GEMCITABINE VERSUS FOLFIRINOX IN PATIENTS WITH ADVANCED PANCREATIC ADENOCARCINOMA HENT1 POSITIVE: BACK TO THE FUTURE

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BACKGROUND

Human equilibrative nucleoside transporter 1 (hENT1) is a transmembrane protein which acts as a nucleoside transporter and is the main mediator of Gemcitabine (GEM) uptake into human cells. Several studies showed a positive predictive role of hENT1 expression in adjuvant pancreatic adenocarcinoma (PAC) treated with GEM. In this retrospective study we compared GEM versus FOLFIRINOX (a more effective and toxic regimen) in a series of patients affected by metastatic PAC (m-PAC) in which hENT1 evaluation was available.

METHODS

149 patients affected by histologically confirmed unresectable locally advanced- or m-PAC, treated in our institution from 2009 to 2013, have been screened for inclusion in this retrospective study. 70 patients, treated with GEM or FOLFIRINOX in first-line therapy, fulfilled clinical inclusion criteria for survival analysis. 31 patients, whose stored tumor samples were available and contained sufficient quality/quantity DNA for evaluation of hENT1 expression by RT-PCR, underwent this exploratory analysis (Tab 1). The primary endpoint was OS and the secondary endpoint was PFS. Safety was assessed in terms of grade 3-4 adverse events (AEs).

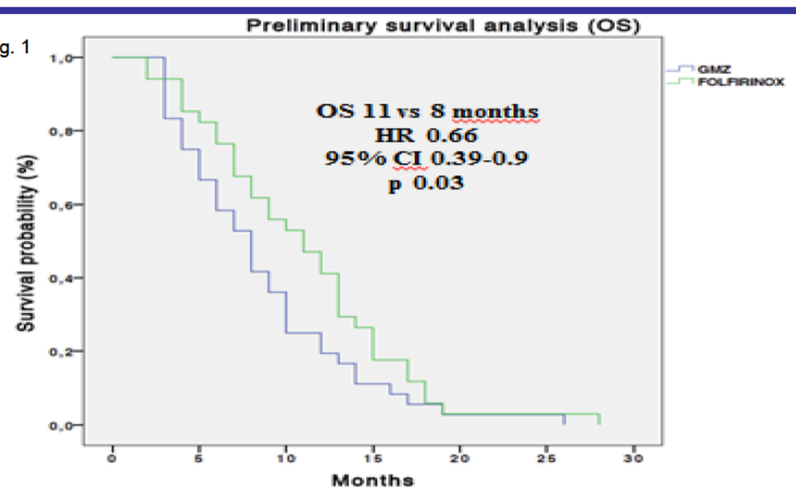
RESULTS

The survival analysis, carried out on 70 patients regardless of hENT1 expression, showed a longer OS (11 vs 8 months; HR 0.66, 95% CI: 0.34-0.9; p=0.03) (Fig. 1) and PFS (6 vs 3 months; HR 0.76, 95% CI: 0.38-1.25; p=0.1) in the group treated with FOLFIRINOX compared to GEM. Within the exploratory analysis, which included 31 patients (Tab. 1), no differences were found in hENT1 positive (hENT1+ve) patients treated with FOLFIRINOX compared to GEM in terms of OS (8.5 vs 7 months, HR: 0.89; 95% CI: 0.3-2.5; p=0.8) (Fig. 2) and PFS (5.5 vs 5 months, HR: 0.8, CI 95%: 0.2-2.2; p=0.61). The incidence of hematologic and non hematologic -G3-4 AEs was also higher in the FOLFIRINOX group (Tab. 2). GEM-treated hENT1+ve patients showed a statistically significant improvement both of OS (8 vs 2 months; p=0.0012) (Fig. 3) and PFS (5 vs 1 months; p=0.0004) in comparison to GEM-treated hENT1 negative (hENT1-ve) patients. On the contrary, FOLFIRINOX-treated hENT1+ve patients had OS and PFS similar to FOLFIRINOX-treated hENT1-ve patients.

Tab. 1

Patient's characteristic	FOLFIRINOX (n= 14)	GEMCITABINE (n=17)
Age – yr	43-77	58-82
Male – n	11	7
Female – n	3	10
T location – n Head	8	11
T location – n Body/Tail	6	6
Metastatic stites – n 1 site	7	12
Metastatic stites – n > 1 site	7	5
Biliary stent – n	7	12
PS ECOG 0 – n	5	6
PS ECOG 1 – n	5	6
PS ECOG 2 – n	4	5
hENT 1 $^{+ve}$ - n	7	12
hENT 1 $^{-ve}$ - n	7	5

Fig. 1



Tab. 2

G 3-4 Adverse Event	FOLFIRINOX (n = 14)	GEMCITABINE (n = 17)
Hematologic		
Neutropenia	6	3
Febrile neutropenia	1	/
Thrombocytopenia	1	/
Anemia	1	/
Non-hematologic		
Vomiting	2	1
Diarrhea	2	/
Sensory neuropathy	2	/
Thromboembolism	1	/

Fig. 2

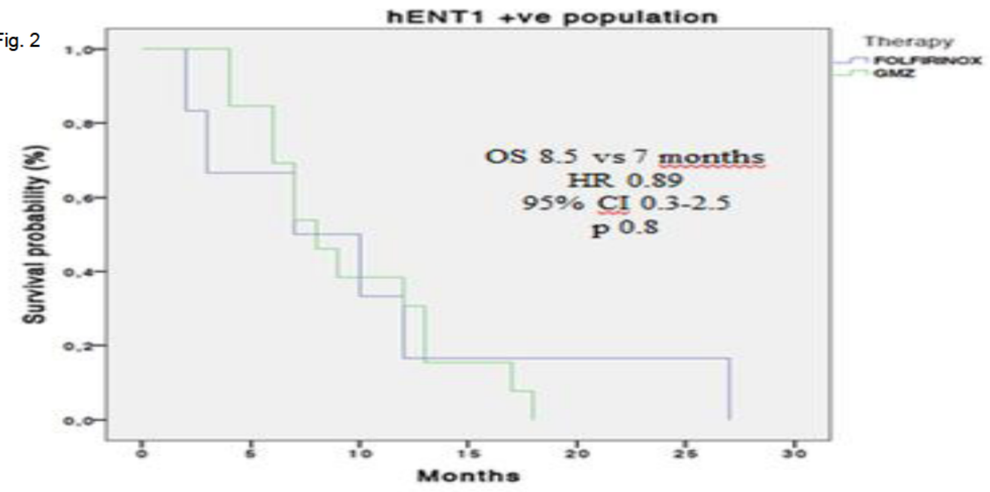
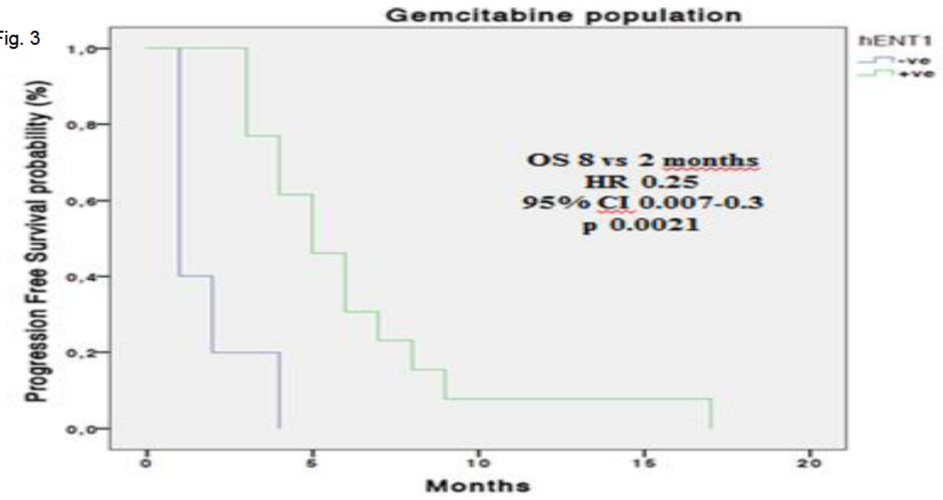


Fig. 3



CONCLUSIONS

In our exploratory analysis GEM seems as effective as FOLFIRINOX in terms of survival with a better safety profile in hENT1+ve m-PAC. Whether confirmed in prospective studies, GEM monotherapy or GEM-based therapy might be the standard first-line regimen in this selected population.

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