Oral Paclitaxel and Encequidar (oPac+E) versus IV paclitaxel (IVPac) in the Treatment of Metastatic Breast Cancer (mBC) Patients (Study KX-ORAX-001): Progression Free Survival (PFS) and Overall Survival (OS) Updates (Abstract PD1-08)

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Background

- Paclitaxel has poor oral bioavailability due to excretion by gastrointestinal p-glycoprotein.
- Encequidar (E) is a potent specific minimally absorbed p-glycoprotein inhibitor which enables absorption of oral paclitaxel (oPac).
- oPac+E is a combination of paclitaxel liquid-filled capsules and an encequidar tablet.
- Systemic exposure (AUC) of oPac+E 205mg/m^2/day x 3 is equivalent to IV paclitaxel (IVPac) 80mg/m^2.
- Peak concentrations (Cmax) is 1/7th of IVPac.
- The combination oPac+E does not contain Cremophor.
- Corticosteroid and antihistamine premedications are not required for prophylaxis of hypersensitivity reactions.
- oPac+E was associated with a lower incidence of neuropathy and alopecia but a higher incidence of infections, low-grade gastrointestinal adverse events and grade 4 neutropenia compared to IV paclitaxel.
- oPac+E is administered at home, minimizing hospital/clinic visits.
- Results from the pivotal phase III trial, KX-ORAX-001, including the final analysis of confirmed tumor response rate, early PFS and OS were presented at SABCS, 2019, Abstract # GS6-01.
- At the final analysis for the primary endpoint, the confirmed tumor response rate was significantly higher in the oPac+E arm vs IVPac (35.8% vs 23.4%, p=0.011 ITT, population).
- Updated progression free survival (PFS) and overall survival (OS) analyses comprising 14 additional months of follow-up data are presented in this poster.

Study Design

- Randomized, multinational study in women with metastatic breast cancer (mBC).
- Patients were randomized 2:1 to receive oPac+E (205mg/m^2/day x3 weekly) or IVPac 175 mg/m^2 every three weeks.
- Treatment continued until progression of disease or toxicity.
- The primary efficacy endpoint was confirmed tumor response as assessed by blinded independent central review (BICR) on two consecutive evaluations (Figure 1).
- Key secondary efficacy endpoints included Duration of Response, Progression Free Survival (PFS) and Overall Survival (OS).

Prespecified Analysis Populations

Intent to treat (ITT): – All randomized patients (n=402: oPac+E 265; IVPac 137)

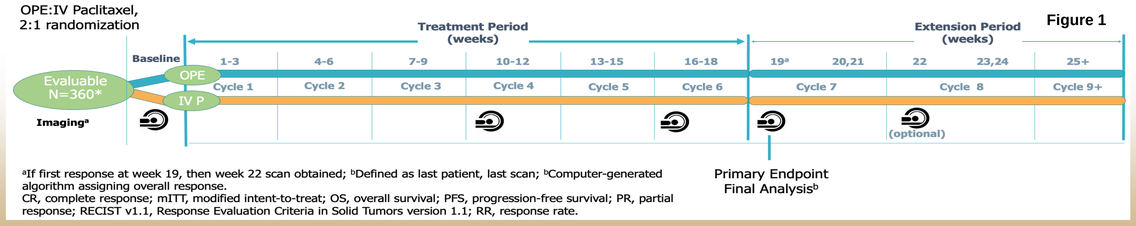
Modified intent to treat (mITT): RECIST measurable disease and received at least 7 days of oPac+E or 1 dose of IVPac (n=360: oPac+E 235; IVPac 125)

Baseline Characteristics in KX-ORAX-001 (ITT Population)

402 patients were enrolled of which 399 received treatment.

	Treatment	
	IVPac N=137	oPac+E N=265
Age (Years)		
Mean (SD)	55.8 (11.51)	58.1 (11.99)
Median	56.0	60.0
Race, n (%)		
Black	2 (1)	4 (2)
Caucasian	10 (7)	22 (8)
Hispanic/Latino	123 (90)	236 (89)
Other	2 (1)	3 (1)
Baseline ECOG, n (%)		
0	79 (58)	159 (60)
1	58 (42)	106 (40)
Receptor Status Group, n (%)		
HER2 Negative, ER and PR Negative	25 (18)	27 (10)
HER2 Negative, ER or PR Positive	72 (53)	157 (59)
HER2 Positive, ER or PR Positive	12 (9)	29 (11)
HER2 Unknown, ER and PR Unknown	18 (13)	30 (11)
Other	10 (7)	22 (8)
Prior Taxane Exposure, n (%)	43 (31)	76 (29)
Prior Anthracycline Exposure n (%)	79 (58)	153 (58)
% of Subjects with Visceral Metastases	106 (77)	204 (77)
Prior Chemotherapy Regimens in metastatic setting		
No prior chemotherapy	93 (68)	185 (70)
1 Line	27 (20)	54 (20)
≥ 2 Lines	17 (12)	25 (9)

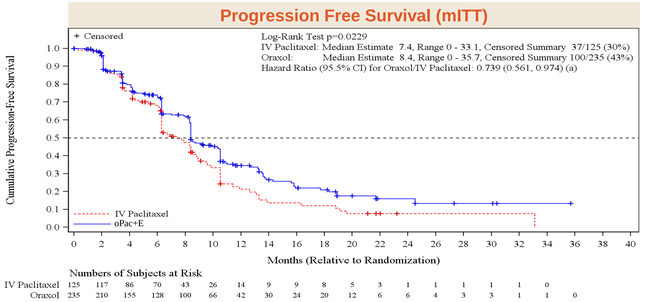
Figure 1



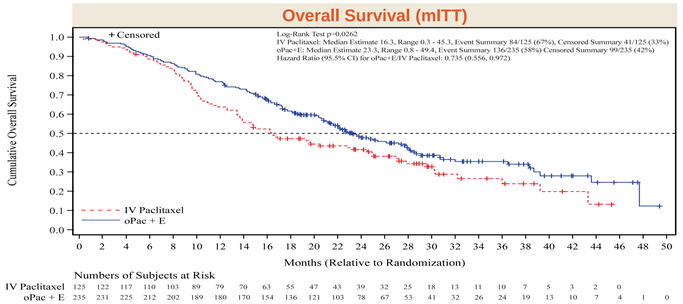
[a]If first response at week 19, then week 22 scan obtained; [b]Defined as last patient, last scan; [c]Computer-generated algorithm assigning overall response.
CR, complete response; mITT, modified intent-to-treat; OS, overall survival; PFS, progression-free survival; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; RR, response rate.

Results

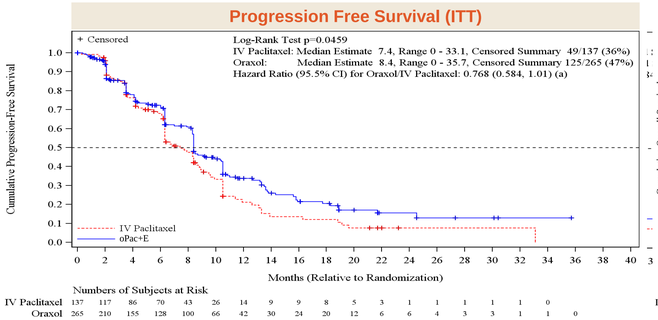
Progression Free Survival (mITT)



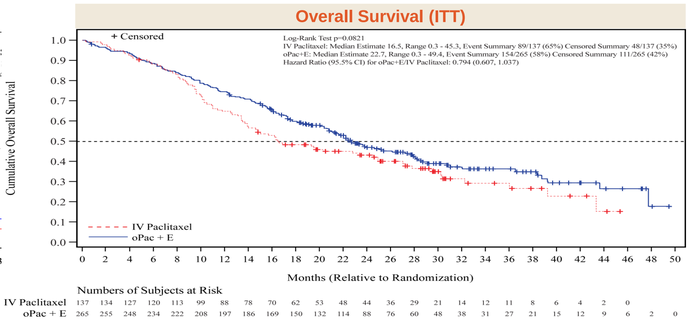
Overall Survival (mITT)



Progression Free Survival (ITT)



Overall Survival (ITT)



Progression Free Survival (mITT)

Treatment (n)	Events (%)	Median (mo) (range)	Hazard Ratio[1] (CI)	p-value
oPac+E (235)	57%	8.4 (0-35.7)	0.739 (0.561,0.974)	0.023
IVPac (125)	70%	7.4 (0-33.1)		

Progression Free Survival (ITT)

Treatment (n)	Events (%)	Median (mo) (range)	Hazard Ratio[1] (CI)	p-value
oPac+E (265)	53%	8.4 (0-35.7)	0.768 (0.584,1.010)	0.046
IVPac (137)	64%	7.4 (0-33.1)		

[1]Cox Proportional Hazard

Overall Survival (mITT)

Treatment (n)	Events (%)	Median (mo) (range)	Hazard Ratio[1] (CI)	p-value
oPac+E (235)	58%	23.3 (0.8-49.4)	0.735 (0.556,0.972)	0.026
IVPac (125)	67%	16.3 (0.3-45.3)		

Overall Survival (ITT)

Treatment (n)	Events (%)	Median (mo) (range)	Hazard Ratio[1] (CI)	p-value
oPac+E (265)	58%	22.7 (0.3-49.4)	0.794 (0.607,1.037)	0.082
IVPac (137)	65%	16.5 (0.3-45.3)		

[1]Cox Proportional Hazard

Conclusions

- oPac+E achieved the primary efficacy endpoint of the trial, superiority in confirmed radiologic response rate when compared to IVPac at the dose/schedule approved for MBC.
- Responses were of long duration.
- When compared to IVPac, PFS and OS in the prespecified mITT were statistically significant in the oPac+E treated patients.
- Strong trends of OS superiority were observed in favor of oPac+E vs IVPac in the ITT population.
- These findings support the clinical relevance of the increased tumor response rates observed with oPac+E. (NCT 02594371)