MADRID 2014 ESMO congress

TARGET: A randomized phase II trial comparing vintafolide versus vintafolide plus docetaxel, versus docetaxel alone in second-line treatment of folate-receptor-positive non-small cell lung cancer patients

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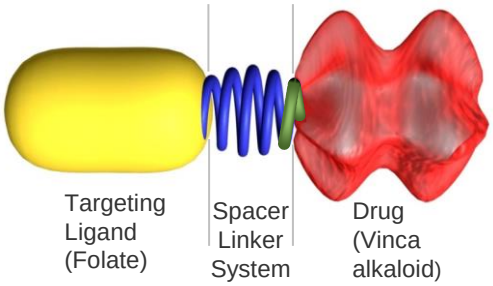
Disclosures

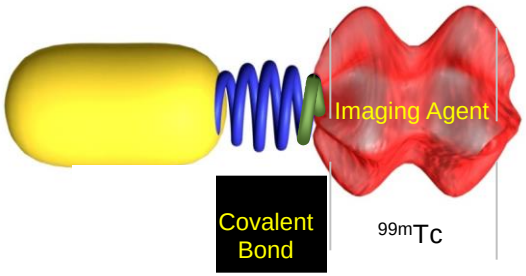
- ESMO conference registration by Endocyte

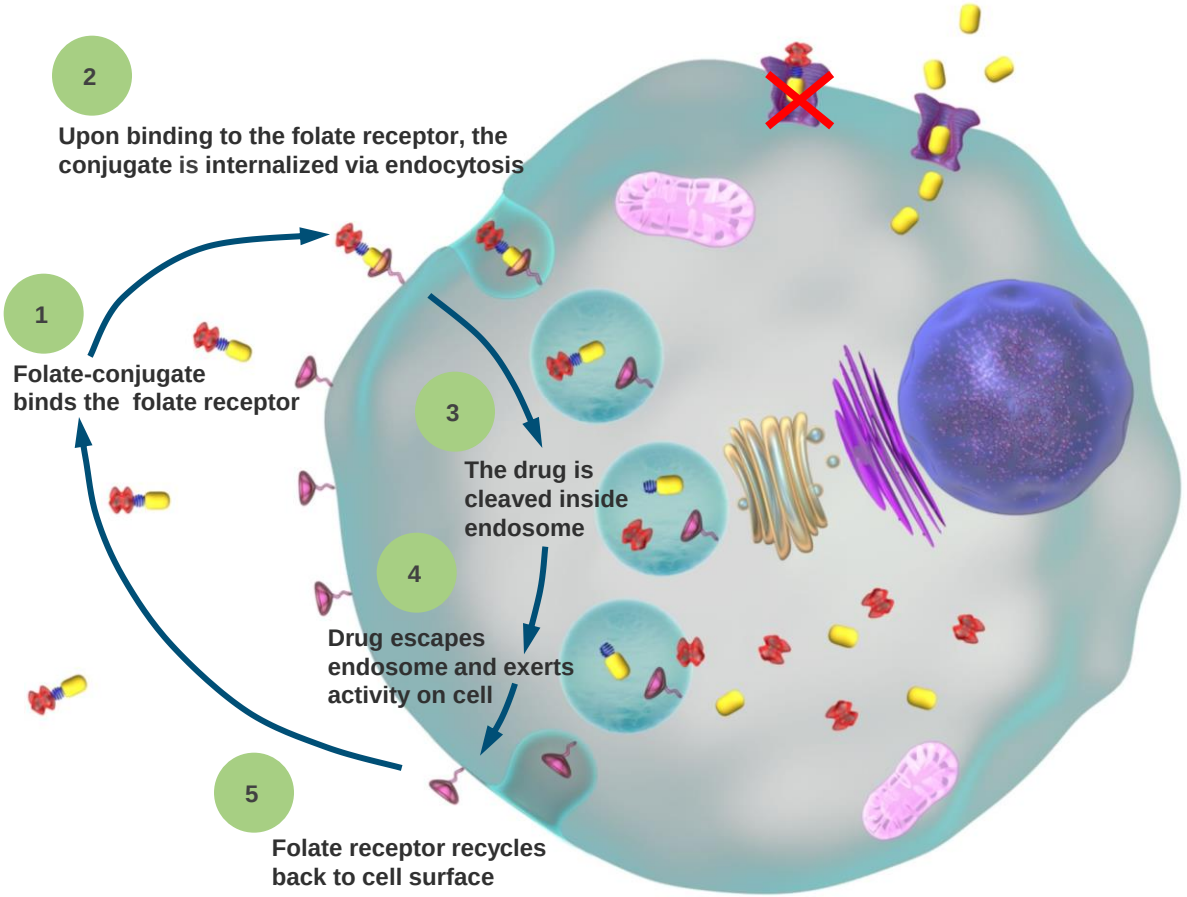
Mechanism of Action

Vintafolide (EC145)

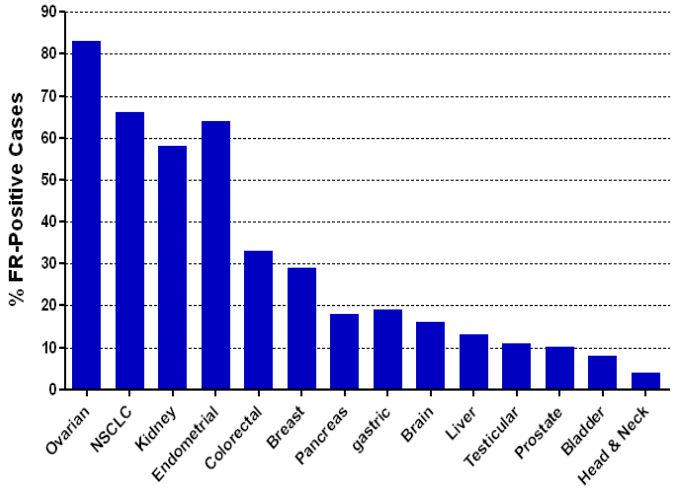


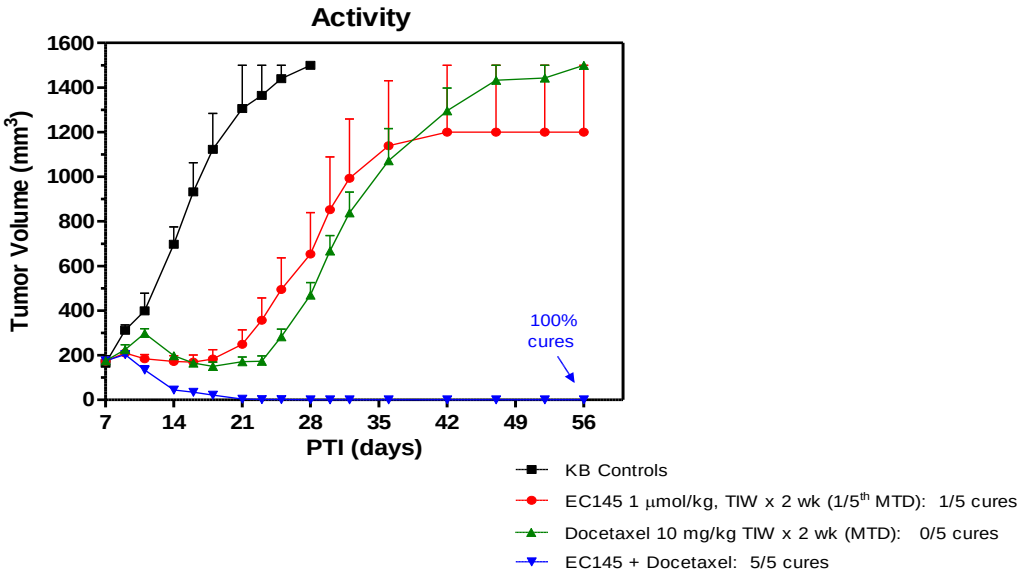
^{99m}Tc-etarfolatide (EC20)





Rationales for TARGET Study

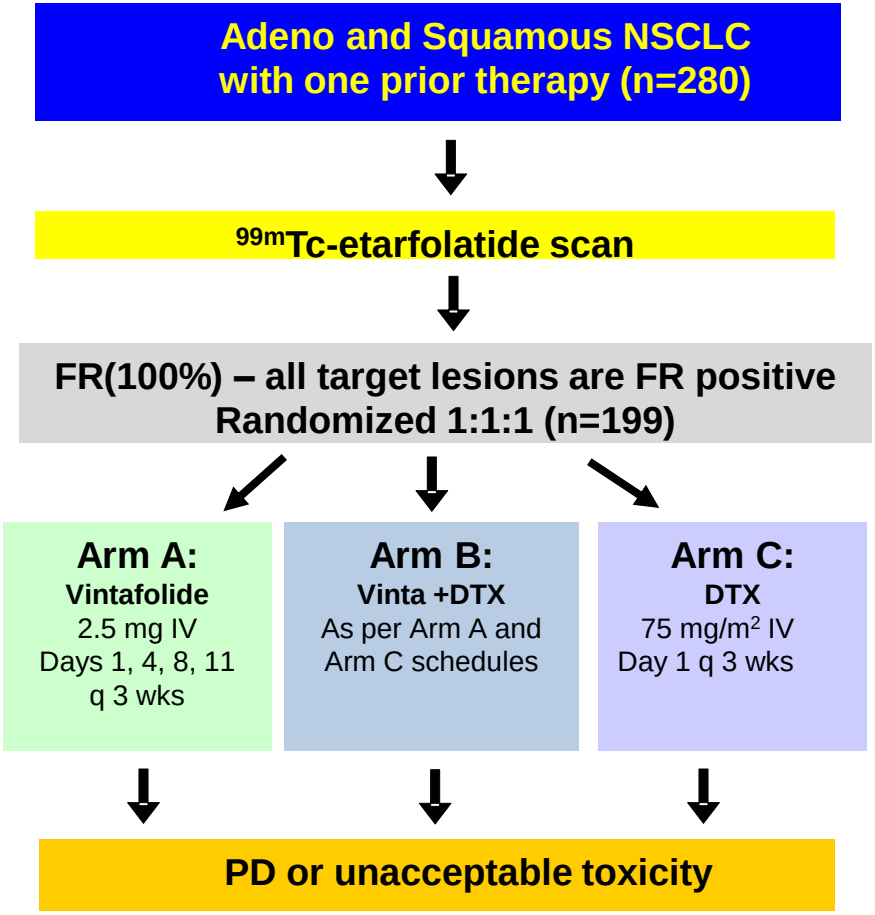




Single-agent vintafolide activity in heavily pre-treated NSCLC patients	FR(100%)* N=14
Disease Control Rate (CR + PR + SD)	57.1%
Median PFS	7.1 months
Median OS	10.8 months

* FR(100%) = all target lesions positive for FR

Study Design



- **Stratification Factors**
  - Time since last chemo (< 3 vs ≥ 3 m)
  - Best response to last chemo
  - Stage IIIB vs. IV
  - Prior EGFRi treatment (Y vs N)
- **Primary Endpoint: PFS**
  - 75% Power for 50% Improvement 1-Sided Alpha= 0.10
  - Futility Interim at 50% PFS events
- **Secondary Endpoints**
  - ORR, DCR, OS

Patient Disease Characteristics

	Vintafolide N=63	Vinta + DTX N=68	DTX N=68
Median age (yrs)	64.0	63.5	63.0
ECOG PS 0 1 2	 22% 76% 2%	 27% 73% 0%	 27% 73% 0%
Adenocarcinoma	65%	63%	72%
Smoker	76%	90%	85%
Stage IV	82%	85%	87%
Time since last chemo < 3 months	 51%	 49%	 50%
Best response to last chemo CR/PR/SD	73%	72%	71%
Prior EGFR inhibitor treatment	16%	15%	13%

Drug Administrations

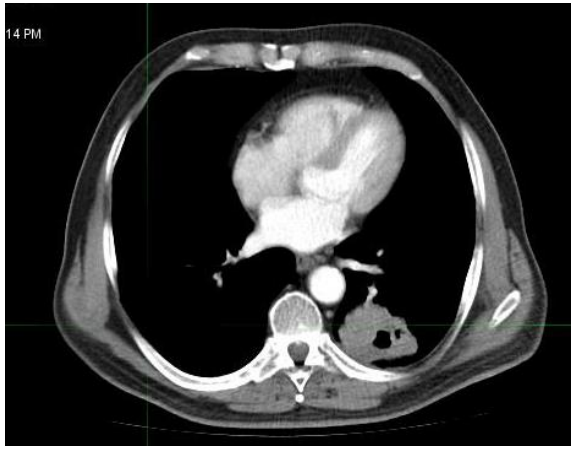
	Vintafolide N=63	Vinta + DTX N=68		DTX N=68
Median # of cycles	2.0 (1-19)	4.0 (1-19)		4.0 (1-16)
Relative Dose Intensity	95%	Vinta 74%	DTX 84%	92%
% patients with		Vinta	DTX	
≥ 1 dose omitted	22%	81%	15%	0%
≥ 1 dose adjusted	3%	29%	52%	35%
Reason dose adjusted		Vinta	DTX	
Hematologic toxicity	50%	85%	77%	71%
Non-hematologic toxicity	50%	15%	31%	29%

Efficacy Results – All patients

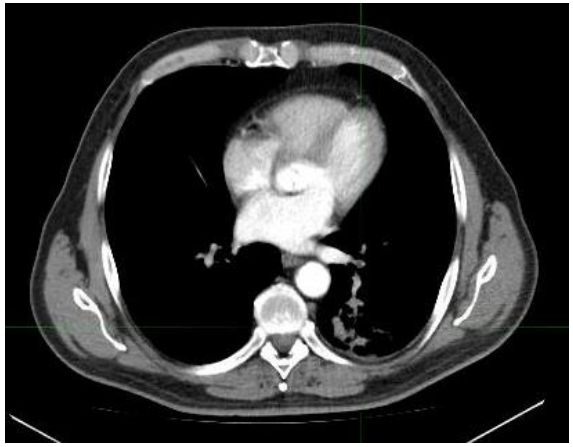
	Vintafolide N=63	Vinta + DTX N=68	DTX N=68
Median PFS (months, 95% CI)	1.6 (1.4; 3.2)	4.2 (2.8; 5.4)	3.3 (1.7;4.2)
PFS HR (vs. DTX; 95% CI)* 1-sided p-value	1.35 (0.92; 1.96) 0.9421	0.75 (0.52;1.09) 0.0696	
Median OS (months, 95% CI)	8.4 (5.6; 12.3)	11.5 (7.3; 13.4)	8.8 (5.4; 12.6)
OS HR (vs. DTX; 95% CI)* 1-sided p-value	1.05 (0.68; 1.61) 0.5818	0.88 (0.58;1.36) 0.2874	
PR	4 (6.3%)	15 (22.1%)	9 (13.2%)
SD	22 (34.9%)	33 (48.5%)	32 (47.1%)

* Unstratified log-rank

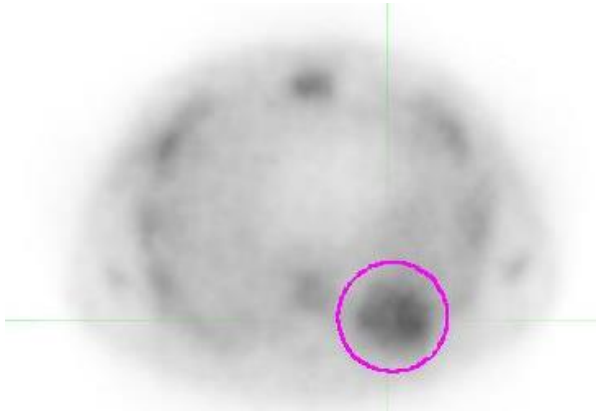
Patient response to Vinta + DTX



Baseline



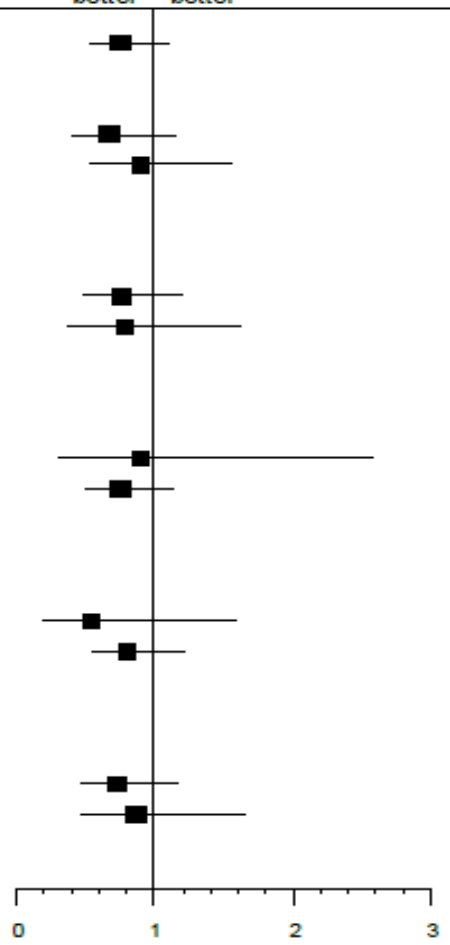
After 2 cycles



^{99m}Tc-etarfolatide scan

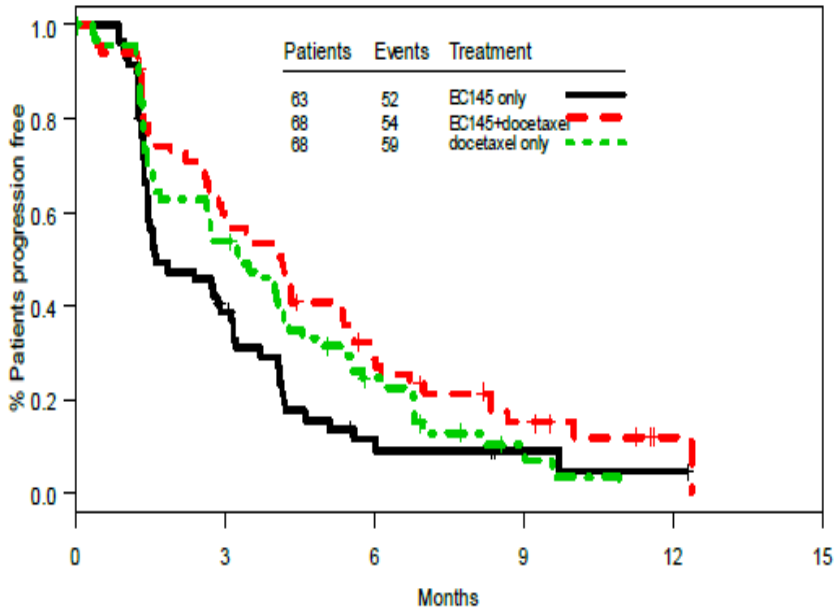
Efficacy Results – PFS Forest Plots

Subgroups	EC145+doce O/N	doce O/N	HR (CI)
Overall	54 / 68	59 / 68	0.75(0.52,1.09)
Time since Last Chemotherapy			
< 3 MONTHS	27 / 33	31 / 34	0.67(0.40,1.14)
>= 3 MONTHS	27 / 35	28 / 34	0.90(0.53,1.55)
Interaction test		χ^2_1 = 0.58 , P = 0.446	
Best Response to Last Chemotherapy			
CR/PR/SD	38 / 49	43 / 48	0.76(0.49,1.18)
PD/UNK	16 / 19	16 / 20	0.78(0.37,1.61)
Interaction test		χ^2_1 = 0.01 , P = 0.920	
Disease Stage at Study Entry			
STAGE IIIB	7 / 10	8 / 9	0.89(0.31,2.58)
STAGE IV	47 / 58	51 / 59	0.75(0.50,1.13)
Interaction test		χ^2_1 = 0.02 , P = 0.876	
Prior Treatment with EGFR Inhibitor			
Y	6 / 10	8 / 9	0.54(0.19,1.58)
N	48 / 58	51 / 59	0.80(0.54,1.20)
Interaction test		χ^2_1 = 0.57 , P = 0.452	
Histology			
ADENO.*	33 / 43	42 / 49	0.73(0.46,1.16)
SQUAMOUS CELL CARCINOMA	21 / 25	17 / 19	0.87(0.46,1.66)
Interaction test		χ^2_1 = 0.18 , P = 0.669	



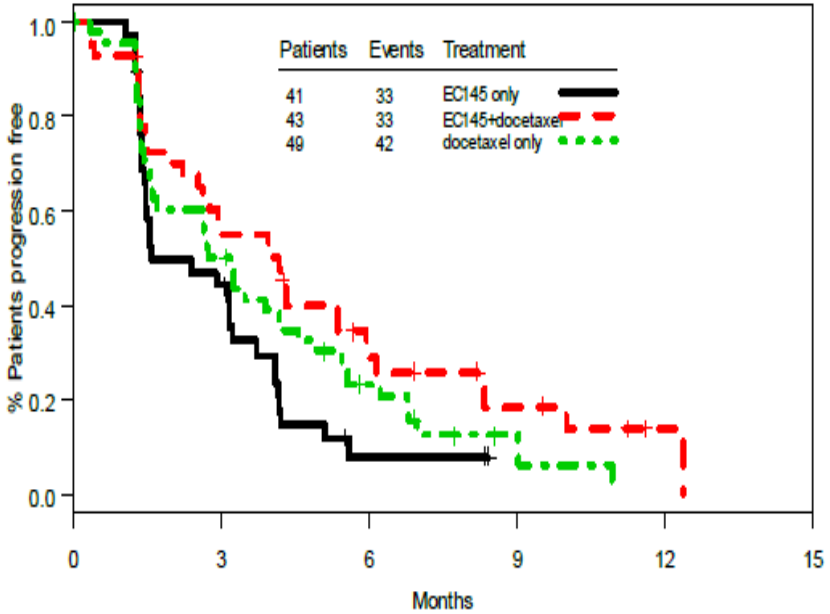
Progression Free Survival

All patients



Number at risk						
EC145 only	63	21	5	2	1	0
EC145+docetaxel	68	38	17	7	1	0
docetaxel only	68	35	13	3	0	0

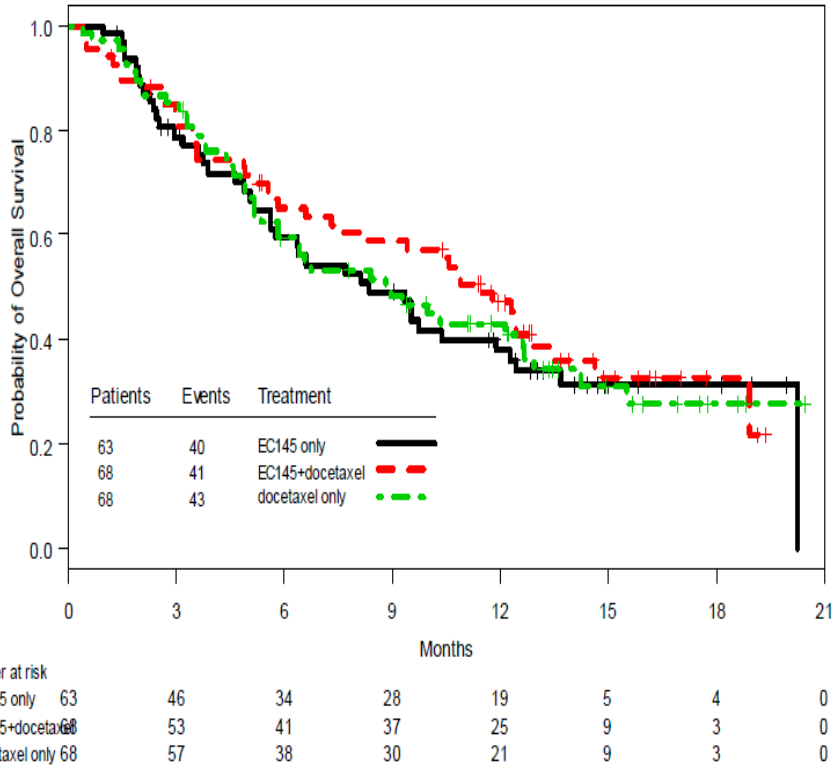
Adenocarcinoma



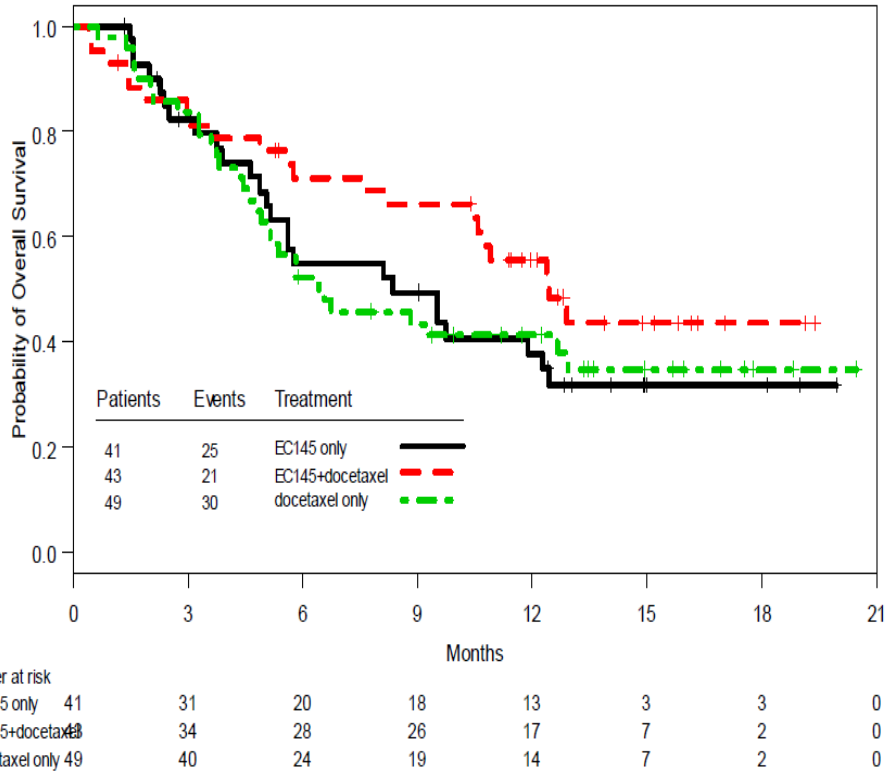
Number at risk						
EC145 only	41	16	2	0	0	0
EC145+docetaxel	43	23	11	5	1	0
docetaxel only	49	24	9	2	0	0

Overall Survival

All patients



Adenocarcinoma



Efficacy Results – Stratified Analyses

All Patients	Vintafolide N=63	Vinta + DTX N=68
PFS HR (vs. DTX; 95% CI) 1-sided p-value	1.35 (0.89; 2.04) 0.9266	0.78 (0.52;1.17) 0.1175
OS HR (vs. DTX; 95% CI) 1-sided p-value	0.96 (0.62; 1.50) 0.4396	0.75 (0.48;1.18) 0.1066

Adenocarcinoma	Vintafolide N=41	Vinta + DTX N=43
PFS HR (vs. DTX; 95% CI) 1-sided p-value	1.32 (0.79; 2.21) 0.8590	0.68 (0.41;1.14) 0.0732
OS HR (vs. DTX; 95% CI) 1-sided p-value	0.88 (0.51; 1.52) 0.3274	0.51 (0.28; 0.94) 0.0147

TEAEs Regardless of Causality

	Vintafolide N=63			Vinta + DTX N=68			DTX N=68		
% TEAEs	G1-4	G3	G4	G1-4	G3	G4	G1-4	G3	G4
Neutropenia	3	0	2	77	15	57	62	18	37
Febrile Neutropenia	0	0	0	13	12	2	6	3	3
Sepsis/Neutropenic Sepsis	0	0	0	7	0	6	2	0	2
Anemia	24	6	0	21	4	2	29	6	0
Thrombocytopenia	0	0	0	7	0	0	4	0	0
Nausea	5	0	0	15	2	0	19	0	0
Vomiting	5	0	0	13	0	0	12	0	0
Constipation	16	0	0	9	0	0	7	0	0
Peripheral neuropathy	18	2	0	34	9	0	21	0	0
Fatigue	14	6	0	27	7	0	34	9	0

Conclusions

- Vintafolide in combination with docetaxel showed clinical meaningful improvement across all efficacy endpoints over single-agent docetaxel
- Best improvement was seen in the pre-defined adenocarcinoma patient subgroup with PFS HR 0.68 and OS HR 0.51
- Safety profile was manageable and expected from the single-agent agents