CAROLEEN: A Real-World Study assessing Adjuvant Treatment Decision Dynamics and Outcomes in High-Risk HR+/HER2- eBC, including Patient Compliance and Quality of Life

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KEY FINDINGS & CONCLUSIONS

- **CAROLEEN is a non-interventional study in high-risk Hormone receptor positive/Human epidermal growth factor receptor 2 negative early breast cancer (HR+/HER2- eBC) patients with indication for treatment with either ribociclib or abemaciclib according to their respective SmPCs in the adjuvant setting assessing cross-sectional baseline, as well as longitudinal treatment outcomes up to 39 months.**
- **Current recruitment performance in CAROLEEN indicates a positive trend in clinical adoption of ribociclib since label extension for the adjuvant treatment of eBC, indicating its use across the full breadth of the approved adjuvant ribociclib label.**

BACKGROUND

► German RW 5 year-iDFS rates per N-stages of HR+/HER2- eBC*

	Total	N0 non-high-risk**	N0 high-risk**,***	N1***	N2-N3***
Patients, N (%)	1,008	314 (31)	92 (9)	428 (42)	174 (17)
5-year rate, % [95% CI]	85.8 [82.0; 88.8]	94.5 [89.6; 97.1]	87.4 [73.2; 94.4]	87.6 [81.0; 92.1]	63.4 [50.6; 73.7]

** Real-world data set of German patients receiving standard treatments according to physician`s choice between 2007 and 2016[1] (before approval of adjuvant CDK4/6i therapy), confirming international data from the US flatiron database[2].*
*** High-risk status was defined per NATALEE (pivotal ribociclib phase-3 trial) criteria: node-positive disease (N1 – N3) or node-negative (N0) with additional risk factors (e.g., T4, T3, T2 G3, T2 G2 with Ki67 ≥20%).*
**** Ribociclib in-label population with high risk of recurrence.*

► In-label use of ribociclib and abemaciclib

	N0		N1	N2-N3
Ribociclib[4]	T2	T3-T4	all patients[a]	
	with G3 or G2 with high genomic risk[b] or KI-67 ≥20%	all patients		
Abemaciclib[5]	no approval		for tumors ≥5 cm or G3	all patients

[a] T2-T4 N1mi (to be judged as N1) are included. T0/T1 N1mi (Stage IB) are excluded.
[b] Oncotype Dx risk score ≥26 or high-risk profile in Prosigna/PAM50, MammaPrint or Endopredict.

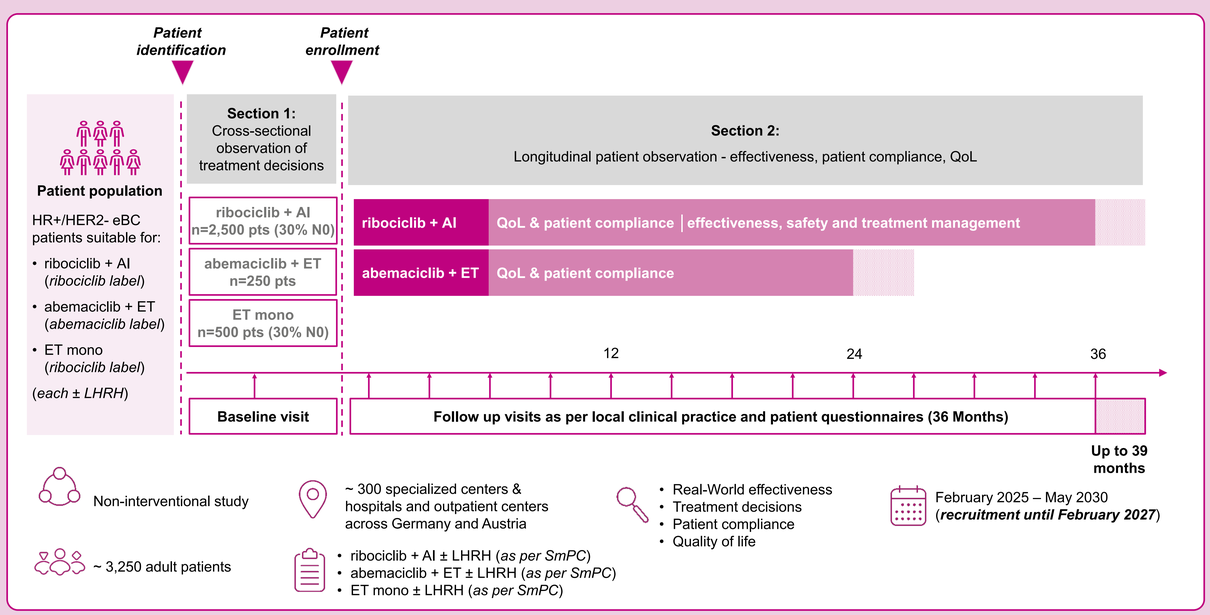
- Treatment of patients with Hormone receptor positive/Human epidermal growth factor receptor 2 negative (HR+/HER2-) early breast cancer (eBC) is with curative intent, while the risk of disease recurrence remains high in certain patients, depending on stage, tumor characteristics and individual risk factors. Real-world data show similar risk profile of node negative patients with high risk-features compared to node positive patients.
- Advancements in adjuvant therapy options for HR+/HER2- high-risk eBC underscore the necessity for real-world data with approved treatments, which noteworthily, have a different definition of the high-risk population according to their labels.
- The CAROLEEN study seeks to explore aspects influencing treatment decisions, patient compliance, clinical adoption of CDK4/6i treatment (i.e., ribociclib or abemaciclib), and their outcomes in the real-world setting.

iDFS, invasive disease-free survival DFS; RW, real-world

STUDY DESIGN

- CAROLEEN is a non-interventional study featuring a cross-sectional analysis at baseline and a longitudinal evaluation of long-term outcomes over a period of up to 39 months (**Figure 1 - Figure 3**).
  - The cross-sectional observation assesses drivers of treatment choices and clinical adoption in the ribociclib cohort by collecting data of patients treated with either ribociclib + aromatase inhibitor (AI) ± *luteinizing hormone-releasing hormone* (LHRH), abemaciclib + endocrine therapy (ET) ± LHRH or ET monotherapy ± LHRH (patients with indication for ribociclib according to the approved criteria).
  - The longitudinal observation examines real-world effectiveness, safety, and treatment management in the ribociclib cohort as well as patient-reported outcomes, including quality of life and patient compliance, in both the ribociclib and abemaciclib cohorts.
- Thus, the study aims to translate the benefits demonstrated in clinical trials into real-world settings, generating evidence on clinical decision-making, treatment outcomes and patient compliance for patients in routine practice in high-risk HR+/HER2- eBC management.

Figure 1. Study design



AI, aromatase inhibitor; eBC, early breast cancer; ET, endocrine therapy; HER2, Human epidermal growth factor receptor 2; HR, Hormone receptor; LHRH, luteinizing hormone-releasing hormone; N0, node negative; QoL, quality of life; | LHRH to be given in pre- or perimenopausal women or men.

OBJECTIVES

Figure 2. Primary and secondary objectives (excerpt)

Primary objective

- Evaluation of invasive disease-free survival (iDFS) for adjuvant therapy with ribociclib + AI ± LHRH in patients with HR+/HER2- early breast cancer at 36 months using 'Standardized Definitions for Efficacy Endpoints (in adjuvant breast cancer trials)' (STEEP) criteria[3]

Secondary objectives (excerpt)

Section 1

- Identification of differences in baseline characteristics between ribociclib + AI ± LHRH, abemaciclib + ET ± LHRH and ET mono ± LHRH, and changes thereof compared to patients included at a later timepoint
- Reasons for treatment decision documented by the treating physician
- Assessment of patients' individual perception of risk of recurrence and treatment decision by questionnaire at baseline

Section 2

- Evaluation of iDFS, invasive breast cancer-free survival (iBCFS), recurrence-free survival (RFS) and distant disease-free survival (DDFS) for ribociclib + AI ± LHRH using STEEP criteria[3] at different timepoints
- Evaluation of safety and tolerability of ribociclib + AI ± LHRH
- Evaluation of QoL for ribociclib + AI ± LHRH and abemaciclib + ET ± LHRH by European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ)-C30, EORTC QLQ-BR42 and Hospital Anxiety and Depression Scale (HADS D)
- Evaluation of patient compliance to ribociclib + AI ± LHRH and abemaciclib + ET ± LHRH as assessed by the Medication Adherence Report Scale (MARS-D), physician adherence rating (ribociclib cohort only), and neutrophil count (ribociclib cohort only)

AI, aromatase inhibitor; DDFS, distant disease-free survival; eBC, early breast cancer; EORTC QLQ, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; ET, endocrine therapy; HER2, Human epidermal growth factor receptor 2; HADS, Hospital Anxiety and Depression Scale; HR, Hormone receptor; LHRH, luteinizing hormone-releasing hormone; iBCFS, Invasive breast cancer-free survival; iDFS, invasive disease-free survival; MARS-D, Medication Adherence Report Scale D; RFS, recurrence-free survival; STEEP, Standardized Definitions for Efficacy Endpoints (in adjuvant breast cancer trials)

PATIENTS

Figure 3. Key eligibility criteria and treatments

Key inclusion criteria

- ≥18 years of age
- Histological diagnosis of HR+/HER2- early breast cancer with curative intent
- Indication for treatment with ribociclib + AI ± LHRH as described in the current SmPC of ribociclib[4] **or** abemaciclib + ET ± LHRH as described in the current SmPC of abemaciclib[5] in the adjuvant setting

Key exclusion criteria

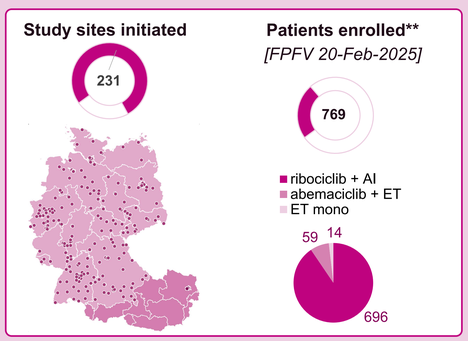
- Patient is simultaneously participating in any investigational trial or simultaneously participating in another Novartis-sponsored non-interventional study with ribociclib.

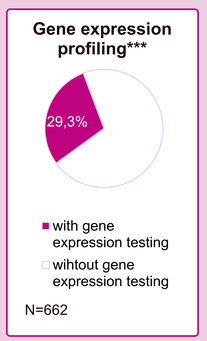
ET, endocrine therapy; HER2, Human epidermal growth factor receptor 2; HR, Hormone receptor; LHRH, luteinizing hormone-releasing hormone; SmPC, summary of product characteristics | LHRH to be given in pre- or perimenopausal women or men.

BASELINE DATA

- Study metrics and selected preliminary baseline data as of 01-Oct-2025 are shown in **Figure 4**.

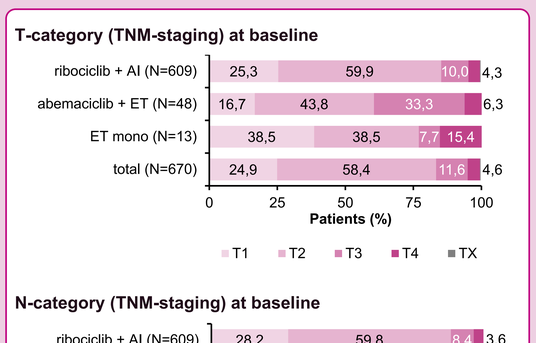
Figure 4. Study metrics and selected baseline data*

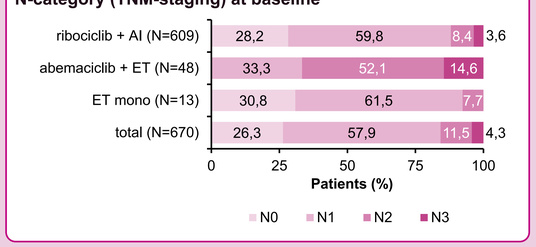




Age and fertility status

	ribociclib + AI	abemaciclib + ET	ET mono
Age (years) [620, 50, 13]	58.1 ± 12.3	60.6 ± 11.7	72.2 ± 7.6
Fertility status (%)[605, 47, 11]			
Pre-menopausal	27.8	23.4	0.0
Peri-menopausal	5.6	2.1	0.0
Post-menopausal	66.6	74.5	100.0





Data cut-off date for preliminary uncleaned data: 01-Oct-2025. **excl. 32 screening failures. * Breast cancer prognostic array, including: Oncotype Dx, Prosigna/PAM50, MammaPrint, and EndoPredict. | Numbers in superscript brackets indicate number of non-missing values. | For clarity reasons labels for values <1% were omitted.*

References

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2. Jhaveri K, Pegram M, Nevenet P et al (2024). Real-world evidence on risk of recurrence in patients with node-negative and node-positive HR+/HER2−early breast cancer from US electronic health records. ESMO. Poster ID 292P
3. Tolaney SM, Garrett-Mayer E, White J, et al (2021). J Clin Oncol; 39(24):2720-31.
4. Summary of product characteristics (SmPC) Kisqali
5. Summary of product characteristics (SmPC) Verzenlos

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Disclosures

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