A multicenter, randomized, double-blind, phase II study to evaluate the tolerability of an induction dose escalation of everolimus in patients with metastatic breast cancer (DESIREE)

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Study Design

N=156

HR+/HER2- mBC

progression/ recurrence while on or after NSAI

R

Everolimus 10 mg arm (EVE 10mg)
week 1-3: 4 x 2.5 mg /d (blinded)
week 4-24: 10 mg/d (open-label)

Dose escalation arm (EVE esc)
week 1: 2.5 mg (1 x verum + 3 x placebo/d)
week 2: 5 mg (2 x verum + 2 x placebo/d)
week 3: 7.5 mg (3 x verum + 1 x placebo/d
week 4-24: 10 mg/d (open-label)

Primary endpoint:
Mucositis grade ≥2 or <2 and discontinuation due to AE, patients' or investigators' decision within the first 12 weeks of treatment (Mucositis episode)

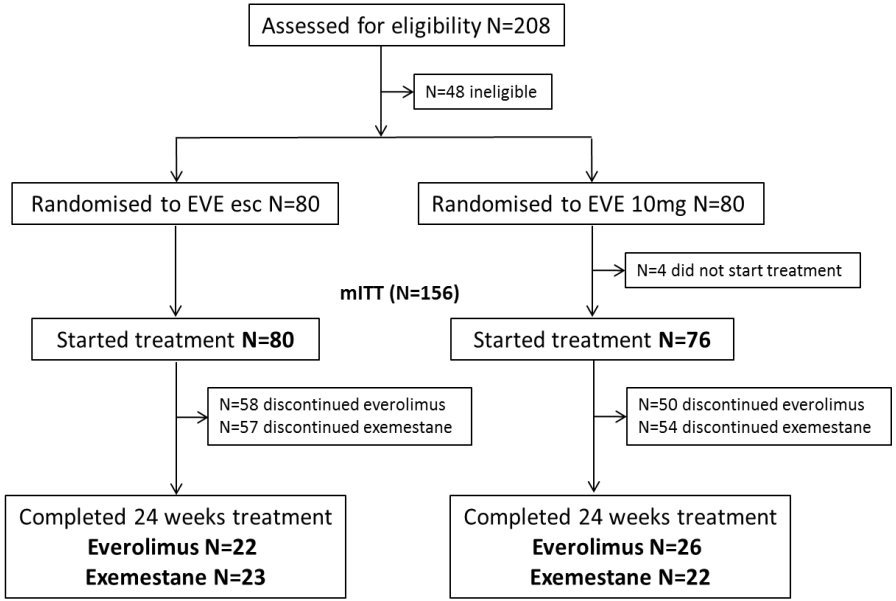
Key secondary endpoints:
- Clinical benefit rate
- Relative total dose intensity
- Safety
- Quality of life

Study duration:
24 weeks, EOT visit (week 25-28)

Statistical assumption:
EVE 10 mg: 40% mucositis, EVE esc: 20% mucositis, continuity-corrected $\chi 2$-test, Type-I-error: 20% and Power: 90%

Patient and Tumor Characteristics

Consort diagram



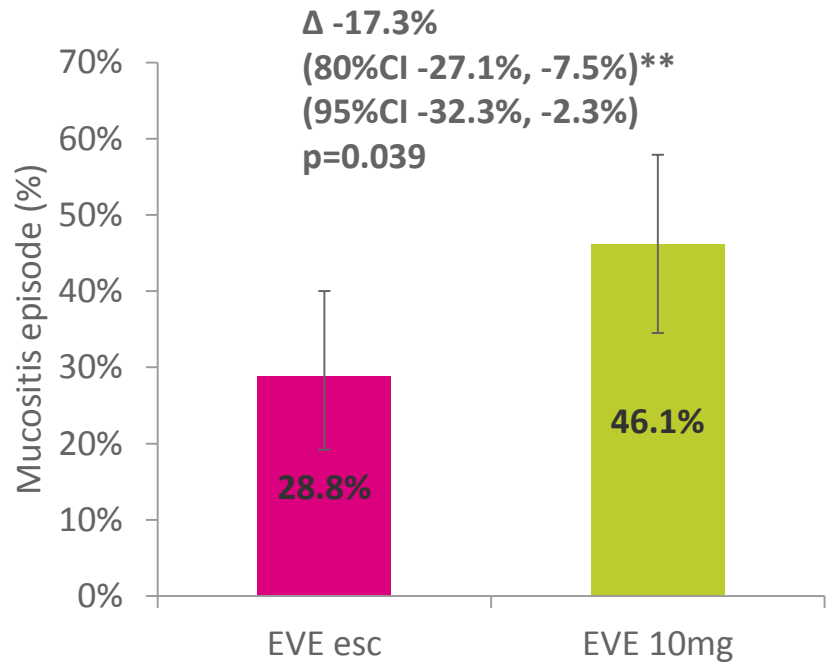
Main baseline characteristics

Parameter	Category	EVE esc N=80 N(%)	EVE 10 mg N=76 N(%)	p-value
Age, years (range)	median	64.5 (33.0-85.0)	63.0 (41.0-81.0)	0.538
BMI, kg/m^2 (range)	median	25.8 (16.5-45.5)	24.6 (15.9-43.9)	0.401
ECOG PS	0	57 (71.3)	63 (82.9)	0.202
	1	20 (25.0)	12 (15.8)	
	2	3 (3.8)	1 (1.3)	
No of metastatic sites	1	22 (27.5)	28 (36.8)	0.512
	2	30 (37.5)	28 (36.8)	
	3	19 (23.8)	15 (19.7)	
	≥4	9 (11.3)	5 (6.6)	
Selected metastatic sites*	Liver	45 (56.3)	32 (42.1)	0.081
	Lung	21 (26.3)	17 (22.4)	0.582
	Pleura	12 (15.0)	7 (9.2)	0.331
Previous metastatic treatment lines	0	6 (7.5)	7 (9.2)	0.849
	1-2	59 (73.8)	53 (69.7)	
	>2	15 (18.8)	16 (21.1)	

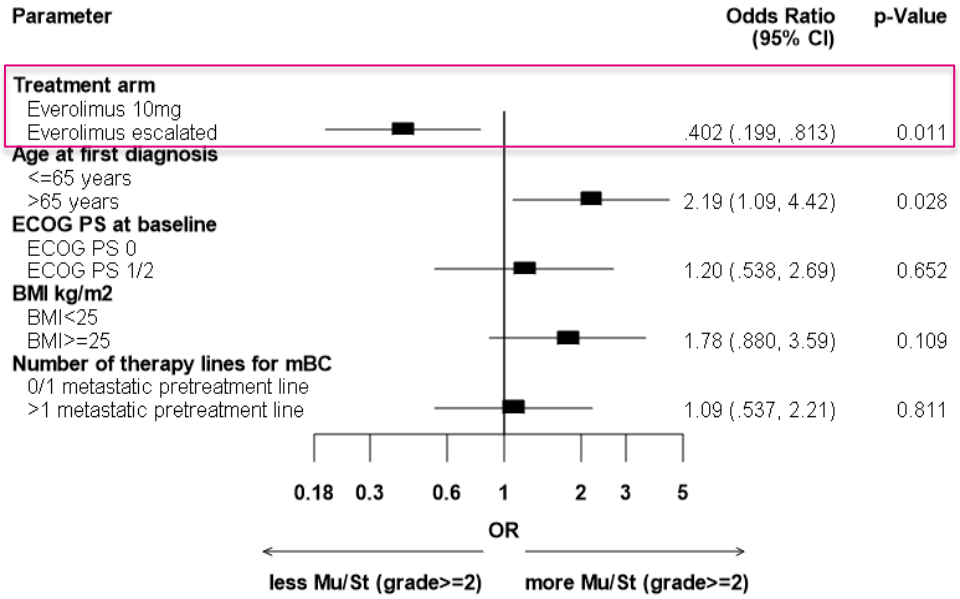
*some patients had more than one metastatic site

Primary Endpoint

Mucositis episode* at 12 weeks



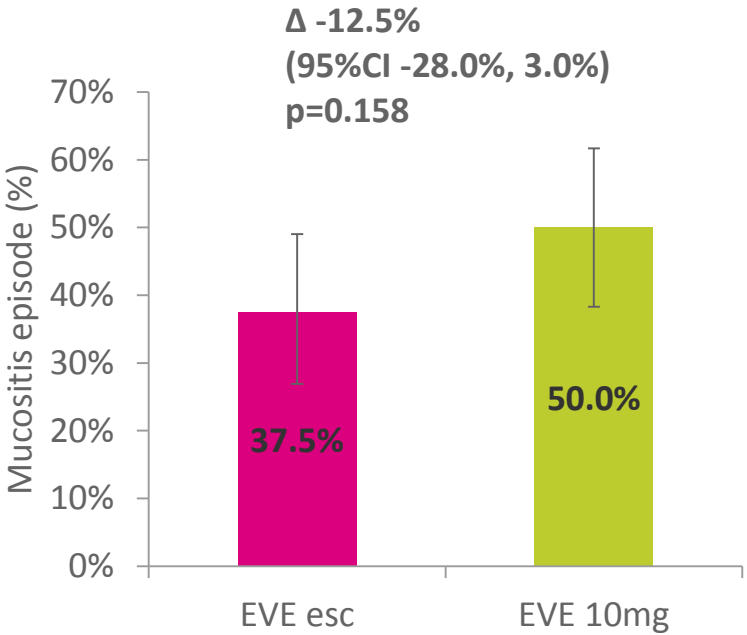
Multivariate logistic regression analysis



*mucositis grade ≥2 or <2 + discontinuation due to AE, patients' or investigators' decision
**design: Type-I-error 20%

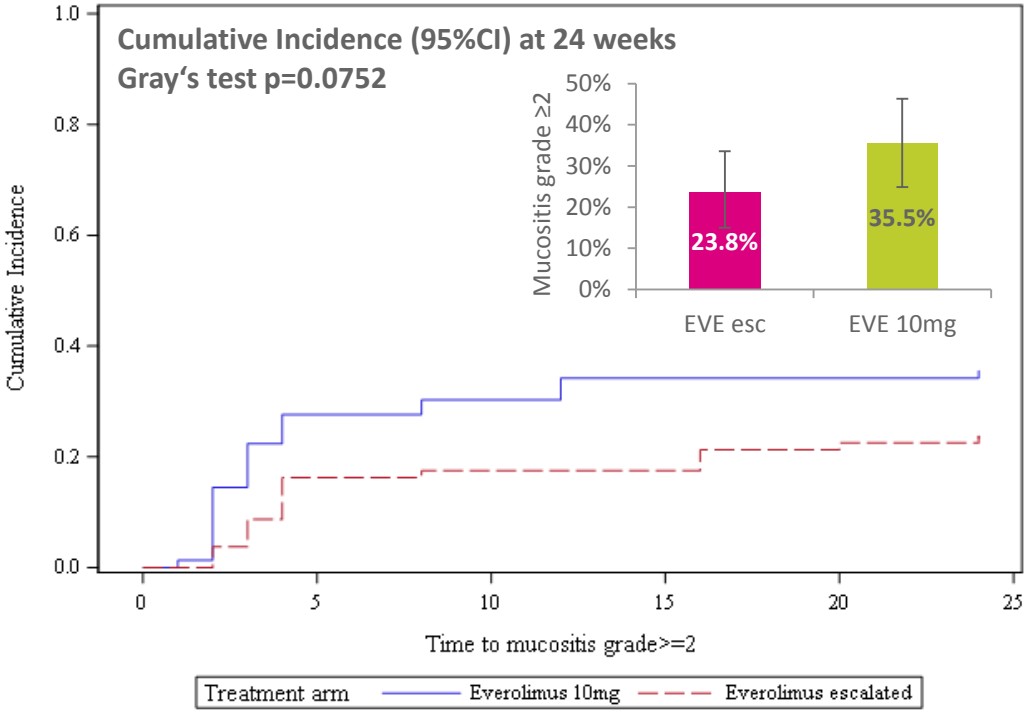
Secondary Tolerability Endpoints

Mucositis episode* at 24 weeks

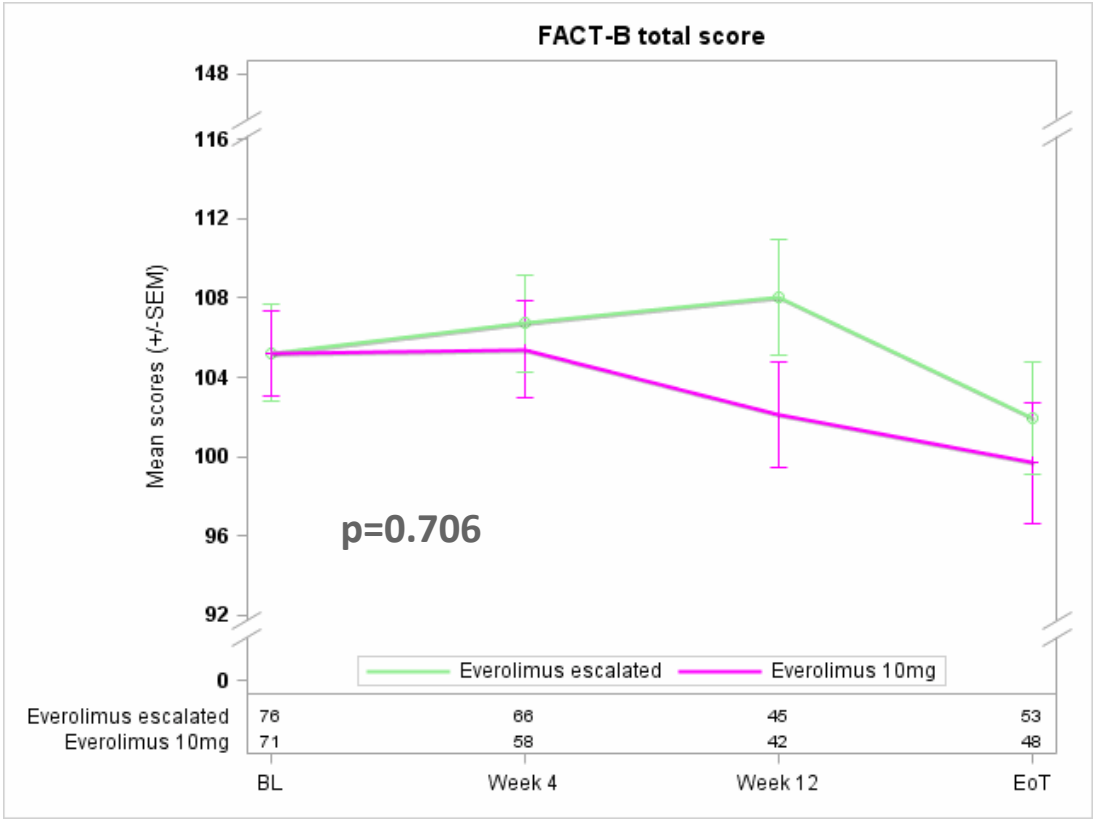


*mucositis grade ≥2 or <2 + discontinuation due to AE, patients' or investigators' decision

Time to onset of mucositis grade ≥2



Quality of Life (QoL)



- QoL was prospectively captured by FACT-B questionnaire
- Higher FACT-B total scores (range 0-148) indicate better QoL.
- Considering the metastatic setting, FACT-B total score was generally high in both treatment arms and not significantly different between the arms:

  Mean [SD]:

  EVE esc 105.5 [20.5]

  EVE 10mg 103.5 [18.6]

Conclusions

- DESIREE met its primary objective: fewer patients had mucositis grade ≥2 when the everolimus was escalated within the first 4 weeks.
- A dose escalation schema of everolimus over three weeks can be successfully used in patients with HR+/HER2- mBC to prevent the onset of mucositis grade ≥2 without affecting efficacy.
- Unirad study dose reductions of everolimus were less common in patients starting with 5mg compared to full dose (28.4% vs 46.85)[1]

[1]Bachelot T et al. ESMO virtual plenary 2021

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