Conclusion: TP300 was well tolerated but no objective responses were observed in 16 evaluable patients with GC or GOJ carcinoma, and recruitment of further patients was discontinued.

6591 POSTER

Improved 6-month Survival Rate in Subjects With Prostate Stem Cell Antigen (PSCA) Positive Tumours in a Global, Randomized Phase 2 Trial Comparing Gemcitabine Vs. Gemcitabine + Ags-1c4d4 (asp6182) in Metastatic Pancreatic Cancer (mPC)

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Background: AGS-1C4D4 (ASP6182) (A) is a CHO-derived fully human monoclonal antibody (MAb) generated from AGS-PSCA (P) a hybridoma MAb. PSCA is a cell surface protein expressed by about 50% of pancreatic cancers, and A significantly inhibited the growth and metastasis of established orthotopic HPAC tumours in combination with gemcitabine (G). These results are of the primary analysis preplanned for when the last randomized patient was followed for 6 months. Final overall survival data is expected by August 2011.
Methods: Previously untreated patients with pathologically-confirmed mPC and ECOG performance status (PS) of 0 or 1 were randomized 1:2 to G (1000 mg/m^2 IV over 30 minutes weekly $\times$7, 1 week rest, then weekly $\times$3 q4weeks) or G plus A (48 mg/kg loading dose, then 24 mg/kg q3weeks over 60 minutes IV), stratified by region (North America vs. Europe/Russia). Primary endpoint was 6-month (mo) survival rate (SR) in the intention-to-treat (ITT) population. With a planned sample size of 185 pts, the study was designed to detect an improvement in 6-mo SR from 45% to 65% with 90% power and one-sided $\alpha = 0.10$. Tumour samples were collected for pre-planned secondary analyses by PSCA expression.
Results: 196 pts (63 in G arm, 133 in G+A arm) enrolled 04/09–05/10 at 55 centers in USA, Canada, Spain, France, and Russia. For G/G+A arms: median age 63/62 years, male 40/56%, PS 1 83/73%, deaths to date 73/71%. Grade 3/4 adverse events (G/G+A; %): any 63/78%, neutropenia 14/26%, thrombocytopenia 2/9%, and pulmonary embolism 2/6%. Tumour tissue was available from 118 pts (60%) for immunohistochemistry (IHC): 64 pts strong/moderate (+) and 54 weak/no staining (−) for PSCA. Efficacy data for 6-mo SR are shown in the table. Disease control rate (95% CI) was 49% (36, 62) for G arm and 50% (41, 58) for G+A arm in the ITT population, and 57% (34, 78) for G arm and 70% (54, 83) for G+A arm in the PSCA+ population.

Population	6-mo. SR (%) (95% CI)			
	ITT	PSCA unavailable	PSCA −	PSCA +
G + A	56 (47, 64)	55 (41, 68)	34 (19, 52)	74 (59, 87)
G	44 (32, 58)	44 (23, 66)	32 (13, 57)	57 (34, 78)
Difference (G+A)–A (95% CI)	11 (−4, 26)	11 (−13, 35)	3 (−25, 30)	17 (−10, 42)
P-Value*	0.07	0.19	0.42	0.08

*One-sided Cochran-Mantel-Haenszel test.

Conclusions: A trend toward improved 6-mo SR was seen in mPC patients with tumours that stained strong or moderate for PSCA expression who were treated with G or G+A. Follow-up is ongoing for secondary endpoints.

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5-Fluorouracil/Leucovorin, Oxaliplatin and Irinotecan (FOLFOXIRI) as First-Line Treatment of Advanced Gastric Cancer

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Background: The aim of the present study was to evaluate the efficacy and safety of FOLFOXIRI as first-line treatment in patients with advanced gastric cancer (AGC) based on results of J. Lee y col. (Annals of Oncology 18: 88−92, 2007).

Material and Methods: 35 patients (p) diagnosed with locoregional, recurrent or metastatic AGC, <75 years old, chemotherapy naïve, PS 0−3, with accurate renal, hepatic and bone marrow functions, were treated from April/27 to March/11 with 5-Fluorouracil 2000 mg/m^2 48 h continuous infusion/d1−3, Leucovorin 100 mg/m^2/d1 and Irinotecan 150 mg/m^2/d1; cycles were administered every 2 weeks, up to 12 cycles, tumour progression or unacceptable toxicity. A total of 35 p were evaluable for toxicity and 33 p for response (2 p early exits from the study).
Results: Median age: 64 years (51−75); male/female: 26/9; PS 0/1/2/3: 3/20/10/2. Advanced locoregional 5 p, metastatic 28 p and recurrent 2 p. Affected organs 1/2/>2: 2/10/23. Sites: Distal lymph nodes 30%, peritoneum 22%, liver 20% and others 26%. A total of 367 cycles were administered with a median of 10 per patient. Effectiveness analysis: 1 RC and 23 RP (RR global 72.7%) and 8 p EE (24.2%). Most relevant toxicities per patient were: anemia G1+2: 77%, neutropenia G3+4: 48%, thrombocytopenia G1+2: 37%, neurotoxicity G1+2:45%, mucositis G1+2: 22%, diarrhea G1+2: 48% and emesis G3+4:42%. 17 p (48%) underwent dose reduction. 6 p received second line QT. Rescue gastrectomy was performed in 2 p. Median time to progression was 8.9 months and median overall survival was 10.3 months.
Conclusions: FOLFOXIRI treatment as first-line treatment of AGC on daily based practice has demonstrated a high activity with a manageable acute toxicity profile, reproducing previously reported results in series of selected patients.

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Phase II Trial of MiniDOX in "Suboptimal" Patients With Advanced Gastric Cancer (AGC). TTD 08−02 (Nº EudraCT: 2008-001825-32)

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Background: Chemotherapy has improved the overall survival (OS) in patients (p) with AGC. We defined "Suboptimal" p as those with PS ECOG-2 and/or weight loss 10−25% and/or age $\geqslant$70 years. This population is usually underrepresented in AGC clinical trials.
Methods: We explored in 43 previously untreated "suboptimal" AGC p the "miniDOX" regimen (docetaxel(D) 40 mg/m^2 iv, d1; oxaliplatin (O) 80 mg/m^2 iv d1; capecitabine (C) 625 mg/m^2 po bid, d1 to 21, every 21d; after 6 courses only C was maintained). D and O dose were allowed to be increased to 45 $\rightarrow$ 50 and to 90 $\rightarrow$ 100 mg/m^2 respectively if less than grade 2 toxicity after the first 2 courses. One included p that did not received any dose of chemotherapy, was included in the ITT efficacy analysis but not in the safety analysis. After the inclusion of the first 10 p the protocol was amended: close vigilance of thromboembolic disease and prophylactic use of G-CSF was recommended. Primary endpoint was Response Rate (RR) and toxicity was the main secondary objective.
Results: *Patient characteristics*: PS ECOG-2:12 p, Weigh loss 10−25%:23 p; median age 73.3 years (40.2–87.7); 32 males; locally advanced: 8 p/metastatic:35 p; Primary site: Gastric 32 p/EGJ 11; Lauren histological type: diffuse 8 p/intestinal 19 p/mixed 1 p/unknown 15 p; Prior gastrectomy: 10 p. In 19 p the dose of D and O were increased to 45 and 90 mg/m^2 respectively and in 8 p to 50 and 100 mg/m^2. Six courses of O and D were administered in 46% and 53% respectively and 58% were treated with 6 or more courses of C. Worst toxicity per p (Grade 3−4): neutropenia: 5 p; febrile neutropenia: 3 p; thrombocytopenia: 1 p; Pulmonary embolism (PE): 4 p (3 of them suffered sudden death and the PE was suspected but not confirmed); diarrhoea: 9 p; paronychia: 2 p; ictus: 1 p; renal failure: 1 p (this p suffered infection/bacteraemia without neutropenia and died); Hand-foot syndrome: 4 p and asthenia: 5 p. Response: CR: 1 p, PR: 27 p (RR: 65%), SD: 8 p, Progression: 2 p, No determined: 5 p; With a median follow-up of 9.2 months, 21 p have died (toxicity: 4 p, progressive disease: 16 p, toxicity of second line treatment 1 p) and 22 p are alive with disease. Median and one year actuarial progression free survival and OS are 5.6 months/17% and 14.6 months/58% respectively.
Conclusions: Although the toxicity (mainly PE) of miniDOX has been important, its activity has been very interesting in "suboptimal" pts with AGC and this combination should be further investigated in this setting.