Nature Reviews Endocrinology | Published online 14 Jul 2017; doi:10.1038/nrendo.2017.96

TARGETED THERAPIES

Lenvatinib SELECTs survival benefit

Until the past 4 years, no treatment option existed for patients with refractory differentiated thyroid cancer, who were treated routinely with supportive care. The first drug to be approved for these patients by the FDA was sorafenib in 2013, followed by lenvatinib in 2015 — both approvals were on the basis of progression-free survival (PFS) improvements, with no demonstrated overall survival benefit. Now, a study has shown that the oral multikinase inhibitor lenvatinib, which targets VEGF, FGFR, RET and KIT, increases overall survival in patients with differentiated thyroid cancer who are refractory to radioiodine therapy.

In the double-blind, phase III SELECT trial, 392 patients were randomly assigned to receive lenvatinib or placebo. Patients were divided into two age groups: those younger than 65 years and those older than 65 years. PFS outcomes did not differ significantly between older and younger patients in either arm. When age was analyzed as a continuous variable, a significant correlation between age and a shorter overall survival was noted for patients receiving placebo, but not for those treated with lenvatinib. Among the older cohort, the median overall survival was 18.4 months in the placebo arm, and for patients treated with lenvatinib was not reached, but is expected to exceed 22 months. In the younger cohort, overall survival was not reached for either age group. Overall, the incidence of adverse events was considerably higher in older patients compared with younger patients (89% versus 67%).

Marcia Brose, lead author of the study, comments on the importance of these trial data: "for the first time ever we have now proven that a multikinase inhibitor, lenvatinib, extends overall survival for patients with radioiodine-refractory differentiated thyroid cancer. This was shown only for the patients over 65 years of age, which in itself is noteworthy because this study also demonstrates the drug is tolerable in these patients". The overall survival data were not mature at the time of study reporting. Nevertheless, owing to extensive patient crossover in the placebo arm, longer follow-up durations will unlikely result in different outcomes.

Brose highlights the implications for future research: "this is a disease that has been shown to be responsive to kinase inhibitors; these patients are now doing better and our data show that some of these patients are living longer." These promising latest data have renewed interest in identifying additional agents that can be used either sequentially or in combination with lenvatinib, which might enhance the clinical benefit described herein.

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This article originally appeared in Nat. Rev. Clin. Oncol. (http://dx.doi.org/10.1038/nrclinonc.2017.103)

ORIGINAL ARTICLE Brose, M. S. *et al.* Effect of age on the efficacy and safety of lenvatinib in radioiodine-refractory differentiated thyroid cancer in the phase III SELECT trial. *J. Clin. Oncol.* http://dx.doi.org/10.1200/JCO.2016.71.6472 (2017)

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