Sponsor

Novartis

Generic Drug Name

Ribociclib

Trial Indications

Hormone Receptor–positive/Human Epidermal Growth Factor Receptor 2–negative advanced or metastatic breast cancer

Protocol Number

CLEE011A3002

Protocol Title

Real-world effectiveness and safety in HR+/HER2- advanced or metastatic BC patients treated with ribociclib or alpelisib: a European non-interventional retrospective study (REASSURE)

Clinical Trial Phase

Not applicable

Phase of Drug Development

Not applicable

Study Start/End Dates

Study Start Date: 11 June 2021 (Final Protocol)

Study Completion Date: 30 November 2023 (Full Stats Analysis Final)

Reason for Termination

Not applicable

Study Design/Methodology

The study was a multinational and multicenter cohort study of patients with hormone receptor–positive/human epidermal growth factor receptor 2–negative (HR+/HER2-) advanced or metastatic breast cancer (aBC/mBC) treated with ribociclib or alpelisib between the period of 01 January 2018 and 30 September 2021. Patients who were receiving active treatment for malignancies other than BC or participating in a clinical trial were excluded. This study was conducted retrospectively with secondary use of data.

Centers

Not applicable. Patient data were collected in a retrospective fashion from 2 different sources:

a) IQVIA's oncology evidence network (OEN; L'Institut Curie [Curie], Instituto Português de Oncologia do Porto [IPO-Porto], and Institut de Cancérologie de l'Ouest [ICO]).
b) Local sites / clinics proposed by Novartis affiliates in the Czech Republic.

Objectives:

Primary objective

To estimate real-world progression-free survival (rwPFS) in patients with locally advanced/metastatic not amenable to surgery HR+/HER2- BC (progressed following prior therapy or de novo) for whom the treating physician took the decision to initiate treatment with ribociclib before entering the study.

Selected secondary objectives

- Characterize HR+/HER2- advanced/metastatic BC patients treated with ribociclib with respect to demographics and clinical characteristics at index date (baseline).

Test Products, Doses, and Modes of Administration

Patients had received ribociclib or alpelisib per their dosing regimens prior to this observational study.

Statistical Methods

Continuous variables were described by the number of observations, mean, standard deviation, median, first and third quartiles (interquartile range [IQR]: Q1, Q3), the minimum and maximum value, in addition to two-sided 95% confidence intervals (CIs) of the mean. Categorical variables were described using counts and percentages of patients within each category. All analyses were conducted on overall data source cohorts and the subpopulations of interest, provided that the sample sizes were adequate. A Kaplan-Meier (K-M) curve was generated to describe rwPFS and for other time-to-event analyses.

Note: in the time-to-event analysis, 'NA' and 'not reached' refer to the estimates that were not available or not reached as there were too few events (due to small sample sizes) and the follow-up period was too short for the curve to interact with 0.5.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion criteria:

- Aged 18 years or older at ribociclib or alpelisib treatment initiation.
- Male and female gender.
- Confirmed diagnosis of locally advanced/metastatic not amenable to surgery HR+/HER2- BC (progressed following prior therapy or de novo) for whom the treating physician took the decision to initiate treatment with ribociclib or alpelisib.
- Patients with at least one prescription for ribociclib or alpelisib during the index period (1 January 2018 to 30 September 2021).

Exclusion criteria:

- Patients participating in any interventional clinical trial that included investigational or marketed products at the time of index (ribociclib, alpelisib, and other); patients participating in other investigator-initiated research or non-interventional study (NIS) could be included as long as their standard of care was not altered by the study.
- Patients on active treatment for malignancies other than HR+/HER2- aBC/mBC at the time of index.

- IPO-Porto only:
    - Patients who had participated or were participating in any interventional clinical trial that included investigational or marketed products at the time of index (ribociclib, alpelisib, and others).
    - Patients who underwent part of the treatment for locally advanced/metastatic not amenable to surgery HR+/HER2- BC outside the center.

Participant Flow Table

Source	Number of Patients Enrolled
ICO	123
Curie	72
IPO-Porto	81
Czech Republic	159

Baseline Characteristics

Refer to Secondary Outcome Results

Primary Outcome Results

The data was not pooled across sites, due to the need for patient level data to remain at each site. As a result, the analysis is presented for each site separately.

ICO: Real-world progression-free survival from index in the overall ribociclib cohort

	Overall
Number of Patients	106
Number of events*	50
Number of Censored Patients	56
Median (95% CI) months	29.7 (20.7-NA)
25% survival (95% CI)	13.3 (8.2-18.5)
75% survival (95% CI)	NA (33.1-NA)

Abbreviations: CI: confidence interval; NA: not available.
*Events: first documented disease progression or death.

Curie: Real-world progression-free survival from index in the overall ribociclib cohort

	Overall
Number of Patients	38
Number of Events*	16
Number of Censored Patients	22
Median (95% CI) months	31.0 (28.0-NA)
Q1-Q3	26.0-NA

Abbreviations: CI: confidence interval; Q1-Q3: first and third quartiles; NA: not available.
*Events: first documented disease progression or death.

IPO-Porto: Real-world progression-free survival from index in the overall ribociclib cohort

	Overall
Number of Patients	81
Number of Events*	33
Number of Censored Patients	48
Median (95% CI) months	31.2 (18.6-NA)
Q1-Q3	10.3- NA

Abbreviations: CI: confidence interval; Q1-Q3: first and third quartiles; NA: not available.
*Events: first documented disease progression or death.

Czech Republic: Real-world progression-free survival from index in the overall ribociclib cohort

	Overall
Number of Patients	159
Number of Events*	73
Number of Censored Patients	86
Median (95% CI) months	19.1 (16.9-26.7)
Q1-Q3	8.0-37.3

Abbreviations: CI: confidence interval; Q1-Q3: first and third quartiles.
*Events: first documented disease progression or death.

Selected secondary Outcome Results

The data was not pooled across sites, due to the need for patient level data to remain at each site. As a result, the analysis is presented for each site separately.

1. Institut de Cancérologie de l'Ouest (ICO)

ICO: Patient demographics and clinical characteristics at ribociclib index in the overall cohort

Characteristic	Overall	
	N=106	%
Age at initiation of ribociclib (index date) (years)		
N	106	
Mean (Std Dev)	56.3 (13.0)	
95_CInorm	53.8 - 58.8	
Median (Q1 - Q3)	56.6 (45.6 - 67.4)	
Min - Max	27.7 - 82.1	
Missing	0	
Age at initiation of ribociclib (years)		
<65	74	69.8%
≥65	32	30.2%
Missing	0	
Sex		
Male	0	0.0%
Female	106	100.0%
Missing	0	
Year at index date		
2019	16	15.1%
2020	71	67.0%

Characteristic	Overall	
	N=106	%
2021	19	17.9%
Missing	0	
History of BC		
No	96	90.6%
Yes	10	9.4%
Missing	0	
Diabetes		
No	103	97.2%
Yes	3	2.8%
Missing	0	
Cardiovascular disease		
No	80	75.5%
Yes	26	24.5%
Missing	0	
Body Mass Index at index date (BMI) (kg/m²)		
N	84	
Mean (Std Dev)	25.1 (5.3)	
95 CInorm	23.9 - 26.2	
Median (Q1 - Q3)	23.8 (21.7 - 27.2)	
Min - Max	14.5 - 42.9	
Missing	22	
Body Mass Index (BMI) at index date (kg/m²)		
Underweight <18.5	<6	
Healthy/normal weight 18.5 - <25	49	58.3%
Pre-obesity 25 - <30	20	23.8%
Obesity	<20	

Characteristic	Overall	
	N=106	%
≥30		
Missing	22	
Menopausal status		
Pre-menopausal	41	39.0%
Post-menopausal	64	61.0%
Missing	1	
Primary tumor type		
Invasive ductal	89	84.0%
Lobular carcinoma	<106	
Other	<6	
Missing	0	
Disease site		
Non- visceral	76	73.1%
Visceral	<6	
Multiple	<106	
Missing	<6	
Primary metastatic disease		
No	65	61.3%
Yes	41	38.7%
Missing	0	
Metastatic sites at index date		
0	<6	
1	47	44.3%
2	26	24.5%
3	19	17.9%
≥4	<106	
Missing	0	
Local/breast metastases at index date		

Characteristic	Overall	
	N=106	%
No	<106	
Yes	<6	
Missing	0	
Bone metastases at index date		
No	25	23.6%
Yes	81	76.4%
Missing	0	
Lung metastases at index date		
No	85	80.2%
Yes	21	19.8%
Missing	0	
Liver metastases at index date		
No	80	75.5%
Yes	26	24.5%
Missing	0	
Central nervous system metastases at index date		
No	<106	
Yes	<6	
Missing	0	
Lymph node metastases at index date		
No	61	57.5%
Yes	45	42.5%
Missing	0	
Other metastases at index date		
No	83	78.3%
Yes	23	21.7%
Missing	0	
Time from diagnosis to metastasis		

Characteristic	Overall	
	N=106	%
≤24 months	9	8.5%
>24 months	56	52.8%
mBC at diagnosis	41	38.7%
Missing	0	
Asymptomatic disease		
No	<106	
Non-applicable (locally advanced)	<6	
Yes	53	50.0%
Missing	0	
Grading		
G1	<6	
G2	77	75.5%
G3	20	19.6%
Missing	<6	
Stage		
0	<6	
I	18	17.1%
IIA	24	22.9%
IIB	9	8.6%
IIIA	9	8.6%
IIIB	<6	
IIIC	<6	
IV	40	38.1%
Missing	<6	
Baseline Eastern Cooperative Oncology Group (ECOG)		
0	37	44.6%
1	41	49.4%
2	<6	
3	<6	

Characteristic	Overall	
	N=106	%
4	0	0.0%
Missing	23	
Prior chemotherapy		
No	83	78.3%
Yes	23	21.7%
Missing	0	
Prior surgery		
No	76	71.7%
Yes	30	28.3%
Missing	0	
Prior radiotherapy (RT)		
No	79	74.5%
Yes	27	25.5%
Missing	0	
Prior adjuvant endocrine therapy (ET)		
No	71	67.6%
Yes	34	32.4%
Missing	1	
Prior lines of ET		
0	88	83.0%
1	17	16.0%
2	<6	
≥3	<6	
Missing	0	
Primary endocrine resistance		
No	89	84.0%
Yes	17	16.0%
Missing	0	

Characteristic	Overall	
	N=106	%
Sensitivity to prior hormonal therapy		
No	10	9.4%
Yes	96	90.6%
Missing	0	
Prior everolimus treatment		
No	<106	
Yes	<6	
Missing	0	
CDK4/6i across lines		
Adjuvant	0	0.0%
1st metastatic line	91	85.8%
2nd metastatic line	<106	
≥3rd metastatic line	<6	
Missing	0	
Previous lines of therapies		
0	89	84.0%
1	<106	
2	<6	
≥3	0	0.0%
Missing	0	
Baseline neutrophil-to-lymphocyte ratio (NLr)		
N	104	
Mean (Std Dev)	3.1 (2.2)	
95_CInorm	2.7 - 3.5	
Median (Q1 - Q3)	2.5 (1.7 - 3.6)	
Min - Max	0.8 - 14.5	
Missing	2	
Baseline platelet-to-lymphocyte ratio (PLr)		

Characteristic	Overall	
	N=106	**%**
N	103	
Mean (Std Dev)	236.5 (146.2)	
95 CInorm	207.9 - 265	
Median (Q1 - Q3)	190.8 (143.2 - 280.3)	
Min - Max	48.6 - 892.6	
Missing	3	
Baseline lymphocytes-to-monocytes ratio (LMr)		
N	104	
Mean (Std Dev)	4.2 (2.8)	
95 CInorm	3.6 - 4.7	
Median (Q1 - Q3)	3.4 (2.3 - 5.0)	
Min - Max	0.8 - 14.6	
Missing	2	

Abbreviations: 1L: first line of therapy; LoT: line of therapy; Std Dev: standard deviation; 95_CInorm: 95% confidence interval from normal distribution; Q1 – Q3: first and third quartile; kg/m²: kilograms per meter squared; CDK4/6i: cyclin-dependent kinase 4/6 inhibitor.

2. L'Institut Curie (Curie)

Curie: Patient demographics and clinical characteristics at ribociclib index date in the overall cohort

Characteristic	Overall	
	N=38	%
Age at index date (years)		
N	38	
Mean (Std Dev)	51.6 (13.2)	
Mean 95 CInorm	51.6 (47.2 - 55.9)	
Median (Q1-Q3)	50.0 (42.0 - 60.8)	
Min-Max	27.0 - 76.0	
Missing/Unknown	0	
Age at initiation of ribociclib (years)		
<65	30	79.0%
≥65	8	21.0%
Missing/Unknown	0	
Sex		
Male	1	3.0%
Female	37	97.0%
Missing/Unknown	0	
Year of index		
2019	13	34.0%
2020	15	39.0%
2021	10	26.0%
Missing/Unknown	0	

Characteristic	Overall	
	N=38	%
History of BC		
No	26	68.0%
Yes	12	32.0%
Missing/Unknown	0	
New_Diabetes mellitus		
No	38	100.0%
Yes	0	0.0%
Missing/Unknown	0	
New_heart_failure		
No	38	100.0%
Missing/Unknown	0	
New_Hypertension		
No	31	82.0%
Yes	7	18.0%
Missing/Unknown	0	
New_Myocardial infarction		
No	38	100.0%
Missing/Unknown	0	
New_other_cardio		
No	36	95.0%
Yes	2	5.0%

Characteristic	Overall	
	N=38	%
Missing/Unknown	0	
Body Mass Index (BMI) (kg/m²)		
N	32	
Mean (Std Dev)	26.2 (4.9)	
Mean_95_CInorm	26.2 (24.4 - 28.0)	
Median (Q1-Q3)	25.0 (23.8 - 28.1)	
Min-Max	18.0 - 39.2	
Missing/Unknown	6	
Body Mass Index (BMI) Categories (kg/m²)		
Underweight <18.5	1	3.0%
Healthy/normal weight 18.5 - <25	15	47.0%
Pre-obesity 25 - <30	9	28.0%
Obesity ≥30	7	22.0%
Missing/Unknown	6	
Menopausal status		
No (pre-menopausal)	18	53.0%
Yes (post- menopausal)	16	47.0%
Missing/Unknown	4	
Primary tumor type		
Invasive ductal	26	72.0%
Lobular carcinoma	6	17.0%
Other	4	11.0%
Missing/Unknown	2	

Characteristic	Overall	
	N=38	%
Disease site		
Multiple	15	39.0%
No-Visceral	22	58.0%
Visceral	1	3.0%
Missing/Unknown	0	
Primary metastatic disease		
No	32	84.0%
Yes	6	16.0%
Missing/Unknown	0	
Metastatic sites at index date		
1	16	42.0%
2	5	13.0%
3	10	26.0%
4+	7	18.0%
Missing/Unknown	0	
Bone metastases at index date		
No	2	5.0%
Yes	36	95.0%
Missing/Unknown	0	
Lung metastases at index date		
No	30	79.0%
Yes	8	21.0%

Characteristic	Overall	
	N=38	%
Missing/Unknown	0	
Liver metastases at index date		
No	27	71.0%
Yes	11	29.0%
Missing/Unknown	0	
Central nervous system metastases at index date		
No	37	97.0%
Yes	1	3.0%
Missing/Unknown	0	
Lymph node metastases at index date		
No	23	61.0%
Yes	15	39.0%
Missing/Unknown	0	
Other metastases at index date		
No	31	82.0%
Yes	7	18.0%
Missing/Unknown	0	
Time from diagnosis to metastasis (months)		
> 24	32	84.0%
mBC at diagnosis	6	16.0%
Missing/Unknown	0	
Asymptomatic disease		

Characteristic	Overall	
	N=38	%
No	18	47.0%
Yes	20	53.0%
Missing/Unknown	0	
Disease recurrence (months)		
≤12	6	16.0%
>12	32	84.0%
Missing/Unknown	0	
Grade Histopronostic (SBR/EE)		
Grade 1	0	0.0%
Grade 2	10	48.0%
Grade 3	11	52.0%
Missing/Unknown	17	
Stage		
Stage 0	1	3.0%
Stage I	9	25.0%
Stage IIA	12	33.0%
Stage IIB	6	17.0%
Stage IIIA	2	6.0%
Stage IV	6	17.0%
Missing/Unknown	2	
Baseline Eastern Cooperative Oncology Group (ECOG)		
0	26	74.0%
1	6	17.0%

Characteristic	Overall	
	N=38	%
2	3	9.0%
Missing/Unknown	3	
Prior chemotherapy		
No	33	87.0%
Yes	5	13.0%
Missing/Unknown	0	
Prior surgery		
No	38	100.0%
Missing/Unknown	0	
Prior radiotherapy (RT)		
No	35	92.0%
Yes	3	8.0%
Missing/Unknown	0	
Prior adjuvant endocrine therapy (ET)		
No	36	95.0%
Yes	2	5.0%
Missing/Unknown	0	
Prior lines of ET		
0	36	95.0%
1	2	5.0%
2	0	0.0%
3	0	0.0%

Characteristic	Overall	
	N=38	%
4	0	0.0%
Missing/Unknown	0	
Primary endocrine resistance		
No	17	81.0%
Yes	4	19.0%
Missing/Unknown	17	
Sensitivity to prior hormonal therapy		
No	7	33.0%
Yes	14	67.0%
Missing/Unknown	17	
Prior everolimus treatment		
No	38	100.0%
Missing/Unknown	0	
CDK4/6i across lines		
1	24	69.0%
2	8	23.0%
≥3	3	9.0%
Missing/Unknown	3	
Previous lines of therapies		
0	27	75.0%
1	6	17.0%
2	3	8.0%

Characteristic	Overall	
	N=38	%
3+	0	0.0%
Missing/Unknown	2	

Abbreviations: 1L: first line of therapy; Std Dev: standard deviation; 95_CInorm: 95% confidence interval from normal distribution; Q1 – Q3: first and third quartile; kg/m²: kilograms per meter squared; SBR/EE: Elston-Ellis modification of Scarff-Bloom-Richardson; CDK4/6i: cyclin-dependent kinase 4/6 inhibitor.

3. Instituto Português de Oncologia do Porto (IPO-Porto)

IPO-Porto: Patient demographics and clinical characteristics for the overall ribociclib cohort

Characteristic		Overall	
Cohort Size		**N=81**	**100.0%**
Demographic characteristics			
Age at initiation of ribociclib (index date) (years)	N	81	100.0%
	Mean (Std Dev)	59.7 (10.9)	
	Median (Q1-Q3)	59.0 (51.0 - 68.0)	
	Min-Max	32.0 - 83.0	
	Missing/Unknown	0	0.0%

Characteristic		**Overall**	
Cohort Size		**N=81**	**100.0%**
Age at initiation of ribociclib Categories (years)	<65	52	64.2%
	≥65	29	35.8%
Sex	Female	<81	
	Male	<6	
Year of index	2018	14	17.3%
	2019	23	28.4%
	2020	17	21.0%
	2021	27	33.3%
History of breast cancer	No	<81	
	Yes	<6	
Cerebrovascular disease	No	81	100.0%
Chronic obstructive pulmonary disease (COPD)	No	<81	
	Yes	<6	
Dementia	No	<81	
	Yes	<6	
Depression	No	<81	
	Yes	<6	
Diabetes mellitus	No	75	92.6%
	Yes	6	7.4%

Characteristic		Overall	
Cohort Size		**N=81**	**100.0%**
Heart Failure	No	81	100.0%
Hypertension	No	48	59.3%
	Yes	33	40.7%
Hypothyroidism	No	81	100.0%
Ischemic heart disease	No	<81	
	Yes	<6	
Liver disease	No	81	100.0%
Myocardial infarction	No	81	100.0%
Osteoporosis	No	<81	
	Yes	<6	
Peripheral vascular disease	No	69	85.2%
	Yes	12	14.8%
Renal Disease	No	<81	
	Yes	<6	
Rheumatological disease	No	71	87.7%
	Yes	10	12.4%
Ulcer disease	No	<81	
	Yes	<6	
Other	No	71	87.7%
	Yes	10	12.4%
Charlson Comorbidity Index	0	49	60.5%
	1	23	28.4%

Characteristic		Overall	
Cohort Size		**N=81**	**100.0%**
	2	9	11.1%
Body Mass Index (BMI) (kg/m²)	N	<81	
	Mean (Std Dev)	28.1 (5.7)	
	Median (Q1-Q3)	28.1 (23.0 - 32.0)	
	Min-Max	14.0 - 44.8	
	Missing/Unknown	<6	
Body Mass Index (BMI) Categories (kg/m²)	<18.5 Underweight	<6	
	≥30 Obesity	25	30.9%
	18.5-24.9 Normal weight	23	28.4%
	25.0-29.9 Pre-obesity	27	33.3%
	Missing/Unknown	<6	
Smoker	Missing/Unknown	<12	
	Current Smoker	<6	
	Former Smoker	8	9.9%
	Never	61	75.3%
Menopausal Status	Missing/Unknown	<6	
	No (pre-menopausal)	<20	
	Yes (post-menopausal)	61	75.3%

Characteristic		Overall	
Cohort Size		**N=81**	**100.0%**
Primary Tumor Type	Missing/Unknown	<13	
	Invasive ductal	68	84.0%
	Lobular carcinoma	<13	
Disease Site	Multiple	47	58.0%
	Non-visceral	17	21.0%
	Visceral	17	21.0%
Primary metastatic disease	No	50	61.7%
	Yes	31	38.3%
Metastatic sites at index date	1	31	38.3%
	2	24	29.6%
	3	13	16.1%
	≥4	13	16.1%
Local/breast metastases at index date	No	46	56.8%
	Yes	35	43.2%
Bone metastases at index date	No	18	22.2%
	Yes	63	77.8%
Lung metastases at index date	No	59	72.8%
	Yes	22	27.2%
Liver metastases at index date	No	62	76.5%
	Yes	19	23.5%

Characteristic		Overall	
Cohort Size		**N=81**	**100.0%**
Central nervous system metastases at index date	No	81	100.0%
Lymph node metastases at index date	No	66	81.5%
	Yes	15	18.5%
Other metastases at index date	No	61	75.3%
	Yes	20	24.7%
Time from diagnosis to metastasis	≤24 months	12	14.8%
	>24 months	38	46.9%
	mBC at diagnosis	31	38.3%
Asymptomatic disease	No	29	35.8%
	Yes	52	64.2%
Disease recurrence	≤12 months	39	48.2%
	>12 months	42	51.9%
Grading	G1	<6	
	G2	47	58.0%
	G3	30	37.0%
	Missing/Unknown	<6	
Stage	I	13	16.1%
	IIA	15	18.5%

Characteristic		**Overall**	
Cohort Size		**N=81**	**100.0%**
	IIB	<6	
	IIIA	11	13.6%
	IIIB	<6	
	IIIC	<6	
	IV	31	38.3%
	Missing/Unknown	<6	
Baseline Eastern Cooperative Oncology Group (ECOG)	0	31	38.3%
	1	41	50.6%
	2	<9	
	3	<6	
Prior chemotherapy (CT)	No	<81	
	Yes ([neo] adjuvant; for metastatic disease)	<11	
Prior surgery	No	69	85.2%
	Yes	12	14.8%
Prior radiotherapy (RT)	No	73	90.1%
	Yes	8	9.9%
Prior adjuvant endocrine therapy (ET)	No	66	81.5%
	Yes ([neo] adjuvant; for metastatic disease)	15	18.5%
Prior lines of ET	0	<81	

Characteristic		Overall	
Cohort Size		**N=81**	**100.0%**
	1	<6	
Primary Endocrine Resistance	No	69	85.2%
	Yes	12	14.8%
Sensitivity to prior hormonal therapy	No	12	14.8%
	Yes	69	85.2%
Prior everolimus treatment	No	81	100.0%
CDK4/6i across lines	1st	<81	
	2nd	<9	
	≥3 lines	<6	
Previous lines of therapies	0	<81	
	1	<9	
	2	0	0.0%
	3	<6	
Baseline neutrophil-to-lymphocyte ratio (NLr)	N	81	100.0%
	Mean (Std Dev)	3.3 (4.0)	
	Median (Q1-Q3)	2.1 (1.5 - 3.7)	
	Min-Max	0.9 - 32.9	
	Missing/Unknown	0	0.0%
Baseline platelet-to-lymphocyte ratio (PLr)	N	81	100.0%
	Mean (Std Dev)	160.7 (75.6)	
	Median (Q1-Q3)	132.3 (108.7 - 217.3)	
	Min-Max	1.2 - 371.6	
	Missing/Unknown	0	0.0%

Characteristic		Overall	
Cohort Size		**N=81**	**100.0%**
Baseline lymphocytes-to-monocytes ratio (LMr)	N	81	100.0%
	Mean (Std Dev)	3.7 (1.6)	
	Median (Q1-Q3)	3.6 (2.2 - 4.9)	
	Min-Max	0.3 - 7.5	
	Missing/Unknown	0	0.0%

Abbreviations: 1L: first line of therapy; Std Dev: standard deviation; Q1 – Q3: first and third quartile.

4. Local sites/clinics proposed by Novartis affiliates in the Czech Republic.

Czech Republic: Patient demographics and clinical characteristics for the overall ribociclib cohort

		Overall	
	Cohort size	**N=159**	**100.0%**
Demographic characteristics			
Age at initiation (index date) (years)	Total	159	100.0%
	Mean (Std Dev)	61.0 (12.1)	
	Mean_95_CInorm	61.0 (59.1-62.9)	
	Median (Q1-Q3)	63.0 (53.0-71.0)	
	Min-Max	33.0 - 79.0	
	N	159	100.0%

		Overall	
	Cohort size	**N=159**	**100.0%**
	Missing	0	0.0%
Age at initiation Categories (years)	<65 years	86	54.1%
	≥65 years	73	45.9%
	Missing	0	0.0%
Year of index	2018	0	0.0%
	2019	31	19.5%
	2020	39	24.5%
	2021	89	56.0%
	Missing	0	0.0%
History of breast cancer	Yes	93	58.5%
	No	<67	
	Patient records not available	<6	
Cerebrovascular disease	Yes	<6	
	No	<159	
	Patient records not available	<6	
Chronic obstructive pulmonary disease (COPD)	Yes	<6	
	No	<160	
	Patient records not available	0	0.0%
Dementia	Yes	0	0.0%
	No	159	100.0%
	Patient records not available	0	0..0%
Depression	Yes	<17	
	No	144	90.6%

		Overall	
	Cohort size	**N=159**	**100.0%**
	Patient records not available	<6	
Diabetes mellitus	Yes	19	12.0%
	No	140	88.1%
	Patient records not available	0	0.0%
Heart Failure	Yes	<6	
	No	<159	
	Patient records not available	<6	
Hypertension	Yes	68	42.8%
	No	91	57.2%
	Patient records not available	0	0%
Hypothyroidism	Yes	23	14.5%
	No	136	85.5%
	Patient records not available	0	0.0%
Ischemic heart disease	Yes	<6	
	No	<157	
	Patient records not available	0	0.0%
Liver disease	Yes	19	12.0%
	No	140	88.1%
	Patient records not available	0	0.0%
Myocardial infraction	Yes	0	0.0%
	No	159	100.0%

		Overall	
	Cohort size	**N=159**	**100.0%**
	Patient records not available	0	0.0%
Osteoporosis	Yes	<11	
	No	150	94.3%
	Patient records not available	<6	
Peripheral vascular disease	Yes	<6	
	No	<157	
	Patient records not available	0	0.0%
Renal disease	Yes	<6	
	No	<161	
	Patient records not available	0	0.0%
Rheumatological disease	Yes	<6	
	No	<158	
	Patient records not available	0	0.0%
Ulcer disease	Yes	<6	
	No	<161	
	Patient records not available	0	0.0%
Other	Yes	<29	
	No	132	83.0%
	Patient records not available	<6	
Charlson Comorbidity Index (CCI)	>2	64	40.3%
	0	14	8.8%

		Overall	
	Cohort size	**N=159**	**100.0%**
	1	16	10.1%
	2	17	10.7%
	No available patient records	48	30.2%
Body Mass Index (BMI) (kg/m^2)	Total	159	100.0%
	Mean (Std Dev)	27.6 (5.5)	
	Mean_95_CInorm	27.6 (26.8-28.5)	
	Median (Q1- Q3)	27.0 (23.9-30.9)	
	Min-Max	16.2 - 47.6	
	N	159	100.0%
	Missing	0	0.0%
Body Mass Index (BMI) Categories (kg/m^2)	<18.5 Underweight	<6	
	≥30 Obesity	51	32.1%
	18.5-24.9 Normal weight	51	32.1%
	25.0-29.9 Pre-obesity	53	33.3%
	Missing	<6	
Smoker	Never	91	57.2%
	Former smoker	26	16.4%
	Current smoker	18	11.3%
	Missing/Unknown	24	15.1%
Menopausal status	Yes (post-menopausal)	128	80.5%
	No (pre-menopausal or peri-menopausal)	<33	
	Missing/Unknown	<6	

		Overall	
	Cohort size	**N=159**	**100.0%**
Primary tumor type	Invasive ductal	113	71.1%
	Lobular carcinoma	30	18.9%
	Other	7	4.4%
	Missing/Unknown	9	5.7%
Disease site	Non-visceral	80	50.3%
	Visceral	38	23.9%
	Multiple	41	25.8%
	Missing	0	0.0%
Primary metastatic disease	Yes	<64	
	No	97	61.0%
	Missing/Unknown	<6	
Metastatic sites at index date	≥4	52	32.7%
	1	38	23.9%
	2	38	23.9%
	3	20	12.6%
	Missing/Unknown	11	6.9%
Local/breast metastases at index	Yes	31	19.5%
	No	128	80.5%
	Missing/Unknown	0	0.0%
Bone metastases at index date	Yes	110	69.2%
	No	49	30.8%
	Missing/Unknown	0	0.0%
Lung metastases at index date	Yes	<40	
	No	121	76.1%
	Missing/Unknown	<6	
Liver metastases at index date	Yes	<44	
	No	117	73.6%
	Missing/Unknown		

		Overall	
	Cohort size	**N=159**	**100.0%**
		<6	
Central nervous system metastases at index date	Yes	<6	
	No	<158	
	Missing/Unknown	0	0.0%
Lymph node metastases at index date	Yes	80	50.3%
	No	<79	
	Missing/Unknown	<6	
Other specified locations at index date	Yes	<31	
	No	127	79.9%
	Missing/Unknown	<6	
Time from diagnosis to metastasis	≤24 months	15	9.4%
	>24 months	83	52.%
	mBC at diagnosis	61	38.4%
Asymptomatic disease at index	Missing/Unknown	<6	
	No	58	36.5%
	Not applicable – locally advanced	<18	
	Yes	83	52.2%
Disease recurrence	≤12 months	50	31.5%
	>12 months	87	54.7%
	Missing/Unknown	22	13.8%
Grading of primary tumor	G1	22	13.8%
	G2	85	53.5%
	G3	34	21.4%
	Missing/Unknown	18	11.3%
Stage	0	<6	

		Overall	
	Cohort size	**N=159**	**100.0%**
	I	15	9.4%
	IIA	30	18.9%
	IIB	20	12.6%
	IIIA	15	9.4%
	IIIB	<6	
	IIIC	8	5.0%
	IV	58	36.5%
	Missing/Unknown	<6	
Baseline Eastern Cooperative Oncology Group (ECOG)	0	74	46.5%
	1	80	50.3%
	2	<6	
	3	0	0.0%
	4	0	0.0%
	Missing/Unknown	<6	
Prior chemotherapy (CT)	Yes	22	13.8%
	No	46	28.9%
	Missing/Unknown	91	57.2%
Prior radiotherapy (RT)	Yes	31	19.5%
	No	128	80.5%
	Missing/Unknown	0	0.0%
Prior surgery	Yes	28	17.6%
	No	131	82.4%
	Missing/Unknown	0	0.0%
Prior adjuvant endocrine therapy (ET)	Yes	81	50.9%
	No	<80	
	Missing/Unknown	<6	
Prior Lines of ET	0	23	14.5%

		Overall	
	Cohort size	**N=159**	**100.0%**
	1	47	29.6%
	2	<13	
	3+	<6	
	Missing	78	49.1%
Primary endocrine resistance	Yes	9	5.7%
	No	140	88.1%
	Missing/Unknown	10	6.3%
Sensitivity to prior hormonal therapy	Yes	92	57.9%
	No	33	20.8%
	Missing/Unknown	34	21.4%
Prior everolimus therapy	Yes	<6	
	No	<71	
	Missing	90	56.6%
CDK4/6i across lines	≥3 lines	<12	
	1st	128	80.5%
	2nd	19	12.0%
	Missing/Unknown	<6	
Previous lines of therapies (generated)	0	101	63.5%
	1	42	26.4%
	2	13	8.2%
	3	<6	
	4	<6	
	5	<6	
Baseline neutrophil-to-lymphocyte ratio (NLr)	Total	159	100.0%
	Mean (Std Dev)	2.8 (3.0)	
	Mean_95_CInorm	2.8 (2.4-3.3)	
	Median (Q1- Q3)	2.1 (1.5-3.2)	

		Overall	
	Cohort size	**N=159**	**100.0%**
	Min-Max	0.6 - 30.0	
	N	159	100.0%
	Missing	0	0.0%
Baseline platelet- to-lymphocyte ratio (PLr)	Total	159	100.0%
	Mean (Std Dev)	216.6 (357.0)	
	Mean_95_CInorm	216.6 (161.2-272.1)	
	Median (Q1- Q3)	151.1 (119.7-220.0)	
	Min-Max	42.9 - 4340.0	
	N	159	100.0%
	Missing	0	0.0%
Baseline lymphocytes-to-monocytes ratio (LMr)	Total	159	100.0%
	Mean (Std Dev)	5.1 (7.6)	
	Mean_95_CInorm	5.1 (4.0-6.3)	
	Median (Q1- Q3)	3.6 (2.6-5.2)	
	Min-Max	0.0 - 80.0	
	N	159	100.0%
	Missing	0	0.0%

Abbreviations: 1L: first line of therapy; Std Dev: standard deviation; 95_CInorm: 95% confidence interval from normal distribution; Q1 – Q3: first and third quartile; kg/m²: kilograms per meter squared; CDK4/6i: cyclin-dependent kinase 4/6 inhibitor.

Safety Results

Not applicable

Adverse Events by System Organ Class

Not applicable

Most Frequently Reported AEs Overall by Preferred Term n (%)

Not applicable

Serious Adverse Events and Deaths

Not applicable

Other Relevant Findings

Not applicable

Conclusion

This real-world study provides recent evidence on treatment with ribociclib among patients with advanced breast cancer/metastatic breast cancer (aBC/mBC). Overall, median real-world progression-free Survival (rwPFS) estimates were in line with estimates from MONALEESA trials and previous real-world evidence (RWE) studies, confirming applicability of trial results to real-world settings. Moreover, there was heterogeneity between data captured across countries, as well as differences in usual treatment practices at site and individual clinician levels as this study reflects real-life clinical care. In future, a follow-up study with a larger sample size (potentially via a harmonized analysis using a common data model to pool data across multiple sources), would confer sufficient statistical power to establish more precise insights into outcomes and contributing factors of patients with aBC/mBC.

Date of Clinical Study Report

19 April 2024