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Overall Survival Subgroup Analysis by Metastatic Site From the Phase 3 MONALEESA-2 Study of First-Line Ribociclib + Letrozole in Postmenopausal Patients With HR+/HER2− Advanced Breast Cancer

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Disclosure Information

Dr O'Shaughnessy reports personal fees and consultant/advisory boards for AbbVie, Agendia, Amgen Biotechnology, Aptitude Health, AstraZeneca, Bayer, Bristol Myers Squibb, Celgene Corporation, Clovis Oncology, Daiichi Sankyo, Eisai, G1 Therapeutics, Genentech, Gilead Sciences, GRAIL, Halozyme Therapeutics, Heron Therapeutics, Immunomedics, Ipsen Biopharmaceuticals, Lilly, Merck & Co., Myriad, Nektar Therapeutics, Novartis, Pfizer, Pharmacyclics, Pierre Fabre, Puma Biotechnology, prIME Oncology, Roche, Samsung Bioepis, Sanofi, Seagen, Syndax Pharmaceuticals, Taiho Oncology, Takeda, and Synthon.

Introduction

- The phase 3, randomized, double-blind MONALEESA-2 trial recently reported a statistically significant OS benefit with first-line ribociclib + letrozole over placebo + letrozole in postmenopausal patients with HR+/HER2– advanced breast cancer (median, 63.9 vs 51.4 months; hazard ratio, 0.76; 95% CI, 0.63-0.93; *P* = .004)[1]
- Here we present an exploratory OS analysis of patients in MONALEESA-2 in subgroups by location of metastases, number of metastatic sites, and prior therapy

HER2–, human epidermal growth factor receptor 2 negative; HR+, hormone receptor positive; OS, overall survival.

1. Hortobagyi GN, et al. ESMO 2021. Abstract LBA17_PR.

MONALEESA-2 Study Design

- Postmenopausal women with HR+/ HER2– ABC
- No prior therapy for advanced disease
- Prior (neo)adjuvant ET, including TAM, allowed[a]
- N = 668

Stratified by the presence or absence of liver and/or lung metastases

R 1:1

Ribociclib (600 mg/day)
3 weeks on/1 week off
+
letrozole (2.5 mg/day)
n = 334

Placebo
+
letrozole (2.5 mg/day)
n = 334

Primary endpoint
- PFS (locally assessed per RECIST 1.1)

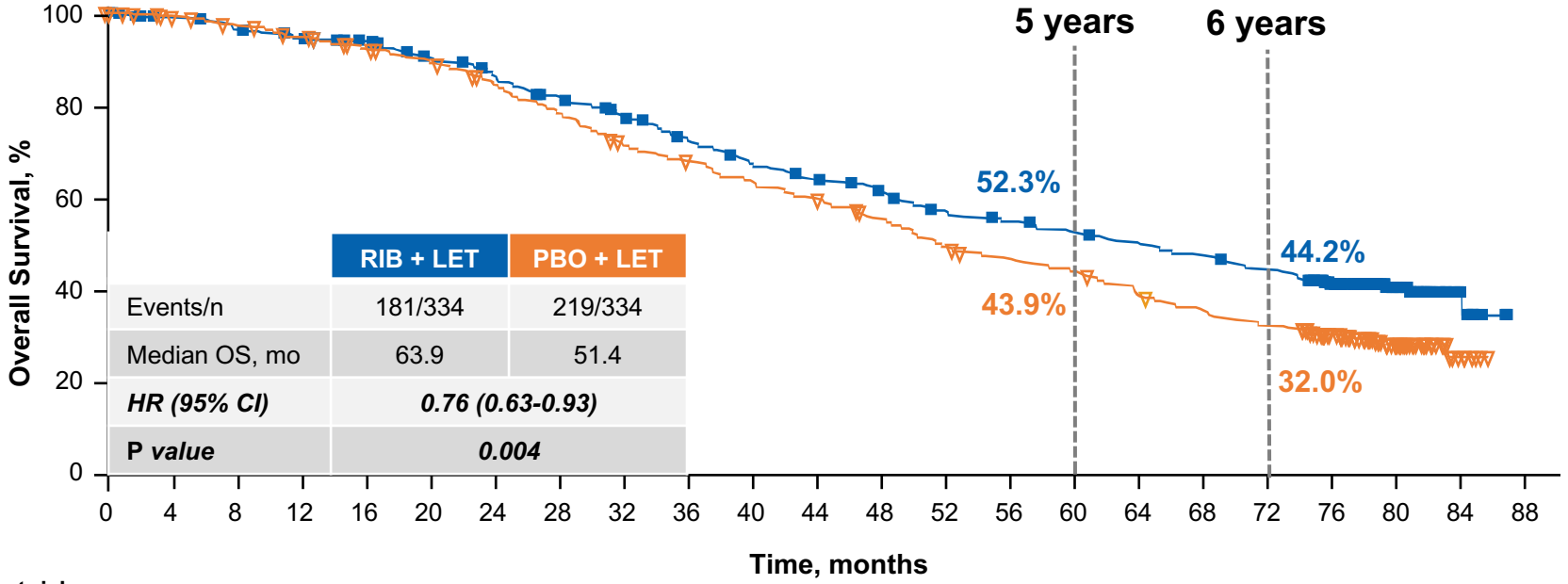
Key secondary endpoint
- OS

Select secondary endpoints
- ORR
- CBR
- Safety
- QOL

ABC, advanced breast cancer; CBR, clinical benefit rate; ET, endocrine therapy; HER2–, human epidermal growth factor receptor 2 negative; HR+, hormone receptor positive; NSAI, nonsteroidal aromatase inhibitor; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; QOL, quality of life; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors version 1.1; TAM, tamoxifen.

[a] Treatment-free interval > 12 months from completion of treatment until randomization required for prior NSAI use.

Ribociclib Achieved Statistically Significant OS Benefit in the ML-2 ITT Population



	RIB + LET	PBO + LET
Events/n	181/334	219/334
Median OS, mo	63.9	51.4
HR (95% CI)	***0.76 (0.63-0.93)***	
P *value*	***0.004***	

No. at risk

RIB + LET	334	323	315	305	300	284	270	253	237	220	202	191	180	165	158	150	142	135	125	101	48	8	0
PBO + LET	334	326	316	306	293	283	265	244	222	209	195	183	167	149	139	131	114	104	94	73	38	6	0

HR, hazard ratio; ITT, intention to treat; LET, letrozole; ML-2, MONALEESA-2; OS, overall survival; PBO, placebo; RIB, ribociclib.

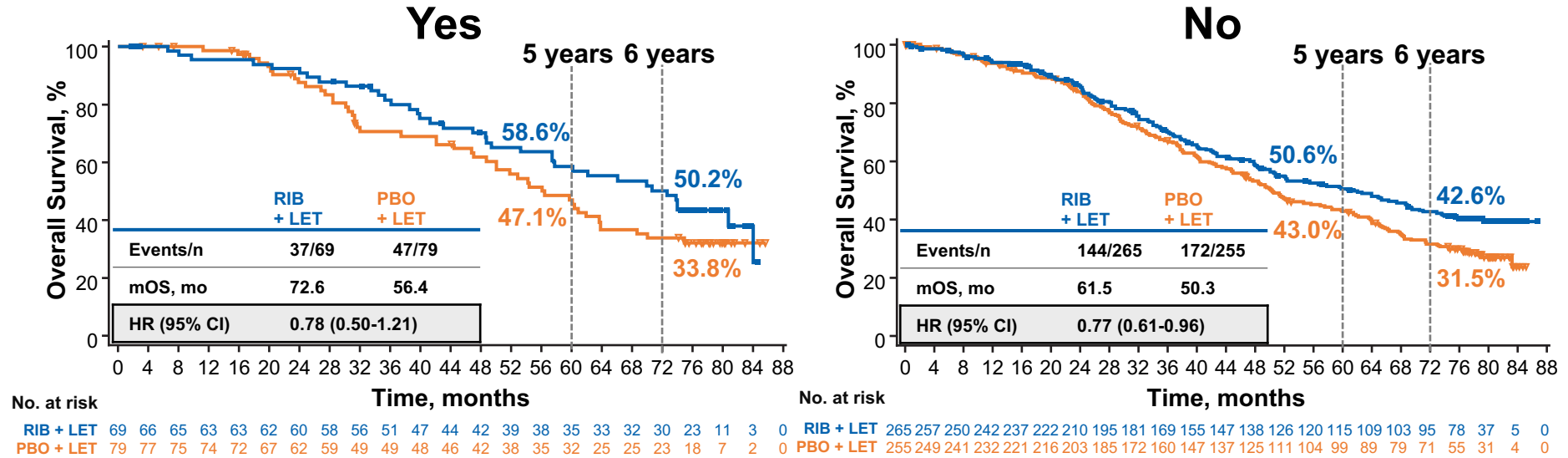
1. Hortobagyi GN, et al. ESMO 2021. Abstract LBA17_PR.

Methods

- The data cutoff for this analysis was June 10, 2021
- Prespecified subgroups determined by baseline location of metastases, number of metastatic sites, and prior therapy were included in this exploratory OS analysis:
  - Bone-only metastases
  - Liver involvement
  - Liver or lung involvement
  - Number of metastatic sites
  - Prior chemotherapy
  - Prior endocrine therapy
- OS was estimated using the Kaplan-Meier method
- Hazard ratios were estimated using stratified (bone-only metastases, number of metastatic sites, prior chemotherapy, and prior endocrine therapy) or unstratified (liver and liver or lung involvement) Cox proportional hazards models
- This analysis was exploratory; it was not powered for significance or adjusted for multiplicity

HR, hazard ratio; OS, overall survival.

OS With Ribociclib in Patients With Bone-Only Metastases

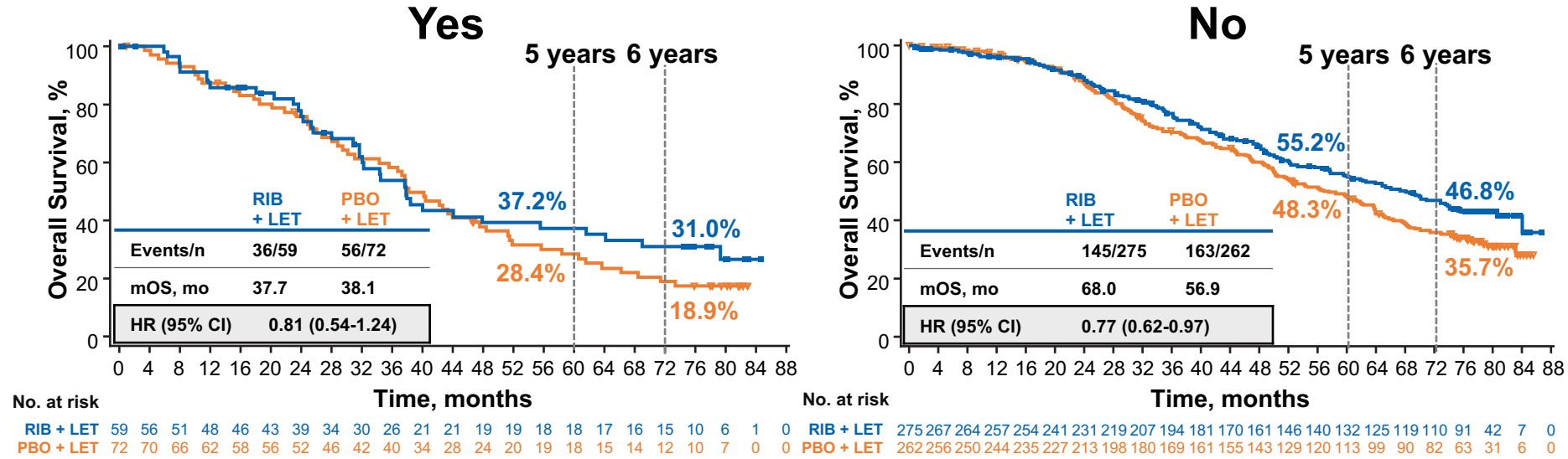


- OS benefit in patients with or without bone-only metastasis was consistent with that in the ITT population[1]

HR, hazard ratio; ITT, intention to treat; LET, letrozole; OS, overall survival; PBO, placebo; RIB, ribociclib.

1. Hortobagyi GN, et al. ESMO 2021. Abstract LBA17_PR.

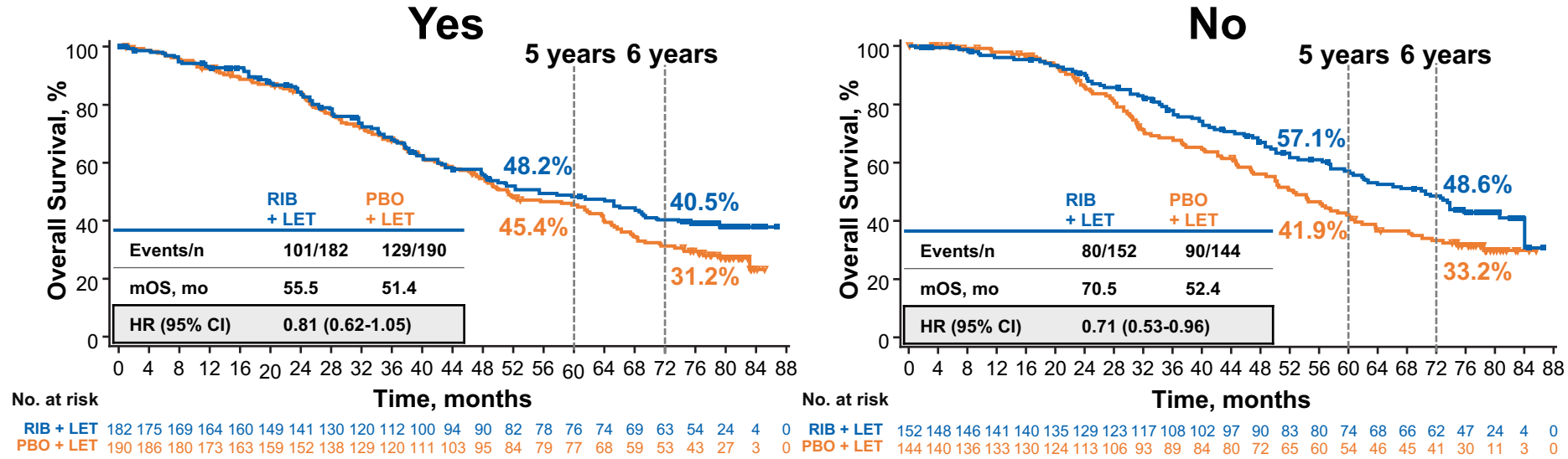
OS With Ribociclib in Patients With Liver Metastases



- At 5 and 6 years, OS benefit was observed in patients with liver metastases

HR, hazard ratio; LET, letrozole; OS, overall survival; PBO, placebo; RIB, ribociclib.

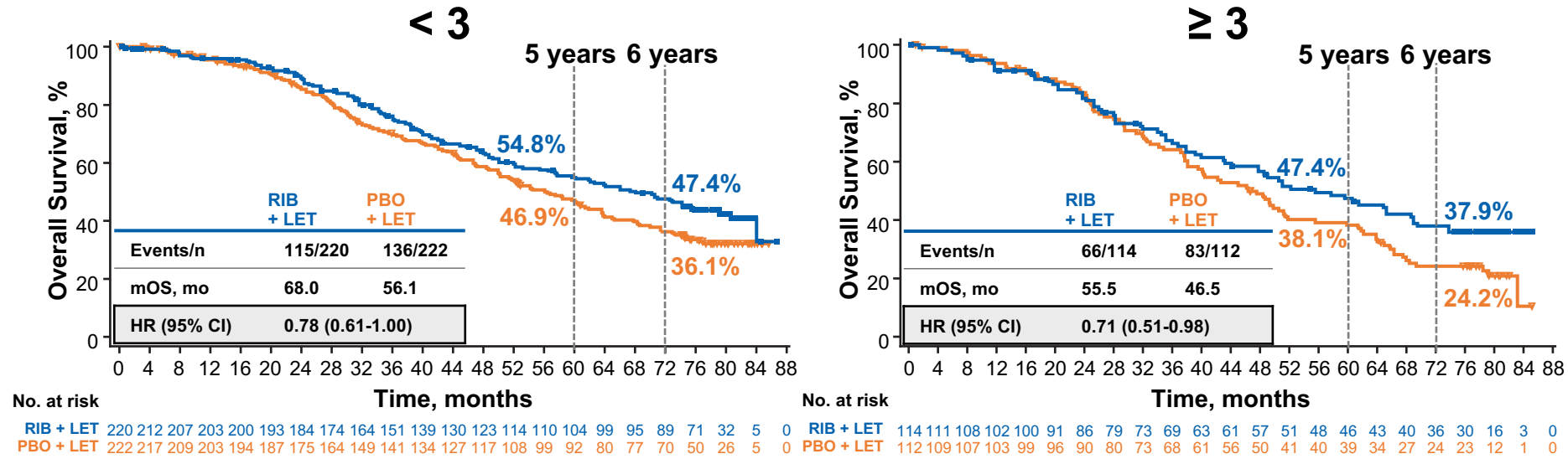
OS With Ribociclib in Patients With Liver or Lung Metastases



- At 5 and 6 years, OS benefit was observed in patients with liver or lung metastases

HR, hazard ratio; LET, letrozole; OS, overall survival; PBO, placebo; RIB, ribociclib.

OS With Ribociclib in Patients by Number of Metastatic Sites

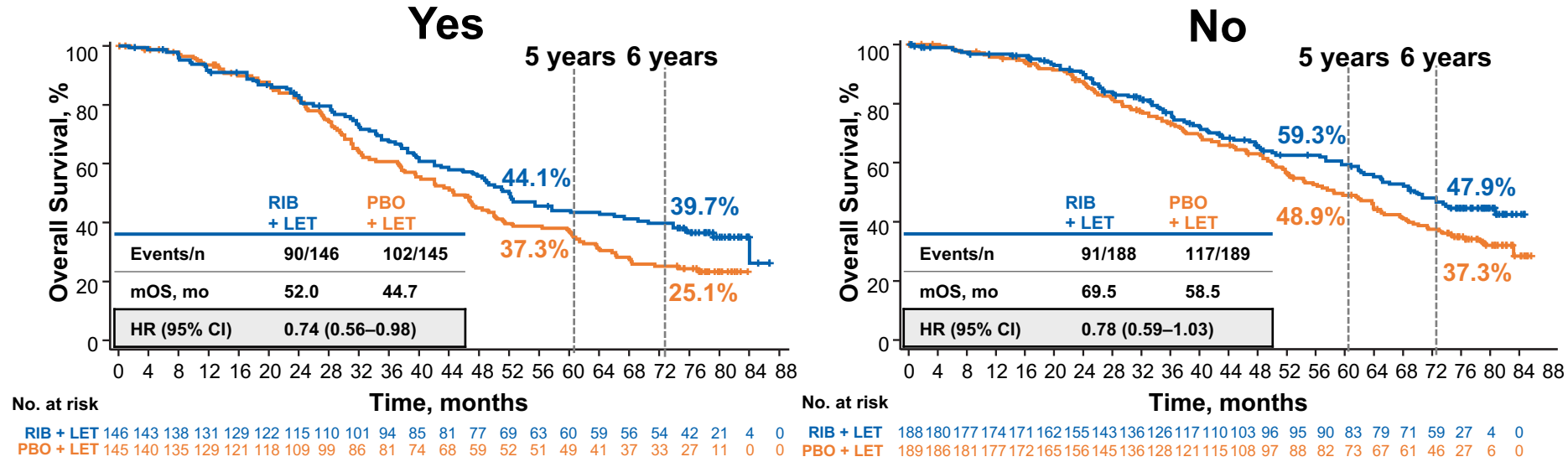


- OS benefit in patients with < 3 or ≥ 3 metastatic sites was consistent with that in the ITT population[1]

HR, hazard ratio; ITT, intention to treat; LET, letrozole; OS, overall survival; PBO, placebo; RIB, ribociclib.

1. Hortobagyi GN, et al. ESMO 2021. Abstract LBA17_PR.

OS With Ribociclib in Patients Who Received Prior Chemotherapy



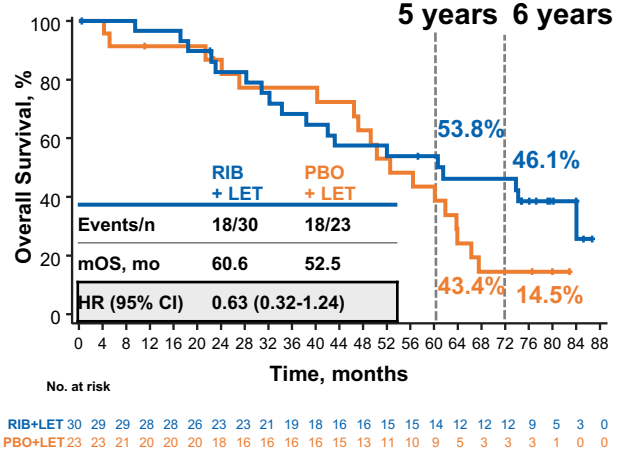
- OS benefit in patients who had or had not received prior (neo)adjuvant chemotherapy was consistent with that in the ITT population[1]

HR, hazard ratio; ITT, intention to treat; LET, letrozole; OS, overall survival; PBO, placebo; RIB, ribociclib.

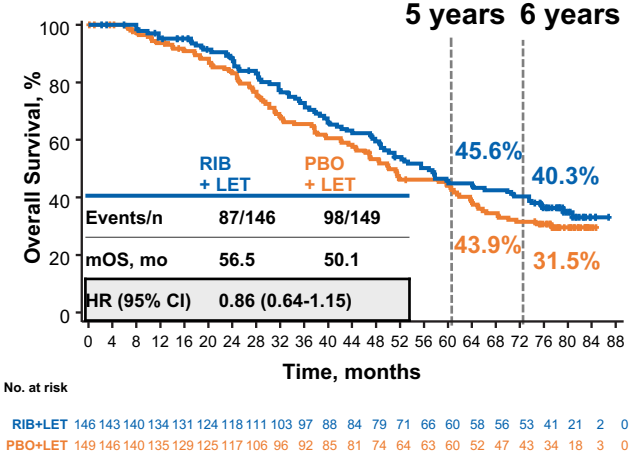
1. Hortobagyi GN, et al. ESMO 2021. Abstract LBA17_PR.

OS With Ribociclib in Patients Who Received Prior Endocrine Therapy

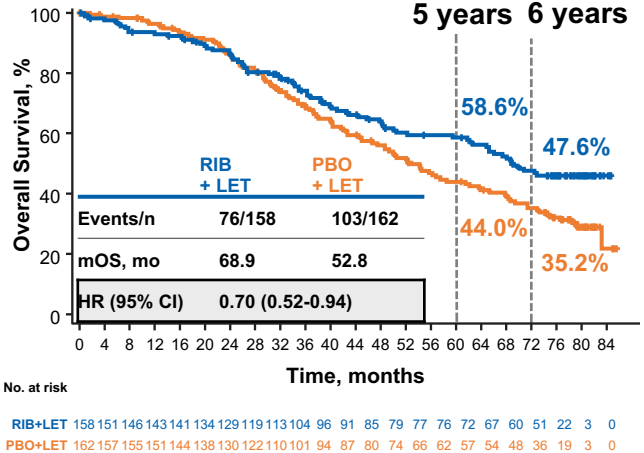
NSAI and Others[a]



Tamoxifen ± NSAI



No Prior ET



- OS benefit in patients who had or had not received prior (neo)adjuvant endocrine therapy was consistent with that in the ITT population[1]

ET, endocrine therapy; HR, hazard ratio; ITT, intention to treat; LET, letrozole; NSAI, nonsteroidal aromatase inhibitor; OS, overall survival; PBO, placebo; RIB, ribociclib.

[a] Patients in the "others" category took gonadotropin-releasing hormone (mainly goserelin).

1. Hortobagyi GN, et al. ESMO 2021. Abstract LBA17_PR.

Conclusions

- Independent of metastatic site (bone, liver, or liver or lung), number of metastatic sites (< 3 or ≥ 3), or prior (neo)adjuvant chemotherapy or endocrine therapy, this exploratory subgroup analysis demonstrated improved survival with first-line ribociclib + letrozole compared with placebo + letrozole in postmenopausal patients with HR+/HER2– advanced breast cancer in the MONALEESA-2 trial
- Consistent improvement in long-term survival at 5 and 6 years with ribociclib was observed in all subgroups analyzed
- MONALEESA-2, -3, and -7 have demonstrated a consistent overall survival benefit with ribociclib regardless of endocrine therapy partner, line of therapy, or menopausal status[1-3]

HER2–, human epidermal growth factor receptor 2 negative; HR+, hormone receptor positive; OS, overall survival.

1. Slamon DJ, et al. *N Engl J Med*. 2020;382:514-524. 2. Im S-A, et al. *N Engl J Med*. 2019;381:307-316.
3. Yardley DA, et al. ASCO 2020. Poster P139.

Acknowledgments

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