

gests, approaches to the same challenges around the world.

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1. Boulware LE, Marinopoulos S, Phillips KA, et al. Systematic review: the value of the periodic health evaluation. *Ann Intern Med* 2007;146:289-300.

2. Yarnall KSH, Pollak KI, Østbye T, Krause KM, Michener JL. Primary care: is there enough time for prevention? *Am J Public Health* 2003;93:635-41.

Treatment of Growing Teratoma Syndrome

TO THE EDITOR: Growing teratoma syndrome consists of an enlarging mature teratoma arising during or after chemotherapy for a nonseminomatous germ-cell tumor, with normal serum levels of al-

pha-fetoprotein and human chorionic gonadotropin.¹ The preferred treatment is complete surgical resection² because teratomas are resistant to chemotherapy and radiation therapy.

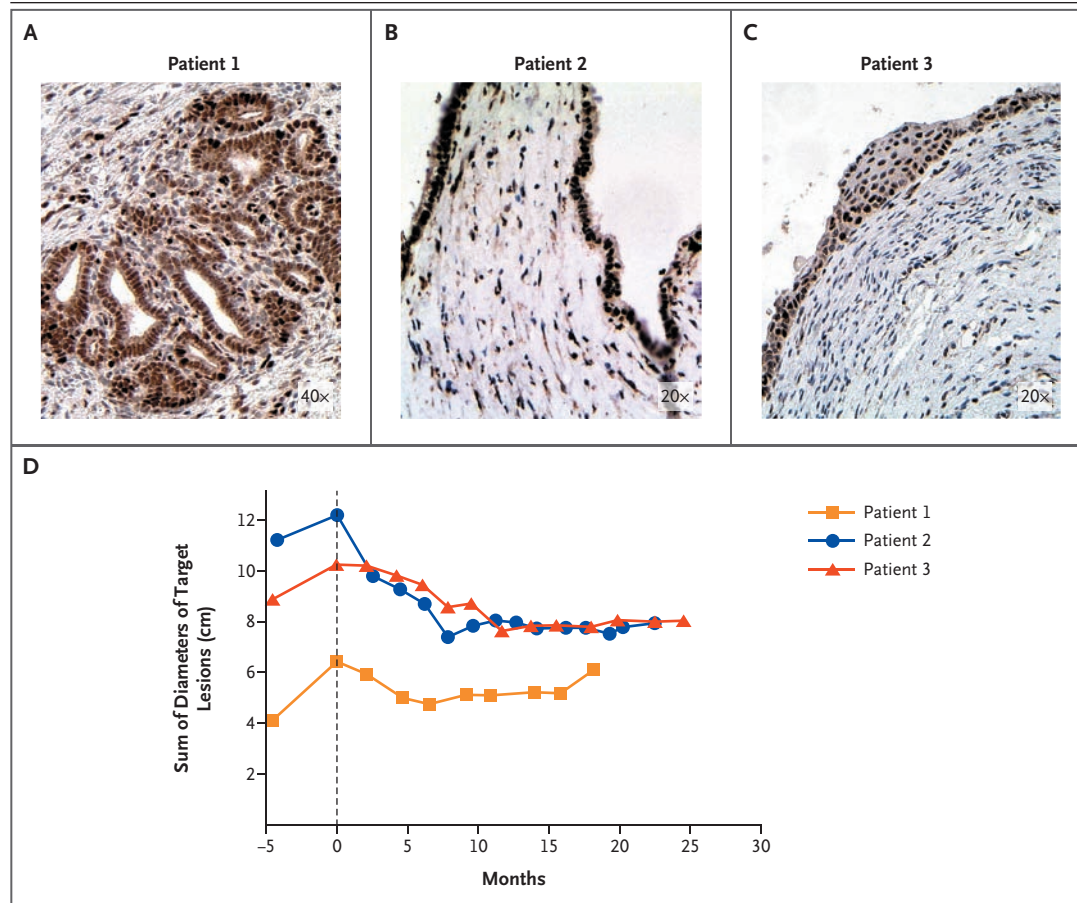


Figure 1. Immunohistochemical and Radiologic Findings in Three Patients with Growing Teratoma Syndrome after Treatment with PD0332991.

Immunohistochemical staining of paraffin-embedded primary tumor blocks with the use of a mouse monoclonal antibody in a 1:50 dilution (EDTA retrieval, Laboratory Vision) was performed. Panel A shows staining of mature teratoma cells in a specimen obtained from Patient 1 (magnification, $\times 40$). Panel B shows staining of cells obtained from Patient 2 (magnification, $\times 20$), and Panel C shows staining of cells obtained from Patient 3 (magnification, $\times 20$). There is strong nuclear staining of retinoblastoma protein (pRB) in the epithelial component of the teratomas. Panel D shows the effect of treatment (initiated at time 0) represented by the sums of the longest diameters of the target lesions at each radiologic evaluation. All patients had progressive disease before the initiation of treatment.

Although embryonal carcinomas express little or no retinoblastoma protein (pRB),³ mature teratomas express high levels of pRB. Normally, cyclin-dependent kinase 4/6 (CDK4/6) stimulates cell growth by phosphorylating pRB. The development of selective CDK inhibitors,⁴ including PD0332991 (Pfizer), which selectively inhibits CDK4/6, suggests a new treatment for growing teratoma syndrome.

We report on the clinical course of three men, 22 to 37 years of age, with growing teratoma syndrome who were treated in a phase 1 trial of PD0332991 for refractory solid tumors (ClinicalTrials.gov number, NCT00141297).⁵ This trial was sponsored and funded by Pfizer. The patients initially presented with metastatic non-seminomatous germ-cell tumors. They received four cycles of cisplatin-based chemotherapy, with normalization of serum tumor markers. Each patient underwent two or more operations for growing teratoma syndrome after chemotherapy. Subsequently, progressive disease that was not amenable to further surgery developed in all the patients. Written informed consent was obtained from the patients in this protocol, which was approved by the institutional review board of the University of Pennsylvania.

There was a strong nuclear expression of pRB in the epithelial component of the teratomas in all three patients (Fig. 1A, 1B, and 1C). At enrollment, all patients had radiologic evidence of disease progression (Fig. 1D). Patient 1 received oral PD0332991, 150 mg daily, for 21 days on an every-28-days cycle. The dose was decreased to 100 mg because of neutropenia. He had stable disease for 18 months. Patient 2 initiated treatment with PD0332991, 200 mg daily, for 14 days on an every-21-days cycle. The dose was decreased to 150 mg because of headaches and vomiting. Neutropenia also developed. He had a partial response (according to the Response Evaluation

Criteria in Solid Tumors) for 22 months and continued to receive treatment. Patient 3 initiated treatment with PD0332991 at a dose of 125 mg daily for 21 days on an every-28-days cycle. He also had neutropenia. He had stable disease for 24 months and continued to receive treatment.

These preliminary data suggest that PD0332991 has therapeutic benefit in patients with growing teratoma syndrome in whom the tumor is inoperable. We suggest further evaluation of CDK inhibitors in pRB-expressing teratomas.

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1. Logothetis CJ, Samuels ML, Trindade A, Johnson DE. The growing teratoma syndrome. *Cancer* 1982;50:1629-35.

2. Speiss PE, Kassouf W, Brown GA, et al. Surgical management of growing teratoma syndrome: the M. D. Anderson Cancer Center experience. *J Urol* 2007;177:1330-4.

3. Bartkova J, Lukas C, Sørensen CS, et al. Deregulation of the RB pathway in human testicular germ cell tumours. *J Pathol* 2003;200:149-56.

4. Schwartz GK, Shah MA. Targeting the cell cycle: a new approach to cancer therapy. *J Clin Oncol* 2005;23:9408-21.

5. O'Dwyer PJ, LoRusso P, DeMichele A, et al. A phase I dose escalation trial of a daily oral CDK 4/6 inhibitor PD-0332991. *J Clin Oncol* 2007;25:Suppl:150s. abstract.

Excess Iodine from an Unexpected Source

TO THE EDITOR: It is standard practice to induce a decrease in the body's iodine stores before treatment with radioiodine for thyroid cancer. Such patients should avoid an iodine-rich diet,^{1,2} and physicians should be aware that some over-the-counter supplements contain iodine.

A 55-year-old man had a large mass on the

right side of his neck, which was identified in a specimen from a fine-needle aspiration biopsy as papillary thyroid carcinoma. He had a total thyroidectomy, with a modified dissection of the right side of the neck. Pathological examination revealed a multifocal, papillary thyroid carcinoma, the largest being 1.8 cm in diameter, with capsular and