

Real-World Patient-Reported Outcomes After Initiation of Adjuvant Ribociclib Plus Endocrine Therapy in Early HR+/HER2– Breast Cancer: A Multicentre Prospective Observational Study in Croatia (PRO-QoL-Cro)

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Study

Planned

Administrative details

EU PAS number

EUPAS1000001116

Study ID

1000001116

DARWIN EU® study

No

Study countries

Study description

PRO-QoL-Cro is a multicentre, prospective, non-interventional, single-arm cohort study with primary data collection at three centres in Croatia: University Hospital Centre Split, University Hospital Centre Osijek and Clinical Hospital Dubrava.

The population is adults with HR+/HER2-negative breast cancer, AJCC 8th edition anatomic stage II to III, who initiate adjuvant ribociclib plus endocrine therapy in routine clinical practice, with adjuvant endocrine therapy started within 12 months before baseline. Treatment is prescribed solely according to clinical judgement and the Summary of Product Characteristics. The study does not influence treatment decisions or require study-specific investigations.

The overall aim is to generate real-world evidence on patient-reported outcomes, covering health-related quality of life, breast cancer-specific symptoms and functioning, work productivity and informal care needs, during the first six months after initiation of adjuvant ribociclib plus endocrine therapy.

The primary objective is to estimate the within-patient change in the EQ-5D-5L utility index from baseline (Month 0) to Month 6. As no Croatian value set exists, scoring uses the Hungarian value set in the primary analysis and the Italian value set in sensitivity analyses.

Secondary objectives are to describe changes in EORTC QLQ-BR23 functioning and symptom domains, in work productivity and activity impairment measured with the WPAI:GH, and in informal care needs operationalised as informal care hours per week, and to explore associations of PRO trajectories with treatment-related side effects, sociodemographic characteristics and prior endocrine

therapy duration (up to 3 vs 4 to 12 months).

Assessments occur at Months 0, 1, 3 and 6. Clinical characteristics, adverse events and treatment modifications are recorded from routine medical records to support interpretation. Of 76 participants to be enrolled, 64 are expected to be evaluable for the primary endpoint.

Study status

Planned

Research institutions and networks

Institutions

University Hospital Centre Split

University Hospital Centre Osijek; Clinical Hospital
Dubrava

Contact details

Study institution contact

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Primary lead investigator

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Study timelines

Date when funding contract was signed

Planned: 22/09/2026

Study start date

Planned: 28/09/2026

Data analysis start date

Planned: 30/11/2027

Date of final study report

Planned: 31/03/2028

Sources of funding

- Other

More details on funding

Pharmaceutical company and other private sector - Novartis Hrvatska d.o.o.

Study protocol

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Other

Study topic, other:

Medical condition to be studied

Study type:

Non-interventional study

Scope of the study:

Evaluation of patient-reported outcomes

Data collection methods:

Combined primary data collection and secondary use of data

Study design:

Multicentre, prospective, single-arm, non-interventional cohort study with primary data collection. Patient-reported outcomes are assessed at Months 0, 1, 3 and 6 after initiation of adjuvant ribociclib plus endocrine therapy.

Main study objective:

The primary objective is to estimate the within-patient change in health-related quality of life, as measured by the EQ-5D-5L utility index, from baseline (Month 0) to Month 6 after initiation of adjuvant ribociclib plus endocrine therapy in routine clinical practice.

Secondary objectives are: (1) to describe changes in EORTC QLQ-BR23 functioning and symptom domains over 6 months; (2) to evaluate changes in work productivity and activity impairment as measured by the WPAI:GH over 6 months; (3) to evaluate changes in informal care needs, operationalised as informal care hours per week, over 6 months; (4) to explore associations between treatment-related side effects and changes in patient-reported outcomes over time; (5) to explore associations between sociodemographic characteristics and patient-reported outcome trajectories over time; and (6) to explore whether the duration of prior endocrine therapy (up to 3 versus 4 to 12 months) is associated with patient-reported outcome trajectories during the 6 months.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

KISQALI

Study drug International non-proprietary name (INN) or common name

RIBOCICLIB

Anatomical Therapeutic Chemical (ATC) code

(L01EF02) ribociclib

ribociclib

Medical condition to be studied

Breast cancer

Additional medical condition(s)

Hormone receptor-positive, HER2-negative early breast cancer, AJCC 8th edition
anatomic stage II to III

Population studied

Short description of the study population

Adults aged 18 years or older, women and men, with histologically confirmed hormone receptor-positive, HER2-negative breast cancer of AJCC 8th edition anatomic stage II or III, who initiate adjuvant ribociclib in combination with

endocrine therapy according to the Summary of Product Characteristics in routine clinical practice, and in whom adjuvant endocrine therapy was initiated within 12 months before baseline. Participants must be able to understand and complete the study questionnaires and must provide written informed consent.

Patients are not eligible if they have evidence of metastatic disease (AJCC stage IV) or locoregional or distant recurrence before baseline, prior treatment with a CDK4/6 inhibitor, an active second primary malignancy before initiation of ribociclib, contraindications to ribociclib or endocrine therapy according to the Summary of Product Characteristics, severe cognitive impairment, current participation in another interventional clinical trial, or are pregnant or breastfeeding.

Consecutive eligible patients are invited at three participating centres in Croatia until the planned sample size is reached.

Age groups

- **Adult and elderly population (≥ 18 years)**

- Adults (18 to < 65 years)
 - Adults (18 to < 46 years)
 - Adults (46 to < 65 years)
- Elderly (≥ 65 years)
 - Adults (65 to < 75 years)
 - Adults (75 to < 85 years)
 - Adults (85 years and over)

Estimated number of subjects

76

Study design details

Setting

Three hospital oncology departments in Croatia: University Hospital Centre Split, University Hospital Centre Osijek and Clinical Hospital Dubrava.

Consecutive eligible patients are identified and invited during routine outpatient visits within the enrolment period. Baseline is the day of initiation of adjuvant ribociclib in combination with endocrine therapy. Each participant is followed for six months, with assessments at Month 0, Month 1 (day 28 plus or minus 7 days), Month 3 (day 90 plus or minus 14 days) and Month 6 (day 180 plus or minus 21 days), calculated from baseline. Questionnaires are completed by participants on paper before the clinical consultation and, at baseline, before the first dose whenever feasible. Clinical data are abstracted from routine medical records, including selected data collected retrospectively for up to 12 months before baseline to characterise prior treatment and clinical context. There is no comparator arm and no randomisation. Treatment decisions, including dose modifications and discontinuation, are made solely by the treating physician according to clinical judgement and the Summary of Product Characteristics.

Comparators

None. The study is single-arm. Each participant serves as her or his own reference, and the measure of interest is the within-patient change from baseline (Month 0) to Month 6. Exploratory subgroup contrasts are prespecified, including duration of endocrine therapy before baseline (up to 3 versus 4 to 12 months).

Outcomes

Primary endpoint: within-patient change in the EQ-5D-5L utility index from baseline (Month 0) to Month 6.

Secondary endpoints, assessed at Months 0, 1, 3 and 6 and summarised as change from baseline to Month 6 and modelled as trajectories over time:

EORTC QLQ-BR23 functioning scales: body image, future perspective, sexual functioning;

EORTC QLQ-BR23 symptom scales: systemic therapy side effects, breast symptoms, arm symptoms, upset by hair loss;

WPAI:GH overall work impairment, absenteeism, presenteeism and activity impairment, with work-related domains analysed in participants employed at baseline and activity impairment in all participants;

informal care needs, measured as informal care hours per week, with caregiver type summarised descriptively.

Supportive descriptive outcomes: treatment interruptions, dose reductions and permanent discontinuation of ribociclib, adverse events, hospitalisations, sick leave and analgesic use.

Data analysis plan

All outcomes are summarised descriptively at each assessment. The primary endpoint is analysed using a mixed model for repeated measures on the EQ-5D-5L utility index, with participant as a random effect and assessment time point as a fixed effect, adjusted for prespecified covariates including centre, age, anatomic stage and duration of endocrine therapy before baseline. Utility scoring uses the Hungarian value set in the primary analysis and the Italian value set in sensitivity analyses. EORTC QLQ-BR23 scales are scored according to the EORTC scoring manual. WPAI:GH domains are calculated using the standard scoring formulas. Informal care is analysed in two parts: the proportion of participants receiving any care, and hours per week among those receiving care; extreme values are checked against source responses and summarised using robust methods where appropriate. Changes are directionally

harmonised across instruments. Missing data are assumed missing at random in the primary analysis, with sensitivity analyses under alternative assumptions and a descriptive account of reasons for missing assessments. Estimates are presented with 95 percent confidence intervals; no formal hypothesis testing is planned for the primary endpoint.

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data source(s), other

Primary data collection at three participating centres in Croatia: patient-reported outcome questionnaires completed on paper by participants at study visits, and clinical data abstracted from routine hospital medical records. No pre-existing registry or database is used.

Data sources (types)

[Electronic healthcare records \(EHR\)](#)

[Patient surveys](#)

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Yes

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Yes

Data characterisation moment

after creation of study variables

Data characterisation details

Data are collected on paper source forms and entered into an EpiData database with predefined ranges and logical checks. Patient-reported outcome data are entered twice by independent operators and discrepancies are resolved against

the paper source document, with corrections documented in a query log. Completeness of each questionnaire is checked at the study visit before the participant leaves the clinic, and the reason for any missing assessment is recorded in the case report form. Derived scores are recalculated independently and compared before the analysis dataset is locked.