2021 ESMO congress

LBA17

Overall survival (OS) results from the phase III MONALEESA-2 (ML-2) trial of postmenopausal patients (pts) with hormone receptor positive/human epidermal growth factor receptor 2 negative (HR+/HER2–) advanced breast cancer (ABC) treated with endocrine therapy (ET) ± ribociclib (RIB)

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Background

ML-2 (NCT01958021) is a randomized phase III clinical trial investigating first-line (1L) RIB, a cyclin-dependent kinase 4/6 inhibitor (CDK4/6i), + letrozole (LET) vs placebo (PBO) + LET in postmenopausal pts with HR+/HER2– ABC. ML-2 previously reported a statistically significant improvement in progression-free survival (PFS; primary endpoint) with RIB + LET vs PBO + LET (HR, 0.56; 95% CI, 0.43-0.72). We report the protocol-specified final analysis of OS (key secondary endpoint).

Methods

Postmenopausal pts with HR+/HER2– ABC were randomized 1:1 to receive RIB + LET or PBO + LET. Pts were excluded if they received a prior CDK4/6i, chemotherapy (CT), or ET in the advanced setting. OS was evaluated with a stratified log-rank test and summarized using Kaplan–Meier methods. This protocol-specified analysis was planned after 400 deaths.

Results

The intention-to-treat population included 668 pts (RIB: 334; PBO: 334). At data cutoff (10 June 2021), 47 pts were still on treatment (RIB: 30 [9.0%]; PBO: 17 [5.1%]) and the median follow-up was 79.7 mo (min, 74.6 mo). Final OS was evaluated after 400 deaths (RIB: 181 [54.2%]; PBO: 219 [65.6%]). RIB + LET showed a significant OS benefit vs PBO + LET (median, 63.9 vs 51.4 mo; HR, 0.76; 95% CI, 0.63-0.93; *P*=.004) and met the boundary of statistical significance. Estimated 6-year OS rate was 44.2% for RIB vs 32.0% for PBO. Time to first CT (median, 50.6 vs 38.9 mo; HR, 0.74; 95% CI, 0.61-0.91) and CT-free survival (median, 39.9 vs 30.1 mo; HR, 0.74; 95% CI, 0.62-0.89) showed a consistent benefit for RIB vs PBO. Among pts who discontinued study treatment, 87.8% vs 90.2% received a subsequent antineoplastic therapy for RIB vs PBO, respectively, and 21.7% and 34.4% received a subsequent CDK4/6i. No new safety signals were observed.

Conclusions

To date, this is the first report of a statistically significant and clinically meaningful OS benefit with a 1L CDK4/6i in postmenopausal pts with HR+/HER2– ABC. After a median follow-up of >6.5 y, median OS improvement was >12 mo for 1L RIB + LET vs PBO + LET.

Clinical trial identification

NCT01958021 (CLEE011A2301).

Editorial acknowledgement

This abstract was developed with editorial assistance provided by Casey Nielsen, PhD of MediTech Media, LLC. Editorial

support was funded by Novartis Pharmaceuticals Corporation.

Legal entity responsible for the study

Novartis Pharmaceuticals Corporation.

Funding

Novartis Pharmaceuticals Corporation.

Disclosure

G.N. Hortobagyi: Financial Interests, Personal, Research Grant, Grant support to institution to conduct trial. Personal fees member/chair Steering Committee: Novartis. S.M. Stemmer: Financial Interests, Institutional, Research Grant: Rabin Medical Center. H.A. 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