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ABIGAIL: International, open-label, multicenter, non-inferiority, randomized phase II study of abemaciclib plus endocrine therapy with or without a short course of induction paclitaxel in patients with previously untreated HR-positive/HER2-negative advanced breast cancer with aggressive disease criteria

Juan de la Haba-Rodríguez, Javier Cortés, Serena Di Cosimo, Isabel Blancas, Patricia Cortez-Castedo, Ana López, Elena López-Miranda, Helena Pla-Juher, Cinta Albacar, Jose Ponce-Lorenzo, Vicente Carañana, Lorena París, María Valero, Manuel Ruíz-Borrego, Vega Iranzo, Ana Garrido, Daniel Alcalá-López, Leonardo Mina, Juan José García-Mosquera, Antonio Llombart-Cussac

Declaration of interest

Juan de la Haba-Rodríguez, MD, PhD

- Research grants from Roche and Pfizer.
- Consultancy/advisory fees from AstraZeneca, Amgen, Roche/Genentech, Novartis, Lilly, AstraZeneca-Daiichi, and Pfizer.
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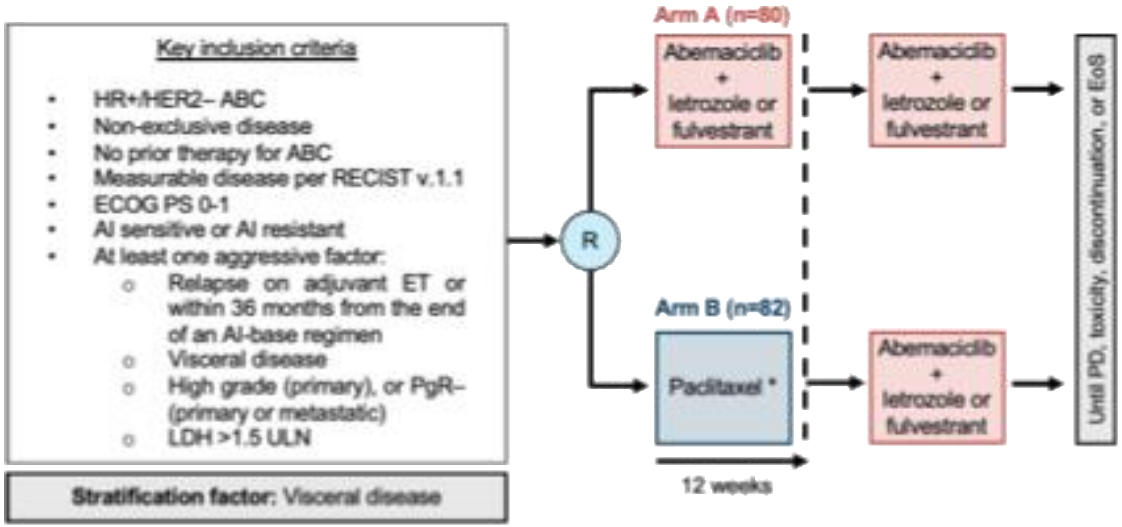
Background & Study design

- CDK4/6 inhibitors, such as abemaciclib, plus endocrine therapy (ET) represent one of the standard first-line therapies for HR+/HER2- advanced breast cancer (ABC) [1-4].
- However, chemotherapy as induction treatment is still used for patients at risk of rapid progression [5].
- ABIGAIL is an international, open-label, multicenter, randomized, non-inferiority, phase II trial (NCT04603183).

[1] Sledge Jr – J Clin Oncol 2017 | [2] Goetz – J Clin Oncol 2017 | [3] Sledge Jr – JAMA Oncol 2020 | [4] Goetz – Ann Oncol 2024 | [5] Cardoso – Ann Oncol 2018



Primary objective:
Compare 12-week ORR per BICR in both groups.

Key secondary endpoints:
PFS, OS, clinical benefit rate,, time to response, duration of response, safety, maximum tumor shrinkage.

Newcombe hybrid score method was used. Based on 10% dropout rate, N ≥160 was necessary to attain 80% power at nominal level of two-sided α=0.05.

* According to response, clinicians can determine if patients extend paclitaxel to a maximum of 6 cycles after the first 12 weeks of treatment.

ABC, advanced breast cancer; AI, aromatase inhibitor; BICR, blinded independent central review; ECOG PS, Eastern Cooperative Oncology Group Performance status; EoS, end of study; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; LDH, lactate dehydrogenase; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PgR, progesterone receptor; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors; ULN, upper limit of normal.

Key baseline characteristics

	Abemaciclib + ET *N* = 80	Paclitaxel *N* = 82
Age, years		
Median (range)	57 (26-82)	60 (34-85)
ECOG performance status		
0	52 (65%)	52 (63.4%)
1	28 (35%)	30 (36.6%)
Disease stage at study entry		
Unresectable locally advanced	2 (2.5%)	2 (2.4%)
Metastatic	78 (97.5%)	80 (97.6%)
Recurrent	49 (61.3%)	57 (69.5%)
De novo	29 (36.2%)	23 (28.1%)
Menopausal status		
Premenopausal	24 (30.0%)	20 (24.4%)
Postmenopausal	55 (68.7%)	62 (75.6%)
Missing	1 (1.3%)	0 (0%)

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Efficacy Results: Primary Endpoint

12-week objective response rate (ORR) per BICR

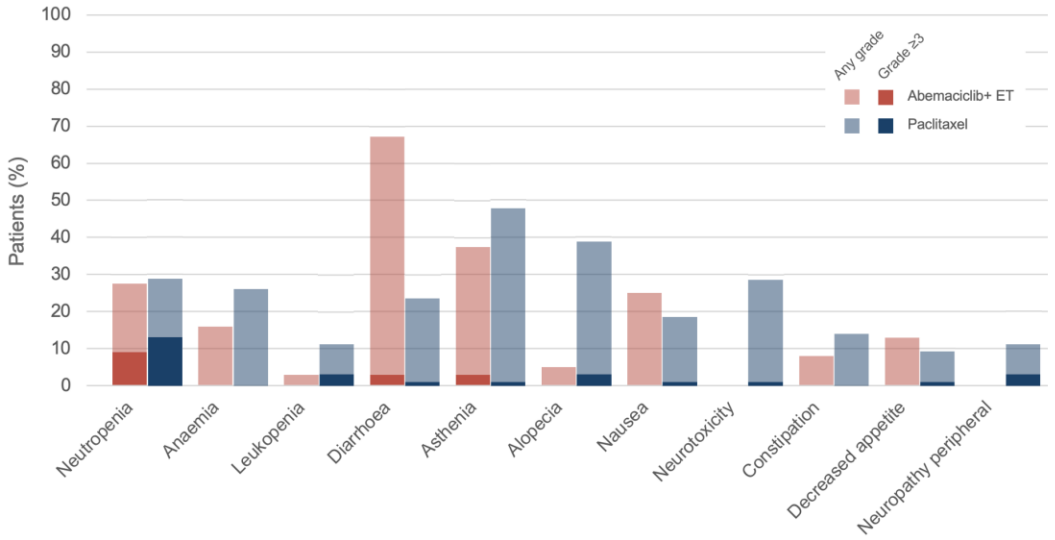
- The primary endpoint was met with a 12-week ORR per BICR of 58.8% in abemaciclib + ET, and 40.2% in paclitaxel (p = 0.0193).

	Abemaciclib + ET *N* = 80	Paclitaxel *N* = 82	Odd ratio (95% CI)	*p* value
12-week ORR in ITT population				
Complete response, partial response	47 (58.8%)	33 (40.2%)	**2.11 (1.13-3.96)**	**0.0193**
Stable disease, progressive disease , or discontinuation	33 (41.2%)	49 (59.8%)		
Response at 12 weeks since randomization				
Complete response	0 (0%)	0 (0%)		
Partial response	47 (58.8%)	33 (40.2%)		
Stable disease	24 (30.0%)	37 (45.2%)		
Progressive disease	1 (1.2%)	7 (8.5%)		
Not evaluable	8 (10.0%)	5 (6.1%)	–	
Death*	2 (2.5%)	2 (2.4%)		
Withdrawal of consent	2 (2.5%)	1 (1.3%)		
Toxicity	2 (2.5%)	0 (0%)		
Non-radiological progression	1 (1.25%)	0 (0%)		
Incorrect randomization	1 (1.25%)	2 (2.4%)		

*Deaths were due to causes different from treatment-related toxicity.

Safety Results at 12 weeks

Treatment-emergent adverse events (TEAEs) in ≥10% of patients



	Abemaciclib + ET		Paclitaxel	
12 week-TEAEs, %	**Any grade**	**G≥3**	**Any grade**	**G≥3**
Neutropenia	27	9	29	13
Anaemia	16	0	26	0
Leukopenia	3	0	11	3
Diarrhoea	68	3	23	1
Asthenia	37	3	48	1
Alopecia	5	0	39	3
Nausea	25	0	18	1
Neurotoxicity	0	0	28	1
Constipation	8	0	14	0
Decreased appetite	13	0	9	1
Neuropathy peripheral	0	0	11	3

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Conclusions

- The ABIGAIL trial met its primary endpoint with a 12 week-ORR of 58.8% in patients treated with abemaciclib + ET vs. 40.2% in patients treated with paclitaxel (p=0.0193).
- The toxicity profile observed after the first 12 weeks was as expected according to each treatment strategy.
- The ABIGAIL trial demonstrated that abemaciclib combined with endocrine therapy shows superior efficacy at 12 weeks compared to standard chemotherapy as a front-line treatment strategy for HR+/HER2- ABC patients with aggressive disease characteristics.
- This study is currently ongoing to evaluate long-term efficacy and other secondary endpoints, including PFS.

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Presentation

Lay language summary

European Society for Medical Oncology (ESMO)
Via Ginevra 4, CH-6900 Lugano
T. +41 (0)91 973 19 00
esmo@esmo.org

esmo.org