ORIGINAL ARTICLE

The Treatment of Primary Breast Cancer in Older Women With Adjuvant Therapy

A Retrospective Analysis of Data From Over 3000 Patients From the PATH Biobank, With Two-Year Follow-up

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SUMMARY

Background: Breast cancer is the most common cancer in women in Germany. Mortality from breast cancer has declined over the past 15 years, but less so in women aged 70 or older than in younger women. The discrepancy might be explained by age-related differences in treatment.

Methods: Data from the Patients' Tumor Bank of Hope (PATH) database of women who underwent adjuvant treatment for the treatment of an invasive primary tumor without distant metastases (year of diagnosis, 2006–2011) were retrospectively analyzed. The clinical and tumor-biological findings and treatment data over two years of follow-up were compared across three age groups (under age 50, ages 50 to 69, and ages 70 and up). Chi-square tests were carried out to reveal significant differences, and post-hoc multiple comparisons were performed with and without Bonferroni correction. Treatment data were adjusted for staging and grading and tested for age-dependence with logistic regression.

Results: Follow-up data were available for 3257 (65%) of 4981 women, of whom 61% were in the middle age group and 22% in the oldest. Compared to women aged 50 to 69, those aged 70 and up less commonly received breast-conserving treatment (68.8% vs. 86.4%), chemotherapy (27.5% vs. 44.1%), radiotherapy (81.8% vs. 92.4%), and trastuzumab (52.9% vs. 79.3%; $p < 0.001$ for all differences). All differences remained significant after statistical adjustment.

Conclusion: The cause of these age-related differences is unclear. It cannot be determined from these data whether concomitant disease, the older patients' individual decisions, or other factors were responsible for their not receiving treatment as often as the younger patients did.

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In 2010 some 70 340 women in Germany developed invasive tumors of the breast. Patients' mean age at diagnosis was 64 (1). Breast cancer is the most common tumor disorder in women in Germany (1). Currently, about 17 500 women die from breast cancer every year (1), of whom more than half are older than 70 (2). Breast cancer mortality is slightly decreasing in Germany (1). Two factors have materially contributed to this development: optimized imaging methods have resulted in early and certain diagnosis, which means that more women who were identified as having tumor stages with a favorable prognosis were treated. Secondly, disease management programs (3), certified breast centers, and the development of new, targeted therapeutic approaches (4) have contributed to better healthcare provision and improved survival (1, 5, 6). According to data from a meta-analysis undertaken by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) (7), adjuvant treatment with classic medications has led to an estimated relative reduction in cumulative 15-year mortality of almost 60%. Furthermore, it is assumed that in future, as many as 75% of potential deaths will probably be prevented by administering adjuvant systemic therapy (7). Guideline-conform care provision is considered crucial for the purposes of improving the quality of the result (disease-free survival, overall survival) (8). According to the S3 guideline for the diagnostic evaluation, therapy, and follow-up care of breast cancer, the therapeutic decisions of doctors and patients should include treatment options, risks, and benefits, depending on the patient's age, among other factors. The present publication focuses on the question of age group-specific differences in the treatment of breast cancer. To this end, the researchers analyzed the annotated dataset of the Patients' Tumor Bank of Hope (PATH) Biobank.

Methods

Data source: PATH Biobank

In 2002, numerous unanswered research questions prompted the setting up of the PATH Foundation. Its aim is to collect blood and tumor tissues, as well as normal tissues adjacent to tumors, from and for breast

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TABLE 1

Clinical data and medical history of PATH patients differentiated by age group (valid %)*¹

		Age groups						Total N = 3257 (100)		p*3
		<50 years n = 575 (17.7)		50–69 years n = 1980 (60.8)		>69 years n = 702 (21.6)				
Menopausal status*2	Pre	406	(85.3)	89	(5.0)	0	(0.0)	495	(16.8)	<0.001
	Peri	32	(6.7)	55	(3.1)	1	(0.1)	88	(3.0)	
	Post	38	(8.8)	1633	(91.9)	692	(99.9)	2363	(80.3)	
	Not known	99		203		9		311		
Tumor size(T)	pT1	378	(66.4)	1433	(73.1)	345	(49.8)	2156	(66.9)	<0.001
	pT2	170	(29.9)	483	(24.6)	295	(42.6)	948	(29.4)	
	pT3	17	(3.0)	34	(1.7)	36	(5.2)	87	(2.7)	
	pT4	4	(0.7)	10	(0.5)	17	(2.5)	31	(1.0)	
	Not known	6		20		9		35		
Node status (N)	pN0	360	(63.7)	1394	(71.3)	436	(65.1)	2197	(67.7)	<0.001
	pN1	153	(27.1)	419	(21.4)	158	(23.6)	750	(23.1)	
	pN2	36	(6.4)	98	(5.0)	45	(6.7)	191	(5.9)	
	pN3	16	(2.8)	43	(2.2)	31	(4.6)	107	(3.3)	
	Not known	10		26		32		68		
Distant metastases (M)	cM0	543	(100)	1845	(100)	659	(100)	3047	(100)	n. a.
	Not known	32		135		43		210		
Grading	G1	67	(11.8)	377	(19.3)	71	(10.3)	515	(16.0)	<0.001
	G2	337	(59.4)	1220	(62.4)	459	(66.3)	2015	(62.7)	
	G3	164	(28.9)	359	(18.4)	162	(23.4)	685	(21.3)	
	Not known	7		24		10		41		
Estrogen receptor	Positive	472	(83.5)	1693	(86.7)	602	(86.4)	2767	(86.1)	0.151
	Not known	10		28		5		43		
Progesterone receptor	Positive	449	(79.6)	1507	(77.2)	515	(74.2)	2471	(77.0)	0.073
	Not known	11		27		8		46		
HER2/neu status	Positive	76	(13.5)	201	(10.4)	80	(11.5)	369	(11.2)	0.112
	Not known	12		44		9		65		
Triple negative	Yes	59	(10.6)	160	(8.3)	62	(9.0)	281	(8.8)	0.246
	Not known	16		48		11		75		

n. a., not applicable; PATH, Patients' Tumor Bank of Hope

*¹ The percentages of valid cases results from the number of cases in the column minus the "Not known" cases in the table cell.

*² As reported in physician's letter. If a patient was older than 60, her status was classified as postmenopausal.

*³ Global Chi-square test

cancer patients and store these tissues. The specimens are systematically enhanced with patients' data and are made available for research purposes, following an application process.

Since 2004, more than 7600 women have consented to providing a tissue specimen and to having their data stored in the PATH Biobank. In addition to the decentralized storage of the biospecimens in the institutes for pathology at the participating seven breast cancer centers (German Cancer Society/German Society for Senology), all relevant clinical and tumor biological

data from doctors' and pathology reports are being collected and made available. Additional information is gained by following up the patients and surveying them. The first follow-up takes place after 2 years (9).

Selection of patients

The data of women with invasive breast cancer and tissue collection/storage in 2006–2011 were included, as was patient-reported follow-up information up to 2013. Breast cancer patients were contacted two years after providing a specimen for storage, as long as they had

TABLE 2

Therapy data of PATH patients differentiated by age groups (valid %)

		Patients <50 years n = 575 (17.7)		Patients 50–69 years n = 1980 (60.6)		Patients >69 years n = 702 (21.6)		Total N = 3257 (100)		p*
BCT	Valid n	566	(100)	1964	(100)	699	(100)	3229	(100)	<0.001
	Yes	444	(78.4)	1696	(86.4)	481	(68.8)	2621	(81.2)	
	Not known	9		16		3		28		
T1 tumor and BCT	Valid n	376	(100)	1431	(100)	344	(100)	2151	(100)	<0.001
	Yes	320	(85.1)	1301	(91.0)	294	(85.5)	1915	(89.1)	
	Not known	2		2		1		5		
T2 tumor and BCT	Valid n	168	(100)	483	(100)	295	(100)	946	(100)	<0.001
	Yes	119	(70.8)	381	(78.9)	177	(60.0)	677	(71.6)	
	Not known	2		0		0		2		
Radiotherapy	Valid n	551	(100)	1883	(100)	638	(100)	3072	(100)	<0.001
	Yes	481	(87.3)	1739	(92.4)	522	(81.8)	2742	(89.3)	
	Not known	18		73		58		139		
Radiotherapy after BCT	Valid n	429	(100)	1621	(100)	444	(100)	2494	(100)	<0.001
	Yes	411	(95.8)	1591	(98.1)	415	(93.5)	2417	(96.9)	
	Not known	12		57		31		100		
Chemotherapy	Valid n	522	(100)	1725	(100)	592	(100)	2839	(100)	<0.001
	Yes	361	(69.2)	761	(44.1)	163	(27.5)	1285	(45.3)	
	Not known	49		222		87		358		
Antihormonal therapy if hormone receptor is positive	Valid n	483	(100)	1679	(100)	570	(100)	2732	(100)	0.003
	Yes	456	(94.4)	1583	(94.3)	515	(90.4)	2554	(93.4)	
	Not known	21		81		44		146		
Trastuzumab if HER2/neu status is positive	Valid n	75	(100)	188	(100)	68	(100)	331	(100)	<0.001
	Yes	70	(93.3)	149	(79.3)	32	(52.9)	255	(77.0)	
	Not known	1		13		12		26		

BCT, breast conserving therapy; PATH, Patients' Tumor Bank of Hope

* Global Chi-square test

given their consent at the time of their initial diagnosis (90.2% consent rate) and current contact details were available (89.6%). The data of patients who received neoadjuvant therapy and of those with distant metastases were not included in our analysis because these conditions alone meant that the treatment given was different. In neoadjuvant therapy, the tumor dignity is assessed by means of a punch biopsy. It is technically not possible to generate a biospecimen. In case of a pathological complete remission (pCR), no tissue remains after concluding neoadjuvant therapy, or the tissue has changed to a degree that makes it impossible to draw conclusions about the original tumor. In synchronous breast cancer, the case with the poorer prognosis was included in the analysis. In patients who were included in the database with a primary tumor and also with a recurrence, only the primary cancer was included. The same approach was applied to other secondary cancers.

Statistical analysis

The description for the total cohort and three age-stratified cohorts (age at diagnosis <50, 50–69, >69 years) was done on the basis of TNM classification, tumor biology, and therapy. Quantitative data were reported with absolute frequencies and relative frequencies. Where significant age differences were identified in the global Chi square test, <5% post-hoc multiple comparisons with and without Bonferroni correction were done in case of a two-tailed probability of error. With the Bonferroni correction, the significance level was set at $p < 0.0013$, since 36 individual tests were undertaken ($0.05/36$). In order to prove associations between age groups and therapies, logistic regressions—adjusted for staging and grading—were calculated. The oldest age group was defined as the reference value. To estimate effects, we calculated odds ratios (OR) with 95% confidence intervals (CI). We used the statistics package SPSS 22.0 for our analyses.

Proportion of women treated with radiotherapy and chemotherapy by age group.
The figure shows 95% confidence intervals and significant differences after Bonferroni correction

Results

In the diagnostic period from 2006 to 2011, the PATH database included information from 4981 patients meeting the inclusion criteria. Follow-up data and self-reported therapy data up to 2013 were available for 3257 (65.4%) of these women. At the time when the data were assembled for the purpose of evaluation, mortality was 4.7%.

No relevant differences were seen with regard to clinical characteristics and medical histories between the patients with follow-up—who are the subject of what follows—and all others who had been included in the analysis. The median age was 61 years (*eTable*).

Of the 3257 patients who participated in the follow-up interview, 575 (17.7%) were younger than 50 at the time of diagnosis, 1980 (60.8%) were 50–69 years old, and 702 (21.6%) were older than 69 years. Age-dependency was noted for medical histories and clinical characteristics. Younger patients had significantly higher rates of smaller tumors than patients in the oldest age group. The group of 50–69-year olds had the smallest rate of patients with poorly differentiated tumors. Compared with the two younger age groups, patients older than 69 years had the highest rates of larger tumors. Regarding estrogen, progesterone, and HER2/neu status, no significant differences were seen between age groups (*Table 1*).

Regarding self-reported therapeutic measures, 81.2% of patients had undergone breast-conserving surgery (*Table 2*). In total, 89.1% underwent radiotherapy and 45.3% received adjuvant chemotherapy. The post-hoc multiple comparisons showed significant differences between all three age groups for breast-conserving therapy (BCT) (all $p < 0.001$). Patients in the youngest and oldest age groups with T1 tumors had breast conserving treatment significantly less often than the 50–69-year olds (85.1% versus 91.0%,

$p = 0.004$ and 85.5% versus 91.0%, $p = 0.011$; non-significant at the Bonferroni corrected significance level of $p \leq 0.0013$), whereas women aged >69 with T2 tumors received BCT significantly less often than patients in the two younger age groups (60.0% versus 78.9% versus 70.8%; $p < 0.001$ and $p = 0.035$); significance was not reached after Bonferroni correction of the significance level of $p \leq 0.0013$). Radiotherapy was administered significantly less often in patients >69 years of age compared with 50–69-year-olds, in connection with BCT (93.5% versus 98.1%; $p < 0.001$) as well as overall (81.8% versus 92.4%; $p < 0.001$). Adjuvant chemotherapy was administered significantly less often in the oldest age group than in the other two age groups (27.5% versus 44.1% versus 69.2%; all $p < 0.001$) (*Figure*). Patients older than 69 with positive hormone receptor status were treated significantly less often with antihormonal therapy (90.4% of >69 year-olds versus 94.3% of 50–69 year-olds; $p = 0.003$; and 90.4% of women >69 years of age versus 94.4% of women <50 years of age, $p = 0.016$; both p values are non-significant at the Bonferroni corrected significance level of $p \leq 0.0013$). Although the proportions of HER2/neu positive cancers in the age groups were comparable (13.5% versus 10.4% versus 11.5%), patients older than 69 were treated significantly less often with trastuzumab than patients in the other two age groups (52.9% versus 79.3% versus 93.3%; between the intermediate and youngest age groups $p = 0.031$; non-significant at the Bonferroni corrected significance level of $p \leq 0.0013$, otherwise $p < 0.001$).

We controlled for staging and grading in multivariate analyses. The age dependent therapeutic differences described earlier largely remained: patients in the intermediate and youngest age groups more often received BCT (OR 2.12, 95% CI 1.68 to 2.67 and OR 1.34, 95% CI 1.00 to 1.79) and adjuvant chemotherapy (OR 5.83, 95% CI 4.37 to 7.79 and OR 15.4, 95% CI 10.64 to 21.53). In patients aged 50–69, radiotherapy was used more often than in patients older than 69 (OR 2.45, 95% CI 1.85 to 3.25). However, in the patients younger than 50, the odds ratio of radiotherapy was not significantly higher (OR 1.38, 95% CI 0.98 to 1.94) (*Table 3*).

Discussion

The present article investigates the question of whether age-group specific differences exist in the treatment of breast cancer. To this end, 3257 (65.4%) datasets of 4981 patients were selected from the PATH database and classified into three age groups. In all age groups, information given by the patients themselves at the time of their initial diagnosis and at the time of their 2-year follow-up were largely complete and reliable (10). The results regarding age-dependent healthcare provision confirmed the results of Watermann and colleagues, who evaluated patients' data covering the period 1995 to 2000 in Germany (11). Our data also confirmed the results reported by Kiderlen and colleagues, who analyzed European data covering the time period 2008 to 2012 on the age-dependent treatment of

TABLE 3

Therapy data by age groups adjusted for grading and staging pT and pN*

	Breast conserving therapy		Chemotherapy		Radiotherapy	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
>69 years	1		1		1	
50–69 years	2.12	(1.68–2.67)	5.83	(4.37–7.79)	2.45	(1.85–3.25)
<50 years	1.34	(1.00–1.79)	15.14	(10.64–21.53)	1.38	(0.98–1.94)
pT1	1		1		1	
pT2	0.41	(0.33–0.51)	3.41	(2.72–4.29)	0.57	(0.44–0.74)
pT3	0.05	(0.03–0.09)	1.97	(1.02–3.81)	0.83	(0.36–1.90)
pT4	0.02	(0.00–0.08)	1.06	(0.37–3.07)	0.76	(0.17–3.46)
G1	1		1		1	
G2	0.84	(0.61–1.16)	3.52	(2.59–4.79)	0.90	(0.63–1.29)
G3	0.76	(0.53–1.08)	29.76	(20.23–43.79)	0.99	(0.65–1.51)
N0	1		1		1	
N1	0.70	(0.56–0.88)	6.00	(4.73–7.61)	1.07	(0.80–1.42)
N2/N3	0.39	(0.28–0.53)	8.85	(5.73–13.68)	5.68	(2.59–12.45)

CI, confidence interval; OR, odds ratio; pT, primary tumor assessed as pathological; pN, regional lymph nodes assessed as pathological

* Not adjusted for metastases, as only cases without distant metastases were included

breast cancer (12). In order to avoid an accumulated alpha error, we additionally calculated the results by using Bonferroni correction and reporting these in cases where the uncorrected results differed. It is more difficult to achieve a significant testing result when using this conservative method; consequently, possible logical and stochastic dependencies between the test statistics will be subject to underestimates.

Study cohort

Patients who are registered with the PATH Biobank or another prevention study are of a slightly younger age and have more favorable tumor stages than all women with cancer in Germany (pT1: 52%; pT2: 37%; pT3: 5%; pT4: 6%) (1, 13, 14). This would explain the lower death rate at the time when data from the PATH patients were collated for evaluation. Mortality was consistent with mortality in the VERDI study after only one year (15). Patients who are included in therapeutic studies are often younger than average and present with rather more favorable tumor stages (15–18), since typical comorbidities are often exclusion criteria that rule out study participation (19, 20). Evident insights for older breast cancer patients are therefore available to an unsatisfactory degree, although most gynecological-oncological patients are older than 65. The number of women >59 years of age in Germany is predicted to rise by 3.1 million over the following 15 years (a 23% increase), which means that the proportion of potentially older breast cancer patients will also rise. Of the PATH participants included in the present study, one fifth (n = 702) were older than 69 (21).

When all women who had been included in the PATH Biobank at the time of the study and whose data were included in the present analysis were compared with the women who participated in the follow-up, no clinical selection process became obvious. In order to exclude possible biases, patients with distant metastases at primary diagnosis and those receiving neo-adjuvant therapy were excluded from our analysis. In spite of the lower response rate at follow-up compared with other studies regarding health services research in oncology (22, 23), these patients represented all included PATH participants, but not all breast cancer patients in Germany.

Therapeutic care provision

The prognosis and therapy of breast cancer are determined by the stage at initial diagnosis and the tumor biology. The cancers of younger PATH patients are not significantly more often HER2/neu positive or triple negative. Patients in this age group are therefore not affected to a greater degree by tumors with a tendentially more unfavorable prognosis (24). With regard to the tumor stage, the intermediate age group of 50–69 year-olds, which is relevant for breast cancer screening, has the highest rates of T1 and the smallest rate of T3 and T4 tumors. Patients in the oldest age group of >69 years more often present with advanced and poorly differentiated tumors.

Several studies have shown that medical care provision depends on patients' age (14, 25, 26). This was confirmed by the self-reported therapy information provided by PATH patients. The observed differences

in BCT are largely consistent with those observed in the OVIS study (14). According to the benchmarking annual report 2012 issued by the West German Breast Center, 27% of women were not treated by using breast-conserving surgery because of tumor size and multicentric tumors or because of the patient's own wishes (27). When looking at all systemic therapies in total, an age gradient is obvious in participants in the PATH Biobank as well as in participants in the OVIS study: younger patients receive systemic treatment more often than older women (14). In women in the PATH Biobank, this is mainly because of the fact that chemotherapy is used more often in younger women, although older patients can equally benefit from modern chemotherapy, in spite of their higher risk of therapy related hematological toxicity and mortality (28).

Population based analyses have confirmed the data presented here: patients older than 69 are more likely not to receive adjuvant radiotherapy than patients in other age groups, even though radiotherapy after BCT optimizes local tumor control in patients of all ages and reduces the recurrence rate (29–32). Earlier studies investigated the reduction in mortality owing to the use of radiotherapy in older women (33–37). The Prime II study into breast cancer showed that after a median follow-up period of 5 years, the incidence of ipsilateral in-breast recurrences (1.3% in the group of patients who had received radiotherapy compared with 4.3% in the group that had not received radiotherapy) does not affect 5-year survival (93.3%), recurrence-free survival, or distant metastases (38). The Prime II study was conducted by using modern therapeutic approaches. Patients were randomized into two groups with or without irradiation of the entire breast in the diagnostic period 2003–2009. On the basis of these data, the indication for postoperative radiotherapy in older patients could be discussed for individual cases if the tumor biology is favorable and the tumor is small, although this is not yet included in the current S3 guideline. The recommendations of the German Gynaecological Oncology Working Group (Arbeitsgemeinschaft Gynäkologische Onkologie) consider in individual cases an individualized approach in older, and especially in fragile, patients (8, 39). We were not able to ascertain whether this development forms the basis for the confirmed difference in the frequency at which radiotherapy is used.

The rarer use of antihormonal therapy and trastuzumab in patients older than 69 is consistent with the observation that fewer older women receive adjuvant medication. For antihormonal treatment, the range of adverse effects in association with the length of the period over which the medication is given, of mostly 5 years, may affect the decisions of patients and doctors (40). The fact that trastuzumab is administered significantly more rarely to patients older than 69 should be seen in association with the already reported less common chemotherapeutic care, as adjuvant chemotherapy is a prerequisite (e1). Further, its administration in

therapeutic cycles over a period of several months and its intravenous application may cause some women to opt against trastuzumab treatment.

According to the S3 guideline, older patients should receive systemic adjuvant therapy that is comparable to that given to younger breast cancer patients. Organ function and comorbidities are crucial in making this decision.

Conclusion

Older breast cancer patients in the PATH cohort have breast conserving surgery less often and receive radiotherapy and chemotherapy and targeted treatment less often than younger women. The extent to which comorbidities and other factors are the reasons behind the therapeutic abstinence of the patients included in the PATH data is currently not known. Because of the way in which the data were collected, this retrospective analysis did not investigate the relevance and influence that doctors' attitudes towards treatment may have in combination with patients' attitudes. Further studies are needed to answer this question, especially interviews with experts and patients, and a better stratification of the age group, depending on life expectancy and comorbidities. Independently of the requirement of participatory decision making in the individual case, the way in which therapeutic care is closely associated with a patient's age, as we described in this article, may lead to speculate why US breast cancer patients >70 years of age have a higher 5-year survival rate than German patients (e2).

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Conflict of interest statement

PATH is an independent foundation under the civil code. It is not for profit and works independently of commercial interests. With its tissue bank, the PATH Foundation aims to promote and support molecular biological research projects relating to the diagnosis and therapy of cancer. The supporters and sponsors of the PATH Foundation are Roche Pharma, Grenzach; Amgen, Munich; AstraZeneca, Wedel; Bristol-Myers Squibb, Munich; Förderverein Robert Janker Krebsstiftung e.V. [friends' association of the Robert Janker cancer foundation, reg assoc], Bonn; GlaxoSmithKline, Munich; Henkel Foundation, Düsseldorf; MammaMia, the breast cancer magazine; Notaries Zimmermann und Hauschild, Düsseldorf; Novartis Pharma, Nuremberg; Pfizer Oncology, Berlin; Pierre Fabre, Freiburg; the Initiative for the Area of Bochum and Herne; Unterweyer Healthcare Communication, Hamburg; many private donors and the Verein Brustkrebs Deutschland.

Dr Anzeneder is a PATH Biobank employee.

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KEY MESSAGES

- Clinical data and characteristics gleaned from patients' medical histories and self reported therapeutic measures have been found to be age-dependent and unfavorable for older patients with breast cancer.
- The question of why older women in the PATH group receive breast conserving therapy less often, have radiotherapy or chemotherapy less often, and receive targeted treatment less often remains unanswered on the basis of the present study.
- Research is needed into whether similar treatment patterns are to be found in unselected cohorts of patients that include older patients with different comorbidities and life expectancies.

Dr Kunz has received a speaker's honorarium from Roche, for a lecture on senology.

Dr Waldmann has received travel expenses from PATH on the occasion of a PATH users' meeting.

The remaining authors declare that no conflict of interest exists beyond those outlined above.

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Supplementary material
 For eReferences please refer to:
www.aerzteblatt-international.de/ref3515

eTable:
www.aerzteblatt-international.de/15m0577

Supplementary material to:

The Treatment of Primary Breast Cancer in Older Women With Adjuvant Therapy

A Retrospective Analysis of Data From Over 3000 Patients From the PATH Biobank,
With Two-Year Follow-up

by Elke Peters, Tobias Anzeneder, Christian Jackisch, Thomas Dimpfl,
Georg Kunz, Alexander Katalinic, and Annika Waldmann

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eTABLE

Clinical data and medical history data PATH patients with and without follow-up (valid%)*¹

		Follow-up				Total	
		Yes, n = 3 257 (65.4)		No, n = 1 724 (34.6)		No = 4 981	
Age at surgery	Mean (SD)	60.78 (11.31)		60.70 (13.08)		60.75 (11.96)	
	Minimum–Maximum	23–93		27–92		23–93	
Menopausal status* ²	Pre	495	(16.8)	310	(20.1)	820	(17.9)
	Peri	88	(3.0)	49	(3.2)	137	(3.1)
	Post	2 363	(80.2)	1 185	(76.7)	3 548	(79.0)
	Not known	311		180		491	
Age groups	< 50 years	575	(17.7)	359	(20.8)	934	(18.8)
	50–69 years	1 980	(60.8)	909	(52.7)	2 889	(58.0)
	> 69 years	702	(21.6)	456	(26.5)	1 158	(23.2)
Tumor size(T)	pT1	2 156	(66.9)	1 031	(60.5)	3 187	(64.7)
	pT2	948	(29.4)	574	(33.7)	1 522	(30.9)
	pT3	87	(2.7)	65	(3.8)	152	(3.1)
	pT4	31	(1.0)	34	(2.0)	65	(1.3)
	Not known	35		20		55	
Node status (N)	pN0	2 190	(68.7)	1 093	(65.2)	3 283	(67.5)
	pN1	730	(22.9)	390	(23.3)	1 120	(23.0)
	pN2	179	(5.6)	109	(6.5)	288	(5.9)
	pN3	90	(2.8)	84	(5.0)	174	(3.6)
	Not known	68		48		116	
Distant metastases (M)	cM0	3 047	(100)	1 593	(100)	4 640	(100)
	Not known	210		131		341	
Grading	G1	515	(16.0)	259	(15.2)	774	(15.7)
	G2	2 016	(62.7)	1 006	(59.0)	3 022	(61.4)
	G3	685	(21.3)	441	(25.8)	1 126	(22.9)
	Not known	41		18		59	
Estrogen receptor	Positive	2 767	(86.1)	1 419	(83.2)	4 186	(85.1)
	Negative	447	(13.9)	287	(16.8)	734	(14.9)
	Not known	43		18		61	
Progesterone receptor	Positive	2 471	(77.0)	1 240	(72.7)	3 711	(75.5)
	Negative	740	(23.0)	465	(27.3)	1 205	(24.5)
	Not known	46		19		65	
HER2/neu status	Positive	357	(11.2)	214	(12.6)	571	(11.7)
	Negative	2 835	(88.8)	1 479	(87.4)	4 314	(88.3)
	Not known	65		31		96	
Triple negative	Yes	281	(8.8)	177	(10.5)	458	(9.4)
	No	2 901	(91.2)	1 514	(89.5)	4 415	(90.6)
	Not known	75		33		108	

*¹ Patients who received neoadjuvant therapy or those with distant metastases were excluded.

*² As reported in the physician's letter. If a patient was >60, her status was classified as postmenopausal.