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Italian Association  
for Neuroendocrine  
Tumours

**XXII Riunione Nazionale I.T.M.O.**

# ONCOLOGIA: EVOLUZIONE DELLE CONOSCENZE

**Coordinatore:**  
**Prof. Emilio Bajetta**

**Monza, 1 luglio 2016**

**Sede:**

Aula Padiglione "Faggi"  
Istituto di Oncologia Policlinico di Monza  
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## Neoplasie del Pancreas Esocrino e l'Innovazione

# Terapie inefficaci o indicazioni superate?

*Alberto Zaniboni*

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# Premessa

- L'adenocarcinoma del pancreas rimane tra le pochissime neoplasie nelle quali né terapie a bersaglio molecolare né l'immunoterapia sembrano al momento di applicabilità clinica routinaria
- La chemioterapia tradizionale (Folfirinox, Abraxane/Gemcitabina e Gemcitabina) sono i riferimenti clinici abituali per i trattamenti medici neoadiuvanti, adiuvanti e palliativi
- Le ultime novità sono ancora focalizzate su sviluppi della chemioterapia classica (Naliri)
- Esiste ancora un ruolo per schemi terapeutici/ farmaci ritenuti "superati"?



**NCCN Guidelines Version 1.2016**  
**Pancreatic Adenocarcinoma****Table 2: Potential Indications for Various Therapies in the Treatment of Pancreatic Adenocarcinoma**

Regimen	Resectable (adjuvant)	Borderline Resectable (neoadjuvant)	Locally Advanced	Metastatic (good performance status)
Gemcitabine	✓ (category 1)		✓ (category 1 for poor performance status)	✓ (category 1 for good and poor performance status)
Gemcitabine/Albumin-Bound Paclitaxel		✓	✓	✓ (category 1; preferred)
Gemcitabine/Erlotinib			✓	✓ (category 1; survival benefit is small)
Gemcitabine/Cisplatin			✓ (especially if possible hereditary cancer)	✓ (especially if possible hereditary cancer)
Gemcitabine/Capecitabine			✓	✓
Fixed-dose-rate gemcitabine			✓	✓ (category 2B)
GTx [Fixed-dose-rate gemcitabine/docetaxel/capecitabine]			✓ (category 2B)	✓ (category 2B)
5-FU/Leucovorin	✓ (category 1)			
FOLFIRINOX		✓	✓	✓ (category 1; preferred)
Capecitabine	✓ (category 2B)		✓ (category 2B)	✓ (category 2B)
Continuous Infusion 5-FU	✓		✓ (category 2B)	✓ (category 2B)
Fluoropyrimidine/Oxaliplatin (eg, FOLFOX, CapeOx)			✓ (category 2B)	✓ (category 2B)
Radiation	✓ (fluoropyrimidine- or gemcitabine- based)	✓ (subsequent chemoradiation is sometimes included)	✓ (in select patients without systemic metastases; fluoropyrimidine- or gemcitabine-based)	✓ (palliative only)

Come ho trattato gli ultimi 100 pazienti  
in stadio IV in prima linea?

Gemcitabina  
25

GEMOX  
28

Abraxane/GEM  
33

Folfirinox  
8

Folfox  
6

e i prossimi 100?

GEMCITABINA DA SOLA?

## EDITORIAL

## Genomic Testing for Gemcitabine-Based Treatment of Pancreatic Cancer

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Pancreatic cancer is a deadly condition with a single-digit overall five-year survival rate. Most tumors are metastatic upon diagnosis, and patients are left with palliative treatment options. Nucleoside analogue-based chemotherapy and, more recently, oxaliplatin, irinotecan, fluorouracil, and leucovorin (FOLFIRINOX) are the options most frequently recommended for most patients with advanced disease. Gemcitabine as a single agent remains a standard first line of defense for metastatic disease, especially in patients with poor performance status.

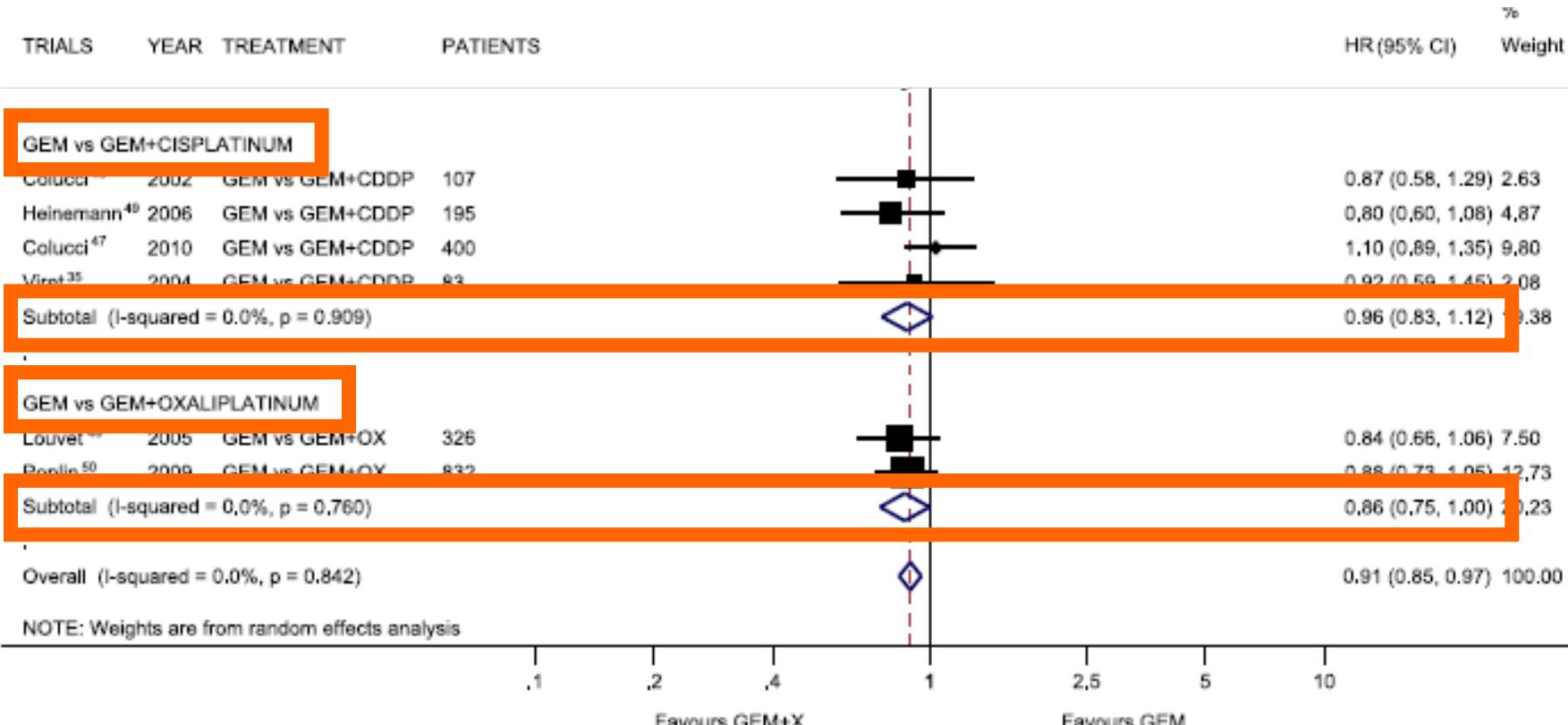
results of electrophoretic mobility shift assay indicate that the G-to-A mutation reduces Sp1/3 binding to the promoter of the WWOX gene, leading to low levels of WWOX expression in pancreatic cancer cells.

The association of WWOX rs11644322 and low overall survival among patients with metastatic pancreatic cancer treated with gemcitabine-based therapy should be explored to assess if such genomic testing can screen appropriate patients for gemcitabine therapy. After additional clinical trials on large popu-

**ANCORA GEMOX?**

Available at [www.sciencedirect.com](http://www.sciencedirect.com)EJC  
EUROPEAN JOURNAL OF CANCER

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# BRCA and Pancreas Adenocarcinoma

- 5-8% of PDAC patients germline BRCA1 or 2 mutation
  - Ashkenazi Jewish 5-16%
  - Familial PDAC 5-19%
  - Familial breast/ovary cancer 5-10%
- BRCA Founder mutations in AJ descent (2-3%)
  - BRCA 1:185delAG, 5382insC
  - BRCA 2:6174delT

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Memorial Sloan Kettering  
Cancer Center

# Genetic Factors

- A family history of pancreatic cancer is seen in 20% of patients<sup>1,2</sup>
- In some of these families (5%–10% of patients), the high risk is due to a hereditary pancreatic cancer syndrome, in which cancer is caused by one of several germline mutations<sup>1,2</sup>
- **Familial pancreatic cancer**
  - Defined as two or more first-degree relatives with pancreatic cancer
  - Individuals with family history have a range from a 1.9- to a 13-fold increased risk<sup>3–5</sup>
  - Familial pancreatic cancer is genetically heterogeneous, with some cases caused by germline mutations<sup>6–8</sup>:
    - *BRCA2* (2.8%–17.2%)
    - *PALB2* (1%–3%)

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2. Kanji ZS, et al. *CMAJ*. 2013;185(14):1219-1226.

3. Jacobs EJ, et al. *Int J Cancer*. 2010;127:1421-1428.

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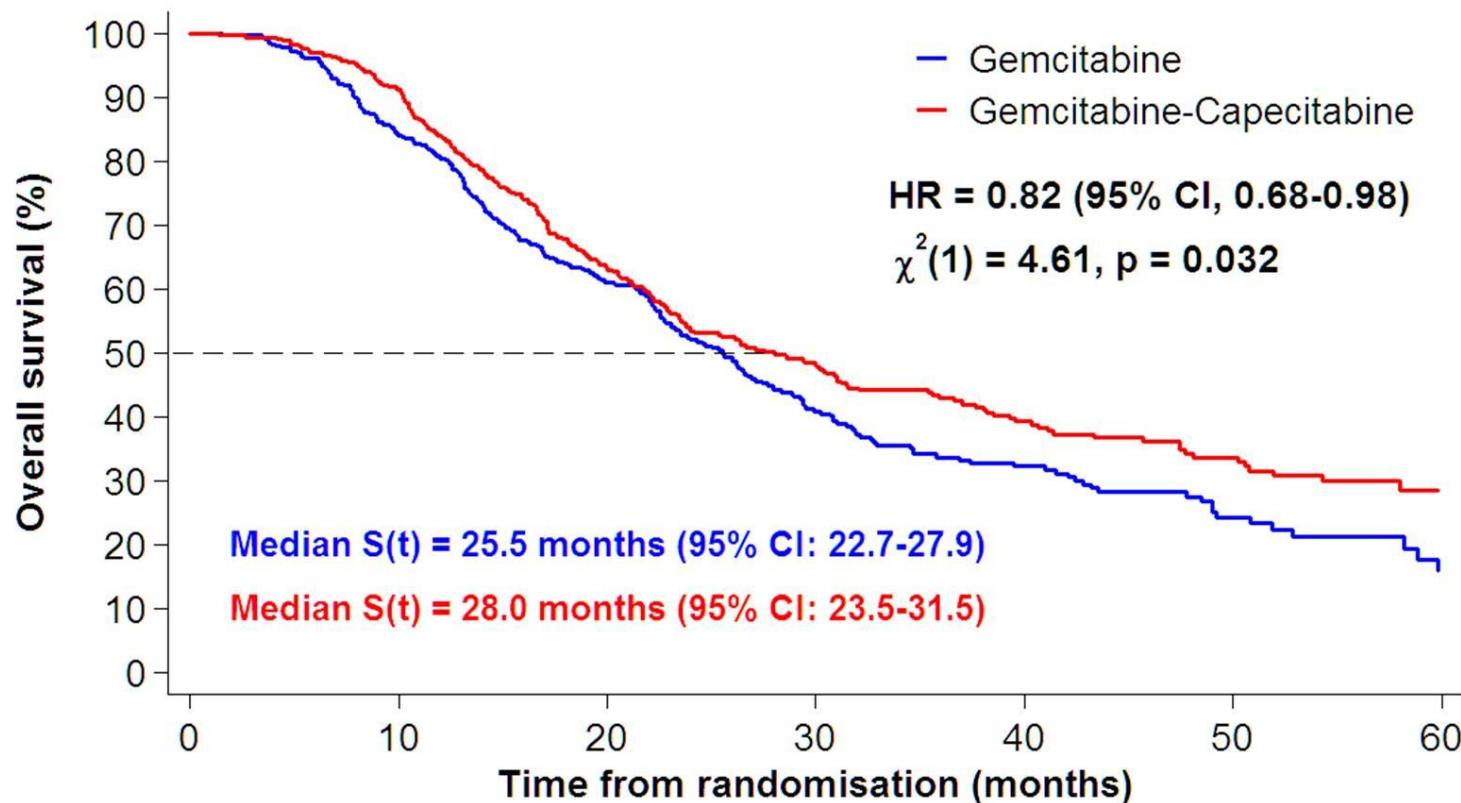
6. Shi C, et al. *Arch Pathol Lab Med*. 2009;133:365-374.

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**CAPECITABINA + GEMCITABINA?**

# Survival by Treatment



## No. at Risk

Gem	366	302	207	109	61	27	9
GemCap	364	328	219	139	83	50	19





June 2016