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Impact of germline *BRCA1/2* status on outcomes for patients with HR+/HER2- metastatic breast cancer treated with CDK4/6 inhibitors: a systematic review and meta-analysis

Michele Bottosso [a,b,1], Christian Zurlo [a,b,1], Federica Miglietta [a,b], Anna Chiara Cattelan [a,b], Daniela Iannaccone [a,b], Maria Vittoria Dieci [a,b], Gaia Griguolo [a,b,*], Fabio Girardi [b,2], Valentina Guarneri [a,b,2]

[a] Department of Surgery, Oncology and Gastroenterology, University of Padova, Padova, Italy
[b] Division of Oncology 2, Istituto Oncologico Veneto IRCCS, Padova, Italy

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ABSTRACT

Background: Almost 60 % of breast cancers (BCs) diagnosed in germline BRCA1/2 mutation (gBRCAm) carriers are HR+/HER2-. Sparse data suggest limited CDK4/6 inhibitors benefit among gBRCAm carriers. However, prespecified subgroup analyses from pivotal trials are lacking, and current data quality is poor given the small patient populations.

Methods: We conducted a systematic review and meta-analysis of studies evaluating CDK4/6 inhibitors outcomes in patients with HR+/HER2-metastatic BC according to gBRCA status. Progression free survival (PFS) and overall survival (OS) were compared between gBRCAm patients and those with wild type (wt) or unknown (wt/unk) gBRCA status.

Results: Of 1339 potentially eligible records, 14 studies were included, covering a population of 618 gBRCAm patients. Studies were mostly retrospective, with moderate-to-high risk of bias according to ROBINS-E algorithm. Three studies included only gBRCA tested patients; all others also allowed gBRCA untested patients.

Meta-analysis of studies with available data for gBRCAm vs. gBRCAwt patients resulted in an HR for PFS of 1.68 (95 %CI 1.37–2.05) and an HR for OS of 1.73 (95 %CI 1.12–2.67). Inclusion of patients with unknown gBRCA status led to similar results (gBRCAm vs. gBRCAwt/unk), with an HR for PFS of 2.02 (95 %CI 1.59–2.57) and for OS of 1.46 (95 %CI 1.08–2.00).

Conclusions: Emerging data suggest that gBRCAm patients with advanced HR+/HER2- BC may experience shorter PFS and OS with CDK4/6 inhibitor compared to gBRCAwt. Given the low level of evidence and the high risk of bias in available studies, further research is needed to understand molecular mechanisms and identify the optimal treatment sequence.

1. Introduction

Breast cancer (BC) is one of the leading causes of cancer mortality among women worldwide, with an estimated mortality rate of 12.7 per 100 000 in 2022 [1,2]. Hormone receptor (HR)+/HER2- BC represents the most common subtype of metastatic BC, accounting for more than 70 % of diagnoses [3]. For patients with metastatic HR+/HER2- BC, the addition of CDK4/6 inhibitors to endocrine therapy (ET) has led to remarkable progression-free survival (PFS) and overall survival (OS) improvements, thus representing current standard first-line treatment [4].

Among unselected BC patients, around 5–10 % carries a deleterious germline mutation in cancer susceptibility genes. In particular, germline *BRCA1/2* pathogenic variants (g*BRCA*m) represent the most frequent alteration in cancer susceptibility genes observed in BC patients. Even if g*BRCA1* pathogenic mutations are well-known to be associated with an

* Corresponding author. Department of Surgery, Oncology and Gastroenterology, University of Padova, Padova, Italy.
E-mail address: gaia.griguolo@unipd.it (G. Griguolo).
[1] Contributed equally as first author.
[2] Contributed equally as last author.

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increased risk of developing triple-negative (HR-/HER2-) BC, the majority of BCs (almost 60 %) diagnosed in g*BRCA*m carriers present a HR+/HER2- subtype [5,6].

In this context, several reports have suggested that g*BRCA*m carriers receiving CDK4/6 inhibitors in combination with ET for metastatic BC might present worse clinical outcomes as compared to g*BRCA* wild type (g*BRCA*wt) patients [7,8]. However, current data quality is poor, considering that each study only included a small number of g*BRCA*m patients (between 5 and 145) and that most were retrospective reports. Additionally, prespecified subgroup analyses from pivotal trials are lacking [7,9].

We therefore conducted a systematic review and meta-analysis of studies evaluating outcomes of HR+/HER2- metastatic BC patients treated with CDK4/6 inhibitors according to g*BRCA* status.

2. Methods

2.1. Identification of eligible studies

We queried Embase, MEDLINE, PubMed, ASCO, ESMO and SABCS proceedings to identify all potentially eligible studies from database inception to29th May 2025. We used a database specific, pre-specified search strategy (Supplementary Table 1) including terms for the disease domain and the study design domain. We did not set language or time restrictions. Duplicate records were removed using a citation tool (Zotero v.6.0.36).

Records were therefore selected with a stepwise process: by title, abstract and, lastly, appraising full text. Records were independently assessed by two reviewers (MB and CZ) to ensure consistent data collection. Discordant cases were evaluated by a third reviewer (FG). The same two reviewers extracted data from the selected studies on a predefined table. Both published abstracts and full articles that met the inclusion criteria were included for analysis. Every phase of the process was recorded and summarized in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines [10].

Risk of bias assessment for each included study was evaluated by two independent investigators (MB and CZ) using the ROBINS-E tool, and potential disagreements were discussed with a third reviewer (FG) [11].

Study was registered in the international prospective register of systematic reviews (CRD42024500780).

2.2. Methods for the meta-analysis

Studies were deemed eligible if they included patients receiving any CDK4/6 inhibitor and provided PFS or overall survival (OS) estimates by g*BRCA* status. PFS and OS were compared according to g*BRCA* status (g*BRCA*m vs. g*BRCA*wt and vs. a combined group of g*BRCA*wt patients and unknown status [wt/unk]). To allow for heterogeneity between studies, a random-effects meta-analysis was used. In a random-effects meta-analysis the pooled effect is obtained from a distribution of true effects rather than being a weighted average of a fixed, true effect. Heterogeneity was measured through I^2 and graded according to the Cochrane Handbook for Systematic Reviews of Interventions [12].

A pre-specified subgroup analysis was conducted to explore possible sources of inconsistency between studies due to differences in publication type (full article vs. abstract/poster) or study size (less than 250 vs. 250 or more). The subgroups were compared through the *Q statistic*, a measure of the deviation of the effect estimates from the mean.

A meta-regression was performed to investigate the impact of publication type and study size on effect estimates. A meta-regression is an extension of a meta-analysis, in which the estimated coefficient describes how the outcome variable varies with a unit change of the potential effect modifier.

Lastly, possible publication or reporting bias was assessed using a funnel plot and Egger's test for statistical significance. A funnel plot is a scatter plot where the effect estimates are plotted against a measure of precision such as the study's standard error.

All analyses were performed with the statistical software STATA (version 18), packages *metan*, *meta regress*, *meta funnel*.

3. Results

3.1. Systematic review

The database search produced 1339 records. Records were evaluated for eligibility based on title and abstract. Full text of the remaining 69 studies was subsequently examined and studies were excluded due to irrelevant publication type, irrelevant setting, or irrelevant outcomes. Fourteen studies were finally identified and included in the systematic review (Fig. 1). Characteristics of eligible studies are reported in Table 1.

Included studies covered a population of 16884 patients, 618 of whom carrying g*BRCA*m (range 5–145). Most studies were retrospective, with only 2 prospective trials. Three studies included only g*BRCA* tested patients, while all other studies also allowed g*BRCA*unk patients.

Seven studies only assessed patients receiving CDK4/6 inhibitors as first-line therapy. Palbociclib was the only CDK4/6 inhibitor prescribed in 3 studies and the most commonly used in the others. Median follow-up ranged between 16 and 46 months and was not reported for 6 studies.

The risk of bias assessment, according to ROBINS-E tool, is reported in Supplementary Fig. 1. None of the studies had a low risk of bias; for nine studies there were some concerns about possible bias, while for five studies the risk of bias was very likely.

3.2. Meta-analysis

The meta-analysis of studies with available data for g*BRCA*m vs. g*BRCA*wt patients resulted in an HR for PFS of 1.68 (95 %CI 1.37–2.05) and an HR for OS of 1.73 (95 %CI 1.12–2.67). I^2 was 54.2 % for PFS and 70.5 % for OS (Fig. 2).

Expanding the analysis with the inclusion of patients with unknown g*BRCA* status (g*BRCA*m vs. g*BRCA*wt/unk) led to similar results, with an HR for PFS of 2.02 (95 %CI 1.59–2.57) and for OS of 1.46 (95 %CI 1.08–2.00). I^2 was 67.7 % for PFS and 65.6 % for OS (Fig. 3).

A sensitivity analysis was conducted only including patients receiving CDK4/6 inhibitors as their first line of treatment to explore outcomes in a more homogeneous patient population. Results suggested that the treatment effect was not dependent on the line of therapy (Supplementary Fig. 2).

A subgroup analysis was performed to explore the impact of publication type or population size as possible sources of heterogeneity. After such a stratification, there was weak evidence against the hypothesis of homogeneity between subgroups after stratifying by size but not by publication type, meaning that small studies are likely to provide estimates that are biased upward. However, heterogeneity only slightly and inconsistently improved, suggesting that there was some residual confounding that could not be addressed. (Fig. 4; Supplementary Fig. 3).

Meta-regression was used to measure the association between outcome and size or publication type. For size and publication type the regression coefficients were −0.34 and 0.22, respectively. Although there was some evidence of dependence of the observed effects on these covariates, the association in both cases was not significant (Fig. 5, Supplementary Fig. 4).

A funnel plot was used to rule out publication bias. There was evidence of "small study" effect (Egger test p-value = 0.006), but the number of studies was rather limited (Supplementary Fig. 5).

4. Discussion

To our knowledge, this is the first systematic review and meta-analysis evaluating the impact of g*BRCA* status on the outcome of patients with HR+/HER2- metastatic BC treated with CDK4/6 inhibitors.

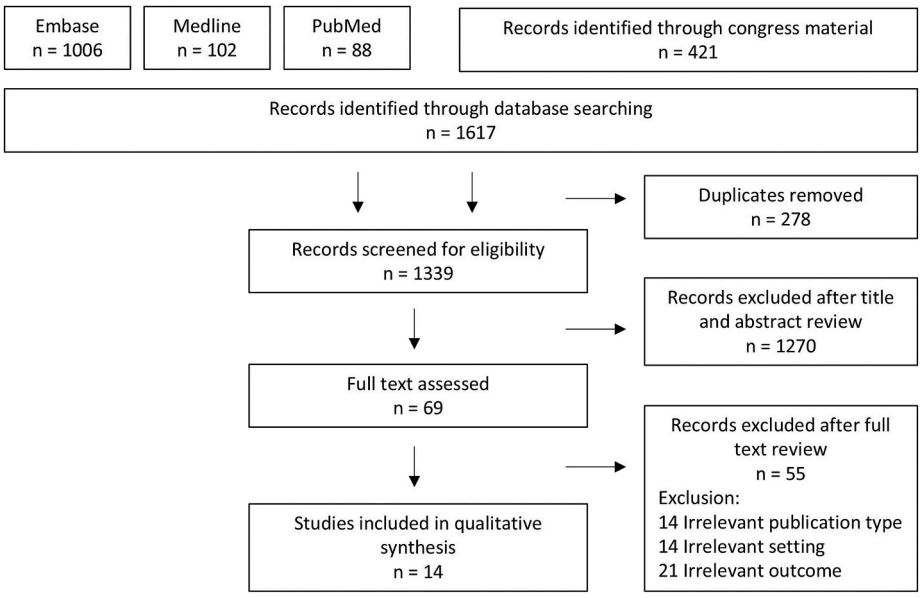

Fig. 1. PRISMA flowchart.

Most studies identified through the systematic review process were retrospective and often monocentric, therefore susceptible to potential selection bias. Indeed, according to the ROBINS-E algorithm, nine studies were classified as having some concerns regarding potential bias, while five were considered at high risk of bias. The evaluated studies presented significant heterogeneity in terms of patients' characteristics: 7 studies were limited to first-line patients, while the others included pretreated patients.

Significant heterogeneity was also observed among the control groups. While three studies included only patients tested for g*BRCA* status, most studies also included untested patients, and separate data for the different control groups (with or without the inclusion of g*BRCA*unk) were often unavailable. Since the inclusion of untested patients (potentially carrying unknown g*BRCA*mut) might have reduced the observed PFS and OS differences, a conservative study selection using only g*BRCA*wt controls was applied.

Moreover, immortal time bias may represent a potential limitation, particularly given that most studies do not specify the timing of *BRCA* testing. Genetic testing performed after treatment initiation may select patients surviving long enough to be tested, potentially skewing survival outcomes. In the Safonov study, which contributed substantial weight to the meta-analysis, a left-truncation analysis accounting for the interval between treatment initiation and *BRCA* testing showed no significant difference in median PFS. As similar bias cannot be excluded in other studies, this finding highlights potential methodological limitations and underscores the need for cautious interpretation of the pooled results. Additionally, some studies did not provide HRs for PFS or OS and were therefore excluded from the meta-analysis. Furthermore, several datasets have been presented only as congress abstracts, with full publications not yet available.

The quality of the studies was consistently moderate to low, but these observations were likely to be due to the nature of the studies and the patient population, warranting larger studies prospectively assessing outcomes for *gBRCA*m patients. Heterogeneity between studies was moderate to high and was only in part explained by subgroup analyses on publication type or size of the study. This calls for caution when interpreting our results, which however are the best available to date.

While ET in combination with a CDK4/6 inhibitor represents the standard of care for metastatic HR+/HER2- BC, including patients with g*BRCA*m, our results show that g*BRCA*m patients present worse outcomes, in terms of both PFS and OS, as compared to g*BRCA*wt patients when receiving this treatment. These data highlight the need for further prospective studies to identify the best therapeutic strategy in this setting, as well as the best treatment sequence. For instance, several early phase trials are currently evaluating the association of PARP inhibitors and ET (with or without CDK4/6 inhibitors according to treatment setting) for metastatic HR+/HER2- BC. In particular, the phase I/II HOPE trial is evaluating the safety of a combination of olaparib, palbociclib and fulvestrant in patients with g*BRCA*m HR+/HER2-metastatic BC (NCT03685331), the phase I/II PETRA trial is testing the combination of the oral SERD camizestrant with saruparib, a novel PARP1-selective inhibitor (NCT04644068), while the phase II ELEMENT trial is evaluating the combination of elacestrant and niraparib in g*BRCA*m patients (NCT06201234). Although preliminary, results from these trials might potentially pave the way to newer, more personalized treatment options for g*BRCA*m patients diagnosed with HR+/HER2- metastatic BC.

Whether the worse outcomes observed in g*BRCA*m as compared to g*BRCA*wt patients might be linked to an intrinsic negative prognostic impact of g*BRCA*m in the context of HR+/HER2- metastatic BC or to a reduced benefit derived by these patients from CDK4/6 inhibitors (and potentially ET) still remains to be clarified. Indeed, previous literature appears to be inhomogeneous and somehow divergent regarding the prognostic impact of g*BRCA* status among patients with metastatic BC. In fact, while no significant impact of g*BRCA* status on PFS and OS was observed in the prospective PRAEGNANT registry [25], a more recent analysis of the ESME real-world database reported, in the HR+/HER2- metastatic BC subgroup, a significantly lower PFS1 and non-significantly lower OS for g*BRCA*m carriers as compared to g*BRCA*wt (PFS1: HR 1.23, 95 %CI: 1.03–1.46, p = 0.024; OS: HR 1.22, 95 % CI: 0.97–1.52, p = 0.089) [26]. However, in this analysis, in which patients included mostly received chemotherapy as first-line treatment and were treated before the widespread use of CDK4/6 inhibitors (first-line treatment started between 2008 and 2016), the magnitude of the negative effect associated with g*BRCA*m appears to be smaller than that observed in our metanalysis.

These observations suggest that there might be potential differences in tumor biology in HR+/HER2- BCs arising in g*BRCA*m (as compared to their g*BRCA*wt counterpart), and that the molecular mechanisms underlying reduced benefit from CDK4/6 inhibitors in this patient subgroup need to be studied. Indeed, several potential mechanisms have been proposed. A first report by Sofonov et al. identified an enrichment

Table 1
Characteristics of studies identified through the systematic review process.

Study	Study type	N patients	Median follow-up (months; 95 % CI)	PFS (months)		OS (months)	
				Median (95 %CI)	HR (95 %CI)	Median (95 %CI)	HR (95 %CI)
Frenel JS et al., 2020 [13]	Prospective[e]	20 g*BRCA*m[a] 125 g*BRCA*wt 997 g*BRCA*wt + unknown	21.2 (0–34)	14.3 (10.4-NR) NA 26.7 (24.1–29.4)	NA	NA	NA
Collins JM et al., 2021 [7]	Retrospective	85 g*BRCA*m 774 g*BRCA*wt 2109 g*BRCA*wt + unknown	NA	10 (7–11) 10 (9–11) 11 (10–12)	g*BRCA*m vs g*BRCAwt*: HR 1.24 (0.96–1.59) g*BRCA*m vs g*BRCA*wt + unknown: HR 1.38 (1.08–1.75)	26 (21-NR) 37 (31–51) 33 (31–35)	g*BRCA*m vs g*BRCAwt*: HR 1.50 (1.06–2.14) g*BRCA*m vs g*BRCA*wt + unknown: HR 1.22 (0.88–1.71)
Kim JY et al., 2021 [14]	Retrospective[e]	5 g*BRCA*m 56 g*BRCA*wt 244 g*BRCA*wt + unknown	31 (NA-NA)	5.7 (NA-NA) 37.7 (NA-NA) 29.0 (NA-NA)	g*BRCA*m vs g*BRCAwt* + unknown: HR 8.54 (2.57–28.36)	NA	NA
Safonov A et al., 2022 [15]	Prospective[e]	45 g*BRCA*m 960 g*BRCA*wt	NA	4.4 (4.0–7.0) 10.2 (9.0–11.2)	g*BRCA*m vs g*BRCAwt*: HR 2.12 (1.48–3.03)	NA	NA
Bruno L et al., 2022 [16]	Retrospective	15 g*BRCA*m[b] 45 g*BRCA*wt 157 g*BRCA*wt + unknown	41.7 (38.7–44.8)	10.2 (5.7–14.7) 15.6 (7.8–23.4) 17.6 (12.9–22.2)	g*BRCA*m vs g*BRCAwt*: HR 2.11 (1.10–4.05) g*BRCA*m vs g*BRCA*unknown: HR 2.58 (1.37–4.85)	31.4 (6.6–56.3) 49.3 (39.2–59.4) NA	g*BRCA*m vs g*BRCAwt*: HR 3.23 (1.30–9.00) g*BRCA*m vs g*BRCA*unknown: HR 2.34 (1.03–5.29)
Park SY et al., 2022 [17]	Retrospective[e]	6 g*BRCA*m 27 g*BRCA*wt 183 g*BRCA*wt + unknown	16 (NA-NA)	9.0 (NA-NA) NR 33.0 (NA-NA)	g*BRCA*m vs g*BRCAwt* + unknown: HR 5.57 (1.91–16.24)	NA	NA
Rodriguez A et al., 2022 [18]	Retrospective	8 g*BRCA*m 70 g*BRCA*wt 172 g*BRCA*unknown	NA	12.1(NA-NA) 12.6 (NA-NA) 13.6 (NA-NA)	NA	28.8 (28.8-NR) NR (44.9-NR) 35.8 (29.7–53.1)	NA
Müller C et al., 2023 [19]	Retrospective	8 g*BRCA*m 83 g*BRCA*wt 439 g*BRCA*wt + unknown	NA	27 (NA-NA) 14 (NA-NA) NA (NA-NA)	NA	NA	NA
Fuentes Antrás J et al., 2023 [20]	Retrospective	15 g*BRCA*m[c] 53 g*BRCA*wt 85 g*BRCA*unknown	46 (7–84)	9.9 (NA-NA) 26.8 (NA-NA) 23.7 (NA-NA)	g*BRCA*m vs g*BRCAwt*: HR 4.0 (2.0–7.9)	28.1[e] NR 49.2	g*BRCA*m vs g*BRCAwt*: HR 3.5 (1.6–7.7)
Safonov A et al., 2023 [8]	Retrospective[e]	145 g/t*BRCA*m 4464 g*BRCA*wt + unknown	NA	14.3 (10.0–16.5) 22.0 (20.7–23.7)	g*BRCA*m vs g*BRCAwt*: HR 1.6 (1.3–2.0) g*BRCA*m vs g*BRCAwt* + unknown: HR 1.93 (1.70–2.36)	40.7 (31.0–51.5) 49.7 (48.3–53.1)	g*BRCA*m vs g*BRCAwt* + unknown: HR 1.21 (0.95–1.53)
Palazzo A et al., 2023 [21]	Retrospective	40 g*BRCA*m 209 g*BRCA*wt	37.5 (31.4–43.5)	10.7 26.7	g*BRCA*m vs g*BRCAwt*: HR 1.61 (1.09–2.44)	40.1 69.0	g*BRCA*m vs g*BRCAwt*: HR 1.72 (1.01–2.94)
Scheel R et al., 2024 [22]	Retrospective	20 g*BRCA*m[c] 231 g*BRCA*wt 64 g*BRCA*unknown	NA	14.9 31.3	g*BRCA*m vs g*BRCAwt*: HR 2.31 (1.27–4.22)	NA	NA
Guinel T et al., 2024 [23]	Retrospective[e]	90 g*BRCA*m[c] 523 g*BRCA*wt 4207 g*BRCA*unknown	44.0 (43.1–45.1)	11.2 (8.9–16.1) 15.7 (14.2–17.3) 18.9 (18.0–20.0)	g*BRCA*m vs g*BRCAwt*: HR 1.48 (1.15–1.90)	49.7 (42.2-NR) 50.1 (45.1–57.2)	g*BRCA*m vs g*BRCAwt*: HR 0.93 (0.64–1.36)
Cruellas Lapena M et al., 2025 [24]	Retrospective[e]	116 g*BRCA*m[d] 117 g*BRCA*wt	44	NA	g*BRCA*m vs g*BRCAwt*: 1.55	NA	g*BRCA*m vs g*BRCAwt*: 1.74

Abbreviation: CI Confidence Interval, PFS progression free survival, OS overall survival, g*BRCA* germline *BRCA*, g*BRCA*m germline *BRCA* mutation, g*BRCA*wt germline *BRCA* wild type, NR not reached, NA not available.

[a] Including 1 patient with gATM mutation.
[b] Including 4 patients with gATM mutations and 1 patient with gCHEK2 mutation.
[c] Including patients with gPALB2 mutations.
[d] Including carriers of pathogenic variants in other homologous recombination repair genes.
[e] First line only.

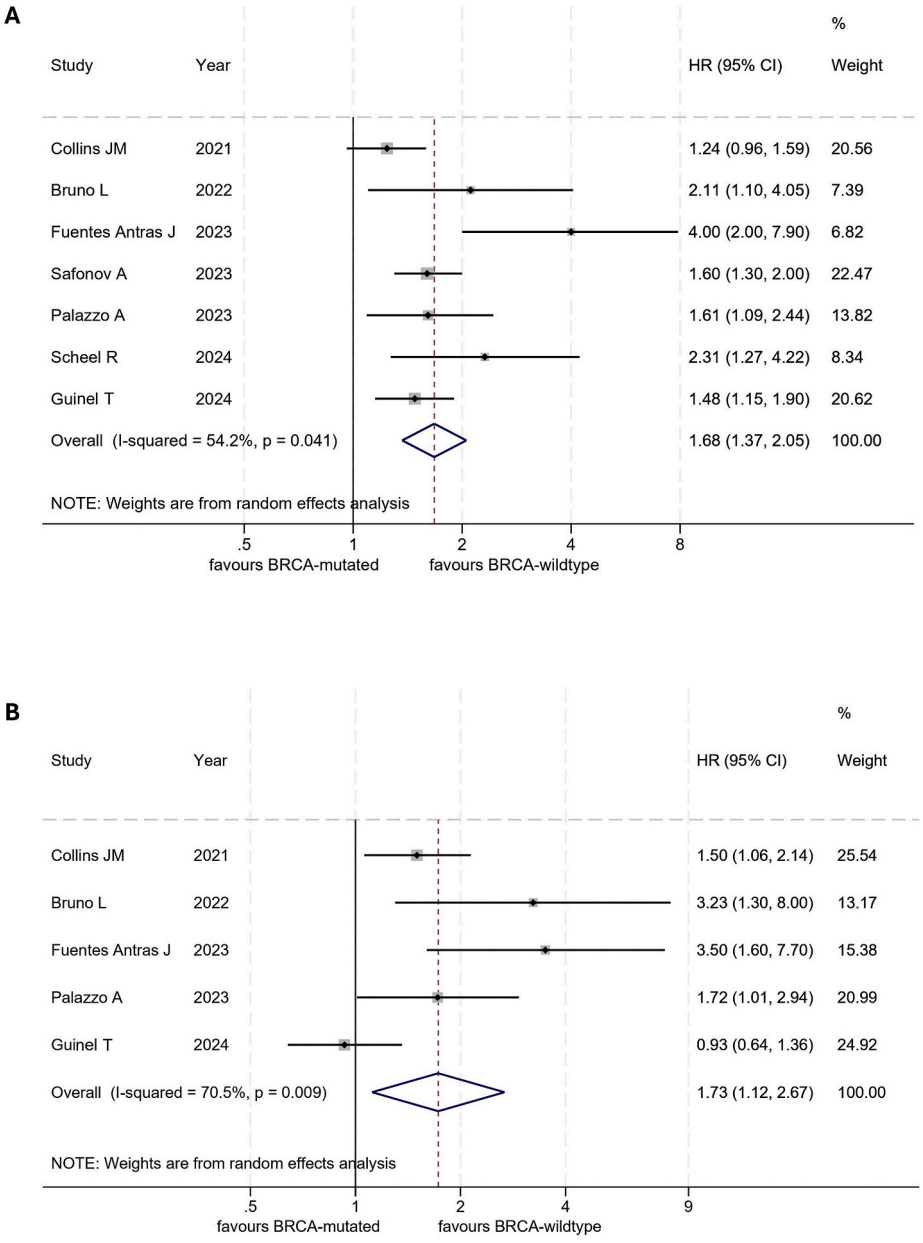

Fig. 2. Hazard ratios for progression free survival (A) and overall survival (B) according to g*BRCA* status.

for RB1 mutations, an alteration typically associated with resistance to CDK4/6 inhibitors, among HR+/HER2- BC arising in g*BRCA*2m patients. Considering the proximity of *BRCA2* and RB1 on the chromosome 13, the authors hypothesized that the co-loss of heterozygosity of *BRCA2* and RB1 could predispose cancer cells to a subsequent biallelic loss of RB1 under the selective pressure of CDK4/6 inhibitor treatment, thus favoring the development of resistance to these agents [15]. However, a subgroup analysis of the PADA-1 trial, reported a higher cumulative incidence of *ESR1* mutations emergence during first line treatment with aromatase inhibitors plus palbociclib in *BRCA1/2-PALB2* mutation carriers (Fine & Gray method p = 0.03) [13]. Moreover, the evaluation of BC molecular intrinsic subtyping according to the PAM50 algorithm in a small cohort of 8 samples of g*BRCA*2m HR+/HER2- BCs reported an extremely high proportion of non-luminal subtypes (63 %) [18]. If confirmed, this observation might also potentially explain (at least in part) the worse outcomes observed in g*BRCA*m patients, as non-luminal subtypes have been reported to be associated with worse outcomes (PFS and OS) in patients receiving CDK4/6 inhibitors [27]. In this context, higher levels of homologous recombination deficiency signature have been associated with reduced sensitivity to endocrine therapy and increased expression of signatures associated with CDK4/6 inhibitors resistance (RB-loss signature) in a correlative analysis of two phase II trials [28].

These data may have potential clinical implications in the adjuvant setting as well. In the context of early-stage HR+/HER2- BC, adjuvant abemaciclib has demonstrated a significant and clinically relevant improvement in invasive disease-free survival and distant relapse-free survival in the MonarchE trial [29]. Similar outcomes have been recently observed with ribociclib in the NataLEE trial [30]. Conversely, high-risk HER2- BC patients with g*BRCA*m derived significant benefit from adjuvant olaparib in the OlympiA trial, which showed improvements in both disease-free survival and OS [31]. Given the similar inclusion criteria and approval indications, these two therapies might compete for use in patients with HR+/HER2- BCs harboring a g*BRCA*m. Specific data on g*BRCA*m carriers in the MonarchE trial have been recently reported, suggesting a maintained benefit in this subgroup,

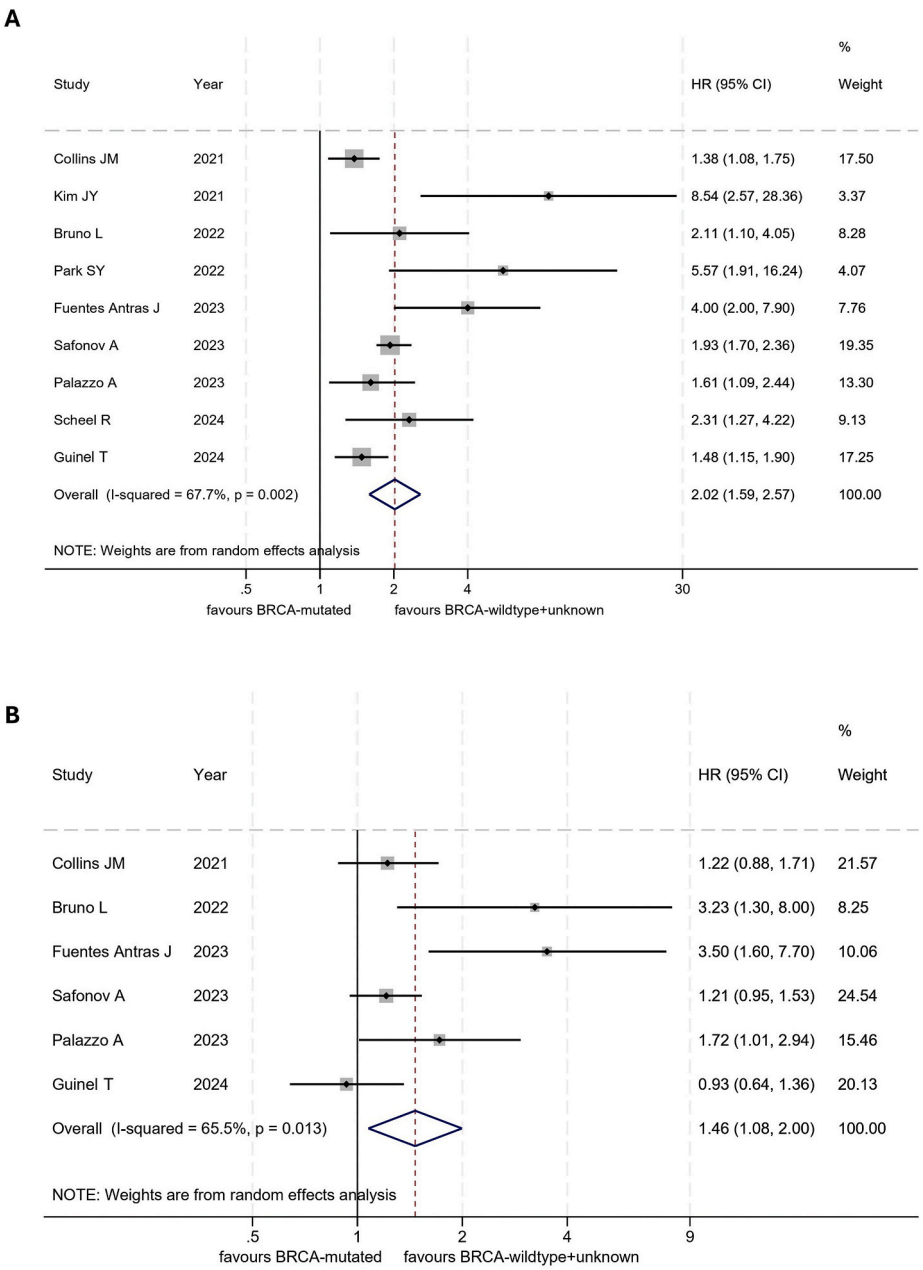

Fig. 3. Hazard ratios for progression free survival (A) and overall survival (B) for patients with gBRCAm vs gBRCAwt + unk.

even though the data are limited by small sample sizes and low number of events [32]. While the worse outcomes observed with CDK4/6 inhibitors in g*BRCA*m patients might concur, in addition to OS benefit observed in the OlympiA trial, to support the use of PARP inhibitors over CDK4/6 inhibitors in clinical settings in which both might be prescribed, the maintained benefit observed in the subgroup analysis of the MonarchE trial highlights that g*BRCA*m patients should not be excluded from treatment with adjuvant CDK4/6 inhibitors, in clinical settings in which these agents have shown to improve patient outcomes, solely based on their mutation status.

Finally, potential confounding factors should be considered when interpreting our results. As expected, significant age differences between g*BRCA*m and g*BRCA*wt patients were reported in most studies. Nevertheless, pivotal phase III trials consistently reported similar HRs across age subgroups, thus age does not seem to be a relevant risk modifier in this context [33,34]. Moreover, potential ethnic differences between the subgroups are not reported, and considering the higher prevalence of g*BRCA2* mutations among black individuals, this might potentially represent a confounding factor [35]. Finally, due to the different approval times of CDK4/6 inhibitors and the years covered by the studies, palbociclib was the most frequently prescribed CDK4/6 inhibitor in the majority of the studies included in our metanalysis, therefore limiting the potential applicability of these results to other CDK4/6 inhibitors.

5. Conclusions

The present meta-analysis suggests that g*BRCA*m patients with advanced HR+/HER2- BC treated with CDK4/6 inhibitors in combination with ET may experience poorer PFS and OS compared to g*BRCA*wt patients. These findings should be interpreted with caution due to the limited quality of available evidence and potential biases across studies. Further research is needed to understand molecular mechanisms underlining these observations and identify optimal treatment sequence

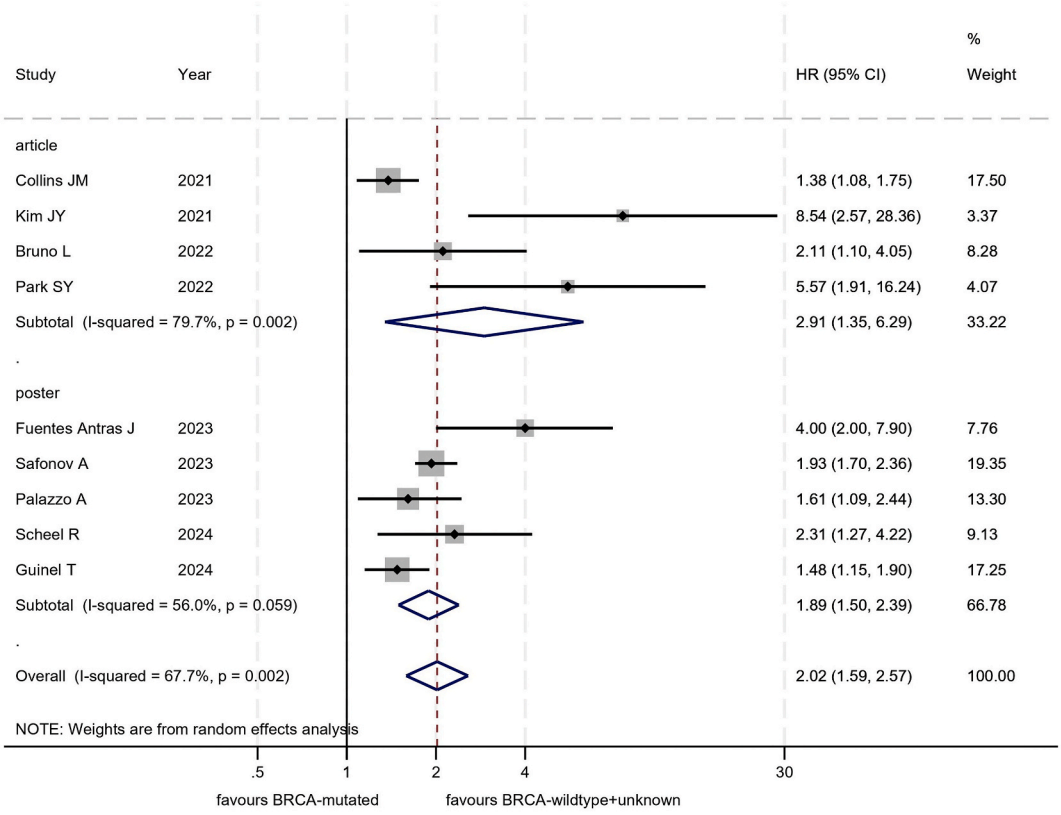

Fig. 4. Subgroup analysis of hazard ratios for progression free survival for patients with gBRCAm vs gBRCAwt + unk according to type of publication (full article vs. abstract/poster).

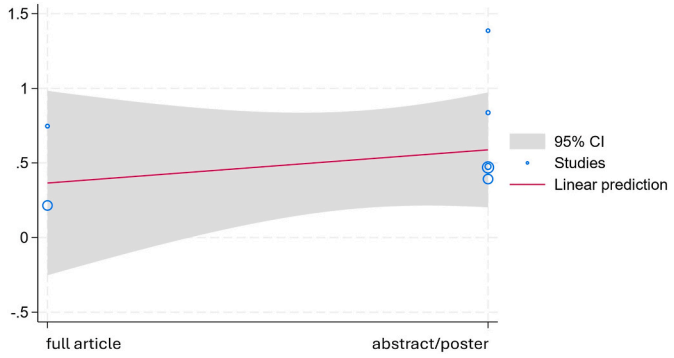

Fig. 5. Meta-regression analysis assessing the association between publication type and progression-free survival (logarithmic scale for hazard ratios).

for this subgroup of patients.

CRediT authorship contribution statement

Michele Bottosso: Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Christian Zurlo:** Writing – original draft, Project administration, Data curation. **Federica Miglietta:** Writing – review & editing, Funding acquisition, Data curation. **Anna Chiara Cattelan:** Project administration, Data curation. **Daniela Iannaccone:** Project administration, Data curation. **Maria Vittoria Dieci:** Writing – review & editing, Funding acquisition, Data curation. **Gaia Griguolo:** Writing – review & editing, Supervision, Funding acquisition, Data curation, Conceptualization. **Fabio Girardi:** Writing – review & editing, Supervision, Formal analysis, Data curation, Conceptualization. **Valentina Guarneri:** Supervision, Funding acquisition, Data curation, Conceptualization.

Data availability

No new data were generated for this work. Data underlying this article are available in the article.

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Declaration of competing interest

MB reports travel support from Eli Lilly. CZ reports travel support from Eli Lilly, Sanofi, Gilead. FM reports personal fees from Roche, Novartis, Pfizer, Seagen, Menarini, MSD, Gilead, Astrazeneca

MVD reports personal fees for consultancy/advisory role from: Eli Lilly, Pfizer, Novartis, Seagen, Gilead, MSD, Exact Sciences, AstraZeneca, Roche, Daiichi Sankyo, Roche. The other authors declare no conflicts of interest. GG reports fees for advisory role from Gilead, Seagen, Menarini, personal fees as an invited speaker from Eli Lilly, Novartis, MSD, travel support Gilead, Eli Lilly, Pfizer, Novartis, Daiichi Sankyo, AMGEN, AstraZeneca. FG reports travel support from Eli Lilly, Gilead, Novartis; honoraria for lectures from AstraZeneca, Eli Lilly, Gilead. VG reports personal fees for advisory board membership for AstraZeneca, Daiichi Sankyo, Eli Lilly, Gilead, MSD, Novartis, Pfizer, Olema Oncology, Pierre Fabre, Roche, Menarini Stemline, personal fees as an invited speaker for AstraZeneca, Daiichi Sankyo, Eli Lilly, Exact Sciences, Gilead, GSK, Novartis, Roche, Zentiva, Menarini Stemline, personal fees for expert testimony for Eli Lilly.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.breast.2025.104544.

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