San Antonio Breast Cancer Symposium® - December 8-11, 2020

Lower rates of neuropathy with Oral Paclitaxel and Encequidar (oPac+E) compared to IV Paclitaxel (IVPac) in treatment of metastatic breast cancer (mBC): Study KX-ORAX-001 (Abstract PS13-06)

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Background

oPac+E

- 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.
  - Hypothesized to decrease incidence/severity of neuropathy.

Clinical implications of oral taxane administration with oPac+E

- oPac+E avoids the need for Cremaphor or premedications for prophylaxis of hypersensitivity reactions.
- oPac +E is administered at home, minimizing clinic visits.

Phase III trial data

- Results of the pivotal phase III trial, KX-ORAX-001, including the final analysis of confirmed tumor response rate, and early PFS and OS data 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 group vs IVPac (35.8% vs 23.4%, p=0.011 ITT, population).

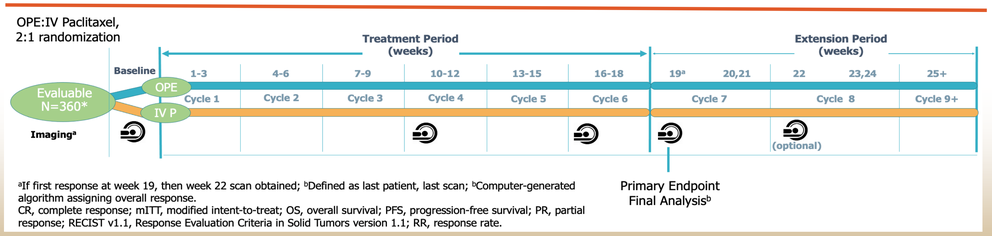
Baseline Characteristics (ITT Population)

402 patients were enrolled; 399 received treatment

	Treatment	
	IVPac N=137	oPac+E N=265
Age (Years)		
Median	56.0	60.0
Min, Max	27, 85	30, 90
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)

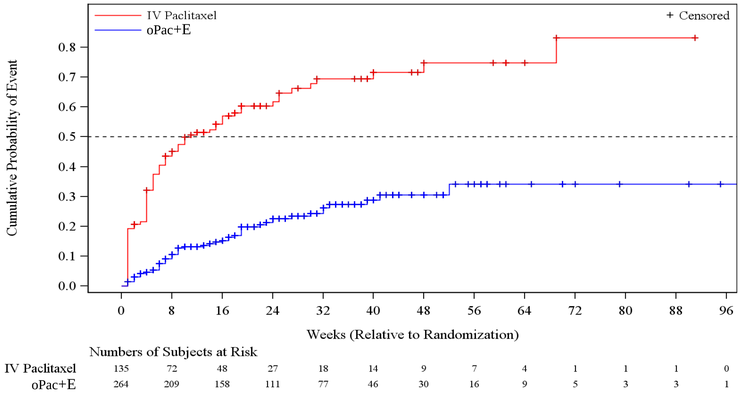
Study Design

- Randomized, multinational study in women with metastatic breast cancer (mBC).
- 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 progressive disease or toxicity.
- The primary endpoint was confirmed tumor response assessed by blinded independent central review (BICR) on two consecutive evaluations Figure 1.
- Key secondary endpoints included Duration of Response, Progression Free Survival and Overall Survival.

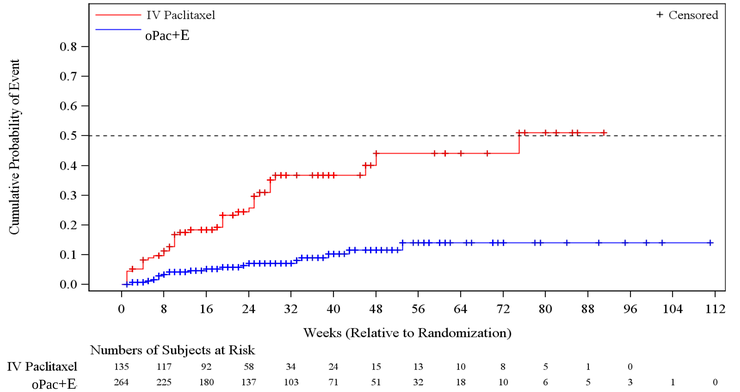


Results

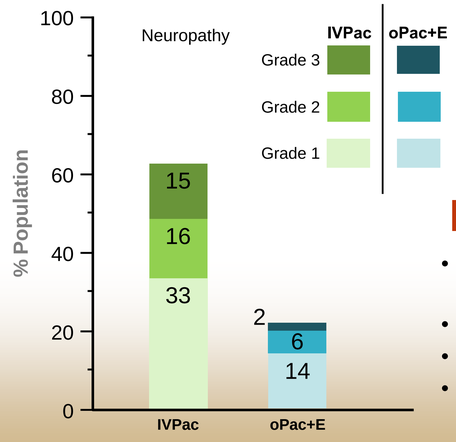
Cumulative Risk of Neuropathy: (Safety Population N=399)



Cumulative Risk of Neuropathy Grade ≥ 2:Lower with oPAC+E (Safety Population N=399)



Lower Incidence of Neuropathy with oPac+E vs IVPac



Most Common (≥10%) Neuropathy Adverse Events

	IVPac		oPac+E	
	All Grades (%)	Grade 3 (%)	All Grades (%)	Grade 3 (%)
Peripheral Neuropathy	36%	7%	8%	1%
Paresthesia	21%	2%	6%	1%
Peripheral Sensory Neuropathy	11%	5%	5%	0%

Less Use of Medications for Neuropathy with oPac+E vs IVPac

	IVPac	oPac+E
PREGABALIN	30%	10%
GABAPENTIN	10%	2%

Conclusions

- oPac+E was associated with a lower incidence of neuropathy, slower onset and lesser severity of neuropathic events compared to IVPac 175mg/m^2 every three weeks.
- Dose reductions due to neuropathy were less frequent with oPac+E (2%) vs IVPac (8%).
- No patients receiving oPac+E vs IVPac (8%) discontinued treatment due to neuropathy.
- Reduction in neuropathy may allow longer use of effective therapy while maintaining dose intensity and offers the potential to improve QOL in patients with breast cancer receiving taxanes.

(NCT 02594371)