

# Brain Metastases in Breast Cancer Network Germany (BMBC, GBG 79): First analysis of 1004 patients from the multicenter registry



Isabell Witzel<sup>1</sup>, Sibylle Loibl<sup>2</sup>, Elena Laakmann<sup>1</sup>, Doris Augustin<sup>3</sup>, Felix Flock<sup>4</sup>, Hans Hermann Dohmen<sup>5</sup>, Gülhis Durmus<sup>6</sup>, Matthias Frank<sup>7</sup>, Tobias Hesse<sup>8</sup>, Atanas Ignatov<sup>9</sup>, Thorsten Kühn<sup>10</sup>, Tanja Neunhöffer<sup>11</sup>, Tjong-Won Park-Simon<sup>12</sup>, Marcus Schmidt<sup>13</sup>, Andrea Stefek<sup>14</sup>, Rudolf Weide<sup>15</sup>, Florian Würschmidt<sup>16</sup>, Tanja Fehm<sup>17</sup>, Volker Moebus<sup>18</sup>, Gunter von Minckwitz<sup>2</sup>, Nicole Burchard<sup>2</sup>, Volkmar Mueller<sup>1</sup>



<sup>1</sup> University Medical Center Hamburg-Eppendorf, Department of Gynecology, Germany; <sup>2</sup> German Breast Group (GBG), Neu-Isenburg, Germany; <sup>3</sup> DONAUSAR Clinic Deggendorf, Germany; <sup>4</sup> Clinic Memmingen, Memmingen, Germany; <sup>5</sup> Clinic St. Elisabeth Straubing GmbH, Straubing, Germany; <sup>6</sup> Rems-Murr-Clinic-Winnenden, Germany; <sup>7</sup> Ortenau Clinic Offenburg-Gengenbach, Germany; <sup>8</sup> Diakonie Clinic Rotenburg (Wumme) Germany; <sup>9</sup> Clinic of the Otto-v.-Guericke-University, Magdeburg, Germany; <sup>10</sup> Clinic Esslingen, Germany; <sup>11</sup> Dr.-Horst-Schmidt-Clinic, Wiesbaden, Germany; <sup>12</sup> Hannover Medical School Germany; <sup>13</sup> University Clinic Mainz; <sup>14</sup> Johanniter-Clinic Genthin-Stendal, Germany; <sup>15</sup> Clinic for hematological and oncological diseases, Koblenz, Germany; <sup>16</sup> Radiology Alliance Hamburg, Germany; <sup>17</sup> on behalf of the Translational Research Board of the Arbeitsgemeinschaft für Gynäkologische Onkologie (AGO-Trafo); <sup>18</sup> on behalf of the Breast Study Group of the Arbeitsgemeinschaft für Gynäkologische Onkologie (AGO-B)

## Background

- The incidence of brain metastases (BM) in breast cancer patients is rising and has become a major clinical challenge
- So far, limited therapeutic options and insights into the biology of BM exist since only a few studies analyzed exclusively patient data of breast cancer patients.
- In order to increase knowledge about breast cancer patients with BM, our open, multicenter registry was initiated in 2014: The Brain Metastases in Breast Cancer Network Germany (BMBC, GBG79).

## Materials and Methods

- Patients with diagnosed BM since 2000 and a history of breast cancer and no history of other malignant or neurological disease can be included in the register.
- Registration of patient data is allowed retrospectively as well as prospectively into a web-based database ("MedCodes").
- Data of the primary tumor, metastatic disease and BM as well as treatment details are collected.
- For this first analysis, 1004 patients from 92 German centers were included.

## Current Status

- 92 participating centers in Germany
- 1004 patients with completed documentation
- 12/2014 start of tissue sample collection for translational research

## Results

- Median age at first diagnosis of BM was 56 years (22 – 90 years).
- 47% of patients (398/848) were HER2 positive, 22% (186/848) were triple-negative and 31% (264/848) had luminal primary tumors indicating a selection of patients with a specific tumor biology who develop BM.
- 57% of the patients (510/891) had up to three BM whereas 43% (381/891) had more than three BM (table 1).
- 22% of patients (221/1004) had BM without evidence of extracranial disease.
- 29% of the patients (288/998) underwent surgery of the BM. Of the patients with surgery and radiotherapy, 74% (176/238) were treated with whole brain radiotherapy, 11% (27/238) with stereotactic radiotherapy and 6% received both (14/238).
- In patients without surgery and with radiotherapy, 88% (496/562) received whole brain radiotherapy, 7% (38/562) stereotactic radiotherapy and 3% received both (14/562) (table 2).
- One year survival rate from diagnosis of BM was 35.2 % (CI95%: 31.9 – 38.5).
- Median time from diagnosis of primary breast cancer to BM was 36.6 months for the entire cohort (CI95% 33.5 – 39.4), 33.5 months (CI95% 29.0 – 37.3) for HER2-positive patients, 43 months (CI95% 35.4 – 48.8) for patients with luminal tumors and 20.1 months (CI95% 17.4 – 25.5) for triple-negative patients (p<0.001).
- Median time from first diagnosis of BM to death in the entire cohort was 7.1 months (CI95%: 5.8 – 7.9).
- Regarding the number of BM, patients with up to three BM had a median survival of 9.2 months (CI95%: 7.8 – 11.2) and patients with 4 or more BM 5.1 months (CI95% 4.0 – 6.2) (p<0.001, Fig. 1).
- Regarding tumor subtypes, HER2-positive patients had the longest median survival with 12.3 months (CI95%: 9.6 – 14.0) compared with 5.7 months (CI95%: 4.0 – 7.3) for luminal primary tumors and 4.0 months (CI95%: 3.1 – 4.6) for triple-negative patients (p<0.001, Fig. 2).
- HER2 positive patients receiving HER2-directed therapy after the diagnosis of BM lived longer than those without (median 18.5, CI95%: 15.0 – 23.8 vs. 13.4 months, CI95%: 9.6 – 18.5, p=0.069).

Patient's characteristics	N	%
Age at first diagnosis of breast cancer, median	51.5 years	21-87 (range)
Age at diagnosis of BM, median	56.0 years	22-90 (range)
Tumor subtype (n=848)		
• TNBC	186	21.9
• Luminal B	264	31.1
• HER2+	398	46.9
Number of BM (n=891)		
• 1	256	28.7
• 2-3	254	28.5
• >4	381	42.8

Table 1: Patient's characteristics (n=1004)

Treatment	N	%
Systemic treatment after the diagnosis of BM	345/458	75.3
• Chemotherapy	117/458	25.5
• Hormone therapy	241/458	52.6
• Targeted therapy	288	28.9
Operative therapy of BM	176	74.0
• and WBRT	27	11.3
• and SRS	14	5.9
• and WBRT + SRS	803	61.3
Radiotherapy of BM	562	56.3
• WBRT	496	88.3
• SRS	38	6.8
• WBRT and SRS	14	2.5

Table 2: Treatment after diagnosis of BM

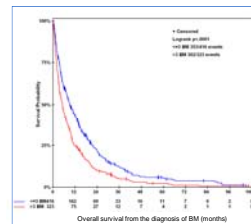


Figure 1: Overall survival from the diagnosis of brain metastases depending on the number of brain metastases (more than three, three or less BM, p<0.001).

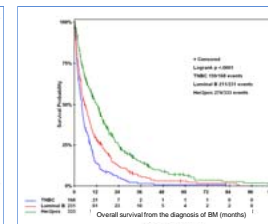
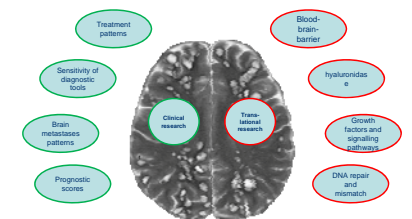


Figure 2: Overall survival from the diagnosis of brain metastases depending on subtype of the primary breast cancer (triple-negative vs. luminal vs. HER2 positive, p<0.001).

## Further Research projects



## Conclusion

- So far, this is the largest analysis of breast cancer patients with BM treated in Germany.
- TNBC patients had a shorter time to development of BM and a shorter survival time compared with other subtypes.
- More than three BM were associated with shorter survival compared with three or less BM..
- The recruitment of the registry is ongoing and we aim to include more than 2000 patients by the end of 2016.

## Contact

1. German Breast Group: www.germanbreastgroup.de/studien/palliativ/bmbc Email: BrainMet@GermanBreastGroup.de  
2. University Medical Center Hamburg-Eppendorf PD Dr. med. Isabell Witzel i.witzel@uke.de Prof. Dr. med. Volkmar Mueller v.mueller@uke.de

## Cooperation

