**Supplementary Data**

**The following investigators participated in the PERTAIN study**

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| **France** | Nathalie Bonichon-Lamichhane, Elisabeth Carola, Jean-Marc Ferrero (author), Laurent Gasnault, Dominique Jaubert, Alain Lortholary, Lionel Uwer, Mathilde Martinez, Marie-Ange Isabelle Moullet, Mouret Reynier, Jean-Maire Naboltz, Jean Baptiste Paoli, Helene Simon, Christian Villaneuva |
| **India** | Suresh Advani, Minish Jain, Pratap Kishore Das, Shekar Patil, Thirumalai Raj Raja |
| **Italy** | Giulia Bianchi, Laura Biganzoli, Giampaolo Biti, Roberto Bordonaro, Giuseppe Cairo, Giacomo Cartenì, Saverio Cinieri, Michelino De Laurentiis, Sabino De Placido (author), Benvenuto Ferrari, Antonella Ferro, Elisa Gallerani, Teresa Gamucci, Francesco Giotta, Lorenzo Livi, Vito Lorusso, Laura Merlini, Paulo Morandi, Antonino Musolino, Lorenzo Pavesi, Silvana Saracchini, Edda Simoncini, Claudio Zamagni |
| **Spain** | Joan Albanell, Isabel Alvarez, Antonio Anton, Lourdes Calvo Martinez, Luis de la Cruz, Juan de la Haba-Rodriguez (author), Jose Angel Garcia-Saenz, Santiago Gonzalez, Jose Ignacio Chacon, Ana Lluch Hernandez, Jose Luis Alonso, Mireia Margeli, Eduardo Martinez, Noelia Martinez, Serafin Morales, Arrate Plazaola, Manuel Ramos |
| **Turkey** | Kadri Altundag, Sercan Aksoy, Elkiran Emin Tamer, Mahmut Gumus, Berna Oksuzoglu, Feyyaz Ozdemir, Ruchan Uslu, Nuriye Yıldırım Özdemir |
| **UK** | Amandeep Dhadda, Timothy Gulliford, Abdel Hamid, Rebecca Herbertson, Anne Kendall, Hartmut Kristeleit, Ian MacPherson, Udaiveer Panwar, Gargi Patel, Christopher Poole, Peter Schmid, Saad Tahir, Matthew Winter |
| **USA**  | Ralph Boccia, Rodolfo Bordoni, Adam Brufsky, Thomas Cosgriff, Jane Carleton, Nagarajan Chandrasekara, Niel Christiansen, Marc Citron, Shaker Dakhil, Paul Devchand, Stephan Divers, Andres Forrero-Torres, Richard Frank, Claudine Isaacs, Sujith Kalmadi, Cynthia Ma, Raul Mena, David Mintzer, Raul H. Oyola, Steven Papish, Ravindranath Patel, Timothy Pluard, Suman Rao, Mothaffar Rimawi (author), Mansoor Saleh, Robert Somer, Adel Tabchy, Grace Wang, Lucas Wong |

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| **Supplementary Table 1.** Representativeness of Study Participants |
| Cancer type(s)/subtype(s)/stage(s)/condition | Human epidermal growth factor receptor 2 (HER2)-positive, hormone receptor (HR)-positive metastatic/locally advanced breast cancer. |
| Considerations related to: |
| Sex | Breast cancer is predominantly detected in females (~99% of cases in the USA) (1), with an estimated global incidence of 2,261,419 new cases in 2020 (11.7% of cancer cases reported) (2, 3). HER2-positive, HR-positive breast cancers are a distinct molecular subtype and have an age-adjusted rate of 12.9 new cases per 100,000 females (~10% of cases of female breast cancers) (4).  |
| Age | In the USA, the median age at diagnosis across all breast cancer subtypes is ~62 years old overall but is slightly younger for Hispanic (57 years), Asian/Pacific Islander (58 years), Black (60 years), and American Indian/Alaska Native (61 years) women than for White women (64 years) (1).  |
| Race/ethnicity | In the USA, there are racial and ethnic variations in breast cancer tumor characteristics, with a 40% higher breast cancer mortality in Black women compared with White women despite lower incidence (1). The incidence of HER2-positive cancers, however, is similar when comparing race and ethnicity, with 4-6% HER2-postive/HR-negative tumors and 9-12%HER2-postive/HR-positive (1). |
| Geography | Breast cancer is the cancer with the highest incidence worldwide, considering both sexes and in females alone (5). Incidence across both sexes is highest in Asia (1,026,171), followed by Europe (531,086), Northern America (281,591), Latin America and the Caribbean (210,100), Africa (186,598), and Oceana (25,873) (3).Globally, breast cancer had the highest rate of mortality in the female population (684,996) in 2020, although it preceded by lung cancer in Australia and New Zealand, Northern Europe, and China, and cervical cancer in many countries in sub-Saharan Africa (5). The number of deaths across both sexes was highest in Asia (346,009), followed by Europe (141,765), Africa (85,787), Latin America and the Caribbean (57,984), Northern America (48,407), and Oceania (5,044) (3). |
| Other considerations | None |
| Overall representativeness of this study | The PERTAIN study has been carried out in patients with HER2-positive, HR-positive metastatic/locally advanced breast cancer.All participants were female with a median age of 59 years (range: 35-87) in the pertuzumab plus trastuzumab arm and 61 years (range: 31-89) in the trastuzumab arm (6).The PERTAIN study was conducted across 80 sites in eight countries (USA, Brazil, France, India, Italy, Spain, Turkey, UK). Most patients enrolled in the study were Caucasian. |

**Supplemental references**

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5. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A*, et al.* Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: A Cancer Journal for Clinicians* **2021**;71:209-49.

6. Rimawi M, Ferrero J-M, de la Haba-Rodriguez J, Poole C, De Placido S, Osborne CK*, et al.* First-line trastuzumab plus an aromatase inhibitor, with or without pertuzumab, in human epidermal growth factor receptor 2-positive and hormone receptor-positive metastatic or locally advanced breast cancer (PERTAIN): a randomized, open-label phase II trial. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* **2018**;36:2826-35.