Sponsor
Novartis Pharmaceuticals

Generic Drug Name
Ribociclib / Kisqali

Trial Indication(s)
Metastatic breast cancer

Protocol Number
CLEE011AUS65

Protocol Title
Description of Treatment Patterns and Description and Comparison of Healthcare Resource Utilization and Costs of Women with Metastatic HR+/HER2- Breast Cancer Treated with CDK4/6 Inhibitors

Clinical Trial Phase
NA

Phase of Drug Development
NA

Study Start/End Dates
Study start date: 08 May 2020

Study Completion date: 31 July 2020

Reason for Termination
NA

Study Design/Methodology

This study used an observational, retrospective cohort design, using US administrative insurance claims data, previously employed in an existing project, to better understand HRU and healthcare costs among women with mBC initiated on a CDK4/6 inhibitor.

Adult women with HR+/HER2- mBC initiated on a CDK4/6 inhibitor were included in the study and were stratified into cohorts based on the first CDK4/6 inhibitor they received (i.e., abemaciclib, palbociclib, or ribociclib), regardless of the line of therapy and menopausal status.

The initiation of the first CDK4/6 inhibitor was defined as the index date. The index treatment was defined as the CDK4/6 inhibitor initiated on the index date (i.e., abemaciclib, palbociclib, or ribociclib).

The 6-month period preceding the index date was considered as the baseline period, and was used to measure patient characteristics.

Outcomes were measured between the index date and 1) the end of the study period (persistence, switch, HRU, costs) OR 2) the end of the index treatment (adherence, dose modification, frequency of monitoring), as relevant. The end of the study period was defined as the earliest occurrence between the end of continuous enrollment and the end of data availability.

Setting

To conduct these analyses, data from the IBM MarketScan® Commercial database (Q1/2001 – Q3/2018) were used.

Centers

Novartis Investigative Site

Objectives:

Primary objective(s)

This study aimed to:

- Describe HRU and healthcare costs of adult women with HR+/HER2- mBC receiving abemaciclib, palbociclib, or ribociclib
- Compare HRU and healthcare costs of adult women with HR+/HER2- mBC receiving abemaciclib, palbociclib, or ribociclib

Secondary objective(s)

- The study aimed to describe treatment patterns and frequency of monitoring of adult women with HR+/HER2- mBC receiving abemaciclib, palbociclib, or ribociclib.

Test Product (s), Dose(s), and Mode(s) of Administration

≥1 ribociclib, palbociclib or abemaciclib medication

Statistical Methods

All analyses were performed using SAS software, Version 9.4 of the SAS System for Windows, SAS Institute Inc., Cary, NC, USA, or using R software, R Foundation for Statistical Computing, Vienna, Austria. All analyses were performed by Analysis Group, Inc. (AGI).

Study Population: Key Inclusion/Exclusion Criteria

Inclusion criteria

- Evidence of treatment with a CDK4/6 inhibitor regardless of the line of therapy. The initiation of the first CDK4/6 inhibitor was defined as the index date, and the first CDK4/6 inhibitor initiated was defined as the index treatment
- BC diagnosis: Two diagnosis codes of BC (International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM]: 174.xx and International Classification of Diseases, 10th Revision, Clinical Modification [ICD-10-CM]: C50.xx [excluding C50.x2 – male BC]) on two medical service claims separated by at least 30 days
- Metastatic disease diagnosis: At least two medical claims for a secondary neoplasm (ICD-9-CM codes: 196.xx–197.xx, 198.xx, ICD-10-CM codes: C77.xx, C78.xx, C79.xx) on separate dates, with the first one occurring no more than 30

days before the first diagnosis for BC HR+/HER2-: At least one prescription fill or administration of an ET (anastrazole, exemestane, ethinyl estradiol, fulvestrant, fluoxymesterone, letrozole, megestrol acetate, tamoxifen, or toremifene), HR+/HER2- therapy (everolimus), or CDK4/6 inhibitor (i.e., abemaciclib, palbociclib, or ribociclib) at any time following the diagnosis of BC, and no claims for treatments indicated for HER2+ BC, including trastuzumab, lapatinib, afatinib, pertuzumab, or ado-trastuzumab, at any time in the data period

- Women of at least 18 years of age as of the index date
- At least 6 months of continuous health plan coverage prior to and at least 1 month of continuous health plan coverage after the index date

Exclusion criteria
None

Participant Flow

A total of 4,320 HR+/HER2- women with at least one claim for treatment with CDK4/6 inhibitor for mBC were included in the analyses: 100 received treatment with abemaciclib, 4,118 received treatment with palbociclib, and 102 received treatment with ribociclib

Baseline Characteristics

	All patients N = 4,320	Abemaciclib N = 100	Palbociclib N = 4,118	Ribociclib N = 102
Demographics (as of the index date)				
Age at the initiation of first CDK4/6 inhibitor therapy (years)				
Mean ± SD	60.3 ± 11.7	59.5 ± 11.8	60.3 ± 11.7	59.4 ± 11.4
Median	60.0	59.0	60.0	58.5
Region, N (%)				
North Central	1,027 (23.8%)	19 (19.0%)	982 (23.8%)	26 (25.5%)
Northeast	901 (20.9%)	27 (27.0%)	863 (21.0%)	11 (10.8%)
South	1,768 (40.9%)	42 (42.0%)	1,683 (40.9%)	43 (42.2%)
West	624 (14.4%)	12 (12.0%)	590 (14.3%)	22 (21.6%)
Type of health plan, N (%)				
CDHP and HDHP	508 (11.8%)	17 (17.0%)	478 (11.6%)	13 (12.7%)
Comprehensive	513 (11.9%)	10 (10.0%)	490 (11.9%)	13 (12.7%)
HMO and POS with capitation	553 (12.8%)	10 (10.0%)	531 (12.9%)	12 (11.8%)
POS without capitation and EPO	307 (7.1%)	12 (12.0%)	286 (6.9%)	9 (8.8%)
PPO	2,401 (55.6%)	49 (49.0%)	2,297 (55.8%)	55 (53.9%)
Unknown	38 (0.9%)	2 (2.0%)	36 (0.9%)	0 (0.0%)
Year of the first observed mBC diagnosis, N (%)				
Prior to 2012	673 (15.6%)	13 (13.0%)	653 (15.9%)	7 (6.9%)
2012	293 (6.8%)	5 (5.0%)	284 (6.9%)	4 (3.9%)
2013	399 (9.2%)	9 (9.0%)	385 (9.3%)	5 (4.9%)
2014	540 (12.5%)	10 (10.0%)	521 (12.7%)	9 (8.8%)
2015	782 (18.1%)	5 (5.0%)	769 (18.7%)	8 (7.8%)
2016	759 (17.6%)	9 (9.0%)	739 (17.9%)	11 (10.8%)
2017	622 (14.4%)	23 (23.0%)	553 (13.4%)	46 (45.1%)
2018	252 (5.8%)	26 (26.0%)	214 (5.2%)	12 (11.8%)
Year of the initiation of first CDK4/6 inhibitor therapy, N (%)				
2015	1,087 (25.2%)	0 (0.0%)	1,087 (26.4%)	0 (0.0%)
2016	1,424 (33.0%)	0 (0.0%)	1,424 (34.6%)	0 (0.0%)
2017	1,208 (28.0%)	26 (26.0%)	1,116 (27.1%)	66 (64.7%)
2018	601 (13.9%)	74 (74.0%)	491 (11.9%)	36 (35.3%)

Reproductive status				
Reproductive status, N (%)				
Premenopausal	359 (8.3%)	8 (8.0%)	330 (8.0%)	21 (20.6%)
Postmenopausal	3,961 (91.7%)	92 (92.0%)	3,788 (92.0%)	81 (79.4%)
Patients aged at least 60 years old	2,216 (55.9%)	49 (53.3%)	2,120 (56.0%)	47 (58.0%)
At least 1 claim for fulvestrant or an aromatase inhibitor and no claims for a GnRH	3,746 (94.6%)	69 (75.0%)	3,610 (95.3%)	67 (82.7%)
At least 1 claim of bilateral oophorectomy[2]	250 (6.3%)	6 (6.5%)	238 (6.3%)	6 (7.4%)
At least 1 record of a diagnosis or procedure code related to postmenopausal status[3]	1,747 (44.1%)	46 (50.0%)	1,663 (43.9%)	38 (46.9%)
Prior treatment for mBC				
Time from mBC diagnosis to index date (months)				
Mean ± SD	26.4 ± 32.4	34.2 ± 40.1	26.3 ± 32.3	20.7 ± 27.1
Median	14.6	17.6	14.7	6.8
Time from mBC diagnosis to index date, N (%)				
< 6 months	1,619 (37.5%)	32 (32.0%)	1,538 (37.3%)	49 (48.0%)
6 - 12 months	416 (9.6%)	10 (10.0%)	394 (9.6%)	12 (11.8%)
12 - 24 months	582 (13.5%)	14 (14.0%)	561 (13.6%)	7 (6.9%)
24 - 36 months	516 (11.9%)	7 (7.0%)	500 (12.1%)	9 (8.8%)
> 36 months	1,187 (27.5%)	37 (37.0%)	1,125 (27.3%)	25 (24.5%)
Number of prior lines of therapy for mBC, N (%)				
0	1,362 (31.5%)	30 (30.0%)	1,291 (31.4%)	41 (40.2%)
1	1,044 (24.2%)	22 (22.0%)	999 (24.3%)	23 (22.5%)
2	646 (15.0%)	15 (15.0%)	617 (15.0%)	14 (13.7%)
3	484 (11.2%)	16 (16.0%)	456 (11.1%)	12 (11.8%)
4	312 (7.2%)	5 (5.0%)	302 (7.3%)	5 (4.9%)
5	184 (4.3%)	5 (5.0%)	174 (4.2%)	5 (4.9%)
6+	288 (6.7%)	7 (7.0%)	279 (6.8%)	2 (2.0%)
No prior lines of therapy for mBC, N (%)	1,362 (31.5%)	30 (30.0%)	1,291 (31.4%)	41 (40.2%)
Received prior line(s) of therapy for mBC, N (%)	2,958 (68.5%)	70 (70.0%)	2,827 (68.6%)	61 (59.8%)
Endocrine therapy[4]	2,684 (62.1%)	61 (61.0%)	2,571 (62.4%)	52 (51.0%)
Chemotherapy[4]	1,570 (36.3%)	42 (42.0%)	1,494 (36.3%)	34 (33.3%)
Other[4]	575 (13.3%)	11 (11.0%)	553 (13.4%)	11 (10.8%)
Prior use of radiation therapy[5], N (%)	1,130 (26.2%)	27 (27.0%)	1,071 (26.0%)	32 (31.4%)
Clinical trial enrollment[6], N (%)	112 (2.6%)	4 (4.0%)	106 (2.6%)	2 (2.0%)

Use of GnRH during baseline period, N (%)	365 (8.4%)	9 (9.0%)	346 (8.4%)	10 (9.8%)
No GnRH use	3,955 (91.6%)	91 (91.0%)	3,772 (91.6%)	92 (90.2%)
Leuprolide	199 (4.6%)	4 (4.0%)	191 (4.6%)	4 (3.9%)
Histrelin	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Goserelin	166 (3.8%)	5 (5.0%)	155 (3.8%)	6 (5.9%)
Triptorelin	3 (0.1%)	0 (0.0%)	3 (0.1%)	0 (0.0%)
Use of concomitant medications during baseline, N (%)				
CYP3A inhibitors[7]	695 (16.1%)	16 (16.0%)	665 (16.1%)	14 (13.7%)
CYP3A inductors[8]	5 (0.1%)	0 (0.0%)	5 (0.1%)	0 (0.0%)
P-inhibitors[9]	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
P-inductors[10]	5 (0.1%)	0 (0.0%)	5 (0.1%)	0 (0.0%)
Medication potentially associated with an increased risk of torsade de pointe[11]	3,260 (75.5%)	79 (79.0%)	3,102 (75.3%)	79 (77.5%)
Organ-level metastatic sites[12], N (%)				
Multiple metastatic sites (excluding lymph nodes)	1,298 (30.0%)	43 (43.0%)	1,222 (29.7%)	33 (32.4%)
Number of metastatic sites (excluding lymph nodes) Mean ± SD Median	 0.7 ± 1.0 0.0	 1.0 ± 1.2 0.0	 0.7 ± 1.0 0.0	 0.7 ± 1.0 0.0
Visceral	1,745 (40.4%)	52 (52.0%)	1,653 (40.1%)	40 (39.2%)
Lung	573 (13.3%)	13 (13.0%)	546 (13.3%)	14 (13.7%)
Liver	997 (23.1%)	30 (30.0%)	946 (23.0%)	21 (20.6%)
Pleura	244 (5.6%)	8 (8.0%)	230 (5.6%)	6 (5.9%)
Retroperitoneum and peritoneum	137 (3.2%)	6 (6.0%)	127 (3.1%)	4 (3.9%)
Mediastinum	87 (2.0%)	5 (5.0%)	80 (1.9%)	2 (2.0%)
Large intestine	41 (0.9%)	1 (1.0%)	39 (0.9%)	1 (1.0%)
Other digestive organs and spleen	83 (1.9%)	1 (1.0%)	81 (2.0%)	1 (1.0%)
Ovary	70 (1.6%)	2 (2.0%)	67 (1.6%)	1 (1.0%)
Genital organs	41 (0.9%)	2 (2.0%)	39 (0.9%)	0 (0.0%)

Adrenal gland	31 (0.7%)	2 (2.0%)	28 (0.7%)	1 (1.0%)
Small intestine	15 (0.3%)	1 (1.0%)	14 (0.3%)	0 (0.0%)
Kidney	10 (0.2%)	0 (0.0%)	10 (0.2%)	0 (0.0%)
Other urinary organs	13 (0.3%)	0 (0.0%)	12 (0.3%)	1 (1.0%)
Other respiratory organs	10 (0.2%)	0 (0.0%)	10 (0.2%)	0 (0.0%)
Bone and bone marrow	3,177 (73.5%)	75 (75.0%)	3,031 (73.6%)	71 (69.6%)
Bone and bone marrow only (may include lymph nodes)	3,029 (70.1%)	67 (67.0%)	2,894 (70.3%)	68 (66.7%)
Central nervous system (CNS)	385 (8.9%)	16 (16.0%)	354 (8.6%)	15 (14.7%)
Brain and spinal cord	314 (7.3%)	14 (14.0%)	289 (7.0%)	11 (10.8%)
Other parts of nervous system	118 (2.7%)	6 (6.0%)	105 (2.5%)	7 (6.9%)
Disseminated neoplasm	114 (2.6%)	0 (0.0%)	108 (2.6%)	6 (5.9%)
Lymph nodes	1,294 (30.0%)	29 (29.0%)	1,243 (30.2%)	22 (21.6%)
Lymph nodes only	932 (21.6%)	17 (17.0%)	899 (21.8%)	16 (15.7%)
Other	606 (14.0%)	16 (16.0%)	580 (14.1%)	10 (9.8%)
Skin	174 (4.0%)	4 (4.0%)	168 (4.1%)	2 (2.0%)
Other[13]	473 (10.9%)	13 (13.0%)	451 (11.0%)	9 (8.8%)
Baseline comorbidities, N (%)				
CCI[14]				
Mean ± SD	6.8 ± 1.1	6.8 ± 1.0	6.8 ± 1.1	6.7 ± 1.1
Median	6.0	6.0	6.0	6.0
Thrombolic event	199 (4.6%)	5 (5.0%)	189 (4.6%)	5 (4.9%)
Pulmonary embolism	123 (2.8%)	4 (4.0%)	116 (2.8%)	3 (2.9%)
QT prolongation	9 (0.2%)	0 (0.0%)	8 (0.2%)	1 (1.0%)
Infection	1,531 (35.4%)	41 (41.0%)	1,461 (35.5%)	29 (28.4%)
Anemia	901 (20.9%)	30 (30.0%)	847 (20.6%)	24 (23.5%)
Neutropenia	283 (6.6%)	12 (12.0%)	262 (6.4%)	9 (8.8%)
Leukopenia	67 (1.6%)	3 (3.0%)	64 (1.6%)	0 (0.0%)

Thrombocytopenia	140 (3.2%)	3 (3.0%)	132 (3.2%)	5 (4.9%)
Comorbidities that may warrant EKG monitoring, N (%)				
Hypertension	1,624 (37.6%)	33 (33.0%)	1,547 (37.6%)	44 (43.1%)
Cardiac arrhythmias	284 (6.6%)	8 (8.0%)	266 (6.5%)	10 (9.8%)
Abnormal EKG	255 (5.9%)	9 (9.0%)	229 (5.6%)	17 (16.7%)
Congestive heart failure	207 (4.8%)	5 (5.0%)	197 (4.8%)	5 (4.9%)
Cardiomyopathy	90 (2.1%)	3 (3.0%)	83 (2.0%)	4 (3.9%)
Myocardial infarction	45 (1.0%)	0 (0.0%)	44 (1.1%)	1 (1.0%)
Angina pectoris	35 (0.8%)	0 (0.0%)	35 (0.8%)	0 (0.0%)
Pericarditis	85 (2.0%)	7 (7.0%)	75 (1.8%)	3 (2.9%)
Left ventricular ejection fraction (LVEF) less than 50%	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other comorbidities, N (%)				
Peripheral vascular disease	215 (5.0%)	8 (8.0%)	202 (4.9%)	5 (4.9%)
Cerebrovascular disease	190 (4.4%)	7 (7.0%)	176 (4.3%)	7 (6.9%)
Dementia	14 (0.3%)	1 (1.0%)	12 (0.3%)	1 (1.0%)
Chronic pulmonary disease	485 (11.2%)	13 (13.0%)	455 (11.0%)	17 (16.7%)
Rheumatic disease	72 (1.7%)	1 (1.0%)	68 (1.7%)	3 (2.9%)
Peptic ulcer disease	42 (1.0%)	1 (1.0%)	41 (1.0%)	0 (0.0%)
Liver disease	819 (19.0%)	17 (17.0%)	788 (19.1%)	14 (13.7%)
Diabetes	666 (15.4%)	22 (22.0%)	625 (15.2%)	19 (18.6%)
Hemiplegia or paraplegia	42 (1.0%)	0 (0.0%)	41 (1.0%)	1 (1.0%)
Renal disease	153 (3.5%)	2 (2.0%)	150 (3.6%)	1 (1.0%)
AIDS/HIV	3 (0.1%)	0 (0.0%)	3 (0.1%)	0 (0.0%)

Means and standard deviations are shown for continuous characteristics; counts and percentages are shown for categorical characteristics, unless otherwise noted

Abbreviations:
CCI: Charlson comorbidity index; CDHP: consumer-driven health plan; CDK: cyclin-dependent kinase; EKG: electrocardiogram; EPO: exclusive provider organization; GnRH: gonadotropin-releasing hormone agonist; HDHP: high-deductible health plan; HER2-: human epidermal growth factor receptor 2 negative; HMO: home health organization; HR+: hormone receptor positive; mBC: metastatic breast cancer; POS: point of service; PPO: preferred provider organization; SD: standard deviation

Primary Outcome Result(s)

Description of Healthcare Resource Utilization

	All patients N = 4,320	Abemaciclib N = 100	Palbociclib N = 4,118	Ribociclib N = 102
Time period				
Duration of follow-up (months)				
Mean ± SD	14.1 ± 10.1	5.2 ± 3.1	14.4 ± 10.2	8.7 ± 4.7
Median	11.9	4.6	12.5	8.3
PPP6M healthcare resource utilization[2]				
Inpatient admissions				
Mean ± SD	0.4 ± 0.9	0.5 ± 1.1	0.4 ± 0.9	0.4 ± 0.9
Median	0.0	0.0	0.0	0.0
Patients with ≥ 1 inpatient admission, N (%)	1,596 (36.9%)	25 (25.0%)	1,542 (37.4%)	29 (28.4%)
Inpatient days				
Mean ± SD	2.8 ± 7.6	3.9 ± 9.9	2.8 ± 7.5	2.5 ± 7.5
Median	0.0	0.0	0.0	0.0
Days with DME services				
Mean ± SD	0.5 ± 1.5	0.5 ± 1.6	0.5 ± 1.5	0.5 ± 1.4
Median	0.0	0.0	0.0	0.0
Days with emergency room services				
Mean ± SD	0.6 ± 1.5	0.9 ± 1.7	0.6 ± 1.5	0.6 ± 1.3
Median	0.0	0.0	0.0	0.0
Days with outpatient services				
Mean ± SD	23.3 ± 13.8	25.8 ± 16.7	23.3 ± 13.7	22.2 ± 11.5
Median	20.4	21.8	20.4	19.8
Home care services				
Mean ± SD	1.8 ± 6.8	1.9 ± 6.4	1.8 ± 6.8	2.1 ± 6.5
Median	0.0	0.0	0.0	0.0
Skilled nursing facility services				
Mean ± SD	0.3 ± 2.1	0.4 ± 1.8	0.3 ± 2.0	0.5 ± 2.9
Median	0.0	0.0	0.0	0.0
Office visits				
Mean ± SD	20.4 ± 11.6	22.9 ± 15.3	20.4 ± 11.6	18.8 ± 9.0
Median	18.2	20.2	18.2	17.3

Ambulatory surgical center visits				
Mean ± SD	0.0 ± 0.3	0.0 ± 0.3	0.0 ± 0.3	0.0 ± 0.0
Median	0.0	0.0	0.0	0.0
Other outpatient services				
Mean ± SD	0.8 ± 2.0	0.6 ± 2.1	0.8 ± 2.0	0.8 ± 2.1
Median	0.0	0.0	0.0	0.0
Days with drug administration-related claims				
Mean ± SD	6.7 ± 5.3	7.0 ± 4.7	6.7 ± 5.3	5.0 ± 4.7
Median	6.2	6.3	6.2	5.3
Days with laboratory tests				
Mean ± SD	10.8 ± 6.6	11.7 ± 7.3	10.8 ± 6.6	10.6 ± 7.1
Median	9.7	10.4	9.6	9.9
PPP6M specific condition-related healthcare resource utilization[2,3]				
Thrombolic event-related resources				
Days with services related to thrombolic event				
Mean ± SD	0.4 ± 2.6	1.3 ± 7.8	0.4 ± 2.3	0.2 ± 1.3
Median	0.0	0.0	0.0	0.0
Inpatient days with services related to thrombolic event				
Mean ± SD	0.2 ± 2.3	1.1 ± 7.5	0.2 ± 2.0	0.1 ± 0.6
Median	0.0	0.0	0.0	0.0
Non-inpatient days with services related to thrombolic event				
Mean ± SD	0.1 ± 0.9	0.2 ± 1.1	0.1 ± 0.9	0.1 ± 1.0
Median	0.0	0.0	0.0	0.0
Patients with ≥ 1 medical service related to thrombolic event, N (%)	360 (8.3%)	7 (7.0%)	348 (8.5%)	5 (4.9%)
Pulmonary embolism-related resources				
Days with services related to pulmonary embolism				
Mean ± SD	0.3 ± 2.6	0.4 ± 1.8	0.3 ± 2.5	0.6 ± 4.1
Median	0.0	0.0	0.0	0.0
Inpatient days with services related to pulmonary embolism				
Mean ± SD	0.2 ± 2.2	0.3 ± 1.7	0.2 ± 2.3	0.2 ± 1.1
Median	0.0	0.0	0.0	0.0
Non-inpatient days with services related to pulmonary embolism				
Mean ± SD	0.1 ± 0.9	0.1 ± 0.5	0.1 ± 0.8	0.4 ± 3.2
Median	0.0	0.0	0.0	0.0

Patients with ≥ 1 medical service related to pulmonary embolism, N (%)	257 (5.9%)	4 (4.0%)	247 (6.0%)	6 (5.9%)
QT prolongation event-related resources				
Days with services related to QT prolongation event				
Mean ± SD	0.0 ± 1.0	0.0 ± 0.0	0.0 ± 0.6	0.7 ± 4.9
Median	0.0	0.0	0.0	0.0
Inpatient days with services related to QT prolongation event				
Mean ± SD	0.0 ± 1.0	0.0 ± 0.0	0.0 ± 0.6	0.6 ± 4.9
Median	0.0	0.0	0.0	0.0
Non-inpatient days with services related to QT prolongation event				
Mean ± SD	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.2
Median	0.0	0.0	0.0	0.0
Patients with ≥ 1 medical service related to QT prolongation event, N (%)	37 (0.9%)	0 (0.0%)	30 (0.7%)	7 (6.9%)
Infection-related resources				
Days with services related to infection				
Mean ± SD	2.4 ± 6.6	3.5 ± 9.1	2.3 ± 6.5	2.5 ± 7.1
Median	0.4	0.0	0.4	0.0
Inpatient days with services related to infection				
Mean ± SD	1.5 ± 5.9	2.5 ± 9.1	1.5 ± 5.8	1.6 ± 6.7
Median	0.0	0.0	0.0	0.0
Non-inpatient days with services related to infection				
Mean ± SD	0.9 ± 2.2	1.0 ± 2.0	0.9 ± 2.3	0.8 ± 1.5
Median	0.0	0.0	0.2	0.0
Patients with ≥ 1 medical service related to infection, N (%)	2,403 (55.6%)	44 (44.0%)	2,314 (56.2%)	45 (44.1%)
Anemia-related resources				
Days with services related to anemia				
Mean ± SD	2.6 ± 7.2	3.4 ± 6.5	2.5 ± 7.2	3.2 ± 8.8
Median	0.0	0.0	0.0	0.0
Inpatient days with services related to anemia				
Mean ± SD	1.2 ± 4.7	1.3 ± 4.7	1.2 ± 4.6	1.7 ± 6.8
Median	0.0	0.0	0.0	0.0
Non-inpatient days with services related to anemia				
Mean ± SD	1.4 ± 4.7	2.1 ± 4.6	1.4 ± 4.7	1.5 ± 3.6
Median	0.0	0.0	0.0	0.0

Patients with ≥ 1 medical service related to anemia, N (%)	1,732 (40.1%)	39 (39.0%)	1,659 (40.3%)	34 (33.3%)
Neutropenia-related resources				
Days with services related to neutropenia				
Mean ± SD	1.1 ± 3.1	0.9 ± 2.7	1.1 ± 3.1	0.8 ± 2.0
Median	0.0	0.0	0.0	0.0
Inpatient days with services related to neutropenia				
Mean ± SD	0.3 ± 2.1	0.3 ± 1.7	0.3 ± 2.1	0.1 ± 0.4
Median	0.0	0.0	0.0	0.0
Non-inpatient days with services related to neutropenia				
Mean ± SD	0.7 ± 2.1	0.6 ± 2.0	0.8 ± 2.2	0.7 ± 2.0
Median	0.0	0.0	0.0	0.0
Patients with ≥ 1 medical service related to neutropenia, N (%)	1,352 (31.3%)	18 (18.0%)	1,310 (31.8%)	24 (23.5%)
Leukopenia-related resources				
Days with services related to leukopenia				
Mean ± SD	0.2 ± 1.6	0.2 ± 1.4	0.2 ± 1.6	0.1 ± 0.7
Median	0.0	0.0	0.0	0.0
Inpatient days with services related to leukopenia				
Mean ± SD	0.1 ± 1.4	0.0 ± 0.3	0.1 ± 1.4	0.1 ± 0.7
Median	0.0	0.0	0.0	0.0
Non-inpatient days with services related to leukopenia				
Mean ± SD	0.1 ± 0.7	0.2 ± 1.3	0.1 ± 0.7	0.0 ± 0.2
Median	0.0	0.0	0.0	0.0
Patients with ≥ 1 medical service related to leukopenia, N (%)	381 (8.8%)	6 (6.0%)	370 (9.0%)	5 (4.9%)
Thrombocytopenia-related resources				
Days with services related to thrombocytopenia				
Mean ± SD	0.6 ± 3.1	0.6 ± 2.6	0.6 ± 3.1	0.5 ± 2.5
Median	0.0	0.0	0.0	0.0
Inpatient days with services related to thrombocytopenia				
Mean ± SD	0.4 ± 2.8	0.4 ± 2.2	0.4 ± 2.9	0.4 ± 2.0
Median	0.0	0.0	0.0	0.0

Non-inpatient days with services related to thrombocytopenia				
Mean ± SD	0.2 ± 1.0	0.2 ± 0.8	0.2 ± 1.0	0.1 ± 0.6
Median	0.0	0.0	0.0	0.0
Patients with ≥ 1 medical service related to thrombocytopenia, N (%)	513 (11.9%)	8 (8.0%)	501 (12.2%)	4 (3.9%)

Means and standard deviations are shown for continuous characteristics; counts and percentages are shown for categorical characteristics, unless otherwise noted

Abbreviations:
DME: durable medical equipment; PPP6M: per-patient-per-6-months; SD: standard deviation

Description of Healthcare Costs

	All patients N = 4,320	Abemaciclib N = 100	Palbociclib N = 4,118	Ribociclib N = 102
Time period				
Duration of follow up period (months)				
Mean ± SD	14.1 ± 10.1	5.2 ± 3.1	14.4 ± 10.2	8.7 ± 4.7
Median	11.9	4.6	12.5	8.3
PPPM healthcare costs[3]				
Total healthcare costs				
Mean ± SD	17,384.5 ± 10,180.6	22,346.8 ± 11,017.0	17,273.9 ± 9,929.1	16,983.9 ± 16,415.1
Median	15,549.1	20,888.5	15,515.6	14,432.5
Medical costs				
Total medical costs				
Mean ± SD	8,357.8 ± 9,788.7	11,285.1 ± 9,995.5	8,299.9 ± 9,562.4	7,828.8 ± 16,227.4
Median	5,550.8	8,170.0	5,570.7	3,875.3
IP costs				
Mean ± SD	2,131.9 ± 6,616.4	2,759.9 ± 6,880.1	2,103.7 ± 6,371.2	2,653.0 ± 13,046.8
Median	0.0	0.0	0.0	0.0
DME costs				
Mean ± SD	17.4 ± 109.1	19.6 ± 79.6	17.5 ± 110.7	14.1 ± 54.3
Median	0.0	0.0	0.0	0.0
Emergency care costs				
Mean ± SD	275.4 ± 942.8	382.1 ± 1,138.7	270.3 ± 923.7	378.3 ± 1,391.6
Median	0.0	0.0	0.0	0.0
OP costs				
Mean ± SD	5,933.1 ± 6,100.0	8,123.5 ± 7,485.6	5,908.4 ± 6,068.4	4,783.4 ± 5,390.1
Median	4,345.6	5,751.3	4,364.6	2,994.5
Home care service costs				
Mean ± SD	156.7 ± 610.5	206.3 ± 625.0	154.6 ± 610.3	192.6 ± 607.2
Median	0.0	0.0	0.0	0.0
Skilled nursing facility costs				
Mean ± SD	41.3 ± 395.6	63.9 ± 377.4	40.4 ± 393.3	57.0 ± 494.7
Median	0.0	0.0	0.0	0.0

Office visit costs				
Mean ± SD	5,694.5 ± 6,028.3	7,815.3 ± 7,330.3	5,672.4 ± 6,003.1	4,507.4 ± 5,146.4
Median	4,100.2	5,409.4	4,110.5	2,573.8
Ambulatory surgical center visit costs				
Mean ± SD	10.5 ± 101.5	11.6 ± 70.2	10.8 ± 103.4	0.0 ± 0.0
Median	0.0	0.0	0.0	0.0
Other OP costs				
Mean ± SD	30.1 ± 244.8	26.4 ± 174.1	30.2 ± 248.6	26.5 ± 117.5
Median	0.0	0.0	0.0	0.0
Laboratory test costs				
Mean ± SD	551.6 ± 1,489.7	579.7 ± 888.2	543.1 ± 1,410.2	868.6 ± 3,598.2
Median	168.1	285.9	167.8	138.3
Medical drug administration costs				
Mean ± SD	2,836.3 ± 3,624.0	3,454.0 ± 3,490.4	2,839.5 ± 3,641.9	2,102.3 ± 2,847.0
Median	1,937.1	2,497.7	1,938.2	944.2
OP costs – excluding drug administration costs				
Mean ± SD	3,137.1 ± 4,445.3	4,701.1 ± 6,074.1	3,110.0 ± 4,413.2	2,699.5 ± 3,507.0
Median	1,782.4	2,218.7	1,778.7	1,665.1
Pharmacy costs				
Total pharmacy costs				
Mean ± SD	9,026.7 ± 4,485.3	11,061.7 ± 4,903.9	8,974.1 ± 4,461.7	9,155.1 ± 4,590.8
Median	9,478.9	12,381.5	9,403.7	9,449.3
CDK4/6 costs[4]				
Mean ± SD	8,242.3 ± 4,650.0	10,637.8 ± 4,926.2	8,176.2 ± 4,629.8	8,563.3 ± 4,599.2
Median	8,555.8	11,477.0	8,431.9	9,240.4
Chemotherapy and endocrine[4]				
Mean ± SD	148.4 ± 411.6	102.6 ± 371.8	152.2 ± 416.5	40.3 ± 147.4
Median	3.3	0.0	3.5	1.4
Other pharmacy costs				
Mean ± SD	636.0 ± 1,566.9	321.3 ± 704.9	645.7 ± 1,576.2	551.6 ± 1,764.6
Median	89.1	84.0	90.2	66.6

Means and standard deviations are shown for continuous characteristics; counts and percentages are shown for categorical characteristics, unless otherwise noted

Abbreviations:
DME: durable medical equipment; IP: Inpatient; OP: outpatient; PPPM: per-patient-per-month; SD: standard deviation; VT: vein thrombosis

Secondary Outcome Result(s)

Dosing Patterns

	All patients N = 4,320	Abemaciclib N = 100	Palbociclib N = 4,118	Ribociclib N = 102
Dosing Patterns				
Starting dose[1], N (%)				
Lower than recommended	587 (13.6%)	37 (37.0%)	541 (13.1%)	9 (8.8%)
Recommended	3,731 (86.4%)	61 (61.0%)	3,577 (86.9%)	93 (91.2%)
Higher than recommended	2 (0.0%)	2 (2.0%)	0 (0.0%)	0 (0.0%)
Dose sequencing[2, 3, 4], N (%)				
Dose decrease	1,342 (31.1%)	24 (24.0%)	1,297 (31.5%)	21 (20.6%)
Dose increase	47 (1.1%)	1 (1.0%)	44 (1.1%)	2 (2.0%)
No dose modification	2,931 (67.8%)	75 (75.0%)	2,777 (67.4%)	79 (77.5%)

Means and standard deviations are shown for continuous characteristics; counts and percentages are shown for categorical characteristics, unless otherwise noted

Frequency of Monitoring in Patients on Treatment for ≥≥ 1 month

	All patients N = 4,320	Abemaciclib N = 100	Palbociclib N = 4,118	Ribociclib N = 102
Patients on treatment for ≥1 month				
Patients on treatment for ≥1 month, N (%)	3,954 (91.5%)	81 (81.0%)	3,792 (92.1%)	81 (79.4%)
EKG monitoring during first month of therapy[1]				
Proportion of patients tested[2], N (%)	308 (7.8%)	13 (16.0%)	264 (7.0%)	31 (38.3%)
Number of tests				
Mean ± SD	1.3 ± 0.9	1.0 ± 0.0	1.3 ± 0.9	1.5 ± 0.6
Median	1.0	1.0	1.0	1.0
Number of tests, N (%)				
1	241 (78.2%)	13 (100.0%)	209 (79.2%)	19 (61.3%)
2	48 (15.6%)	0 (0.0%)	38 (14.4%)	10 (32.3%)
3	15 (4.9%)	0 (0.0%)	13 (4.9%)	2 (6.5%)
4+	4 (1.3%)	0 (0.0%)	4 (1.5%)	0 (0.0%)
CBC monitoring during first month of therapy[1]				
Proportion of patients tested[2], N (%)	3,007 (76.0%)	60 (74.1%)	2,886 (76.1%)	61 (75.3%)
Number of tests				
Mean ± SD	2.1 ± 1.2	2.2 ± 1.4	2.1 ± 1.2	2.0 ± 1.0
Median	2.0	2.0	2.0	2.0
Number of tests, N (%)				
1	1,136 (37.8%)	23 (38.3%)	1,092 (37.8%)	21 (34.4%)
2	1,054 (35.1%)	18 (30.0%)	1,009 (35.0%)	27 (44.3%)
3	507 (16.9%)	10 (16.7%)	488 (16.9%)	9 (14.8%)
4	206 (6.9%)	5 (8.3%)	199 (6.9%)	2 (3.3%)
5	77 (2.6%)	3 (5.0%)	72 (2.5%)	2 (3.3%)
6	12 (0.4%)	0 (0.0%)	12 (0.4%)	0 (0.0%)
7+	15 (0.5%)	1 (1.7%)	14 (0.5%)	0 (0.0%)

Hepatic monitoring during first month of therapy[1]				
Proportion of patients tested[2], N (%)	2,624 (66.4%)	56 (69.1%)	2,509 (66.2%)	59 (72.8%)
Number of tests				
Mean ± SD	1.6 ± 0.9	2.1 ± 1.3	1.6 ± 0.9	1.7 ± 0.8
Median	1.0	2.0	1.0	2.0
Number of tests, N (%)				
1	1,490 (56.8%)	22 (39.3%)	1,440 (57.4%)	28 (47.5%)
2	798 (30.4%)	21 (37.5%)	752 (30.0%)	25 (42.4%)
3	235 (9.0%)	6 (10.7%)	225 (9.0%)	4 (6.8%)
4	69 (2.6%)	5 (8.9%)	62 (2.5%)	2 (3.4%)
5	21 (0.8%)	1 (1.8%)	20 (0.8%)	0 (0.0%)
6+	11 (0.4%)	1 (1.8%)	10 (0.4%)	0 (0.0%)
AST disease monitoring				
Proportion of patients tested[2], N (%)	2,579 (65.2%)	56 (69.1%)	2,465 (65.0%)	58 (71.6%)
Number of tests				
Mean ± SD	1.6 ± 0.9	2.0 ± 1.3	1.6 ± 0.8	1.7 ± 0.8
Median	1.0	2.0	1.0	2.0
Number of tests, N (%)				
1	1,509 (58.5%)	23 (41.1%)	1,458 (59.1%)	28 (48.3%)
2	774 (30.0%)	21 (37.5%)	729 (29.6%)	24 (41.4%)
3	209 (8.1%)	5 (8.9%)	200 (8.1%)	4 (6.9%)
4	62 (2.4%)	6 (10.7%)	54 (2.2%)	2 (3.4%)
5	16 (0.6%)	0 (0.0%)	16 (0.6%)	0 (0.0%)
6+	9 (0.3%)	1 (1.8%)	8 (0.3%)	0 (0.0%)
ALT disease monitoring				
Proportion of patients tested[2], N (%)	2,578 (65.2%)	56 (69.1%)	2,464 (65.0%)	58 (71.6%)
Number of tests				
Mean ± SD	1.6 ± 0.9	2.0 ± 1.3	1.6 ± 0.8	1.7 ± 0.8
Median	1.0	2.0	1.0	2.0
Number of tests, N (%)				
1	1,509 (58.5%)	23 (41.1%)	1,458 (59.2%)	28 (48.3%)
2	773 (30.0%)	21 (37.5%)	728 (29.5%)	24 (41.4%)
3	209 (8.1%)	5 (8.9%)	200 (8.1%)	4 (6.9%)
4	62 (2.4%)	6 (10.7%)	54 (2.2%)	2 (3.4%)
5	16 (0.6%)	0 (0.0%)	16 (0.6%)	0 (0.0%)
6+	9 (0.3%)	1 (1.8%)	8 (0.3%)	0 (0.0%)

ALP disease monitoring				
Proportion of patients tested[2], N (%)	2,572 (65.0%)	56 (69.1%)	2,458 (64.8%)	58 (71.6%)
Number of tests				
Mean ± SD	1.6 ± 0.9	2.0 ± 1.3	1.6 ± 0.8	1.7 ± 0.8
Median	1.0	2.0	1.0	2.0
Number of tests, N (%)				
1	1,503 (58.4%)	23 (41.1%)	1,452 (59.1%)	28 (48.3%)
2	773 (30.1%)	21 (37.5%)	728 (29.6%)	24 (41.4%)
3	210 (8.2%)	5 (8.9%)	201 (8.2%)	4 (6.9%)
4	61 (2.4%)	6 (10.7%)	53 (2.2%)	2 (3.4%)
5	16 (0.6%)	0 (0.0%)	16 (0.7%)	0 (0.0%)
6+	9 (0.3%)	1 (1.8%)	8 (0.3%)	0 (0.0%)
Bilirubin disease monitoring				
Proportion of patients tested[2], N (%)	2,617 (66.2%)	56 (69.1%)	2,502 (66.0%)	59 (72.8%)
Number of tests				
Mean ± SD	1.6 ± 0.9	2.1 ± 1.3	1.6 ± 0.9	1.7 ± 0.8
Median	1.0	2.0	1.0	2.0
Number of tests, N (%)				
1	1,484 (56.7%)	22 (39.3%)	1,434 (57.3%)	28 (47.5%)
2	799 (30.5%)	21 (37.5%)	753 (30.1%)	25 (42.4%)
3	234 (8.9%)	6 (10.7%)	224 (9.0%)	4 (6.8%)
4	68 (2.6%)	5 (8.9%)	61 (2.4%)	2 (3.4%)
5	21 (0.8%)	1 (1.8%)	20 (0.8%)	0 (0.0%)
6+	11 (0.4%)	1 (1.8%)	10 (0.4%)	0 (0.0%)
Imaging during first month of therapy[1]				
Proportion of patients tested[2], N (%)	892 (22.6%)	27 (33.3%)	847 (22.3%)	18 (22.2%)
Number of tests				
Mean ± SD	1.3 ± 0.6	1.3 ± 0.6	1.3 ± 0.6	1.4 ± 0.5
Median	1.0	1.0	1.0	1.0
Number of tests, N (%)				
1	709 (79.5%)	22 (81.5%)	676 (79.8%)	11 (61.1%)
2	141 (15.8%)	3 (11.1%)	131 (15.5%)	7 (38.9%)
3	33 (3.7%)	2 (7.4%)	31 (3.7%)	0 (0.0%)
4	7 (0.8%)	0 (0.0%)	7 (0.8%)	0 (0.0%)
5	2 (0.2%)	0 (0.0%)	2 (0.2%)	0 (0.0%)

Means and standard deviations are shown for continuous characteristics; counts and percentages are shown for categorical characteristics, unless otherwise noted

Safety Results
As this is a study based on secondary use of data, safety monitoring and safety reporting, where there is a safety relevant result, is provided on an aggregate level only; no reporting on an individual case level is required. In studies based on secondary use of data with a safety relevant result, reports of adverse events/adverse reactions are summarized in the study report, i.e. the overall association between an exposure and an outcome. Relevant findings from the study report will be included in the periodic aggregated regulatory reports submitted to Health Authorities (HA).

Other Relevant Findings
None

Conclusion
The objective of this study was to describe treatment patterns and outcomes, as well as compare HRU and healthcare costs, of adult women with metastatic HR+/HER2- breast cancer receiving abemaciclib, palbociclib, or ribociclib using real-world data.

Results showed that among HR+/HER2- mBC women receiving CDK4/6 inhibitors, the majority were postmenopausal and received CDK4/6 inhibitor as first- or second-line therapy for mBC. Across all three treatment cohorts, high levels of persistence and adherence to CDK4/6-based therapy were observed.

Findings also showed that total healthcare costs PPPM while on treatment appeared to be highest in the abemaciclib cohort, while palbociclib and ribociclib cohorts tended to have similar total healthcare costs.

As the present study was one of few early US studies demonstrating real-world evidence of treatment patterns, HRU, and costs among women with mBC treated with CDK4/6 inhibitors, more real-world, comparative studies are warranted to determine long-term treatment patterns and outcomes in these women.

Date of Clinical Study Report:
15 March 2021