Efficacy of Sunitinib in Advanced Medullary Thyroid Carcinoma: Intermediate Results of Phase II THYSU

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In response to a case reported in *The Oncologist* describing the efficacy of sunitinib in medullary thyroid carcinoma (MTC), it was stated that this was the first case reported [1]. We would like to inform readers that the results of a previous ongoing trial (THYSU) were presented at the American Society of Oncology (ASCO) meeting in 2008 [2], confirming the efficacy of sunitinib in MTC and non-MTC (differentiated and anaplastic TC) patients, and this confirmed in an unpublished intermediate analysis (September 24, 2008), which is presented here.

The Phase II Trial of Sunitinib (Sutent®) in Patients with Locally Advanced or Metastatic Anaplastic or Differentiated Thyroid Cancer (THYSU) was designed to investigate the efficacy of sunitinib for progressive, locally advanced, or metastatic TC. Two cohorts of patients were explored based on histology: differentiated and anaplastic TC on the one hand, and MTC on the other. For MTC patients, a two-step study was designed according to Gehan's method [3]. Eleven patients had to be included in the first step. The primary parameter was achievement of objective responses according to the Response Evaluation Criteria in Solid Tumors. Depending on the number of responses, seven to 14 additional pa-

tients could be included in a second step. Sunitinib was given at the standard dose of 50 mg/day, 4 weeks every 6 weeks. At the time of the interim analysis, as presented at the ASCO meeting, 15 patients with progressive MTC had been included in 6 months. Eleven patients were male, and the mean age was 62 years. Ten patients had a Karnofsky performance status ≥ 90 . The mean time from diagnosis to inclusion in the protocol was 2.9 years. Two patients had a local recurrence and all had metastases at one to five sites. Only two patients had received first-line chemotherapy. The mean follow-up duration was 6.2 months (range, 1.2–10.3 months). Patients received an average of four cycles of sunitinib (range, 1–7 cycles). Nine patients had to have their doses of sunitinib reduced. Two patients had a confirmed partial response, three had an unconfirmed partial response (33.3%), and four had stable disease for ≥ 12 weeks (26.7%), with an overall mean tumor shrinkage rate of 27.3%. In all, seven patients with elevated calcitonin levels at inclusion saw their calcitonin level decrease during the sunitinib period, remain stable, or reincrease during the pause. In view of the efficacy at the intermediate analysis, the study was extended to a total of 25 patients with MTC, as well as to the non-MTC population. However, of the

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overall population of the THYSU study (MTC and non-MTC patients), at the intermediate analysis, the safety profile analysis pointed to two serious cardiac side effects for which the data safety monitoring board recommended a closer follow-up of cardiac function with left

ventricular ejection fraction tests every two cycles and brain natriuretic peptide (BNP) dosage at the initiation of and before any cycle. All patients were included after the second step inclusion period and the data have been collected.

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