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ABSTRACTS

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A Placebo-Controlled, Randomized Phase II Study of Conatumumab (C) or AMG 479 (A) or Placebo (P) + Gemcitabine (G) in Patients With Metastatic Pancreatic Cancer (mPC)

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Background: C, a death receptor 5 agonist, and A, an insulin-like growth factor receptor 1 antagonist, are investigational, fully human monoclonal antibodies with preclinical activity in PC models. We conducted a 3-arm, placebo-controlled, randomized phase II study evaluating both agents in mPC pts.

Methods: Eligible patients had no prior therapy for mPC; PS 0–1; no poorly-controlled diabetes. Primary end point: 6-month (mo) overall survival (OS). The study was designed to estimate the efficacy of adding C or A to G; 120 patients provides 80% power to detect a difference between a 6-mo OS of 45% for P and 69% for C or A. Stratification: PS (0 vs. 1). Patients were randomly allocated 1:1:1 to Arm 1: C + G (double-blinded); Arm 2: A + G (open-label due to anticipated thrombocytopenia and hyperglycemia); Arm 3: P + G (double-blinded). Patients received C 10 mg/kg, or A 12 mg/kg, or P intravenously (IV) days (D) 1 and 15 and G 1,000 mg/m² IV over 30 minutes D 1, 8, 15 Q28 D. CT scans: Q 2 cycles.

Results: 125 patients (Arms 1/2/3: 41/42/42 patients) at 37 centers enrolled 3/08-4/09; 41/40/40 received ≥ 1 dose of study drug. Median age 61/66/61 years; male 59/60/62%; PS 1 59/55/62%; liver metastases 66/71/79%. Deaths to date 68/48/57%. Efficacy is shown in the table. Grade 3/4 adverse events (% patients, Arms 1/2/3): neutropenia 22/18/13%; thrombocytopenia 15/15/8%;

fatigue 12/10/5%; hyperglycemia 2/15/3%. No post-dose anti-C nor anti-A antibodies were detected.

Conclusions: The addition of C or A to G is well tolerated and results in trends toward longer PFS, improved 6-mo OS, and higher rates of stable disease, when compared with G + P. Updated efficacy and safety data will be presented.

	Arm 1	Arm 2	Arm 3	Arm 1 vs. 3	Arm 2 vs. 3
6-mo OS (95% CI)	59.7% (42.9, 73.1)	56.6% (40.8, 69.7)	50.1% (33.4, 64.7)	9.6% (-12.5, 31.8)	5.7% (-16.0, 27.4)
Median PFS (95% CI), mo	3.9 (3.4, 5.4)	5.1 (3.2, 6.0)	2.1 (1.9, 3.3)	HR = 0.65 (0.39, 1.07); p = 0.095	HR = 0.60 (0.36, 1.01); p = 0.055
Median OS (95% CI), mo	7.5 (5.8, 10)	7.3 (5.3, NE)	6.2 (4.1, 12.9)	HR = 0.90 (0.5, 1.59); p = 0.71	HR = 0.69 (0.38, 1.25); p = 0.22
Partial response	0/38 (0%)	1/38 (3%)	2/40 (5%)		
Stable disease	24/38 (63%)	19/38 (50%)	13/40 (33%)		
Abbreviations: OS = overall survival; CI = confidence interval; PFS = progression-free survival; HR = hazard ratio					