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Original Research Paper

Sorafenib in iodo-refractory thyroid cancer: Experience of medical oncology department of Pierre and Marie Curie Center Algiers Algeria

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ABSTRACT:
Background: Although thyroid cancer us usally has a excellent prognosis, few therapeutic options are available in the refractory setting, Its multidisciplinary approach is the subject of recommendations regularly updated .The Sorafenib (a multi kinase inhibitor) was recently distinguished as a valid therapeutic option in case the exhaust with standard therapy (surgery ± radioiodine)**. Aim**: is to evaluate the efficacy and safety of sorafenib. **Methods**: We report a retrospective analysis of 53 patients followed for metastatic thyroid cancer and resistant to radioactive iodine, collected in our medical oncology Pierre and Marie Curie center in Algiers. **Results**: Of 53 patients , we treated 40 symptomatic patients with sorafenib, 15 men and 25 women with a sex ratio of 0.6, the average age is 54.58 years (22-79) Histologically we have 15 papillary carcinomas, 13 vesicular carcinomas, 10 poorly differentiated carcinomas, 02 mixed papillary and medullary carcinoma. 38 patients benefited from thyroid surgery, 40 from iratherapy at an average dose of 621 mci. The metastatic sites were: Lung (75%), bone (44%), liver (16%), brain (9%), adrenal (6%), skin (6%). 16% had local and lymph node recurrence .Patients received an average of 11 courses of sorafenib at a daily dose of 800 mg per day 36 patients are evaluable for response, we obtained 25 stabilizations, 04 partial responses and 07 progressions. The average progression-free survival is 13 months. The most common adverse events are: hand foot syndrome grade III (n = 2), moderate hypertension (n = 07), diarrhea grade 2 n=6 , skin reaction grade 3 (n = 1). **Conclusion:** Sorafenib is a promising treatment option for patients with iodine-refractory thyroid cancer

Keywords: Thyroid cancer, iodine refractor, tyrosine kinase inhibitors

INTRODUCTION:

Thyroid cancer is a cancer with a favorable prognosis. Its multidisciplinary care. (1) Sorafenib (a multi-kinase inhibitor) is the first line treatment in cases of failure to standard treatments (surgery ± radioactive iodine)(2)

AIM OF THE STUDY:

Is to evaluate the efficacy and tolerance of sorafenib.

MATERIALS AND METHODS:

We report a retrospective study of 53 patients followed for metastatic thyroid cancer and resistant to radioactive iodine, collected in our medical oncology department at the Pierre and Marie Curie center in Algiers.

RESULTS:

Out of 53 patients, we treated 40 patients symptomatic patients with sorafenib, 15 men and 25 women with a sex ratio of 0.6, the average age is 54.58 years (22-79) Histologically we have 15 papillary carcinomas, 13 vesicular carcinomas, 10 poorly differentiated carcinomas (3), 02 mixed papillary and medullary carcinoma (4). 38 patients benefited from thyroid surgery, 40 from iratherapy at an average dose of 621 mci.

The Metastatic Sites Were:

Lung (75%) , bone (44%), liver (16%), brain (9%), adrenal (6%), skin (6%). 16% had local and lymph node recurrence (5). Patients received an average of 11 courses of sorafenib at a daily dose of 800 mg per day 36

patients are evaluable for response (Figure 1), we obtained 25 stabilizations, 04 partial responses (figure 2) and 07 progressions. The average progression-free survival is 13 is 16.2 months with a Median survival 13 months. Average overall survival is 30.34 months with 79% for one year and 54.4% at two years. The most common side effects are: hand and foot syndrome grade III (n=2), moderate hypertension (n=05), skin rash grade 3 (n=1).

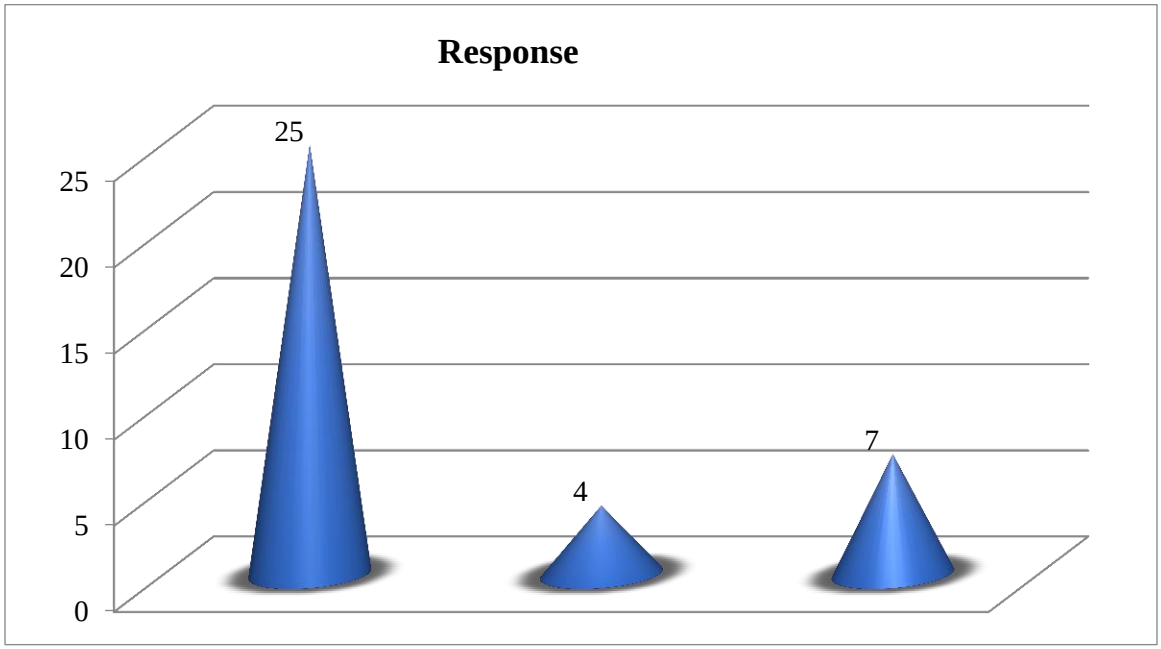

Figure 1: Stabilisation, Partial response, Progression

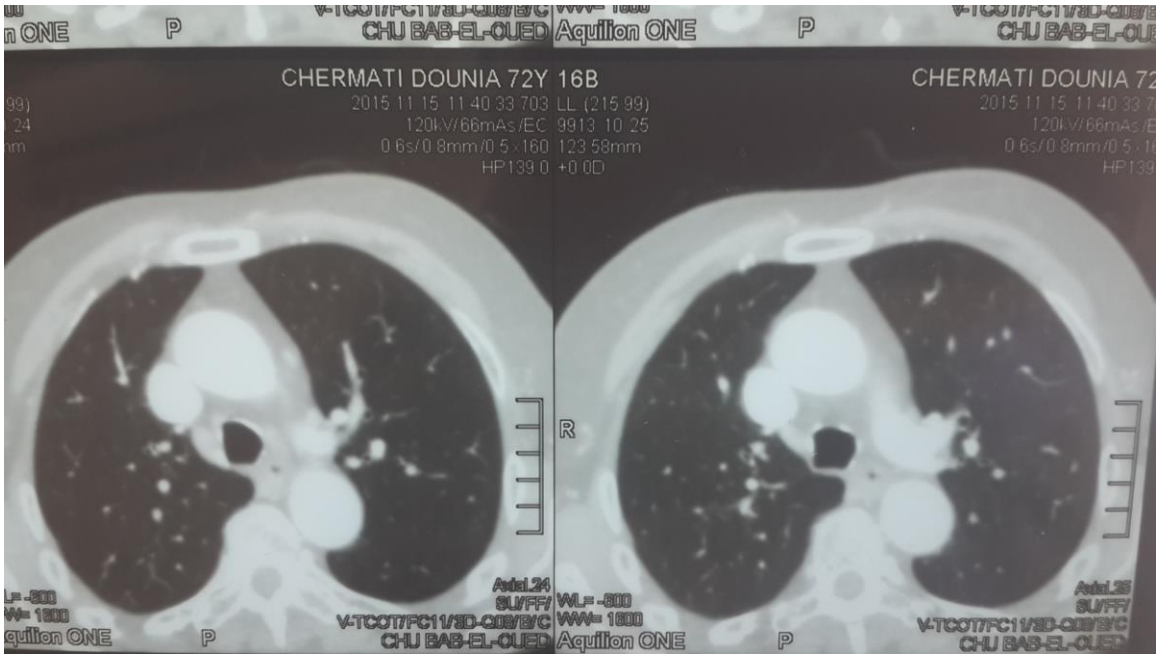

Figure 2 : Lung metastasis after 24 cycles of Sorafenib PR (31%)

DISCUSSION:

- A Differentiated Thyroid Cancer (DTC) can be considered as refractory to iodine when:
- Malignant / metastatic structurally evident disease that does not ever concentrate RAI
- Tumor tissue that loses the ability to concentrate RAI after previous evidence of RAI avid disease
- RAI concentration in some lesions but not in others

- Metastatic disease progresses despite significant concentration of RAI
- Persistent disease after a cumulative dose of 600 mCI (6)

Most often, progression is slow with median survivals of three to seven years for iodor-refractory CTD. It is therefore necessary to carefully assess the risks and benefits of therapy other than symptomatic. However, a disease that progresses (sequential imaging, doubling time of tumor markers: thyroglobulin) between six and fifteen months in principle justifies a therapeutic approach.

- In this situation, the now historic use of adriamycin (with cisplatin) and only offers a low response rate without modifying survival and has been replaced by targeted therapies.(7)
- The results of the DECISION study (8) (phase III, multicenter, randomized, double-blind) comparing sorafenib (n = 207) at a dosage of 400 mg x 2/day to placebo (n = 210) in patients with differentiated thyroid cancer locally advanced or metastatic and refractory to radioactive iodine (I131) or progressing despite treatment with I131
- sorafenib showed its superiority compared to placebo, with a median progression-free survival time of 10.8 months compared to 5.8 months, i.e. an absolute gain of 5 months in favor of sorafenib
- The impact on overall survival has not been demonstrated: the median overall survival was not reached neither in sorafenib group (54 deaths out of 207 patients), nor in the placebo group (54 deaths/210 patients) .
- The percentage of stable disease was comparable in the two groups (74%).
- The percentage of overall response (complete + partial response) was 12.2% (22/196) and 0.5% (1/201) in the sorafenib and placebo groups respectively ($p < 0.0001$), without any complete response .

CONCLUSION:

Understanding of the molecular biology of thyroid cancers has progressed, and significant progress has been made. Kinase inhibitors inhibit VEGF receptor kinases and thus angiogenesis and some of them inhibit other kinases which are involved in particular in the Mitogen-Activated Protein kinase pathway. These inhibitors are effective in differentiated thyroid cancers and in medullary cancers, causing a partial tumor response or long-term stabilization in more than half of patients.

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