1487 - PATTERNS OF METASTASIS ACCORDING TO GERMLINE *BRCA1/2* MUTATION STATUS IN PATIENTS WITH HER2-NEGATIVE METASTATIC BREAST CANCER

Michele Bottosso[1,2], Gaia Griguolo[1,2], Laura Trovò[1,2], Silvia Tognazzo[3], Giovanni Faggioni[2], Eleonora Mioranza[2], Grazia Maria Vernaci[2], Davide Massa[1,2], Valeria Faso[1,2], Davide Napetti[1,2], Alice Menichetti[2], Stefania Zovato[3], Maria Vittoria Dieci[1,2], Valentina Guarneri[1,2]

1. Department of Surgery, Oncology and Gastroenterology, University of Padova, Padova, IT 2. Division of Oncology 2, Istituto Oncologico Veneto IRCCS, Padova, IT; 3. Hereditary Tumors Unit, Istituto Oncologico Veneto IRCCS, Padova, IT

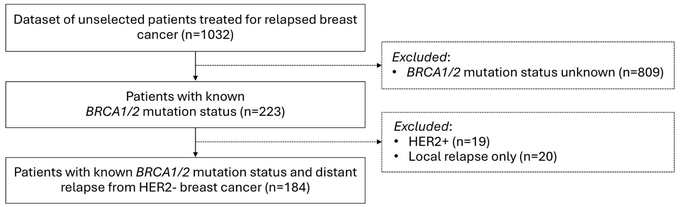
Background

- Breast cancers (BC) arising in *BRCA1/2* pathogenic variants (PVs) carriers show distinct clinical characteristics and subtype distributions.[1,2]
- BC exhibits subtype-specific patterns of metastasis according to hormone receptor (HR) and HER2 status.[3]
- Limited evidence suggests germline *BRCA1/2* PVs may increase metastasis to specific sites, such as the central nervous system (CNS). However, findings are often confounded by differences in subtype distribution among *BRCA1/2* PV carriers.[4,5]
- We investigated the association between germline *BRCA1/2* mutation status and the patterns and frequency of metastasis across BC subtypes.

Methods

Patients treated for HER2- metastatic BC at Istituto Oncologico Veneto (2007-2025) and with known germline *BRCA1/2* mutation status were retrospectively identified (Figure 1).

Figure 1. Study flowchart



Metastatic sites at diagnosis and throughout the disease course were collected. CNS involvement included brain metastases or leptomeningeal disease.

Conclusions

Germline *BRCA1/2* PV are associated with distinct metastatic patterns among patients with HER2- BC. In the HR+ disease, carriers had relatively fewer bone metastases at diagnosis and presented a higher risk of CNS involvement over time.

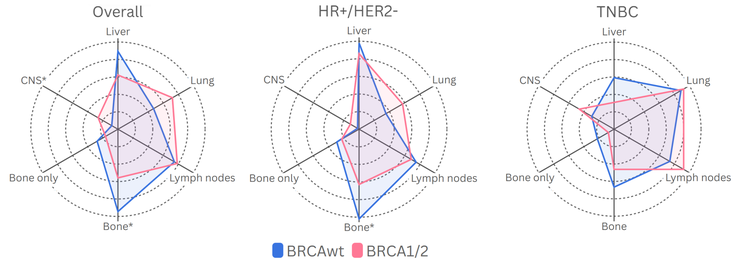
These findings may inform tailored radiological surveillance strategies.

Results

Among 184 patients (33 *BRCA1*, 28 *BRCA2*, 123 noncarriers), 131 presented a HR+ BC and 53 a triple negative BC (TNBC). TNBC was more frequent among *BRCA1* carriers (63.3%), while HR+ BCs were more common among *BRCA2* carriers (82.1%) and noncarriers (78.0 %; p<0.001).

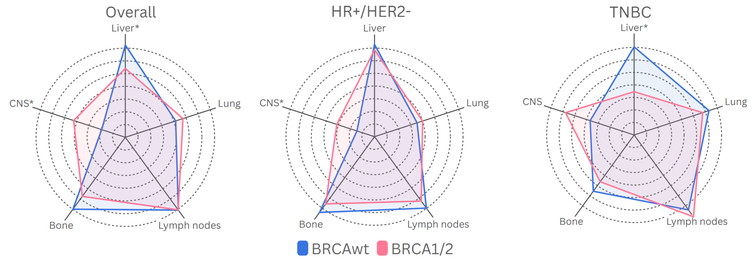
At diagnosis of metastatic BC, *BRCA1/2* carriers with a HR+ BC presented a lower incidence of bone metastases compared to noncarriers (31.4% vs 51.0%, p=0.046). No site differences at first metastatic BC diagnosis were observed among patients with TNBC (Figure 2).

Figure 2. Radar plot summarizing the percentage of metastatic sites involvement at the time of initial metastatic BC diagnosis according to *BRCA1/2* mutation status (asterisks indicate statistically significant differences)



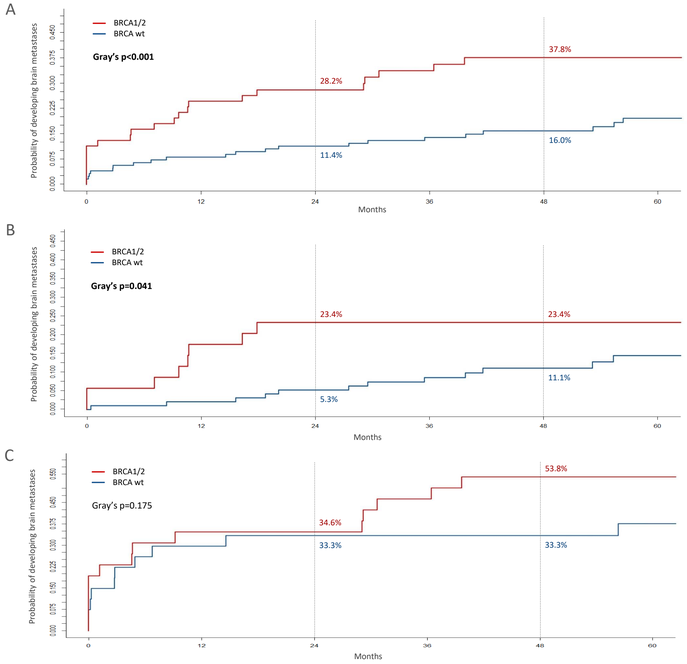
After a median follow-up of 80.7 months, *BRCA1/2* carriers with a HR+ BC presented a higher CNS involvement compared to noncarriers (31.4% vs 14.6%, p=0.030). In TNBC, *BRCA1/2* carriers presented a lower incidence of liver metastases compared to noncarriers (34.6% vs 70.4%, p=0.009) (Figure 3).

Figure 3. Radar plot summarizing the percentage of metastatic sites involvement at last follow-up/death according to *BRCA1/2* mutation status (asterisks indicate statistically significant differences)



Among *BRCA1/2* carriers with HR+ BC, CNS involvement appeared earlier, with a 24-month cumulative incidence of 23.4% as compared to 5.2% in noncarriers (Gray's p=0.041). No differences in the cumulative incidence of CNS involvement were observed among patients with TNBC (34.6% in *BRCA1/2* carrier and 33.3% in noncarriers at 24 months; Gray's p=0.175 (Figure 4).

Figure 4. Cumulative incidence curves for diagnosis of CNS involvement overall (A), among patients with HR+ BC (B), and among patients with TNBC (C) according to *BRCA1/2* mutation status



No significant difference in terms of OS was observed between *BRCA1/2* carriers and noncarriers, both among patients with HR+ BC (39.2 vs 47.6 months, respectively; p=0.246) and among those with TNBC (25.8 vs 15.8 months, respectively; p=0.467).

References:
1. Hu C et al., . N Engl J Med. 2021
2. Atchley DP et al., J Clin Oncol. 2008
3. Lin NU et al., Cancer 2008
4. Song Y et al., Cancer. 2020
5. Garber HR et al., NPJ Breast Cancer. 2022

This presentation is the intellectual property of the author/presenter.
Contact them at **michele.bottosso@iov.veneto.it** for permission to reprint and/or distribute.