexey A. Tryakin, MD, PhD
N.N. Blokhin National Medical Research Center of Oncology, Moscow, Russia
Bashkir State Medical University, Ufa, Russia

Mikhail Y. Fedyanin, MD, PhD
N.N. Blokhin National Medical Research Center of Oncology, Moscow, Russia
Moscow Medical City Hospital "Kommunarka," Moscow, Russia
N.I. Pirogov National Medical and Surgical Center, Moscow, Russia

Sergey A. Tjulandin, MD, PhD
N.N. Blokhin National Medical Research Center of Oncology, Moscow, Russia

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI https://doi.org/10.1200/JCO.23.00629.

REFERENCES

1. Daneshmand S, Cary C, Masterson T, et al: Surgery in early metastatic seminoma: A phase II trial of retroperitoneal lymph node dissection for testicular seminoma with limited retroperitoneal lymphadenopathy. J Clin Oncol 41:3009-3018, 2023
2. Hiester A, Che Y, Lusch A, et al: Phase 2 single-arm trial of primary retroperitoneal lymph node dissection in patients with seminomatous testicular germ cell tumors with clinical stage IIA/B (PRIMETEST). Eur Urol 10.1016/j.eururo.2022.10.021
3. Tandstad T, Smaaland R, Solberg A, et al: Management of seminomatous testicular cancer: A binational prospective population-based study from the Swedish Norwegian Testicular Cancer Study Group. J Clin Oncol 29:719-725, 2011
4. Papachristofilou A, Bedke J, Hayoz S, et al: Single-dose carboplatin followed by involved-node radiotherapy for stage IIA and stage IIB seminoma (SAKK 01/10): A single-arm, multicentre, phase 2 trial. Lancet Oncol 23:1441-1450, 2022

DOI: https://doi.org/10.1200/JCO.23.00629; Published at ascopubs.org/journal/jco on September 7, 2023.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Surgery in Metastatic Seminoma: Negative Trial Should be Treated as Negative

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/authors/author-center.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

Alexey A. Rumyantsev
Stock and Other Ownership Interests: Pfizer, Merck Sharp & Dohme, Sanofi
Honoraria: BioCad
Speakers' Bureau: BioCad, AstraZeneca, Merck KGaA
Travel, Accommodations, Expenses: AstraZeneca, BioCad

Alexandra S. Tyulyandina
Stock and Other Ownership Interests: Ruspharmtech
Honoraria: AstraZeneca/MedImmune, MSD Oncology, BioCad, Eisai, Roche, Novartis, R-Pharm, Merck
Consulting or Advisory Role: AstraZeneca/MedImmune, MSD Oncology, Eisai
Research Funding: AstraZeneca/MedImmune, MSD Oncology, biocad

Alexey A. Tryakin
Stock and Other Ownership Interests: Amgen, Lilly, Merck Serono, Merck, Bayer
Consulting or Advisory Role: BioCad, Roche/Genentech, Bristol Myers Squibb, Eisai, Merck Sharp & Dohme, AstraZeneca, Lilly, Amgen
Speakers' Bureau: Bayer Health, BioCad, Lilly, Merck Serono, Sanofi, Amgen, Bristol Myers Squibb, Eisai, Merck Sharp & Dohme, Pfizer, Bayer, AstraZeneca/Daiichi Sankyo, Novartis
Research Funding: Biocad (Inst)
Travel, Accommodations, Expenses: Novartis, BioCad, Bayer, Veropharm, Sanofi, AstraZeneca, Merck Serono

Sergey A. Tjulandin
Stock and Other Ownership Interests: RosPharmTech
Consulting or Advisory Role: AstraZeneca, BioCad, Novartis, Servier
Speakers' Bureau: AstraZeneca, Novartis, R-Pharm
Research Funding: Merck (Inst), Eisai (Inst), AbbVie (Inst), Novartis (Inst), Bristol Myers Squibb Foundation (Inst), Servier

No other potential conflicts of interest were reported.