RARE PATIENTS IN ROUTINE CARE:

TREATMENT AND OUTCOME IN ADVANCED INVASIVE LOBULAR BREAST CANCER IN THE PROSPECTIVE GERMAN RESEARCH PLATFORM OPAL

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INTRODUCTION

Invasive lobular breast cancer (ILC) is with 5-10% the second most common histologic type of invasive breast cancer after invasive ductal breast cancer (IDC). ILC differs from IDC, for example in its metastatic pattern. However, guidelines do not provide special treatment recommendations for this subtype and specific clinical studies are rare. Here we present prospective data on characteristics, treatment and outcome of patients with advanced ILC in routine care in Germany.

CONCLUSION

Prospective registries, like TMK/OPAL, are a unique source of data on patients with rare tumor subtypes. We show that patients with ABC of an invasive lobular histology present with different tumor characteristics regarding receptor status (more often HR-positive) and metastatic pattern (e.g. more often bone-only, more often peritoneum) than patients with invasive ductal subtype. A multivariate regression analysis showed that especially these tumor characteristics and overall performance status affect mortality risk of the patients. Our data indicate that patients with IDC and ILC benefit from the same treatment strategies, because median OS is comparable despite ILC patients being markedly older. Future research should focus on identifying patients who could benefit from personalized treatment approaches including tumor subtype as a factor to consider.

METHODS

The Tumor Registry Breast Cancer (TMK, NCT01351584) has prospectively documented data of patients with breast cancer by oncologists in Germany since 2007 (Fietz et al. 2017). Since 2017, the OPAL project (NCT03417115) continues the TMK and all specialists (medical and gynecologic oncologists) treating advanced breast cancer (ABC) are participating. Both projects are prospective, observational, open, longitudinal multicenter cohort studies (clinical registries).

Patients at the start of their treatment can be included after signing informed consent. Together over 7500 patients (4250 with ABC) will be recruited from over 200 sites in Germany. There is no treatment specification.

Details on all (sequential) treatments, patient and tumor characteristics, clinical and patient-reported outcomes are documented. Follow-Up is until death or up to 5 years. Data are monitored by data management and on-site. Here, data as of August 31st 2020 are presented. OS was defined as the interval between start of first-line therapy and the date of death from any cause. Patients alive or lost to follow-up were censored at last contact. A Cox proportional hazards model was used to identify potential independent prognostic factors for survival.

RESULTS

Patients with advanced ILC (n=410) were older at start of first-line treatment (median 68 vs. 63 years) while ECOG performance status (ECOG: 0 27% vs 30%) and Charlson Comorbidity Index (CCI 0: 81% vs 84%) were similar compared to patients with IDC (n=1818). The lobular tumor was more often hormone receptor (HR) positive (estrogen and/or progesterone receptor positive: 87% vs 74%) and less often HER2 positive (13% vs 26%). The tumor grading at diagnosis was more frequently G1/2 in the ILC group (72% vs 51%), while the occurrence of primary metastatic disease (tumor stage IV at diagnosis) was similar in both groups (ILC: 36%, IDC: 35%). The type of metastasis at the start of first-line treatment was more often bone-only (19% vs 13%) or peritoneum (8% vs 2%) for the ILC group **(Table 1)**.

Of patients receiving chemotherapy (CT) as first-line treatment for ABC 62% of ILC and 61% of IDC tumors were treated with taxanes. 21% of ILC vs. 25% of IDC tumors received a combination-CT.

Overall, patients with ILC were treated more often with endocrine therapy (ET) +/- CDK4/6-inhibitors (CDK4/6i) than patients with IDC (60% vs 38%), yet, ILC was also more often HR-positive than IDC.

First-line treatment strategy was analyzed for the HR-positive, HER2-negative subgroup. From 2007-16 patients with ILC received more often ET (ILC (n=159) 54% vs IDC (n=688) 44%), while patients with IDC were more often treated with CT first-line. Since approval of CDK4/6i, choice of treatment strategies has been quite similar (ILC (n=155): CDK4/6i: 77%, ET: 14%, CT: 8% and IDC (n=358): CDK4/6i: 75%, ET: 10%, CT: 15%).

Overall survival (OS) from start of first-line treatment was estimated for all patients recruited until 2016 (follow-up of at least 4 years). Median OS was comparable: ILC (n=154) 30.6 months (70% events, 95%-CI 26.1 – 36.9 months) and IDC (n=734) 33.8 months (61% events, 95%-CI 30.6 – 38.4 months). For the HR-positive, HER2-negative subgroup, OS was also similar **(Figure 1)**.

A multivariate Cox regression analysis showed that lobular histology was weakly associated with increased risk of mortality. Further the following factors were associated with a significantly increased risk of overall mortality: ECOG Performance status ≥ 1, negative hormone receptor status, lack of HER2 overexpression, higher grading of the primary tumor (G3/4), advanced, but non metastatic tumor stage at diagnosis (II and III, possibly reflecting the effect of prior neo-/adjuvant chemotherapy treatment), and presence of liver metastasis only, peritoneum metastases, other non-visceral and other visceral (compared to patients with bone-only metastases; **Figure 2**).

Table 1

Characteristic	Invasive lobular		Invasive ductal	
	N	%	N	%
Number of patients	410	100.0	1818	100.0
	Median	25-75% Quartile	Median	25-75% Quartile
Median age at start of first-line	68.4	58.8-75.2	62.7	53.1-72.2
	n	%	N	%
ECOG Performance Status at inclusion				
ECOG 0	109	26.6	536	29.5
ECOG ≥1	143	34.8	538	29.6
Unknown/missing [a]	158	38.5	744	40.9
Comorbidity at inclusion according to CCI [b]				
CCI 0 b	333	81.2	1519	83.6
CCI ≥1 b	77	18.8	298	16.4
Unknown	0	0.0	1	0.1
ER/PR status at inclusion				
ER positive PR positive	259	63,2	1025	56,4
ER positive, PR negative	2	0,5	48	2,6
ER negative, PR positive	88	21,5	267	14,7
ER negative, PR negative	47	11,5	441	24,3
Unknown/missing	14	3.3	37	2
HER2 status at inclusion				
Positive	53	12,9	480	26,4
Negative	355	86,6	1337	73,5
Unknown/missing	2	0,5	1	0,1
Grading at diagnosis				
G1	26	6.3	72	4.0
G2	270	65.9	852	46.9
G3/4	83	20.2	767	42.2
GX/unknown/missing	31	7.6	127	7.0
Tumor stage at diagnosis				
0	3	1.4	16	1.3
I	14	6.3	132	11.0
II	62	28.1	306	25.5
III	52	23.5	217	18.1
IV	66	29.9	379	31.6
Unknown/missing	24	10.9	150	12.5
Metastasis at start of first-line [c]				
Bone only	76	18.5	243	13.4
Liver only	20	4.9	111	6.1
Lung only	4	1.0	69	3.8
Peritoneum	31	7.6	34	1.9
Non-visceral – other [d]	28	6.8	110	6.1
Visceral – other	161	39.3	851	46.3
Unknown/missing	90	22.0	400	22.0

Table 1 Patient and tumor characteristics.

Abbrevations:
CCI Charlson Comorbidity Index; CI, confidence interval; ECOG: Eastern Cooperative Oncology Group; ER: estrogen receptor status; HR, hazard ratio; HER2, human epidermal growth factor receptor 2; PR: progesterone receptor status; Max, Maximum; Min, Minimum; OS, overall survival; StD, standard deviation.

Footnotes Table 1
[a] Collection of data on ECOG performance status started in 2011 and data are missing for patients recruited prior to 2011.
[b] Charlson Comorbidity Index (CCI) according to Quan (Quan et al., 2011).
[c] Metastasis at start of palliative 1st-line therapy (8 weeks before to 4 weeks after start of 1st-line treatment).
[d] Non-visceral: skin, bone and/or lymph node metastasis except bone-only

Referenzen

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Conflicts of Interest:
M. Thill: Consulting Fees (e.g. advisory boards); Author; Amgen, AstraZeneca, Biom'Up, Celgene, Daiichi Sankyo, Eisai, Genomic Health, Lilly, MSD, Norgine, Neodynamics, Novartis, Pfizer, pfm Medical, Roche, RTI Surgical, Tesaro. Fees for Non-CME Services Received Directly from Commercial Interest or their Agents (e.g. speakers' bureaus); Author; Amgen, AstraZeneca, Celgene, Clovis, Eisai, Genomic Health, Hexal, MCI, Medtronic, MSD, Novartis, Omniamed, Pfizer, pfm Medical, Roche, RTI Surgical. Other; Author; manuscript fees: Amgen, Celgene; trial funding: Genomic Health.

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Figure 1

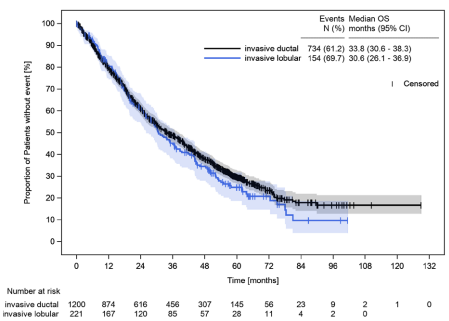

Figure 1 Overall survival since start of first-line treatment of patients with advanced/metastatic invasive lobular vs invasive ductal breast cancer
Survival analysis for patients recruited until 2016 (follow-up of at least 4 years).

Figure 2

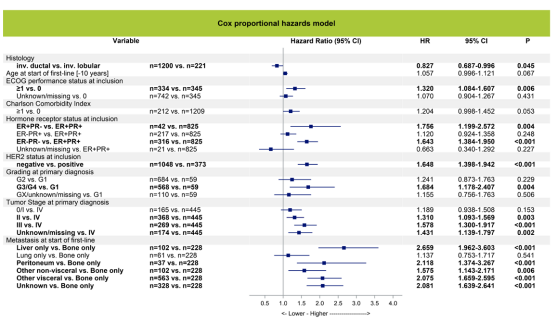

Figure 2 Multivariate regression analysis
Cox proportional hazards model for overall survival.