head and neck cancer

995PD

PHASE II STUDY OF LENVATINIB (LEN), A MULTI-TARGETED TYROSINE KINASE INHIBITOR, IN PATIENTS (PTS) WITH ALL HISTOLOGIC SUBTYPES OF ADVANCED THYROID CANCER (DIFFERENTIATED, MEDULLARY AND ANAPLASTIC)


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Aim: LEN is an oral tyrosine kinase inhibitor targeting VEGFR1-3, FGFR1-4, RET, KIT and PDGFRβ, and showed a prominent improvement in progression free survival (PFS) in pts with radioiodine-refractory differentiated thyroid cancer (RR-DTC) in Phase III study.

Methods: This is an open-label, multi-center phase II study conducted in Japan in pts with advanced thyroid cancer including RR-DTC, medullary thyroid cancer (MTC) and anaplastic thyroid cancer (ATC). Institutional pathological diagnoses were accepted for eligibility. Pts were treated with a starting dose of LEN 24 mg once daily in 28 day cycles until disease progression or development of unmanageable toxicities. Primary objective was safety, and efficacy was assessed by RECIST 1.1 as secondary objective.

Results: From September 2012 to September 2013, 35 pts (all in PS 0-1, median age: 60.0, male/female: 13/22 ) were enrolled and evaluable for safety, including 22 pts with RR-DTC, 4 pts with MTC, and 9 pts with ATC. The most common adverse events (AEs; any Grade; Grade $\geq$ 3) included hypertension (86%; 43%), palmar-plantar erythrodysesthesia syndrome (74%; 6%), fatigue (71%; 3%), decreased appetite (69%; 9%), proteinuria (51%; 0%), stomatitis (51%; 0%), diarrhea (43%; 11%), nausea (40%; 6%) and dysphonia (31%; 0%). Almost all (34/35) subjects required dose reduction, however, no subjects required study drug withdrawal due to AEs. 34 pts were evaluable for efficacy, including 21 pts with RR-DTC, 4 pts with MTC, and 9 pts with ATC. The objective response rate (ORR) based on the investigator assessment was 47.6% in RR-DTC, 25.0% in MTC, and 33.3% in ATC. Median PFS was 6.5 mo (95% CI: 5.6 - 7.3) in MTC and 5.5 mo (95% CI: 1.4 -) in ATC, respectively. Median PFS has not been determined in RR-DTC.

Conclusions: AE profiles were generally similar to the data from previous clinical studies of lenvatinib with manageable toxicity with dose reduction and interruption. LEN demonstrated promising activity in all histologic subtypes of advanced thyroid cancer. Three of 9 pts with ATC have received administration of LEN for more than 6 month, which should be noteworthy.

Disclosure: S. Takahashi, M. Tahara and N. Kiyota: Advisory Board: Eisai. All other authors have declared no conflicts of interest.