**SUPPLEMENTARY DATA**

**Supplementary Table S1.** Patient inclusion criteria

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**Supplementary Table S5.** Response to palbociclib treatment for the nine individual EU countries

**Supplementary Table S1.** Patient inclusion criteria

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| --- | --- |
| **Country** | **Patient inclusion criteria** |
| All countries | * Female; * ≥18 years old; * HR+/HER2- breast cancer diagnosis with confirmed metastatic or advanced disease; * Received palbociclib plus letrozole/aromatase inhibitor or palbociclib plus fulvestrant in line with the licensed indication(s) [Switzerland: postmenopausal women only]; * No prior or current enrolment in an interventional clinical trial for ABC/MBC; * Minimum of three months of follow up data since palbociclib with fulvestrant initiation, or minimum of six months of follow up data since palbociclib with letrozole/aromatase inhibitor initiation. |

**Supplementary Table S2.** Therapeutic indications for IBRANCE (palbociclib) in the EU

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| --- |
| **Therapeutic indications for IBRANCE (palbociclib) in the EU** |
| IBRANCE is indicated for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer:  - in combination with an aromatase inhibitor (Switzerland only: in postmenopausal women);  - in combination with fulvestrant in women who have received prior endocrine therapy (Switzerland only: in postmenopausal women). |
| In pre- or perimenopausal women, the endocrine therapy should be combined with a luteinizing hormone-releasing hormone (LHRH) agonist |

**Supplementary Table S3.** Patient demographics and clinical characteristics for the nine individual EU countries

|  | UK | | DE | | NL | | BE | | IT | | ES | | PT | | FR | | CH | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | P+AI  n=221 | P+F  n=34 | P+AI  n=152 | P+F  n=99 | P+AI  n=27 | P+F  n=37 | P+AI  n=50 | P+F  n=101 | P+AI  n=129 | P+F  n=131 | P+AI  n=148 | P+F  n=111 | P+AI  n=54 | P+F  n=46 | P+AI  n=171 | P+F  n=112 | P+AI  n=30 | P+F  n=70 |
| **Age at palbociclib initiation (years)** |  | | | | | | | | | | | | | | | | | |
| n | 221 | 34 | 152 | 99 | 27 | 37 | 50 | 101 | 129 | 131 | 148 | 111 | 54 | 46 | 171 | 112 | 30 | 70 |
| Mean (SD) | 63.3 (10.8) | 63.6 (7.5) | 54.9 (9.0) | 56.3 (7.9) | 63.1 (11.3) | 61.8 (12.6) | 65.3 (11.9) | 67.8 (9.6) | 65.7 (8.3) | 65.6 (9.1) | 62.9 (10.6) | 64.3 (8.6) | 57.6 (9.8) | 61.2 (9.4) | 65.2 (9.4) | 65.3 (9.7) | 62.3 (11.0) | 67.2 (11.2) |
| Median (range) | 65.0  (31.0, 86.0) | 64.5 (49.0, 81.0) | 55.0 (30.0, 81.0) | 57.0 (39.0, 72.0) | 62.0 (34.0, 87.0) | 63.0 (40.0, 87.0) | 66.5 (35.0, 90.0) | 68.0 (38.0, 90.0) | 66.0 (45.0, 85.0) | 66.0 (32.0, 90.0) | 64.0 (32.0, 84.0) | 64.0 (41.0, 85.0) | 57.0 (34.0, 76.0) | 61.5 (42.0, 82.0) | 65.0 (38.0, 90.0) | 65.0 (34.0, 88.0) | 61.5 (35.0, 82.0) | 68.0 (34.0, 90.0) |
| **Age range, n (%)** |  | | | | | | | | | | | | | | | | | |
| n | 221 | 34 | 152 | 99 | 27 | 37 | 50 | 101 | 129 | 131 | 148 | 111 | 54 | 46 | 171 | 112 | 30 | 70 |
| ≤50 | 30 (13.6) | 1  (2.9) | 43 (28.3) | 27 (27.3) | 3 (11.1) | 7 (18.9) | 5 (10.0) | 4  (4.0) | 2  (1.6) | 7  (5.3) | 20 (13.5) | 7  (6.3) | 11 (20.4) | 5 (10.9) | 7  (4.1) | 6  (5.4) | 4 (13.3) | 4  (5.7) |
| 51-69 | 123 (55.7) | 27 (79.4) | 103 (67.8) | 69 (69.7) | 17 (63.0) | 18 (48.6) | 27 (54.0) | 52 (51.5) | 88 (68.2) | 83 (63.4) | 85 (57.4) | 71 (64.0) | 35 (64.8) | 31 (67.4) | 115 (67.3) | 60 (53.6) | 19 (63.3) | 33 (47.1) |
| >70 | 68 (30.8) | 6 (17.6) | 6  (3.9) | 3  (3.0) | 7 (25.9) | 12 (32.4) | 18 (36.0) | 45 (44.6) | 39 (30.2) | 41 (31.3) | 43 (29.1) | 33 (29.7) | 8 (14.8) | 10 (21.7) | 49 (28.7) | 46 (41.1) | 7 (23.3) | 33 (47.1) |
| **Ethnicity, n (%)** |  | | | | | | | | | | | | | | | | | |
| n | 221 | 34 | 152 | 99 | 27 | 37 | 50 | 101 | 129 | 131 | 148 | 111 | 54 | 46 | 171 | 112 | 30 | 70 |
| White | 175 (79.2) | 24 (70.6) | 134 (88.2) | 87 (87.9) | 27 (100) | 35 (94.6) | 43 (86.0) | 78 (77.2) | 122 (94.6) | 122 (93.1) | 124 (83.8) | 101 (91.0) | 45 (83.3) | 43 (93.5) | 142 (83.0) | 90 (80.4) | 25 (83.3) | 66 (94.3) |
| Hispanic/Latino | 2  (0.9) | 2  (5.9) | 2  (1.3) | 0 | 0 | 0 | 0 | 2  (2.0) | 4  (3.1) | 3  (2.3) | 22 (14.9) | 9 (8.1) | 5  (9.3) | 0 | 6  (3.5) | 2  (1.8) | 0 | 2  (2.9) |
| Middle Eastern | 4  (1.8) | 0 | 9  (5.9) | 2  (2.0) | 0 | 1  (2.7) | 5 (10.0) | 7  (6.9) | 0 | 2  (1.5) | 0 | 0 | 0 | 0 | 8  (4.7) | 8  (7.1) | 1  (3.3) | 1  (1.4) |
| Asian | 21 (9.5) | 4 (11.7) | 1  (0.7) | 1  (1.0) | 0 | 0 | 0 | 4  (4.0) | 2  (1.6) | 3  (2.3) | 0 | 0 | 0 | 0 | 6  (3.5) | 4  (3.6) | 1  (3.3) | 0 |
| Other | 19 (8.6) | 4 (11.7) | 6  (3.9) | 9  (9.1) | 0 | 1  (2.7) | 2  (4.0) | 10 (10.0) | 1  (0.8) | 1  (0.8) | 2  (1.4) | 1  (0.9) | 4  (7.5) | 3  (6.5) | 9  (5.2) | 8  (7.2) | 3 (10.0) | 1  (1.4) |
| **Menopause status, n (%)** |  | | | | | | | | | | | | | | | | | |
| n | 221 | 34 | 152 | 99 | 27 | 37 | 50 | 101 | 129 | 131 | 148 | 111 | 54 | 46 | 171 | 112 | 30 | 70 |
| Perimenopausal | 5  (2.3) | 0 | 3  (2.0) | 3  (3.0) | 0 | 1  (2.7) | 0 | 0 | 0 | 9  (6.9) | 3  (2.0) | 1  (0.9) | 2  (3.7) | 3  (6.5) | 2  (1.2) | 2  (1.8) | 0 | 0 |
| Natural menopause | 192 (86.9) | 33 (97.1) | 125 (82.2) | 78 (78.8) | 25 (92.6) | 30 (81.1) | 44 (88.0) | 98 (97.0) | 125 (96.9) | 114 (87.0) | 127 (85.8) | 102 (91.9) | 43 (79.6) | 39 (84.8) | 161 (94.2) | 104 (92.9) | 25 (83.3) | 65 (92.9) |
| Menopause induced by surgery | 2  (0.9) | 1  (2.9) | 10 (6.6) | 5  (5.1) | 0 | 2  (5.4) | 2  (4.0) | 1  (1.0) | 2  (1.6) | 1  (0.8) | 4  (2.7) | 3  (2.7) | 3  (5.6) | 3  (6.5) | 3  (1.8) | 2  (1.8) | 0 | 0 |
| Menopause induced by LHRH suppression | 22  (10) | 0 | 14 (9.2) | 13 (13.1) | 2  (7.4) | 4 (10.8) | 4  (8.0) | 2  (2.0) | 2  (1.6) | 7  (5.3) | 14 (9.5) | 5  (4.5) | 6 (11.1) | 1  (2.2) | 5  (2.9) | 4  (3.6) | 5 (16.7) | 5  (7.1) |
| **ECOG PS at palbociclib initiation, n (%)** |  | | | | | | | | | | | | | | | | | |
| n | 221 | 34 | 152 | 99 | 27 | 37 | 50 | 101 | 129 | 131 | 148 | 111 | 54 | 46 | 171 | 112 | 30 | 70 |
| 0 | 72 (32.6) | 6 (17.6) | 87 (57.2) | 46 (46.5) | 12 (44.4) | 11 (29.7) | 11 (22.0) | 11 (10.9) | 64 (49.6) | 33 (25.2) | 61 (41.2) | 48 (43.2) | 24 (44.4) | 14 (30.4) | 50 (29.2) | 21 (18.8) | 15 (50.0) | 31 (44.3) |
| 1 | 132 (59.7) | 25 (73.5) | 34 (22.4) | 28 (28.3) | 10 (37.0) | 18 (48.6) | 31 (62.0) | 83 (82.2) | 55 (42.6) | 81 (61.8) | 68 (45.9) | 59 (53.2) | 18 (33.3) | 19 (41.3) | 93 (54.4) | 81 (72.3) | 12 (40.0) | 35 (50.0) |
| 2 | 15 (6.8) | 3  (8.8) | 6  (3.9) | 4  (4.0) | 4 (14.8) | 7 (18.9) | 8 (16.0) | 7  (6.9) | 10 (7.8) | 14 (10.7) | 14 (9.5) | 4  (3.6) | 12 (22.2) | 13 (28.3) | 26 (15.2) | 8  (7.1) | 3 (10.0) | 3  (4.3) |
| 3 | 2  (0.9) | 0 | 2  (1.3) | 0 | 1  (3.7) | 1  (2.7) | 0 | 0 | 0 | 2  (1.5) | 5  (3.4) | 0 | 0 | 0 | 2  (1.2) | 2  (1.8) | 0 | 1  (1.4) |
| 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1  (0.8) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Unknown/not assessed | 0 | 0 | 23 (15.1) | 21 (21.2) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Stage at ABC/MBC diagnosis, n (%)** |  | | | | | | | | | | | | | | | | | |
| n | 221 | 34 | 152 | 99 | 27 | 37 | 50 | 101 | 129 | 131 | 148 | 111 | 54 | 46 | 171 | 112 | 30 | 70 |
| Locoregionally advanced (Stage IIIb, IIIc) | 13 (5.9) | 3  (8.8) | 29 (19.1) | 22 (22.2) | 2  (7.4) | 2  (5.4) | 1  (2.0) | 11 (10.9) | 3  (2.3) | 16 (12.2) | 4  (2.7) | 12 (10.8) | 2  (3.7) | 2  (4.3) | 18 (10.5) | 8  (7.1) | 4 (13.3) | 4  (5.7) |
| Metastatic (Stage IV) | 208 (94.1) | 31 (91.2) | 123 (80.9) | 77 (77.8) | 25 (92.6) | 35 (94.6) | 49 (98.0) | 90 (89.1) | 126 (97.7) | 115 (87.8) | 144 (97.3) | 99 (89.2) | 52 (96.3) | 44 (95.7) | 153 (89.5) | 104 (92.9) | 26 (86.7) | 66 (94.3) |
| **Occurrence of breast cancer, n (%)** |  | | | | | | | | | | | | | | | | | |
| n | 221 | 34 | 152 | 99 | 27 | 37 | 50 | 101 | 129 | 131 | 148 | 111 | 54 | 46 | 171 | 112 | 30 | 70 |
| Recurrent | 80 (36.2) | 29 (85.3) | 40 (26.3) | 93 (93.9) | 15 (55.6) | 27 (73.0) | 22 (44.0) | 98 (97.0) | 21 (16.3) | 121 (92.4) | 41 (27.7) | 97 (87.4) | 19 (35.2) | 38 (82.6) | 58 (33.9) | 91 (81.3) | 14 (46.7) | 58 (82.9) |
| De novo | 141 (63.8) | 5 (14.7) | 112 (73.7) | 6  (6.1) | 12 (44.4) | 10 (27.0) | 28 (56.0) | 3  (3.0) | 108 (83.7) | 10 (7.6) | 107 (72.3) | 14 (12.6) | 35 (64.8) | 8 (17.4) | 113 (66.1) | 21 (18.8) | 16 (53.3) | 12 (17.1) |
| **Metastases sites, n (%)**† |  | | | | | | | | | | | | | | | | | |
| n | 208 | 31 | 123 | 77 | 25 | 35 | 49 | 90 | 126 | 115 | 144 | 99 | 52 | 44 | 153 | 104 | 26 | 66 |
| Bone | 147 (70.7) | 22 (71.0) | 42 (34.1) | 35 (45.5) | 20 (80.0) | 30 (85.7 | 43 (87.8) | 34 (37.8) | 92 (73.0) | 69 (60.0) | 106 (73.6) | 67 (67.7) | 36 (69.2) | 31 (70.5) | 112 (73.2) | 69 (66.3) | 20 (76.9) | 50 (75.8) |
| Liver | 35 (16.8) | 3  (9.7) | 24 (19.5) | 19 (24.7) | 4 (16.0) | 7 (20.0) | 13 (26.5) | 19 (21.1) | 18 (14.3) | 19 (16.5) | 26 (18.1) | 19 (19.2) | 15 (28.8) | 19 (43.2) | 30 (19.6) | 17 (16.3) | 10 (38.5) | 14 (21.2) |
| Lung | 86 (41.3) | 15 (48.4) | 34 (27.6) | 26 (33.8) | 11 (44.0) | 9 (25.7) | 14 (28.6) | 23 (25.6) | 41 (32.5) | 38 (33.0) | 48 (33.3) | 39 (39.4) | 19 (36.5) | 13 (29.5) | 53 (34.6) | 36 (34.6) | 8 (30.8) | 8 (12.1) |
| Lymph nodes | 73 (35.1) | 10 (32.3) | 43 (35.0) | 22 (28.6) | 9 (36.0) | 16 (45.7) | 16 (32.7) | 29 (32.2) | 42 (33.3) | 45 (39.1) | 53 (36.8) | 42 (42.4) | 23 (44.2) | 17 (38.6) | 60 (39.2) | 34 (32.7) | 18 (69.2) | 28 (42.4) |
| Ovary | 1  (0.5) | 0 | 10 (8.1) | 2  (2.6) | 1  (4.0) | 0 | 1  (2.0) | 0 | 0 | 1  (0.9) | 1  (0.7) | 0 | 2  (3.8) | 2  (4.5) | 1  (0.7) | 0 | 0 | 0 |
| **Visceral disease, n (%)** |  | | | | | | | | | | | | | | | | | |
| n | 208 | 31 | 123 | 77 | 25 | 35 | 49 | 90 | 126 | 115 | 144 | 99 | 52 | 44 | 153 | 104 | 26 | 66 |
| Visceral‡ | 104 (50.0) | 16 (51.6) | 63 (51.2) | 45 (58.4) | 15 (60.0) | 13 (37.1) | 26 (53.1) | 38 (42.2) | 53 (42.1) | 55 (47.8) | 65 (45.1) | 54 (54.5) | 32 (61.5) | 30 (68.2) | 73 (47.7) | 50 (48.1) | 15 (57.7) | 21 (31.8) |
| Non-visceral | 104 (50.0) | 15 (48.4) | 60 (48.8) | 32 (41.6) | 10 (40.0) | 22 (62.9) | 23 (46.9) | 52 (57.8) | 73 (57.9) | 60 (52.2) | 79 (54.9) | 45 (45.5) | 20 (38.5) | 14 (31.8) | 80 (52.3) | 54 (51.9) | 11 (42.3) | 45 (68.2) |
| **Prior therapy for ABC/MBC, n (%)**† |  | | | | | | | | | | | | | | | | | |
| n | 1 | 16 | 9 | 17 | 4 | 32 | 2 | 34 | 4 | 49 | 15 | 58 | 9 | 35 | 12 | 78 | 2 | 42 |
| Targeted therapy | 0 | 0 | 0 | 0 | 0 | 2  (6.3) | 0 | 2  (5.9) | 0 | 1 (2.0) | 0 | 3 (5.2) | 0 | 3 (8.6) | 0 | 5  (6.4) | 1 (50.0) | 37 (88.1) |
| Endocrine therapy | 0 | 14 (87.5) | 7 (77.8) | 16 (94.1) | 3 (75.0) | 27 (84.4) | 2  (100) | 33 (97.1) | 4  (100) | 41 (83.7) | 11 (73.3) | 56 (96.6) | 1 (11.1) | 29 (82.9) | 6 (50.0) | 63 (80.8) | 1 (50.0) | 3  (7.1) |
| Chemotherapy | 1  (100) | 2 (12.5) | 2 (22.2) | 1  (5.9) | 1 (25.0) | 5 (15.6) | 0 | 1  (2.9) | 0 | 8 (16.3) | 5 (33.3) | 2  (3.4) | 8 (88.9) | 7 (20.0) | 7 (58.3) | 21 (26.9) | 1 (50.0) | 5 (11.9) |
| Other | 0 | 0 | 0 | 0 | 0 | 1  (3.1) | 0 | 0 | 0 | 0 | 2 (13.3) | 1  (1.7) | 1 (1.11) | 0 | 1  (8.3) | 1  (1.3) | 0 | 0 |
| **Lines of therapy received for ABC/MBC, n (%)** |  | | | | | | | | | | | | | | | | | |
| n | 221 | 34 | 152 | 99 | 27 | 37 | 50 | 101 | 129 | 131 | 148 | 111 | 54 | 46 | 171 | 112 | 30 | 70 |
| 1 | 183 (82.8) | 16 (47.1) | 139 (91.4) | 71 (71.7) | 20 (74.1) | 3  (8.1) | 42 (84.0) | 63 (62.4) | 120 (93.0) | 76 (58.0) | 100 (67.6) | 35 (31.5) | 41 (75.9) | 10 (21.7) | 152 (88.9) | 31 (27.7) | 23 (76.7) | 22 (31.4) |
| 2 | 31 (14.0) | 16 (47.1) | 13 (8.6) | 28 (28.3) | 2  (7.4) | 18 (48.6) | 5 (10.0) | 31 (30.7) | 6  (4.7) | 48 (36.6) | 38 (25.7) | 55 (49.5) | 10 (18.5) | 25 (54.3) | 17 (9.9) | 60 (53.6) | 5 (16.7) | 37 (52.9) |
| 3 | 5  (2.3) | 0 | 0 | 0 | 4 (14.8) | 8 (21.6) | 2  (4.0) | 4  (4.0) | 1  (0.8) | 6  (4.6) | 9  (6.1) | 14 (12.6) | 3  (5.6) | 6 (13.0) | 1  (0.6) | 15 (13.4) | 2  (6.7) | 6  (8.6) |
| ≥4 | 2  (1.0) | 2  (5.8) | 0 | 0 | 1  (3.7) | 8 (21.6) | 1  (2.0) | 3  (3.0) | 2  (1.6) | 1  (0.8) | 1  (0.7) | 7  (6.3) | 0 | 5 (10.9) | 1  (0.6) | 6  (5.4) | 0 | 5  (7.1) |

ABC, advanced breast cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; LHRH, luteinizing hormone-releasing hormone; MBC, metastatic breast cancer; P+AI, palbociclib plus aromatase inhibitor; P+F, palbociclib plus fulvestrant; SD, standard deviation.

BE, Belgium; CH, Switzerland; DE, Germany; ES, Spain; FR, France; IT, Italy; NL, Netherlands; PT, Portugal; UK, United Kingdom.

\* 0 = Fully active, able to carry on all pre-disease performance without restriction.1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work. 2 = Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours. 3 = Capable of only limited selfcare; confined to bed/chair >50% of waking hours. 4 = Completely disabled; cannot carry on any selfcare; totally confined to bed/chair

† The total response percentages may exceed 100% because more than one answer could be selected.

‡ Those with stage IV/mBC defined as having metastases to the lung, brain, liver or ovaries.

**Supplementary Table S4.** Palbociclib treatment patterns for the nine individual EU countries

|  | UK | | DE | | NL | | BE | | IT | | ES | | PT | | FR | | CH | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | P+AI  n=221 | P+F  n=34 | P+AI  n=152 | P+F  n=99 | P+AI  n=27 | P+F  n=37 | P+AI  n=50 | P+F  n=101 | P+AI  n=129 | P+F  n=131 | P+AI  n=148 | P+F  n=111 | P+AI  n=54 | P+F  n=46 | P+AI  n=171 | P+F  n=112 | P+AI  n=30 | P+F  n=70 |
| **Palbociclib follow-up time from initiation (months)** |  | | | | | | | | | | | | | | | | | |
| n | 221 | 34 | 152 | 99 | 27 | 37 | 50 | 101 | 129 | 131 | 148 | 111 | 54 | 46 | 171 | 112 | 30 | 70 |
| Mean (SD) | 13.9 (7.2) | 12.2 (9.2) | 9.5 (3.7) | 6.6 (4.0) | 17.6 (9.2) | 14.6 (9.3) | 13.3 (6.2) | 9.3 (5.6) | 11.7 (7.0) | 8.4 (6.6) | 18.8 (9.3) | 15.3 (10.8) | 11.3 (4.6) | 12.0 (7.0) | 11.0 (4.2) | 10.3 (5.5) | 13.2 (6.1) | 14.0 (7.4) |
| Median (range) | 11.3 (5.9, 35.1) | 8.6 (3.1, 33.9) | 8.2 (6.0, 25.6) | 5.3 (3.0, 24.5) | 15.3 (6.4, 37.9) | 13.9 (3.4, 37.4) | 11.2 (6.3, 33.5) | 7.4 (3.0, 31.3) | 8.5 (5.9, 34.8) | 5.4 (3.0, 32.2) | 17.7 (6.0, 35.8) | 13.1 (3.0, 36.8) | 9.6 (6.7, 27.8) | 10.3 (3.3, 25.9) | 9.6 (6.0, 21.5) | 8.5 (3.2, 21.2) | 11.1 (6.0, 25.5) | 12.7 (3.3, 33.6) |
| **Combination partner, AI, n (%)** |  | | | | | | | | | | | | | | | | | |
| n | 221 | N/A | 152 | N/A | 27 | N/A | 50 | N/A | 129 | N/A | 148 | N/A | 54 | N/A | 171 | N/A | 30 | N/A |
| Letrozole/FEMARA | 192 (86.9) | N/A | 72 (47.4) | N/A | 11 (40.7) | N/A | 47 (94.0) | N/A | 90 (69.8) | N/A | 127 (85.8) | N/A | 46 (85.2) | N/A | 133 (77.8) | N/A | 22 (73.3) | N/A |
| Anastrozole/ARIMIDEX | 17 (7.7) | N/A | 44 (28.9) | N/A | 16 (59.3) | N/A | 1  (2.0) | N/A | 33 (25.6) | N/A | 17 (11.5) | N/A | 6 (11.1) | N/A | 27 (15.8) | N/A | 5 (16.7) | N/A |
| Exemestane/AROMASIN | 12 (5.4) | N/A | 36 (23.7) | N/A | 0 | N/A | 2 (  4.0) | N/A | 6  (4.7) | N/A | 4  (2.7) | N/A | 2  (3.7) | N/A | 11 (6.4) | N/A | 3 (10.0) | N/A |
| **Line of therapy palbociclib received, n (%)** |  | | | | | | | | | | | | | | | | | |
| n | 221 | 34 | 152 | 99 | 27 | 37 | 50 | 101 | 129 | 131 | 148 | 111 | 54 | 46 | 171 | 112 | 30 | 70 |
| 1 | 220 (99.5) | 18 (52.9) | 143 (94.1) | 82 (82.8) | 23 (85.2) | 5 (13.5) | 48 (96.0) | 67 (66.3) | 126 (97.7) | 81 (61.8) | 133 (89.9) | 53 (47.7) | 45 (83.3) | 11 (23.9) | 159 (93.0) | 34 (30.4) | 28 (93.3) | 28 (40.0) |
| 2 | 1  (0.5) | 14 (41.2) | 9  (5.9) | 17 (17.2) | 3 (11.1) | 23 (62.2) | 1  (2.0) | 30 (29.7) | 2  (1.6) | 46 (35.1) | 14 (9.5) | 56 (50.5) | 6 (11.1) | 26 (56.5) | 11 (6.4) | 65 (58.0) | 2  (6.7) | 35 (50.0) |
| 3 | 0 | 0 | 0 | 0 | 1  (3.7) | 7 (18.9) | 1  (2.0) | 4  (4.0) | 1  (0.8) | 4  (3.1) | 1  (0.7) | 1  (0.9) | 3  (5.6) | 5 (10.9) | 1  (0.6) | 10 (8.9) | 0 | 5  (7.1) |
| 4 | 0 | 2  (5.9) | 0 | 0 | 0 | 2  (5.4) | 0 | 0 | 0 | 0 | 0 | 1  (0.9) | 0 | 4  (8.7) | 0 | 3  (2.7) | 0 | 2  (2.9) |
| **Starting dose of palbociclib, mg/day, n (%)** |  | | | | | | | | | | | | | | | | | |
| n | 221 | 34 | 152 | 99 | 27 | 37 | 50 | 101 | 129 | 131 | 148 | 111 | 54 | 46 | 171 | 112 | 30 | 70 |
| 125 | 203 (91.9) | 32 (94.1) | 150 (98.7) | 95 (96.0) | 26 (96.3) | 36 (97.3) | 43 (86.0) | 76 (75.2) | 120 (93.0) | 120 (91.6) | 146 (98.6) | 109 (98.2) | 48 (88.9) | 41 (89.1) | 162 (94.7) | 102 (91.1) | 24 (80.0) | 57 (81.4) |
| 100 | 18 (8.1) | 2  (5.9) | 1  (0.7) | 3  (3.0) | 1  (3.7) | 0 | 6 (12.0) | 25 (24.8) | 9  (7.0) | 10 (7.6) | 1  (0.7) | 1  (0.9) | 6 (11.1) | 5 (10.9) | 7  (4.1) | 8  (7.1) | 5 (16.7) | 12 (17.1) |
| 75 | 0 | 0 | 1  (0.7) | 1  (1.0) | 0 | 1  (2.7) | 1  (2.0) | 0 | 0 | 1  (0.8) | 1  (0.7) | 1  (0.9) | 0 | 0 | 2  (1.2) | 2  (1.8) | 1  (3.3) | 1  (1.4) |
| **Reason for starting palbociclib dose <125 mg/day, n (%)** |  | | | | | | | | | | | | | | | | | |
| n | 18 | 2 | 2 | 4 | 1 | 1 | 7 | 25 | 9 | 11 | 2 | 2 | 6 | 5 | 9 | 10 | 6 | 13 |
| To avoid toxicity | 16 (88.9) | 1 (50.0) | 0 | 1 (25.0) | 1  (100) | 1  (100) | 7  (100) | 6 (24.0) | 5 (55.6) | 7 (63.6) | 1 (50.0) | 2  (100) | 5 (83.3) | 2 (40.0) | 6 (66.7) | 6 (60.0) | 6  (100) | 6 (46.2) |
| ECOG PS score | 5 (27.8) | 0 | 1 (50.0) | 3 (75.0) | 0 | 0 | 2 (28.6) | 3 (12.0) | 3 (33.3) | 1  (9.1) | 0 | 2  (100) | 1 (16.7) | 1 (20.0) | 1 (11.1) | 4 (40.0) | 1 (16.7) | 3 (23.1) |
| Age | 3 (16.7) | 0 | 0 | 1 (25.0) | 0 | 1  (100) | 7  (100) | 14 (56.0) | 6 (66.7) | 5 (45.5) | 2  (100) | 2  (100) | 2 (33.3) | 0 | 4 (44.4) | 3 (30.0) | 1 (16.7) | 7 (53.8) |
| Presence of comorbidities | 4 (22.2) | 0 | 1 (50.0) | 1 (25.0) | 0 | 0 | 3 (42.9) | 1  (4.0) | 0 | 1  (9.1) | 1 (50.0) | 0 | 0 | 3 (60.0) | 1 (11.1) | 2 (20.0) | 1 (16.7) | 1  (7.7) |
| Patient request | 2 (11.1) | 1 (50.0) | 0 | 0 | 0 | 0 | 2 (28.6) | 2 (8.0) | 0 | 2 (18.2) | 0 | 0 | 1 (16.7) | 0 | 0 | 2 (20.0) | 2 (33.3) | 3 (23.1) |
| Other | 0 | 0 | 1 (50.0) | 3 (75.0) | 0 | 0 | 2 (28.6) | 6 (24.0) | 1 (11.1) | 1  (9.1) | 0 | 0 | 4 (66.6) | 4 (80.0) | 0 | 0 | 1 (16.7) | 0 |
| **Dose reduction (any starting dose), n (%)** |  | | | | | | | | | | | | | | | | | |
| n | 221 | 34 | 152 | 99 | 27 | 37 | 50 | 101 | 129 | 131 | 148 | 111 | 54 | 46 | 171 | 112 | 30 | 70 |
| Dose reduced | 45 (20.4) | 4 (11.8) | 22 (14.5) | 11 (11.1) | 6 (22.2) | 5 (13.5) | 10 (20.0) | 6  (5.9) | 14 (10.9) | 10 (7.6) | 40 (27.0) | 15 (13.5) | 13 (24.1) | 7 (15.2) | 25 (14.6) | 12 (10.7) | 6 (20.0) | 17 (24.3) |
| **For those who start at 125 mg/day: Palbociclib dose change, n (%)** |  | | | | | | | | | | | | | | | | | |
| n | 203 | 32 | 150 | 95 | 26 | 36 | 43 | 76 | 120 | 120 | 146 | 109 | 48 | 41 | 162 | 102 | 24 | 57 |
| Dose remained at 125 mg/day | 159 (78.3) | 28 (87.5) | 129 (86.0) | 84 (88.4) | 20 (76.9) | 31 (86.1) | 33 (76.7) | 71 (93.4) | 110 (91.7) | 106 (88.3) | 107 (73.3) | 94 (86.2) | 38 (79.2) | 39 (95.1) | 138 (85.2) | 90 (88.2) | 19 (79.2) | 43 (75.4) |
| Dose changed from 125 mg/day | 44 (21.7) | 4 (12.5) | 21 (14.0) | 11 (11.6) | 6 (23.1) | 5 (13.9) | 10 (23.3) | 5  (6.6) | 10 (8.3) | 14 (11.7) | 39 (26.7) | 15 (13.8) | 10 (20.8) | 2  (4.9) | 24 (14.8) | 12 (11.8) | 5 (20.8) | 14 (24.6) |
| **Reason for dose reduction, n (%)** |  | | | | | | | | | | | | | | | | | |
| n | 45 | 4 | 22 | 11 | 6 | 5 | 10 | 6 | 14 | 10 | 40 | 15 | 13 | 7 | 25 | 12 | 6 | 17 |
| Side effects/toxicity | 40 (88.9) | 3 (75.0) | 19 (86.4) | 11 (100.0) | 6 (100.0) | 5 (100.0) | 10 (100.0) | 6 (100.0) | 14 (100.0) | 10 (100.0) | 38 (95.0) | 14 (93.3) | 13 (100.0) | 7 (100.0) | 23 (92.0) | 11 (91.7) | 5 (83.3) | 16 (94.1) |
| Patient request | 0 | 1 (25.0) | 7 (31.8) | 2 (18.2) | 0 | 0 | 0 | 0 | 0 | 0 | 2  (5.0) | 0 | 0 | 0 | 3 (12.0) | 2 (16.7) | 1 (16.7) | 2 (11.8) |
| Other | 5 (11.1) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1  (6.7) | 0 | 0 | 0 | 0 | 0 | 0 |
| **Palbociclib treatment status, n (%)** |  | | | | | | | | | | | | | | | | | |
| n | 221 | 34 | 152 | 99 | 27 | 37 | 50 | 101 | 129 | 131 | 148 | 111 | 54 | 46 | 171 | 112 | 30 | 70 |
| Treatment ongoing | 173 (78.3) | 28 (82.4) | 112 (73.3) | 83 (83.8) | 20 (74.1) | 25 (67.6) | 43 (86.0) | 91 (90.1) | 117 (90.7) | 101 (77.1) | 96 (64.9) | 69 (62.2) | 47 (87.0) | 36 (78.3) | 159 (93.0) | 96 (85.7) | 22 (73.3) | 45 (64.3) |
| Treatment discontinued | 48 (21.7) | 6 (17.6) | 40 (26.3) | 16 (16.2) | 7 (25.9) | 12 (32.4) | 7 (14.0) | 10 (9.9) | 12 (9.3) | 30 (22.9) | 52 (35.1) | 42 (37.8) | 7 (13.0) | 10 (21.7) | 12 (7.0) | 16 (14.3) | 8 (26.7) | 25 (35.7) |
| **Reason for discontinuation where known, n (%)\*** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| n | 45 | 6 | 39 | 16 | 6 | 12 | 7 | 10 | 12 | 9 | 51 | 42 | 7 | 10 | 12 | 16 | 8 | 25 |
| Progression following initial control/response | 37 (82.2) | 5 (83.3) | 13 (33.3) | 9  (56.3) | 4 (66.7) | 10 (83.3) | 6 (85.7) | 7 (70.0) | 8 (66.7) | 6 (66.7) | 44 (86.3) | 38 (90.5) | 6 (85.7) | 8 (80.0) | 9 (75.0) | 15 (93.8) | 7 (23.3) | 19 (27.1) |
| Progression without initial control/response | 6  (13.3) | 1  (16.7) | 0 | 4 (25.0) | 1  (16.7) | 1  (8.3) | 0 | 1 (10.0) | 4 (33.3) | 2 (22.2) | 4  (7.8) | 3  (7.1) | 1 (14.3) | 1 (10.0) | 0 | 1  (6.3) | 0 | 3  (4.3) |
| Treatment cost | 0 | 0 | 0 | 1  (6.3) | 0 | 0 | 0 | 0 | 0 | 1 (11.1) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1  (1.4) |
| Pill burden/compliance | 0 | 0 | 4  (10.3) | 1  (6.3) | 0 | 0 | 1 (14.3) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Side effects/toxicity | 1  (2.2) | 0 | 4  (10.3) | 3  (18.8) | 0 | 0 | 1 (14.3) | 1 (10.0) | 0 | 0 | 1  (2.0) | 0 | 0 | 0 | 1  (8.3) | 0 | 0 | 1  (1.4) |
| Patient request | 0 | 0 | 21 (53.8) | 4  (25.0) | 0 | 1  (8.3) | 0 | 0 | 0 | 0 | 2  (3.9) | 1  (2.4) | 0 | 0 | 0 | 0 | 1  (3.3) | 1  (1.4) |
| Other | 1  (2.2) | 1  (16.7) | 5  (12.8) | 0 | 1  (16.7) | 0 | 0 | 1 (10.0) | 0 | 0 | 0 | 0 | 0 | 1 (10.0) | 0 | 0 | 0 | 2  (2.9) |

ABC, advanced breast cancer; ECOG, Eastern Cooperative Oncology Group performance status; N/A, not applicable; P+AI, palbociclib plus aromatase inhibitor; P+F, palbociclib plus fulvestrant; PD, progressive disease; SD, standard deviation.

BE, Belgium; CH, Switzerland; DE, Germany; ES, Spain; FR, France; IT, Italy; NL, Netherlands; PT, Portugal; UK, United Kingdom.

\* Data only includes known reasons for discontinuations. N=27 patients discontinued treatment, but the reason was unknown

**Supplementary Table S5.** Response to palbociclib treatment for the nine individual EU countries

|  | UK | | DE | | NL | | BE | | IT | | ES | | PT | | FR | | CH | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | P+AI  n=221 | P+F  n=34 | P+AI  n=152 | P+F  n=99 | P+AI  n=27 | P+F  n=37 | P+AI  n=50 | P+F  n=101 | P+AI  n=129 | P+F  n=131 | P+AI  n=148 | P+F  n=111 | P+AI  n=54 | P+F  n=46 | P+AI  n=171 | P+F  n=112 | P+AI  n=30 | P+F  n=70 |
| **Best response achieved, n (%)** |  | | | | | | | | | | | | | | | | | |
| n | 220 | 34 | 151 | 92 | 27 | 37 | 50 | 91 | 127 | 127 | 146 | 110 | 53 | 45 | 171 | 109 | 30 | 70 |
| Complete response | 19 (8.6) | 2  (5.9) | 81 (53.6) | 35 (38.0) | 3 (11.1) | 1  (2.7) | 4  (8.0) | 5  (5.5) | 14 (11.0) | 6  (4.7) | 12 (8.2) | 8  (7.3) | 6 (11.3) | 4  (8.9) | 39 (22.8) | 16 (14.7) | 5 (16.7) | 5  (7.1) |
| Partial response | 164 (74.5) | 23 (67.6) | 46 (30.5) | 41 (44.6) | 14 (51.9) | 25 (67.6) | 40 (80.0) | 72 (79.1) | 93 (73.2) | 78 (61.4) | 113 (77.4) | 71 (64.5) | 43 (81.1) | 35 (77.8) | 109 (63.7) | 80 (73.4) | 19 (63.3) | 48 (68.6) |
| Stable disease ≥24 weeks | 30 (13.6) | 4 (11.8) | 20 (13.2) | 3  (3.3) | 8 (29.6) | 5 (13.5) | 4  (8.0) | 12 (13.2) | 18 (14.2) | 16 (12.6) | 17 (11.6) | 21 (19.1) | 4  (7.5) | 3  (6.7) | 22 (12.9) | 7  (6.4) | 4 (13.3) | 12 (17.1) |
| Stable disease <24 weeks | 4  (1.8) | 2  (5.9) | 1  (0.7) | 3  (3.3) | 1  (3.7) | 1  (2.7) | 1  (2.0) | 0 | 1  (0.8) | 1  (0.8) | 2  (1.4) | 2  (1.8) | 0 | 1  (2.2) | 1  (0.6) | 1  (0.9) | 2  (6.7) | 3  (4.3) |
| Stable disease (censored) | 0 | 2  (5.9) | 0 | 5  (5.4) | 0 | 3  (8.1) | 0 | 0 | 0 | 26 (20.5) | 0 | 8  (7.3) | 0 | 2  (4.4) | 0 | 5  (4.6) | 0 | 1  (1.4) |
| Progressive disease | 3  (1.4) | 1  (2.9) | 3  (2.0) | 5  (5.4) | 1  (3.7) | 2  (5.4) | 1  (2.0) | 2  (2.2) | 1  (0.8) | 0 | 2  (1.4) | 0 | 0 | 0 |  | 0 | 0 | 1  (1.4) |
| **Objective response rate, n (%)** |  | | | | | | | | | | | | | | | | | |
| Achieved | 183 (83.2) | 25 (73.5) | 127 (84.1) | 76 (82.6) | 17 (63.0) | 26 (70.3) | 44 (88.0) | 77 (84.6) | 107 (84.3) | 84 (66.1) | 125 (85.6) | 79 (71.8) | 49 (92.5) | 39 (86.7) | 148 (86.5) | 96 (88.1) | 24 (80.0) | 53 (75.7) |
| **Clinical benefit rate, n (%)** |  | | | | | | | | | | | | | | | | | |
| Upper bound (inc. Stab Dis censored) | 213 (96.8) | 31 (91.2) | 147 (97.4) | 84 (91.3) | 25 (92.6) | 34 (91.9) | 48 (96.0) | 89 (97.8) | 125 (98.4) | 126 (99.2) | 142 (97.3) | 108 (98.2) | 53 (100) | 44 (97.8) | 170 (99.4) | 108 (99.1) | 28 (93.3) | 66 (94.3) |
| Lower bound (inc. Stab Dis censored) | 213 (96.8) | 29 (85.3) | 147 (97.4) | 79 (85.9) | 25 (92.6) | 31 (83.8) | 48 (96.0) | 89 (97.8) | 125 (98.4) | 100 (78.7) | 142 (97.3) | 100 (90.9) | 53 (100) | 42 (93.3) | 170 (99.4) | 103 (94.5) | 28 (93.3) | 65 (92.9) |
| **PFR (%)** |  | | | | | | | | | | | | | | | | | |
| n | 221 | 34 | 152 | 99 | 27 | 37 | 49 | 101 | 129 | 131 | 148 | 111 | 54 | 46 | 171 | 112 | 30 | 70 |
| 6 | 94.1 | 90.4 | 96.7 | 88.8 | 92.6 | 93.8 | 98.0 | 99.0 | 96.1 | 98.5 | 98.0 | 94.5 | 100 | 94.6 | 99.4 | 95.1 | 96.7 | 92.2 |
| 12 | 85.3 | 74.5 | 88.7 | 72.3 | 82.7 | 82.2 | 91.4 | 87.1 | 93.3 | 93.5 | 85.6 | 73.5 | 81.3 | 76.3 | 95.3 | 83.2 | 88.1 | 74.0 |
| 18 | 79.1 | 65.2 | 84.9 | 72.3 | 74.4 | 52.6 | 81.9 | 65.3 | 89.6 | 84.7 | 71.4 | 43.8 | 75.0 | 64.0 | 78.8 | 57.6 | 39.6 | 53.2 |
| 24 | 53.5 | 65.2 | 84.9 | 72.3 | 74.4 | 52.6 | 81.9 | 49.0 | 82.1 | 69.9 | 60.9 | 30.6 | - | 64.0 | - | - | - | 35.5 |
| **SR (%)** |  | | | | | | | | | | | | | | | | | |
| n | 220 | 32 | 151 | 98 | 27 | 37 | 50 | 82 | 127 | 131 | 148 | 111 | 54 | 45 | 170 | 110 | 29 | 69 |
| 6 | 99.5 | 95.8 | 99.3 | 96.5 | 100 | 100 | 98.0 | 100 | 100 | 100 | 100 | 100 | 100 | 95.3 | 100 | 100 | 100 | 97.1 |
| 12 | 98.1 | 95.8 | 97.9 | 85.8 | 95.2 | 100 | 94.6 | 100 | 98.1 | 100 | 95.1 | 98.6 | 100 | 91.5 | 98.3 | 100 | 100 | 94.9 |
| 18 | 94.4 | 85.2 | 92.2 | 85.8 | 95.2 | 92.3 | 94.6 | 100 | 98.1 | 95.0 | 91.5 | 96.6 | 100 | 85.4 | 98.3 | 100 | 85.7 | 82.3 |
| 24 | 92.2 | 85.2 | 92.2 | 85.8 | 95.2 | 92.3 | 94.6 | 85.7 | 98.1 | 95.0 | 83.2 | 90.8 | 100 | 85.4 | - | - | - | 75.4 |

AI, aromatase inhibitor; F, fulvestrant; P, Palbociclib; P+AI, palbociclib plus aromatase inhibitor; P+F, palbociclib plus fulvestrant; SR, survival rate; PFR, progression-free rate; Stable Dis, stable disease; –, no value available.

BE, Belgium; CH, Switzerland; DE, Germany; ES, Spain; FR, France; IT, Italy; NL, Netherlands; PT, Portugal; UK, United Kingdom.

**Clinical Response.** Complete Response: where ‘Complete Response’ has been recorded at any time (no 24-week minimum); Partial Response: where ‘Partial Response’ has been recorded at any time (no 24-week minimum); Stable disease ≥24 weeks: patient remained on palbociclib for a minimum of 24 weeks, without complete or partial response, death, treatment switch or progression; Stable disease <24 weeks: stable disease recorded for initial response, with a subsequent progression recorded <24 weeks or treatment switch for reason other than progression <24 weeks or death without recorded progression <24 weeks; Progressive disease: progressive disease recorded for initial response without a subsequent partial or complete response recorded.

**Derived Clinical Endpoints.** Clinical Benefit Rate: proportion of patients who achieved a complete or partial response or had stable disease for ≥24 weeks as assessed by the physician; Objective Response Rate: proportion of patients achieving a complete or partial response as assessed by the physician and reported in the patient records; radiologic confirmation was not required and no criteria to re-evaluate were provided; Progression-free Rate: proportion of patients with no evidence of progression or death at 6, 12, 18, and 24 months; Overall Survival Rate: proportion of patients alive at 6, 12, 18, and 24 months.