PS5-05-30

Cycline Dipendent Kinase inhibitors 4/6 and endocrine therapy in the first line of treatment for HR+Her2- advanced breast cancer: a meta-analysis of the published real-world studies

Luca Moscetti, MD [1,2];Isabella Sperduti [3]; Sivia Zaniboni, MD[1]; Lorenzo Belluzzi, MD[1]; Emma Zattarin, MD[1]; Laura Cortesi, MD[4]; Patrizia Vici, MD[3]; Federico Piacentini, MD[1,2]; Claudia Omarini, MD, PhD[1,2]; Elena Barbieri, MD[1,2]; Fabio Canino, MD [1,2]; Monica Barbolini, MD[1]; Federica Caggia [1,2], Massimo Dominici, MD 1; Angela Toss, MD, PhD[1]

[1]University Hospital of Modena, [2]Gruppo Oncologico Italiano Ricerca Clinica, Parma, [3]IRCCS Regina Elena National Cancer Institute, Rome, [4]IRCSS Reggio emilia

Background

First-line treatment for HR+/HER2- advanced breast cancer (ABC) is based on CDK4/6 inhibitors (CDK4/6i) and endocrine therapy (ET). The three available CDK4/6i – palbociclib (P), abemaciclib (A), and ribociclib (R) – demonstrated comparable efficacy in pivotal Phase III trials in terms of progression-free survival (PFS). However, only R achieved a significant overall survival (OS) benefit. Most previous analyses comparing these CDK4/6i focused on efficacy, safety, and tolerability, generally showing no significant differences. Limited real-world (RW) data exist regarding inter-drug comparisons in the RW setting

Methods and Materials

We conducted a meta-analysis of the RW studies in the first-line HR+/HER2-ABC setting (with P, A, and R) to assess potential outcome differences between the three drugs. A systematic literature search was performed using PubMed with the terms: "breast cancer," "real world," "palbociclib," "abemaciclib," "ribociclib" "dalpiciclib". Data extraction began on January 1st, 2020, and the final date for the database search was March 31st, 2025.

Statistical analysis

Treatment comparisons utilized as effect size the percentage (%) of 2-years real-world PFS (rwPFS) and 95% confidence intervals (CI). The % of 2-year rwPFS (%2yPFS) was estimated from the median rwPFS for this analysis Heterogeneity was assessed using the $\chi 2$ Q test ($p<0.05$ indicating significance) and I2 statistics (I2>50% considered significant). The pooled effect size estimate was calculated with a random-effect model using the 2-year PFS as endpoint

Results

67 studies were identified 56 reported the median rwPFS as the primary outcome, one reported time to next treatment (TTNT), 8 reported time to chemotherapy or time to treatment discontinuation, 2 did not reported any outcome. Considering 56 studies involving four CDK4/6 inhibitors reporting rwPFS, no significant differences were observed when comparing all three drugs (%2yPFS 49, 95% IC 46-51, p=0.39 (Fig.1). High heterogeneity was observed across the included studies (I2=81%, p<0.00001). Four out of 56 trials were excluded from the final analysis. The sensitivity analysis conducted in the 52 studies involving four trials with A (%2yPFS 49, CI 95% 40-59), thirty-nine trials with P (%2yPFS 48, CI 95% 45-50) and nine with R (%2yPFS 54, CI 95% 48-60) confirmed the effect size observed (Fig. 2,3,4). In the analysis comparing the three CDK 4/6 inhibitors, no differences were observed when comparing A and P (p=0.751) or A and R (p=0.376), but a possible difference was observed when comparing R and P (p=0.045) (table 1).

Table 1. Comparison in %2yPFS between the three CDSK4/6 inhibitors

	p
Abemaciclib vs Palbociclib	0.751
Abemaciclib vs Ribociclib	0.376
Ribociblib vs Palbociclib	0,045

Figure 2. %2ysPFS in the real world trials with Abemaciclib

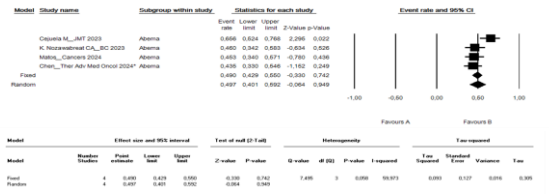


Figure 1. %2ysPFS in the real world trials with CDK4/6 inhibitors

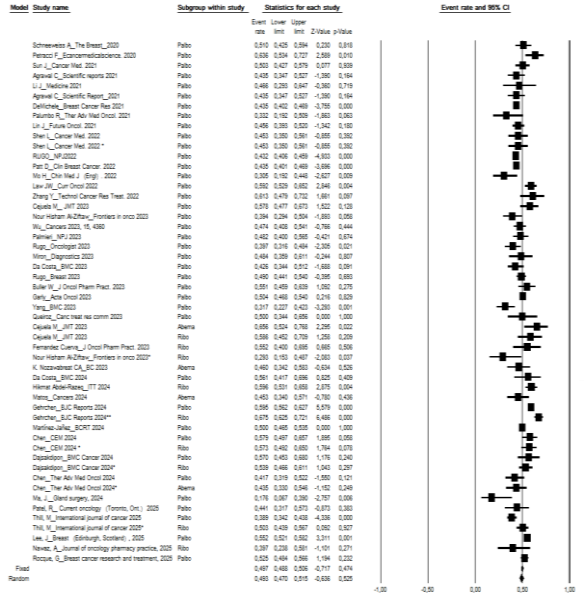


Figure 3. %2ysPFS in the real world trials with Ribociclib

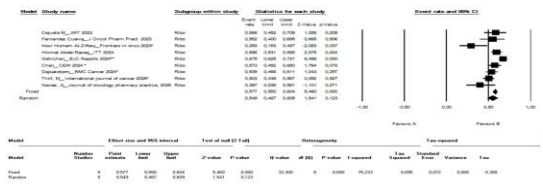
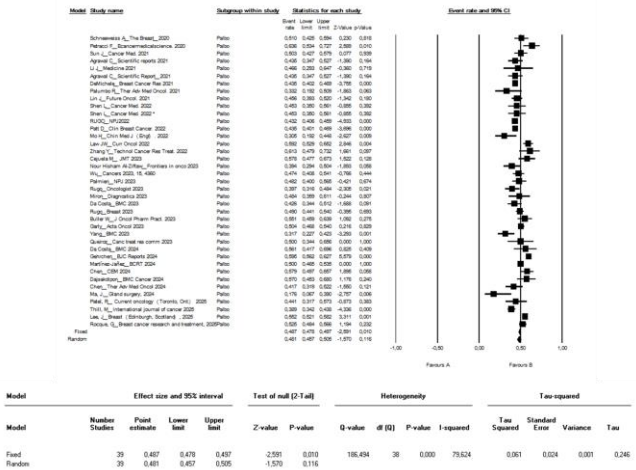


Figure 4. %2ysPFS in the real world trials with Palbociclib.



Discussion

This analysis did not reveal significant differences in 2-year rwPFS, the primary outcome in most real-world studies, among the CDK4/6 inhibitors. Any observed differences between R and P should be interpreted with consideration for the patient characteristics within the studies analysed..

Conclusions

We plan to further refine the analysis by incorporating multiple variables to evaluate inter-trial differences and reduce bias common in real-world settings. The analysis will also be updated to include additional real-world trials published throughout 2025.

Contact

Luca Moscetti
Department of Oncology-Hematology, University Hospital of Modena,
Gruppo Oncologico Italiano Ricerca Clinica
Email: moscetti.luca@aou.mo.it
Website: www.aou.mo.it, www.goirc.org
Phone:+39 059 4223244

This presentation is the intellectual property of the author/presenter. Contact them at moscetti.luca@aou.mo.it for permission to reprint and/or distribute.

© Poster Template by Genigraphics® 1.800.790.4001 www.genigraphics.com