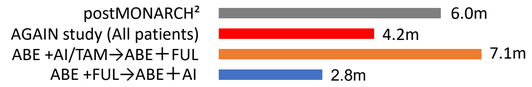
PS2-08-06 Biomarker analysis of patients treated with abemaciclib rechallenge after progression on abemaciclib plus endocrine therapy from the Phase II AGAIN Study (WJOG14220B) <jRCTs031210129>

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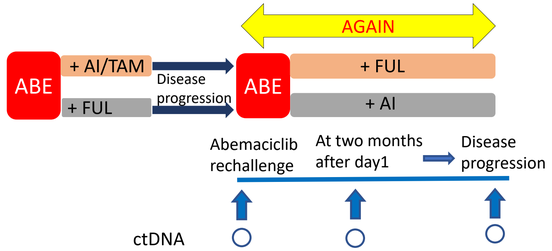
Introduction

We previously conducted a phase II study evaluating abemaciclib (ABE) rechallenge after progression on ABE plus endocrine therapy in patients with hormone receptor-positive, HER2-negative metastatic breast cancer[1]. This study demonstrated a progression-free survival (PFS) benefit for patients treated with ABE plus fulvestrant (FUL) following progression on ABE plus aromatase inhibitor (AI)/tamoxifen (TAM). However, robust biomarkers of resistance to ABE rechallenge are currently lacking. This study presents the results of a biomarker analysis of liquid biopsies, including those collected at the time of disease progression after ABE rechallenge.



Methods and Materials

We obtained liquid biopsies before ABE rechallenge, at 2 months (m) after rechallenge, and at disease progression to identify biomarkers associated with response or resistance to ABE. We analyzed circulating tumor DNA (ctDNA) using a targeted next-generation sequencing panel.



Biomarker ctDNA analyzed by Oncomine Pan-Cancer Cell-Free Assay (ThermoFisher®).

The hazard ratio (HR) and 95% CI for PFS, overall survival (OS) will be calculated using the Cox proportional hazards model.

Results

Figure 1. Frequency of ctDNA alterations at pre-ABE rechallenge and disease progression

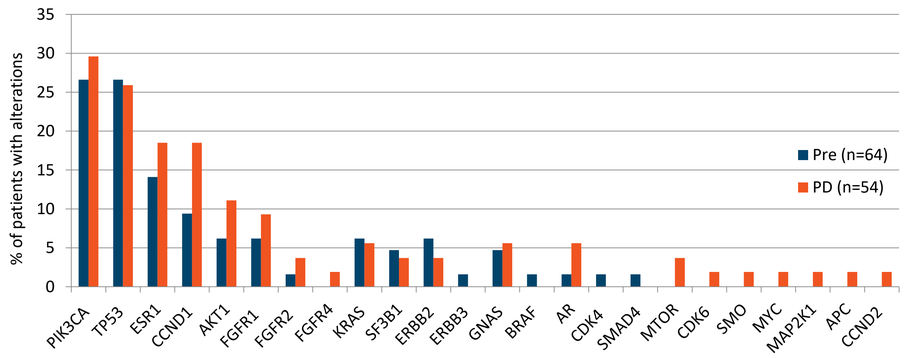


Figure2. PFS in genetic subgroups at disease progression

Subgroup	n	HR (95%CI)	*P* value
CCND1 amplification -	49	reference	
amplification +	5	2.31 (0.88–6.02)	0.09
ESR1 wild-type	51	reference	
mutant	3	0.98 (0.3–3.2)	0.98
PIK3CA wild-type	51	reference	
mutant	3	1.24 (0.38–4.03)	0.72
TP53 wild-type	47	reference	
mutant	7	1.03 (0.46–2.29)	0.94

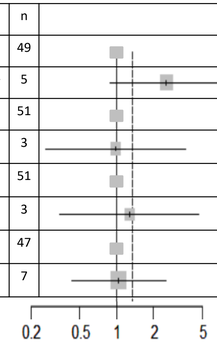


Figure3. OS in genetic subgroups at disease progression

	HR (95%CI)	*P* value
	reference	
	1.95 (0.43–8.86)	0.39
	reference	
	1.06 (0.24–4.8)	0.94
	reference	
	5.08 (0.58–44.56)	0.14
	reference	
	4.17 (1.24–14.02)	0.02

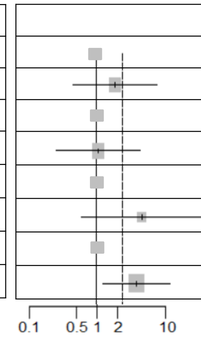
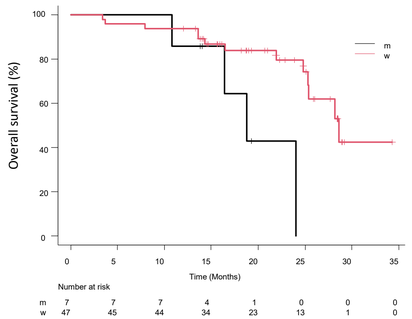
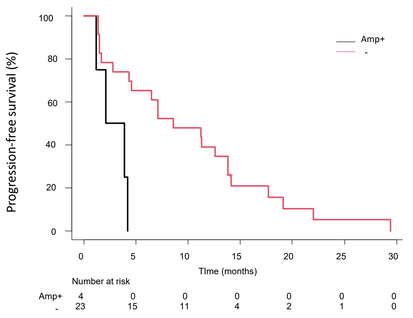


Figure4. *TP53* mutation at disease progression

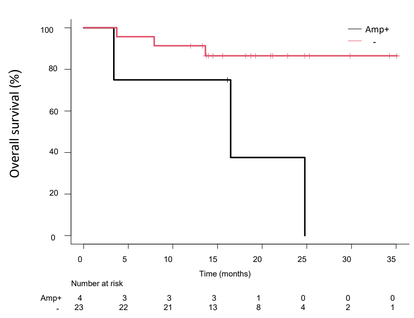


TP53	n	m OS (m) (95% CI)	HR (95% CI)	P value
Mutant	7	18.8 (10.8 – NA)	4.17 (1.24 – 14.02)	0.02
Wild-type	47	28.6 (25.3 – NA)	reference	

Figure 5. *CCND1* amplification at disease progression (ABE +AI/TAM→ABE＋FUL)



CCND1	n	m PFS (m) (95% CI)	HR (95% CI)	P value
Amplification +	4	3.0 (1.2 – NA)	5.13 (1.43 – 18.4)	0.01
-	23	8.6 (4.3 – 13.8)	reference	



m OS (m) (95% CI)	HR (95% CI)	P value
16.5 (3.4 – NA)	6.28 (1.26 – 31.25)	0.01
NA (NA – NA)	reference	

Conclusions

- This is the first biomarker analysis is to examine biomarkers of ABE rechallenge from only ABE.
- In this study of ABE rechallenge, *CCND1* amplification may be associated with resistance to ABE in patients who switched from ABE plus AI/TAM to ABE plus FUL.
- *TP53* mutation was suggested as a prognostic biomarker.

Contact

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Abbreviation

HR; hazard ratio, ABE; Abemaciclib, AI; aromatase inhibitor, TAM; tamoxifen, FUL; fulvestrant

References

1. Meiko N, et al. ESMO congress 2025
2. Kevin K, et al. J Clin Oncol. 2025;43:1101

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