

Pretargeted Anti–Carcinoembryonic-Antigen Radioimmunotherapy for Medullary Thyroid Carcinoma

TO THE EDITOR: In their recent work, Chatal et al¹ describe a significant survival advantage of patients with progressive medullary thyroid carcinoma treated with pretargeted anti–carcinoembryonic-antigen radioimmunotherapy over an untreated control group matched on calcitonin doubling time (median, 110 months v 61 months; $P < .030$). This survival advantage doubled for biologic responders relative to these controls (median, 159 months v 61 months; $P < .010$), and was still evident when biologic responders were compared with biologic nonresponders (median, 159 months v 109 months; $P < .035$).

In delineating clinical risk, Chatal et al relied on calcitonin doubling times, with cut-offs set at 2 years and 5 years. In clinical practice, however, a risk classification based on calcitonin doubling times may not really be helpful because of the need for protracted expectant observation.

Anti–carcinoembryonic-antigen radioimmunotherapy is targeted on membrane-bound carcinoembryonic antigen. There is some evidence to suggest that serum levels of carcinoembryonic antigen from patients with medullary thyroid carcinoma may correspond to the expression of carcinoembryonic antigen in the cancer cells.^{2,3} In addition, the duration of response to pretargeted anti–carcinoembryonic-antigen radioimmunotherapy was previously shown to correlate with the duration of the blood carcinoembryonic antigen response.⁴

The suitability of serum levels of carcinoembryonic antigen for risk stratification of patients with medullary thyroid carcinoma before initial operation has emerged only recently.⁵ Preoperative serum levels of carcinoembryonic antigens greater than 30 ng/mL almost always conflicted with surgical curability and were associated with an approximately 70% rate of involvement of the central and lateral lymph node compartment on the side of the primary tumor. This rate of involvement increased to approximately 90% when the preoperative serum level of carcinoembryonic antigen exceeded 100 ng/mL. In this setting,

involvement of the lateral lymph node compartment on the side opposite to the primary tumor, and distant metastases were seen in three quarters of the patients at the time of operation.⁵ These data suggest that pretherapeutic serum levels of carcinoembryonic antigen, which are available within a few days, may predict the chance of patients with medullary thyroid carcinoma to benefit from anti–carcinoembryonic-antigen radioimmunotherapy.

We wonder if Chatal et al have the data to break down their patients with medullary thyroid carcinoma by pretherapeutic serum level of carcinoembryonic antigen and response to pretargeted anti–carcinoembryonic-antigen radioimmunotherapy. This piece of information would further elucidate the effectiveness of this novel therapeutic modality in select subgroups of patients with medullary thyroid carcinoma.

Andreas Machens and Henning Dralle

Martin Luther University Halle-Wittenberg, Halle (Saale), Germany

REFERENCES

1. Chatal JF, Campion L, Kraeber-Bodéré F, et al: Survival improvement in patients with medullary thyroid carcinoma who undergo pretargeted anti-carcinoembryonic-antigen radioimmunotherapy: A collaborative study with the French Endocrine Tumor Group. *J Clin Oncol* 24:1705-1711, 2006
2. Hamada S, Ishikawa N, Yoshii M, et al: Roles of circulating carcinoembryonic antigen and calcitonin in diagnosis of medullary thyroid carcinoma: A comparative study. *Endocrinol Japon* 23:505-510, 1976
3. Pacini F, Basolo F, Elisei R, et al: Medullary thyroid cancer: An immunohistochemical and humoral study using six separate antigens. *Am J Clin Pathol* 95:300-308, 1991
4. Kraeber-Bodéré F, Rousseau C, Bodet-Milin C, et al: Targeting, toxicity, and efficacy of 2-step, pretargeted radioimmunotherapy using a chimeric bispecific antibody and ¹³¹I-labeled bivalent hapten in a phase I optimization clinical trial. *J Nucl Med* 47:247-255, 2006
5. Machens A, Ukkat J, Hauptmann S, et al: Abnormal carcinoembryonic antigen levels and medullary thyroid cancer progression: A multivariate analysis. *Arch Surg* (in press)

DOI: 10.1200/JCO.2006.06.8171

Authors' Disclosures of Potential Conflicts of Interest

The authors indicated no potential conflicts of interest.