A doctor in a white coat and stethoscope is looking at a tablet computer. The background is a blurred image of the doctor's face and hands holding the tablet.

From publication to practice: How trial data translate to clinical use of CDK4/6 inhibitors in patients with HR+/HER2- advanced breast cancer

What are the implications of the overall survival data for CDK4/6 inhibitors for daily practice?



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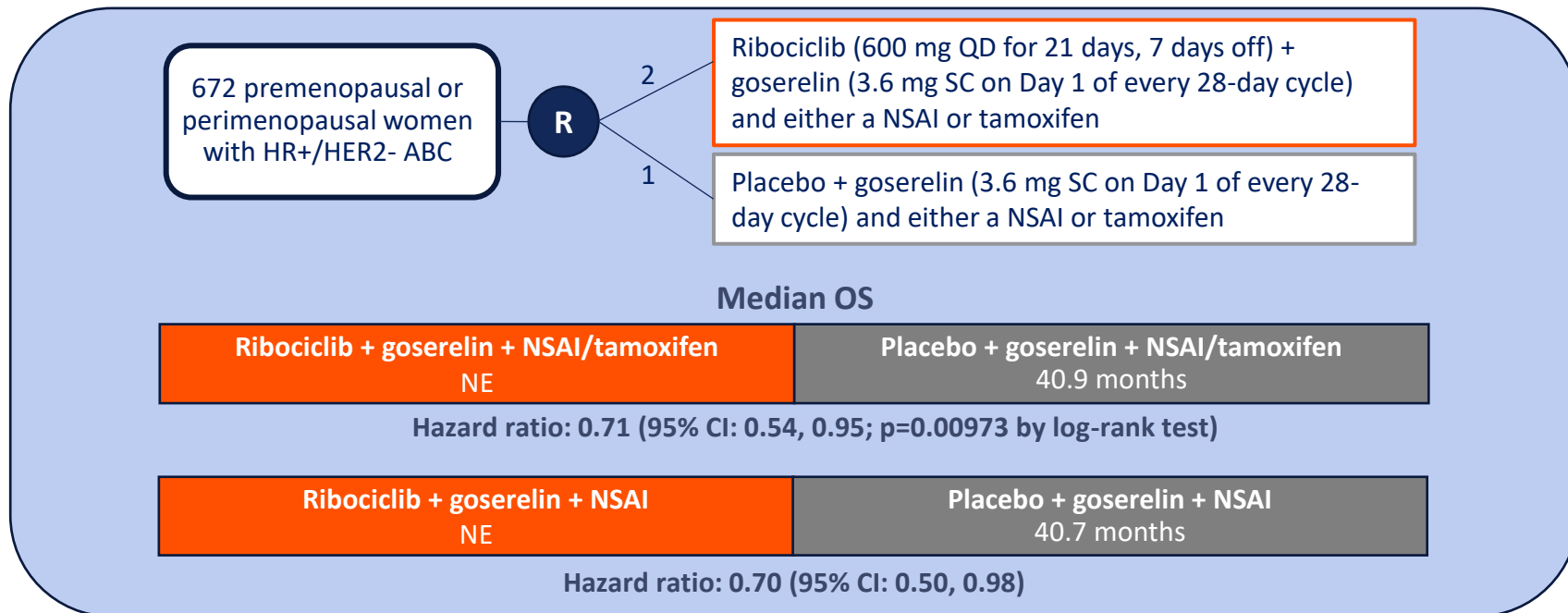
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MONALEESA-7 trial¹

International, randomized, placebo-controlled, Phase III trial



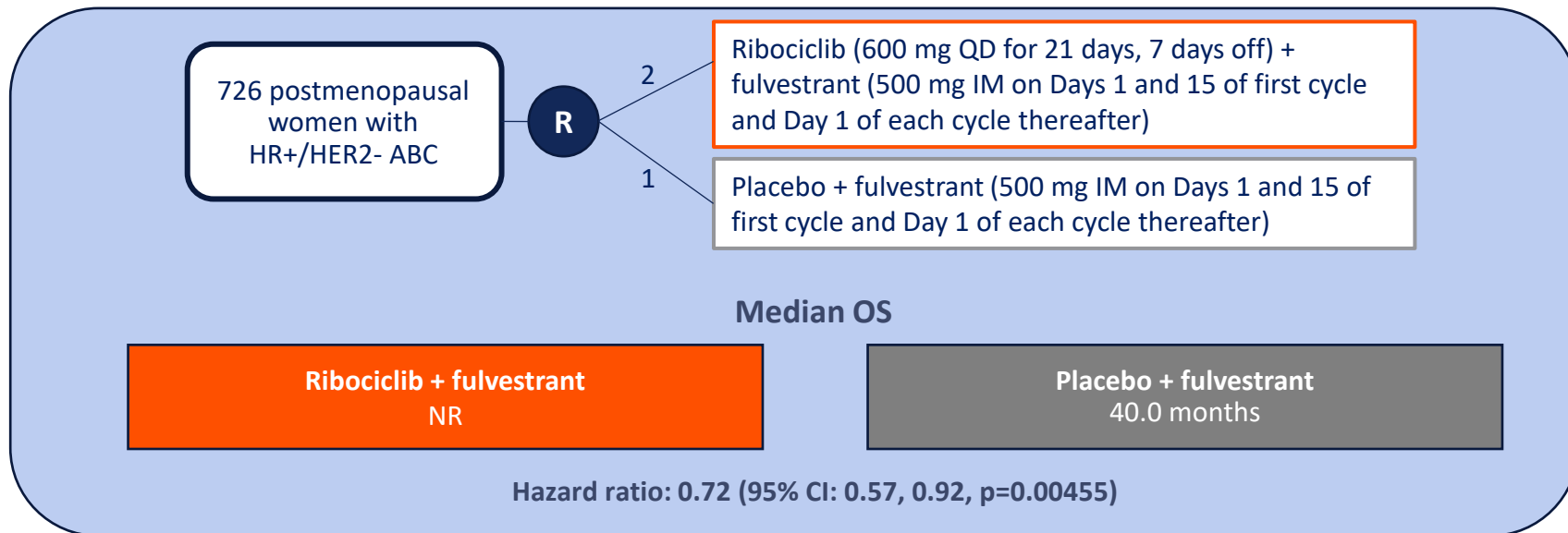
Statistically significant improvement in OS with ribociclib + ET vs. placebo + ET

ABC, advanced breast cancer; CI, confidence interval; ET, endocrine therapy; HR, hormone receptor; HER2, human epidermal growth factor receptor 2; NE, could not be estimated; NSAID, non-steroidal aromatase inhibitor; OS, overall survival; QD, once daily; R, randomized; SC, subcutaneous.

1. Im SA, et al. *N Engl J Med.* 2019;381:307–16.

MONALEESA-3 trial¹

International, randomized, placebo-controlled, Phase III trial



Statistically significant OS benefit with ribociclib + fulvestrant vs. placebo + fulvestrant

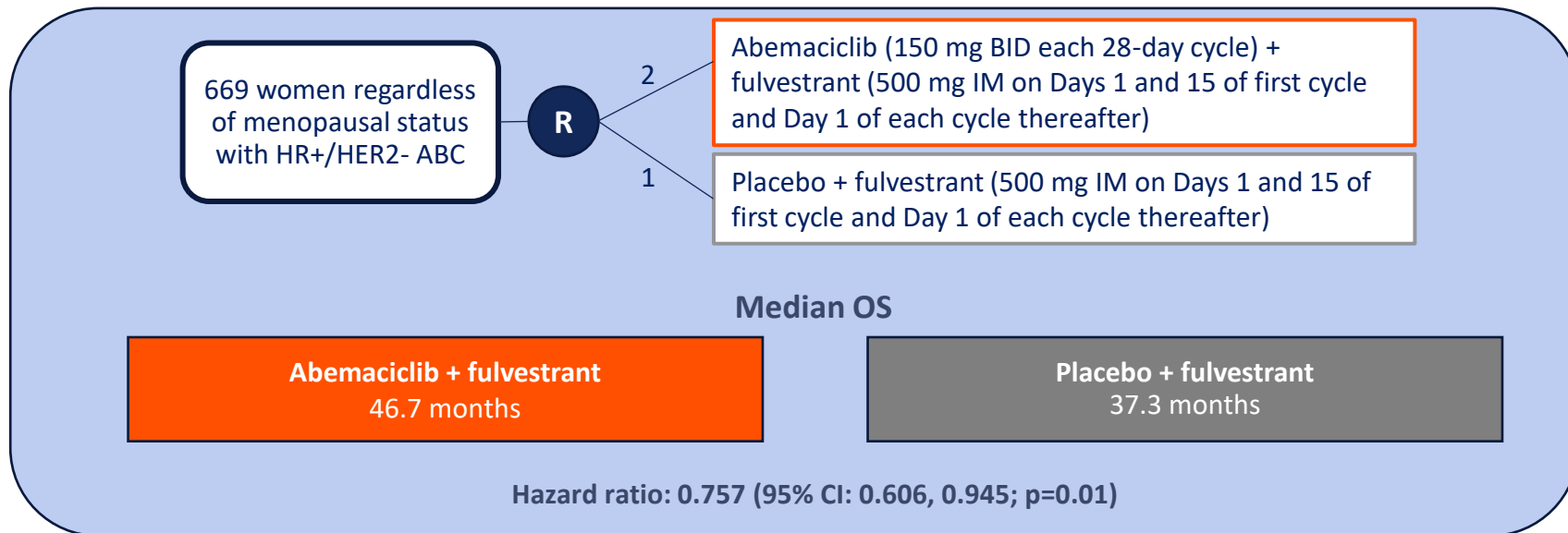
ABC, advanced breast cancer ; CI, confidence interval; HR, hormone receptor; HER2, human epidermal growth factor receptor 2; IM, intramuscular;

NR, not reached; OS, overall survival; QD, once daily; R, randomized.

1. Slamon D, et al. *N Engl J Med.* 2020;382:514–24.

MONARCH-2 trial¹

International, randomized, placebo-controlled, Phase III trial



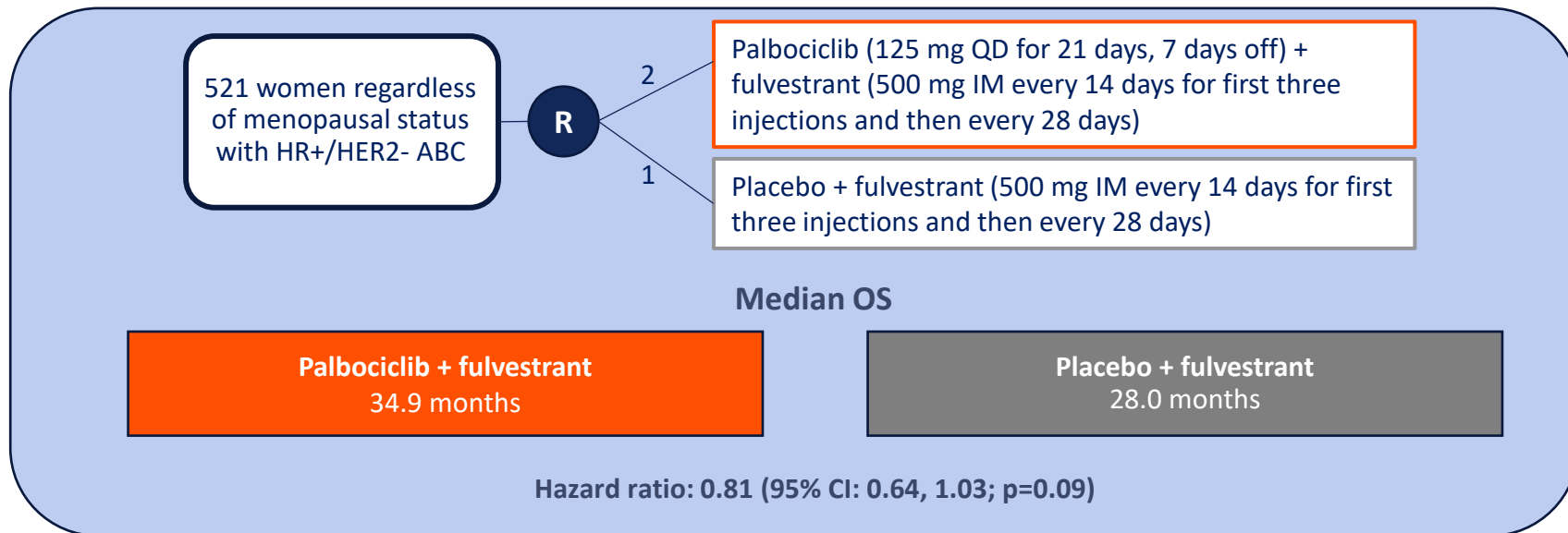
Statistically significant improvement in median OS with abemaciclib + fulvestrant vs. placebo + fulvestrant

ABC, advanced breast cancer; BID, twice daily; CI, confidence interval; ET, endocrine therapy; HR, hormone receptor; HER2, human epidermal growth factor receptor 2; IM, intramuscular; OS, overall survival; R, randomized.

1. Sledge GW, et al. *JAMA Oncol.* 2019;e194782. doi:10.1001/jamaoncol.2019.4782 [Epub ahead of print].

PALOMA-3 trial¹

International, randomized, placebo-controlled, Phase III trial



Difference in OS between palbociclib + fulvestrant vs. placebo + fulvestrant was not significant

ABC, advanced breast cancer; CI, confidence interval; HR, hormone receptor; HER2, human epidermal growth factor receptor 2; IM, intramuscular; OS, overall survival; QD, once daily; R, randomized.

1. Turner NC, et al. *N Engl J Med.* 2018;379:1926–36.

Possible explanations for differences in OS across CDK4/6 inhibitor Phase III trials

Trial differences

- For example, different patient populations within the trials:¹⁻⁵
 - Timing of disease progression
 - Inclusion of patients with *de novo* metastatic disease



Drug differences

- Substantial pharmacological differences between the three CDK4/6 inhibitors⁶



CDK, cyclin-dependent kinase; OS, overall survival.

1. Turner NC, et al. *N Engl J Med.* 2015;373:209–19. 2. Sledge GW, et al. *JAMA Oncol.* 2019;e194782. doi:10.1001/jamaoncol.2019.4782 [Epub ahead of print]. 3. Slamon D, et al. *N Engl J Med.* 2020;382:514–24. 4. Im SA, et al. *N Engl J Med.* 2019;381:307–16. 5. Petrelli F, et al. *Breast Cancer Res Treat.* 2019;174:597–604. 6. Marra A, Curigliano G. *npj Breast Cancer.* 2019;5:27.

Patient selection for CDK4/6 inhibition

No biomarkers to identify patients who will benefit from CDK4/6 inhibitors the most or patients at risk of CDK4/6 inhibitor resistance¹

CDK4/6 inhibitors (+ endocrine therapy backbone) should be considered in all HR+/HER2- patients (first or second line)²⁻⁵

The outcomes of these trials are practice changing

CDK, cyclin-dependent kinase; HR, hormone receptor; HER2, human epidermal growth factor receptor 2.

1. Schoninger SF, Blain SW. *Mol Cancer Ther.* 2019;19:3–12. 2. Turner NC, et al. *N Engl J Med.* 2015;373:209–19. 3. Sledge GW, et al. *JAMA Oncol.* 2019;e194782. doi:10.1001/jamaoncol.2019.4782 [Epub ahead of print]. 4. Slamon D, et al. *N Engl J Med.* 2020;382:514–24. 5. Im SA, et al. *N Engl J Med.* 2019;381:307–16.