# Cancer management and outcome of very young non-pregnant patients with breast cancer diagnosed at 40 years or younger – GBG 29

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BCP Breast Cancer in Pregnancy

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GBG GERMAN BREAST GROUP

BIG Breast International Group

## Background

- Breast cancer (BC) diagnosed in young women who are ≤ 40 years is a relatively rare disease. However, it represents the most common cause of cancer-related deaths in this age group.[1]
- Young age at diagnosis is associated with an increased risk of recurrence and worse survival. The prognostic relevance of young age by itself is controversial. Although some data suggest that BC in young women has a unique biology, other studies have shown that BC subtype varies from that in older patients and worse clinicopathological features and more aggressive subtypes are related with inferior survival outcomes.[2 3]
- To date, general concepts concerning oncological management should be driven by clinicopathological tumor characteristics and should adhere to standardized protocols for patients in general.[4]
- Yet, young patients need more individualized care and to date, little is known about the treatment of young women of ≤ 40 years in everyday clinical practice.

## Patients and Methods

- BCP (GBG 29/BIG 03-02) is a large multicenter, international, observational study with a prospective and retrospective data collection. BCP was established to investigate the oncological management and outcome of BC in pregnancy. Since 2014 non-pregnant patients who are ≤ 40 years are eligible if diagnosed with histological confirmed invasive BC, independent of the type of treatment as control cohort. All patients receive oncological treatment according to local standards.
- All patients fulfilling the following criteria in June, 2018 were included in the full analysis set: patients must not be pregnant at the time of BC diagnosis and age ≤ 40 years.
- Patient characteristics, clinicopathological tumor characteristics, disease stage, treatment modalities, side effects, and pregnancies were collected from medical records. Actual clinical follow-up data of patients was collected from prospectively included patients.
- Continuous data were summarized as median, minimum and maximum, categorical data (including pathological complete response (pCR) rates) as number and valid percent of patients.
- The three year disease free survival (DFS) and overall survival (OS) rates and the corresponding 95% CIs will be estimated using the Kaplan-Meier method.

## Objectives

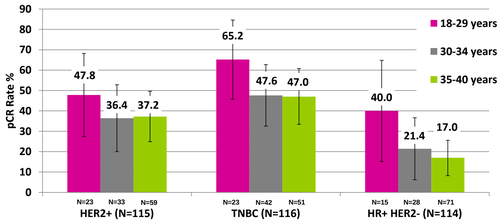
- The aim of this analysis is to report descriptively baseline characteristics, as well as information on diagnostic procedures, BC therapy, short-term (pCR rates for patients treated with neoadjuvant therapy) and long-term (DFS, OS and pregnancies after diagnosis) outcome for non-pregnant women with an age ≤ 40 years.

## Results

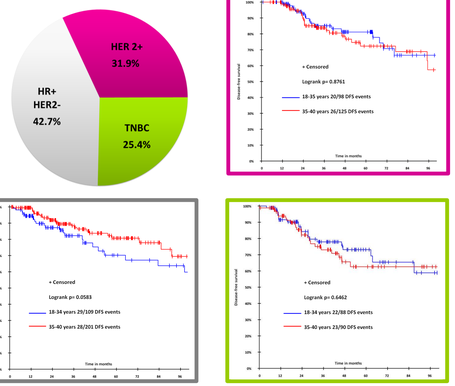
### Table 1. Patient and tumor characteristics

| Parameter | Category | N (valid %) |
|---|---|---|
| Age | Median (min,max) | 35 (19,40) |
| | 18-29 | 137 (14.3) |
| | 30-34 | 267 (27.9) |
| | 35-40 | 552 (57.7) |
| Histological tumor type | Ductal invasive | 815 (86.9) |
| | Lobular subtype | 38 (4.1) |
| | Ductal and lobular invasiv | 5 (0.5) |
| | Other | 80 (8.5) |
| Tumor site | Unilateral | 938 (98.1) |
| | Bilateral | 18 (1.9) |
| cT | cT1 | 380 (41.5) |
| | cT2 | 447 (48.9) |
| | cT3/cT4 | 85 (9.2) |
| cN | cN0 | 586 (67.0) |
| | cN1 | 254 (29.1) |
| | cN2/cN3 | 34 (3.9) |
| Metastasis at primary diagnosis | M0 | 868 (93.2) |
| | M1 | 30 (3.2) |
| | MX | 33 (3.5) |
| Grading | G1 | 38 ( 4.1) |
| | G2 | 377 (40.7) |
| | G3 | 511 (55.2) |
| Ki-67 | <20% | 116 (16.8) |
| | ≥20% | 576 (83.2) |
| Hormone receptor (HR) status | HR positive | 642 (67.4) |
| | HR negative | 311 (32.6) |
| Biological subtype | HER2-/HR+ | 395 (42.7) |
| | TNBC | 235 (25.4) |
| | HER2+/HR+ | 222 (24.0) |
| | HER2+/HR- | 73 (7.9) |

### Figure 1. pCR rates (ypT0 ypN0) according to biological subtype and age groups




### Figure 2. Disease-free survival of young women according to biological subtype and age

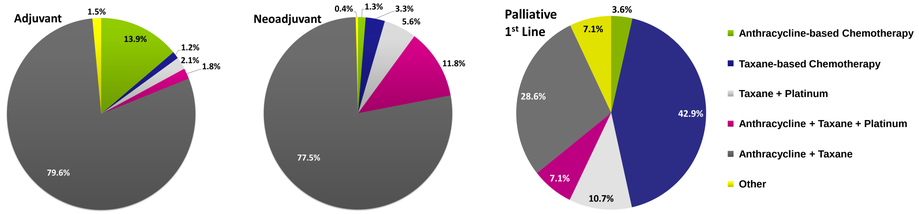



### Table 2. Oncological management

| Parameter | Category | N (valid %) |
|---|---|---|
| **Early Breast Cancer** | | |
| Chemotherapy | Yes | 735 (90.7) |
| | No | 75 (9.3) |
| Setting of chemotherapy | Neoadjuvant | 416 (56.6) |
| | Adjuvant | 319 (43.4) |
| Endocrine therapy | Tamoxifen | 238 (59.9) |
| | Aromatase inhibitor (AI) | 8 (2.0) |
| | Tamoxifen + GnRH analogue | 133 (33.5) |
| | AI+ GnRHa analogue | 15 (3.8) |
| | Sequential endocrine therapy | 3 (0.8) |
| Anti HER2 therapy | Trastuzumab | 123 (65.1) |
| | Trastuzumab + Pertuzumab | 66 (34.9) |
| | None/missing | 106 |
| Breast surgery | Breast conserving surgery | 491 (64.5) |
| | Mastectomy | 241 (31.7) |
| | None | 29 (3.8) |
| Nodal surgery | Sentinel node biopsy | 404 (50.3) |
| | Axillary dissection | 340 (42.3) |
| | None | 59 (7.3) |
| **Metastatic Breast Cancer** | | |
| 1st Line Chemotherapy | Yes | 22 (88.0) |
| | No | 3 (12.0) |
| | Missing | 5 |

- From April 2003 until June 2018, 1812 pregnant and non-pregnant patients have been registered. 964 non-pregnant women ≤ 40 years with a median follow-up of 38.7 months (95%CI; 35.2; 41.3) comprised the analysis set.
- The median age at diagnosis was 35 years (range 19-40). Overall, 90.4% of patients had a stage T1-2 at diagnosis and 67.0% had negative lymph nodes. Further patient and tumor characteristics are shown in Table 1.
- At primary diagnosis 95.3% of patients underwent ultrasound, 88.5% mammography, and 23.5% magnetic resonance imaging of the breasts.
- 82.8% of patients with HR+ HER2- early breast cancer (EBC), 99% with triple-negative EBC, and 95.2% with HER2+ EBC received chemotherapy (CT). Most patients (88.0%) with advanced BC were treated in the 1st line mBC setting with CT. 93.4% of patients with endocrine treatment for EBC received tamoxifen; thereof 35.8 % in combination with a GnRH analogue. Further details about oncological management are shown in Table 2. Figure 3 provides an overview of administered CT regimes in EBC and advanced BC.
- Regardless of biological subtype of BC, the highest pCR rates (ypT0 ypN0) were achieved in the cohort of patients age18-29 years; Figure 1 shows the pCR rates according to biological subtype and age groups.
- The 3-year DFS for patients with EBC was 83.1% (95%CI; 79.6%; 86.0%) and the 3-year OS 94.3% (95%CI; 91.9%; 96.0%). The subgroup analysis per biological subtype suggested a trend towards inferior DFS in the group of patients ≤34 years and HR+ HER2−disease (logrank *p*=0.0583; Figure 2).
- In multivariate analysis DFS and OS were with significantly worse in patients with EBC and initial cN+ and grade 3 tumors (data not shown).
- 33 patients (3.4%) got pregnant after diagnosis of BC with a median time from diagnosis to birth/termination of 3 years (range 2-7).

### Figure 3. Chemotherapy regimes




## Conclusions

- This registry comprises a large cohort of young non-pregnant patients below the age of ≤40 years.
- The reported treatments reflect the modern oncological management of very young patients with almost 91% of all patients receiving neoadjuvant or adjuvant chemotherapy.
- Regardless of biological subtype, the highest pCR rate was achieved in the group of patients <30 years.
- The prognostic relevance of young age by itself could not be shown for patients with HER2+ and triple-negative disease. Yet, similar to previously reported results[5] our data suggest a trend towards inferior DFS in the group of patients ≤34 years and HR+ HER2− disease.
- Registry needs to be continued to get more valid prospective information.

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