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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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

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


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MONALEESA-2 Study Design

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

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

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.

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

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


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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
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\(^1\)

\(^1\) 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.
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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

**Overall Survival, %**

<table>
<thead>
<tr>
<th>No. at risk</th>
<th>RIB + LET</th>
<th>PBO + LET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events/n</td>
<td>101/182</td>
<td>129/190</td>
</tr>
<tr>
<td>mOS, mo</td>
<td>55.5</td>
<td>51.4</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.81 (0.62-1.05)</td>
<td></td>
</tr>
</tbody>
</table>

**Overall Survival, %**

<table>
<thead>
<tr>
<th>No. at risk</th>
<th>RIB + LET</th>
<th>PBO + LET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events/n</td>
<td>80/152</td>
<td>90/144</td>
</tr>
<tr>
<td>mOS, mo</td>
<td>70.5</td>
<td>52.4</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.71 (0.53-0.96)</td>
<td></td>
</tr>
</tbody>
</table>

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

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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 population¹

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.

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OS With Ribociclib in Patients Who Received Prior Chemotherapy

**Yes**

- **Events/n**: 90/146, 102/145
- **mOS, mo**: 52.0, 44.7
- **HR (95% CI)**: 0.74 (0.56–0.98)

**No**

- **Events/n**: 91/188, 117/189
- **mOS, mo**: 69.5, 58.5
- **HR (95% CI)**: 0.78 (0.59–1.03)

- **5 years**: 37.3%
- **6 years**: 39.7%

- **Overall Survival, %**

- **Time, months**

- **No. at risk**

• OS benefit in patients who had or had not received prior (neo)adjuvant chemotherapy was consistent with that in the ITT population\(^1\)

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


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**OS With Ribociclib in Patients Who Received Prior Endocrine Therapy**

- **NSAI and Others**
  - 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.

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**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).


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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\(^1-\^3\).
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