Journal of Cancer and Tumor International

11(4): 7-10, 2021; Article no.JCTI.70420
ISSN: 2454-7360

Lenvatinib in Anaplastic Thyroid Carcinoma (ATC) in a Tertiary Caner Hospital- a Single Institute Experience

Rakesh Sharma[1], P. S. Dattatreya[2], A. V. S. Suresh[2*] and Ch Mohana Vamsy[3]

[1]BOG and OSD, National Board of Examinations, Delhi, India.
[2]Department of Medical Oncology, Omega Hospitals, Hyderabad, India.
[3]Department of Surgical Oncology, Omega Hospitals, Hyderabad, India.

Authors' contributions

This work was carried out in collaboration among all authors. Authors with affiliation RS contributed for the subject management and content writing and accuracy. While with affiliation PSD helped in the biostatistics and manuscript complication. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JCTI/2021/v11i430156
Editor(s):
(1) Dr. Sung-Chul Lim, Chosun University, South Korea.
Reviewers:
(1) Shishir Ojha, Waukesha Memorial hospital, USA.
(2) Raghunadharao Digumarti, KIMS ICON Hospital, India.
Complete Peer review History: https://www.sdiarticle4.com/review-history/70420

Original Research Article

Received 06 May 2021
Accepted 12 July 2021
Published 12 July 2021

ABSTRACT

Anaplastic Thyroid Carcinoma (ATC) is an aggressive rare form of caner with limited treatment options and short survival. In view of initial case reports have shown some good clinical response with lenvatinib, we used the same in our institute. We are presenting a retrospective series of 4 cases between 2018-2021. It showed very promising results with 75% showing clinically meaningful regression of tumor. Hypertension is the most common side effect, which should be aggressively managed. We feel that, lenvatinib remains a safe and effective option to explore in patients with refractory anaplastic thyroid carcinoma.

Keywords: Anaplastic thyroid carcinoma; lenvatinib; India.

1. INTRODUCTION

Anaplastic Thyroid Carcinoma (ATC) is an aggressive rare form of caner with limited treatment options and short survival. Though it represents 2% of all thyroid malignancies, it accounts for 50% of all thyroid cancer related deaths. Until recently there has been no

**Corresponding author: Email: attilivss@gmail.com;*

standard of care available for this cancer. Current survival times for patients with ATC are reported to be extremely short and median Overall Survival (OS) for patients with unresectable disease ranges from 0.5 to 6 months despite multimodal treatment [1]. The newer oral multi targeted tyrosine kinase inhibitor, Lenvatinib showed promising results for the same. The initial case reports have shown some good clinical response, which encouraged the oncologists to use the drug more extensively [1,2,3,4]. Based on the literature, we used the lenvatinib in 4 of the subjects and presenting a case series along with demographics, response and the safety profile.

2. MATERIALS AND METHODS

We present a retrospective analysis of all cases between 2018-2021, who were diagnosed with anaplastic thyroid cancer and had recurrence. Lenvatinib 24 mg once daily was administered at the time of diagnosis of ,metastatic disease and continued until disease progression, unmanageable toxicity. Dose reduction was followed as per the package insert.

The key eligibility criteria for selecting the cases include

1. Aged ≥20 years, either gender
2. Histological confirmed diagnosis of anaplastic thyroid cancer
3. At least one measurable lesion as pre RECIST (Response Evaluation Criteria In Solid Tumors)
4. Eastern Cooperative Oncology Group performance status of ≤2
5. Systolic blood pressure ≤140 mmHg and diastolic blood pressure ≤90
6. Life expectancy of at least more than 2 months
7. Adequate hepatic renal and marrow functions as measured by the labs
8. Consenting and willing to take the medication

The patients underwent 3 weekly clinical examinations, including the documentation of adverse events as per CTC AE (Common Toxicity Criteria – Adverse events) criteria [5], and 6 monthly imaging or whenever clinically indicated, or till progression. The survival follow up was, as per the standard hospital practices.

The purpose of the study is to evaluate the response to treatment, safety and tolerability of Lenvatinib, using RECIST and CTC criteria using descriptive statistics like survival(in weeks) , grade of toxicity.

3. RESULTS

A total of 4 cases were presented during the period with following characters (Table 1). All of the subjects have experienced ≥1 treatment-related adverse event (TRAE). The response to treatment was assessed using RECIT 1.1 criteria [6].

Table 1. Patient characters

	Case 1	**Case 2**	**Case 3**	**Case 4**
Demographics/disease characters				
Age/ Gender	45/F	53/F	69/M	43/F
Duration of symptoms	2 months	1.5 months	2 months	1.5 months
Stage at first diagnosis	T1N0M0	T2N1M0	T2N0M0	T2N0M0
Relapse from date of surgery	130 days	46 days	98 days	110 days
Adjuvant Radiation	Yes	No	Yes	Yes
PS	1	2	1	1
Sites of recurrence	Nodal, local, Lung	Nodal, local, Lung	Nodal, local, Lung	Nodal, local, Lung
Lenvatinib starting dose (mg)	24	24	24	24
Dose reduction- final dose	14	24	14	24
Adverse events				
Hypertension	CTC AE Gr IV	CTC AE Gr I	CTC AE Gr III	CTC AE Gr IV
Diarrhoea	CTC AE Gr II	CTC AE Gr I	CTC AE Gr II	CTC AE Gr II

	Case 1	Case 2	Case 3	Case 4
Fatigue	CTC AE Gr III	CTC AE Gr IV	CTC AE Gr IV	CTC AE Gr III
Nausea	CTC AE Gr II	CTC AE Gr II	CTC AE Gr I	CTC AE Gr II
Best response*	Partial response and continued	Progressed in 6 weeks	Partial response at week 6 progressed at week 12	Partial response at week 6 progressed at week 18
Survival (weeks)	112**	18	23	32

**Partial response defied as more than 20% regression from base line of the sum of maximum diameters and progression defined as new lesions or increase in size of lesions*
*** patient still surviving*

4. DISCUSSION AND CONCLUSION

4.1 Discussion

Most of our patients were females with M:F ratio of 1:3, which is higher than what was reported from the literature probably due to geographical bias [7]. The age range in the present study is 43-69 years, which is in alignment with the literature. The interval from the first diagnosis to recurrence is quite short in this series as reported in literature [1,2,8].

The adverse events observed in our patients are very similar to those reported in phase 2 trial of lenvatinib in medullary thyroid cancer and the phase 3 SELECT trial of lenvatinib in RR-DTC (Radio iodine Refractory- Differentiated Thyroid Cancer) [9,10]. Though hypertension was observed more frequently and in more severe form in our institute, we also observed that these patients did show better and quicker response to therapy. The hypertension was controlled quickly and effectively with medications and in 2 of them, though there was initial dose reduction, we could be brought back to initial dose at later point after antihypertensives. Even though the subjects are on lower doses, we did not observer any signs of disease progression, which means, the drug was probably effective at lower doses as well.

Another key observation is that 75% of our patients had some clinically meaningful regression, which is note worthy as it is much higher than other reports [2,3,4,9,10] and similar to the observations of Soo Young Kim et al. [1]. It is also evident that those who have more hypertension and quicker onset had good response. We feel that Hypertension- may be biological marker of response (like skin rash for the Cetuximab)- however the numbers are too small and it is too early to comment like that .

4.2 Conclusions/Key Limitations and Take Always

1. To conclude, lenvatinib remains a safe and effective option to explore in patients with anaplastic thyroid carcinoma.
2. Hypertension is the most common side effect, which should be aggressively managed and may indicate a good response to therapy
3. The small sample size and retrospective nature of the study limits the extrapolation of the outcomes beyond a point, which is the major drawback of the study.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by

the producing company rather it was funded by personal efforts of the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Soo Young Kim, Seok-Mo Kim, Jun Won Kim, Ik Jae Lee, Tae Joo Jeo3, Hojin Chang, et al. Survival with lenvatinib for the treatment of progressive anaplastic thyroid cancer: A single-center, retrospective analysis. Front. Endocrinol. 2020;11:599.
DOI: 10.3389/fendo.2020.00599
2. Koyama S, Miyake N, Fujiwara K, Morisaki T, Fukuhara T, Kitano H, Takeuchi H. Lenvatinib for Anaplastic Thyroid Cancer and Lenvatinib-Induced Thyroid Dysfunction. Eur Thyroid J. 2018 Jun;7(3):139-144.
DOI: 10.1159/000485972. Epub 2018 Feb 21. PMID: 30023346; PMCID: PMC6047489.
3. Wirth LJ, Brose MS, Sherman EJ, Licitra L, Schlumberger M, Sherman SI, Bible KC, Robinson B, Rodien P, Godbert Y, De La Fouchardiere C, Newbold K, Nutting C, Misir S, Xie R, Almonte A, Ye W, Cabanillas ME. Open-label, single-arm, multicenter, Phase II Trial of Lenvatinib for the Treatment of Patients With Anaplastic Thyroid Cancer. J Clin Oncol. 2021 May 7;JCO2003093. DOI: 10.1200/JCO.20.03093. Epub ahead of print. PMID: 33961488.
4. Tahara M, Kiyota N, Yamazaki T, Chayahara N, Nakano K, Inagaki L, Toda K, Enokida T, Minami H, Imamura Y, Sasaki T, Suzuki T, Fujino K, Dutcus CE, Takahashi S. Lenvatinib for Anaplastic Thyroid Cancer. Front Oncol. 2017 Mar 1;7:25. DOI: 10.3389/fonc.2017.00025. PMID: 28299283; PMCID: PMC5331066.
5. Availablehttp://evs.nci.nih.gov/ftp1/CTCAE/About.html CTCAE v4.03 [minor update 2010]
6. Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, Dancey J, Arbuck S, Gwyther S, Mooney M, Rubinstein L, Shankar L, Dodd L, Kaplan R, Lacombe D, Verweij J. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer. 2009 Jan;45(2):228-47. DOI: 10.1016/j.ejca.2008.10.026. PMID: 19097774.
7. Chintakuntlawar, AV; Foote, RL; Kasperbauer, JL; Bible, KC. Diagnosis and management of anaplastic thyroid cancer. Endocrinology and Metabolism Centers of North America (Review). March 2019;48 (1): 269–84. DOI:10.1016/j.ecl.2018.10.01
8. cancer.org. Thyroid Cancer By the American Cancer Society. In turn citing: AJCC Cancer Staging Manual (7th ed).
9. Schlumberger M, Tahara M, Wirth LJ, Robinson B, Brose MS, Elisei R, et al. Lenvatinib versus placebo in radioiodine-refractory thyroid cancer. N Engl J Med. 2015;372(7):621–30.
DOI:10.1056/NEJMoa1406470
10. Kiyota N, Schlumberger M, Muro K, Ando Y, Takahashi S, Kawai Y, et al. Subgroup analysis of Japanese patients in a phase 3 study of lenvatinib in radioiodine-refractory differentiated thyroid cancer. Cancer Sci. 2015;106(12):1714–21.
DOI:10.1111/cas.12826

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle4.com/review-history/70420