Can a Cure Be Achieved with Taxane-Based Chemotherapy plus Surgery in Patients with Primary Mediastinal Non-Seminomatous Germ Cell Tumors and Progression or Relapse Despite First-Line Chemotherapy?

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Key Words

mediastinal non-seminomatous germ cell tumor,
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Summary

Primary mediastinal non-seminomatous germ cell tumors (NSCGTs) have a poor prognosis in the International Germ Cell Cancer Collaborative Group (IGCCCG) classification. There is no clear standard of treatment at relapse. Between 1995 and 2005, 13 patients experienced progression or relapse, and 1 patient was cured with a taxane-based chemotherapy plus surgical resection at our institution.

Schlüsselwörter

Primärer mediastinaler nichtseminomatöser
Keimzelltumor · Taxane · Rückfall

Zusammenfassung

Primäre mediastinale nichtseminomatöse Keimzelltumoren (NSCGTs) haben in der Germ Cell Cancer Collaborative Group (IGCCCG)-Klassifikation eine schlechte Prognose. Es gibt keinen einheitlichen Standard für die Behandlung bei einem Rückfall. Zwischen 1995 und 2005 zeigten an unserem Institut 13 Patienten eine Progression oder einen Rückfall und 1 Patient wurde durch eine Taxan-basierte Chemotherapie verbunden mit chirurgischer Resektion geheilt.

Primary mediastinal non-seminomatous germ cell tumors (NSCGTs) are rare neoplasms and biologically different from other NSCGTs. This entity was identified as bearing a poor prognosis in the International Germ Cell Cancer Collaborative Group (IGCCCG) classification [1] for advanced NSGCT, and only about 40% of these patients currently obtain long-term survival. In large series of primary mediastinal NSGCT, patients who experience progression or relapse after first-line cisplatin-based chemotherapy are not considered as curable with standard-dose or high-dose chemotherapy [2, 3]. However, a long-term progression-free survival has previously been reported with docetaxel-including treatment in a patient with relapsed primary mediastinal NSGCT [4].

All patients with primary mediastinal NSGCT treated at the Institut Gustave Roussy during a 10-year period were included in this retrospective analysis. Clinical characteristics, treatment at relapse and survival were analyzed for patients with progression or relapse after first-line chemotherapy.

Between 1995 and 2005, 25 patients with primary mediastinal NSGCTs were treated by cisplatin-based chemotherapy, and surgery was used in 17 patients. 13 patients experienced progression or relapse, with a median delay of 4 months (3–9 months) after primary chemotherapy initiation: 4 patients received conventional-dose chemotherapy (vinblastine, ifosfamide and cisplatin (VeIP)), 6 patients received high-dose chemotherapy, and 8 patients received taxane-based chemo-

therapy. All 13 patients eventually died of NSGCT progression, except 1 patient who is progression free 3 years after he was treated with paclitaxel-based chemotherapy and surgery.

This 22-year-old man with primary mediastinal NGCT refractory to salvage chemotherapy entered complete remission after taxane-based chemotherapy and surgery. In June 2004, a 20 cm diameter mass in the anterior mediastinum was diagnosed by chest X-ray and computed tomography (CT) scan. Baseline serum α -fetoprotein (AFP) was 5244 ng/ml ($N < 10$ ng/ml), lactate dehydrogenase (LDH) was 943 UI/l ($N < 600$ UI/l), and human chorionic gonadotropin (HCG) was within the normal range. From June 2004 to August 2004, the patient underwent 4 cycles of cisplatin, etoposide and bleomycin (PEB), with a partial response at the CT staging image. However, the AFP values at the end of treatment failed to attain normality (16 ng/ml), and progressive disease (AFP was 45 ng/ml) was noted in September 2004. The patient therefore received salvage chemotherapy with ifosfamide-containing chemotherapy (VeIP). During the second cycle of salvage chemotherapy, the AFP levels increased to 23 ng/ml after an initial decrease. A third-line chemotherapy was decided in October 2004, consisting in 3 cycles of paclitaxel and epirubicin followed by high-dose chemotherapy (TAXIF regimen) [5]. In March 2005, the residual mass was radically resected, and pathological examination revealed complete necrosis. The AFP levels decreased to within the normal range

(5 ng/ml). In July 2008, more than 3 years later, the patient is without evidence of disease (nonexistent disease (NED)).

Patients with extragonadal germ cell tumors who relapse after initial chemotherapy are classically treated with the same salvage regimens as are patients with testicular germ cell cancer in the same setting. A mediastinal primary site and an inadequate response to cisplatin-based induction chemotherapy have been identified as independent negative prognostic factors, both associated with an approximately twofold higher risk for failure of salvage treatment [5, 6]. This recent series confirms that patients with primary mediastinal NSGCT and a relapse or progression after first-line chemotherapy have a dismal prognosis when managed with conventional-dose or high-dose chemotherapy. Individual patients can profit from taxane-based chemotherapy plus surgical resection, which may contribute to achieve cure.

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Conflict of Interest

The authors did not provide a conflict of interest statement.

References

- 1 The International Germ Cell Cancer Collaborative Group: International germ cell consensus classification: A prognostic factor-based staging system for metastatic germ cell cancers. *J Clin Oncol* 1997; 15:594–603.
- 2 Fizazi K, Culine S, Droz JP, Kramar A, Théodore C, Ruffié P, Le Chevalier T: Primary mediastinal nonseminomatous germ cell tumors: results of modern therapy including cisplatin-based chemotherapy. *J Clin Oncol* 1998;16:725–732.
- 3 Saxman S, Nichols CR, Einhorn LH: Salvage chemotherapy in patients with extragonadal non-seminomatous germ cell tumors: The Indiana University experience. *J Clin Oncol* 1994;12:1390–1393.
- 4 Berruti A, Saini A, Gorzegno G, Tampellini M, Borasio P, Dogliotti L: Durable complete remission after weekly docetaxel administration in a patient with mediastinal non-seminomatous germ-cell tumor refractory to cisplatin-based chemotherapy. *Ann Oncol* 2003;14:1589–1590.
- 5 Lotz JP, Bui B, Gomez F, Théodore C, Caty A, Fizazi K, Gravis G, Delva R, Peny J, Viens P, Duclos B, De Revel T, Curé H, Gligorov J, Guillemaut S, Ségura C, Provent S, Droz JP, Culine S, Biron P; Groupe d'Etudes des Tumeurs Uro-Génitales (GETUG): Sequential high-dose chemotherapy protocol for relapsed poor prognosis germ cell tumors combining two mobilization and cytoreductive treatments followed by three high-dose chemotherapy regimens supported by autologous stem cell transplantation. Results of the phase II multicentric TAXIF trial. *Ann Oncol* 2005;16:411–418.
- 6 Beyer J, Kramar A, Mandanas R, Linkesch W, Greinix A, Droz JP, Pico JL, Diehl A, Bokemeyer C, Schmoll HJ, Nichols CR, Einhorn LH, Siegert W: High-dose chemotherapy as salvage treatment in germ cell tumors: a multivariate analysis of prognostic variables. *J Clin Oncol* 1996;14:2638–2645.
- 7 Hartmann JT, Einhorn L, Nichols CR, Droz JP, Horwich A, Gerl A, Fossa SD, Beyer J, Pont J, Schmoll HJ, Kanz L, Bokemeyer C: Second-line chemotherapy in patients with relapsed extragonadal nonseminomatous germ cell tumors: results of an international multicenter analysis. *J Clin Oncol* 2001;19:1641–1648.