Overall survival results by location and number of metastases in patients with HR+ / HER2− advanced breast cancer from the MONALEESA-2 trial

**Executive Summary**
- **MONALEESA-2** is a phase 3 clinical trial of ribociclib plus letrozole compared with letrozole alone in postmenopausal women with HR+/HER2− advanced breast cancer who had not been treated before for advanced disease
- This document describes results from the MONALEESA-2 trial comparing long-lasting patients receiving each treatment lived; these patients were grouped by the location where the cancer had spread (metastasis) or the number of metastatic sites
- Patients with or without metastases that were in the bone only, in the liver, or in the liver or lung lived longer when treated with ribociclib plus letrozole than those treated with letrozole alone
- Patients with less than 3 sites of metastases at the start of the trial, as well as those who had 3 or more sites, also lived longer with ribociclib plus letrozole than with letrozole alone
- The results of this analysis of MONALEESA-2 demonstrated that ribociclib plus letrozole improved overall survival over letrozole alone for postmenopausal women with HR+/HER2− advanced breast cancer when used as the first therapy for advanced disease, regardless of where they had metastases or how many metastases they had

**MONALEESA-2 study**
- Phase 3 clinical trial
- Patients with HR+/HER2− advanced breast cancer
- Patients who had gone through menopause
- Patients had not been previously treated with endocrine therapy (ET) or chemotherapy for advanced breast cancer
- Included 668 patients in 29 countries (334 patients were randomized to the ribociclib plus letrozole group and 334 patients were randomized to the letrozole alone group)
- The primary goal of the trial was to evaluate how long patients lived without the disease getting worse
- Other key goals of the trial were to evaluate how long patients lived overall and any side effects patients may have experienced while on treatment

**About the medications**
Ribociclib is a targeted therapy used to treat advanced breast cancer that is HR+ and HER2−. Cyclin-dependent kinases 4 and 6 (CDK4/6) are proteins that help breast cancer cells make more copies of themselves. Ribociclib targets CDK4/6 to stop cancer cells from growing. Ribociclib is given in combination with ET.
ET is a type of treatment that blocks the effects of estrogen on breast cancer cells. Since estrogen can drive the growth of breast cancer cells, blocking the effects of estrogen in the body can slow the growth of cancerous cells and prevent the disease from getting worse.

The type of ET used in MONALEESA-2 was letrozole.

**To help you better understand the results**
Median is a statistical term that describes the middle, which separates the lower and upper halves of the data.
Median progression-free survival is an estimate of the time at which 50% of the patients did not have the disease get worse.
Median overall survival is an estimate of the time at which 50% of the patients were still alive.

**Previous published results**

**MONALEESA-2: For patients receiving ribociclib plus letrozole, median progression-free survival was 25.3 months or 16.0 months for patients receiving letrozole alone.**

Median overall survival was 30.9 months for patients receiving ribociclib plus letrozole versus 21.4 months for patients receiving letrozole alone. Patients treated with ribociclib plus letrozole experienced a 24% reduction in the relative risk of death.

**What was the purpose of this analysis of MONALEESA-2?**
This analysis grouped patients, treated with ribociclib plus letrozole or letrozole alone in the MONALEESA-2 trial, by the location or the number of metastases they had.
This analysis looked at survival in these groups of patients.

**What are the key results of this analysis?**
Patients with and without liver metastases treated with ribociclib lived longer overall

<table>
<thead>
<tr>
<th>Patients with and without liver metastases treated with ribociclib lived longer overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>131 patients with liver metastases (20% of all patients)</td>
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<tr>
<td>357 patients without liver metastases (60% of all patients)</td>
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<tr>
<td>Reduction in the risk of death with ribociclib plus letrozole compared with letrozole alone for:</td>
</tr>
<tr>
<td>Patients with liver metastases</td>
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<tr>
<td>Patients without liver metastases</td>
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</table>

**Conclusions**
Researchers grouped patients by the location and number of metastases they had when they entered the MONALEESA-2 trial and looked at how long they lived on each treatment.
Ribociclib plus letrozole extended overall survival compared with letrozole alone, regardless of where the patients had metastases or the number of metastases.
These results show consistent survival benefits of ribociclib plus letrozole over letrozole alone in postmenopausal women with HR+/HER2− advanced breast cancer regardless of if patients had minimal disease burden located in the bone-only, or if they had more widespread disease involving vital organs. All patients derived a survival advantage from ribociclib plus letrozole.

**Study Information**
- **NCT01958021 (MONALEESA-2)**
- **Study number:**
  - **Patient enrollment:**
  - **Total number of patients:**
  - **Reason for exclusion:**
  - **Study phase:**
  - **Study type:**
  - **Study duration:**
  - **Expected completion date:**
  - **Expected trial duration:**
- **Key eligibility criteria:**
  - **Inclusion criteria:**
  - **Exclusion criteria:**
  - **Additional eligibility criteria:**
- **Key outcomes:**
  - **Primary endpoint:**
  - **Secondary endpoints:**
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- **Trial website:**
- **Trial registration:**
- **Trial status:**
- **Trial results:**
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References:
1. Hortobagyi GN, et al. ESMO 2021.; oral presentation LBA17_PR.