decisions harder bringing forward the potential need of taking biopsies in a continuous manner also in the advanced setting to enable optimized treatment decisions for the patient.

5025 POSTER DISCUSSION

Phase 3 Study of Iniparib (I) Plus Gemcitabine (G) and Carboplatin (C) in Metastatic Triple-negative Breast Cancer (mTNBC) − Results of an Exploratory Analysis by Prior Therapy

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Background: Iniparib (I) (BSI-201), an anticancer agent whose mechanism of action is under active investigation, demonstrated improved efficacy outcomes in a randomized phase 2 study when combined with GC in patients (pts) with mTNBC. A confirmatory randomized, open-label phase 3 study (Clinicaltrials.gov number NCT00938652) was conducted (O'Shaughnessy *et al.* ASCO 2011), but did not meet the pre-specified criteria for its co-primary endpoints of overall survival (OS) and progression-free survival (PFS). Here we report results of an exploratory subset analysis from the phase 3 study according to number of prior therapies received.
Methods: Pts were stratified based on receipt of either 0 (n = 297) or 1−2 (n = 222) prior chemotherapies (CT) for metastatic disease. Randomized pts (1:1) received either GC or GCI and, upon central confirmation of disease progression on GC, crossover to GCI was permitted.
Results: From July 2009 to March 2010, 519 pts were randomized. In the overall pt population and within each stratum (1st vs. 2nd/3rd line), demographics, disease characteristics, and prior CT received, were balanced between treatment arms. An exception was receipt of prior bevacizumab (bev) which, although balanced between treatment arms, differed according to strata; 5% of pts in the 1st line received prior bev compared to 63.2% in the 2nd/3rd line. Analysis of PFS and OS by number of lines of therapy − ITT population is detailed in the table.

Prior lines of therapy	GC N	GC Median, mos (95% CI)	GCI N	GCI Median, mos (95% CI)	HR (95% CI)	P-value*
OS†						
All	258	11.1 (9.2–12.1)	261	11.8 (10.6–12.9)	0.88 (0.69–1.12)	0.28
0	149	12.6 (11.9-NC)	148	12.4 (10.6-NC)	1.1 (0.78–1.56)	
⩾1	**109**	**8.1 (6.6–10.0)**	**113**	**10.8 (9.7–13.1)**	**0.65 (0.46–0.91)**	
PFS†						
All	258	4.1 (3.1−4.6)	261	5.1 (4.2−5.8)	0.79 (0.65–0.98)	0.027
0	1 9	4.6 (3.9−5.7)	148	5.6 (4.2−6.9)	0.88 (0.67–1.17)	
⩾1	**109**	**2.9 (1.9−4.1)**	**113**	**4.2 (3.8−5.7)**	**0.68 (0.50–0.92)**	

*2-sided unstratified log-rank test; † pre-specified alpha 0.04 for OS and 0.01 for PFS.

GCI was tolerable with a clinically manageable side effect profile, and adverse events were consistent with the safety profile of GC alone.
Conclusions: In this exploratory analysis by prior therapy, an efficacy benefit was observed in pts receiving GCI vs. GC as 2nd/3rd-line therapy for mTNBC; benefit was not seen for the 1st-line subgroup of pts. The significance of these findings remains uncertain and will need to be validated in future studies.

5026 POSTER DISCUSSION

Sorafenib (SOR) Plus Chemotherapy (CRx) for Treatment (tx) of Patients (pts) With HER2-negative Locally Advanced (adv) or Metastatic (met) Breast Cancer (BC) and Prior Bevacizumab (BEV): Subgroup Analysis of AC01B07

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Background: SOR is a multikinase inhibitor that targets angiogenesis and proliferation. AC01B07 is a double-blind, randomised, placebo (PL)-controlled phase 2b screening trial that assessed SOR when added to CRx in pts with HER2-negative adv BC whose disease progressed during/after a BEV regimen. Primary analysis showed adding SOR significantly prolonged the primary endpoint of progression-free survival (PFS). Tx was tolerable with events consistent with the individual agents. Survival data are pending. Here we report PFS results for predefined and exploratory subgroups.
Methods: Pts were randomised to CRx+SOR (400 mg po twice daily [BID]) or matching PL. The initial CRx used was gemcitabine (GEM 1000 mg/m^2 IV, days 1, 8 of 21) but capecitabine (CAP 1000 mg/m^2 po BID, days 1−14 of 21) became an alternative option later in the study. (NCT00493636; Sponsor, ACORN)
Results: A total of 160 pts were assigned to SOR (n = 81) or PL (n = 79). Prior BEV was for met BC in 156 pts and non-met BC in 4. As expected, more pts received GEM (n = 132) than CAP (n = 28). Overall, PFS was significantly longer for SOR+CRx vs PL+CRx (median 3.4 vs 2.7 mo; hazard ratio [HR] 0.65; 95% confidence interval [CI] 0.45–0.95; 1-sided $P = 0.01$). PFS data across subgroups consistently favored SOR over PL (Table), with the exception of the small (n = 28) CAP subgroup.
Conclusions: Planned subgroup analyses, including the hormone receptor negative subgroup, were consistent with the overall PFS results from AC01B07, demonstrating activity for SOR when added to CRx in the phase 2 setting. This supports further clinical development in all subsets of CRx-treated pts. More studies are needed to understand the disease course and tx options after BEV tx in HER2-negative BC and the various subgroups.

	n	Median PFS (mo)		HR (95% CI)
	n	SOR+CRx	PL+CRx	
Predefined				
Hormone receptor				
Positive	106	3.6	2.7	0.75 (0.48–1.18)
Negative	50	3.1	2.6	0.57 (0.30–1.09)
Visceral disease				
Yes	135	3.2	2.6	0.64 (0.43–0.95)
No	25	4.0	2.9	0.79 (0.29–2.14)
Combination CRx				
GEM	132	3.2	2.5	0.54 (0.36–0.81)
CAP	28	3.6	5.7	2.39 (0.79–7.23)
Exploratory				
Duration of BEV				
⩾6 mo	85	3.1	2.5	0.63 (0.38–1.03)
>6 mo	74	3.9	3.1	0.73 (0.42–1.26)
Time from progression on BEV (met)				
⩽1 mo	129	3.4	2.7	0.65 (0.43–0.97)
>1 mo	27	4.1	2.5	0.75 (0.32–1.76)
Age				
<65 y	135	3.4	2.7	0.64 (0.43–0.95)
⩾65 y	25	3.6	2.7	0.79 (0.28–2.25)
Measurable disease				
Yes	144	3.1	2.6	0.72 (0.49–1.05)
No	15	9.5	2.8	0.26 (0.06–1.06)
Overall	160	3.4	2.7	0.65 (0.45–0.95)