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MonarchE: Evaluation of prognostic and predictive value of Ki-67 index pre and post neoadjuvant chemotherapy (NAC) and changes following NAC

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Background

Two years (y) of adjuvant abemaciclib (abema) + endocrine therapy (ET) improved invasive disease-free survival (IDFS) over ET alone in patients (pts) with HR+, HER2-, node-positive, high-risk disease. In pts who received NAC, abema + ET showed sustained IDFS improvement (HR: 0.65; 95% CI: 0.54-0.73; 4y IDFS rates: 81% abema + ET vs 72% ET alone, Δ9%). In the intent-to-treat population, while high baseline Ki-67 was associated with worse prognosis, benefit was observed with abema regardless of Ki-67 index. Here we evaluate the prognostic and predictive value of baseline (pre-) and post-NAC Ki-67 index and of the changes in Ki-67 following NAC.

Methods

Ki-67 was determined centrally. In pts receiving NAC, Ki-67 index pre- or post-NAC was assessed in subgroups by Ki-67 index (high ≥20%; low <20%) and by changes of Ki-67 index following NAC. Efficacy was assessed using Cox proportional hazard regression model.

Results

Overall, 2057/5637 (36.5%) pts received NAC. Ki-67 index pre-NAC was available for 1359 pts (high, n=879; low, n=480) and of these, 579 pts had Ki-67 index post-NAC (high, n=118; low, n=461). Baseline characteristics and demographics were balanced across treatment arms and subgroups. 4y IDFS rates indicate pts with high Ki-67 pre- and post-NAC have higher risk of recurrence. Among pts who had both pre- and post-NAC Ki-67 results available, NAC reduced the Ki-67 index to low in approximately 75% of high Ki-67 tumors. Pts whose tumors retained a high Ki-67 index following NAC had the highest risk of recurrence. Treatment benefit of abema + ET vs ET alone was consistent across subgroups (Table) regardless of Ki-67 index or changes in Ki-67. Table. Table: 295MO

Population	Arm	Events/Pts, n	4-yr IDFS rates, %	HR (95% CI)
Pre-NAC				
Ki-67 High	Abema + ET	94/436	79.9	0.63 (0.49-0.82)
	ET	140/443	69.2	
Ki-67 Low	Abema + ET	37/233	84.9	0.59 (0.40-0.89)
	ET	64/247	74.5	
Post-NAC				
Ki-67 High	Abema + ET	23/62	63.3	0.53 (0.31-0.90)
	ET	31/56	44.5	
Ki-67 Low	Abema + ET	26/236	91.4	0.45 (0.28-0.72)
	ET	52/225	77.7	

Population	Arm	Events/Pts, n	4-yr IDFS rates, %	HR (95% CI)
Change in Ki-67 pre- to post-NAC				
Remain High	Abema + ET	21/49	57.5	0.63 (0.36-1.10)
ET		26/48	43.5	
Remain low	Abema + ET	11/89	89.1	0.71 (0.33-1.50)
ET		16/88	82.3	
High to Low	Abema + ET	15/147	92.8	0.35 (0.19-0.64)
ET		36/137	74.7	
Low to High	Abema + ET	2/13	NE*	NE*
ET		5/8	NE*	

*Not estimable due to small sample size

Conclusions

Ki-67 index pre- or post-NAC and changes in Ki-67 following NAC were prognostic of pts outcomes, but not predictive of abema treatment benefit in monarchE as benefit with abema in addition to ET was observed across all groups.

Clinical trial identification

NCT03155997.

Legal entity responsible for the study

E. Lilly and Company.

Funding

Eli Lilly and Company.

Disclosure

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