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Matching adjusted indirect comparison of PFS & OS comparing ribociclib + letrozole vs palbociclib + letrozole as first-line treatment of HR+/HER2- ABC: Analysis based on updated PFS & final OS results of MONALEESA-2 & PALOMA-2

Background: CDK4/6i+ET is the preferred 1L tx for pts with HR+/HER2- ABC. All 3 CDK4/6i demonstrated significant improvements in PFS in Phase 3 trials. For postmenopausal (postM) pts, ribociclib (RIB) showed statistically significant OS benefit (MONALEESA-2; ML-2) while palbociclib (PAL) failed to extend OS (PALOMA-2; PAL-2) in a comparable 1L pt population. At the time of this analysis, final OS results for abemaciclib (MONARCH-3) are pending. No CDK4/6i head-to-head studies exist; thus, an anchored matching adjusted indirect comparison (MAIC) of PFS & OS was performed to estimate relative effectiveness of 1L RIB+letrozole (LET) vs 1L PAL+LET.

Methods: PAL-2 & ML-2 (CDK4/6i+LET) included postM pts with HR+/HER2- ABC with no prior tx for ABC & required >12mo from end of (neo)adjuvant tx to recurrence (treatment-free interval, TFI) only if pts received prior NSAI for EBC; the % of pts with TFI ≤12mo in the RIB/PAL arms (ITT) of ML-2 & PAL-2 was 17.7% & 22.1%, respectively. An MAIC of PFS & OS was conducted using individual pt data from the last ML-2 data cut-off (median follow-up [mfu], 80mo) & the last available PAL-2 aggregated data (mfu, 90mo, OS; ≈37mo, PFS). Pts in ML-2 were weighted to match baseline (BL) characteristics in the corresponding arms of PAL-2. HRs for RIB+LET vs PAL+LET were generated via Bucher method.

Results: All available BL pt & disease characteristics reported in PAL-2 were matched with ML-2 (**Table**). After weighting, pt characteristics were well balanced between the 2 trials. Post MAIC, the HR for PFS was 0.80 (95% CI 0.58-1.11; $P=.187$) & the HR for OS 0.68 (95% CI 0.48-0.96; $P=.031$) for RIB+LET vs PAL+LET.

Conclusions: Post MAIC between PAL-2 & ML-2, there was no significant difference in PFS, while OS significantly favored RIB+LET over PAL+LET. These results emphasize findings from the individual studies & put confidence in the use of 1L RIB+LET in postM pts with HR+/HER2- ABC.

		ML-2				PAL-2	
		Unmatched ^a		Matched		PAL+LET	PBO+LET
		RIB+LET	PBO+LET	RIB+LET	PBO+LET		
N		304	299	150	112	444	222
Age, %	<65y	56.9	57.9	59.2	63.5	59.2	63.5
Race, %	White	79.6	82.3	77.5	77.5	77.5	77.5
	Other	20.4	17.7	22.5	22.5	22.5	22.5
ECOG, %	0	60.2	60.5	57.9	45.9	57.9	45.9
	1+	39.8	39.5	42.1	54.1	42.1	54.1
No. met sites, %	<3	66.8	64.9	57.4	53.1	57.5	53.1
Visceral (Liver or Lung), %	Yes	55.3	58.5	48.2	49.5	48.2	49.5
Bone only, %	Yes	20.7	22.4	23.2	21.6	23.2	21.6
Stage at initial diagnosis, %	≥3	54.3	55.5	57.7	55.9	57.7	55.9
Prior surgery, %	Yes	67.4	67.6	73.4	73.9	73.4	73.9
Prior radiotherapy, %	Yes	52.6	50.8	53.2	56.3	53.2	56.3
Prior neoadj CT, %	Yes	13.2	7.7	12.2	14.4	12.2	14.4
Prior adj CT, %	Yes	38.5	41.1	40.5	40.1	40.5	40.1
Prior adj ET, %	Yes	55.6	53.5	56.3	56.8	56.3	56.8
TFI ^b , %	De Novo	36.8	37.8	37.6	36.5	37.6	36.5
	≤12mo	19.1	21.4	22.1	21.6	22.1	21.6
North American, %	Yes	32.6	35.1	37.8	44.6	37.8	44.60

^aSome ML-2 ITT pts were removed to match PAL-2 reported BL data categories.

^bPAL-2 used “disease-free interval” (DFI) to refer to TFI, defined as time from end of (neo)adj tx to recurrence.