

**PROGRESS IN  
PANCREATOLOGY  
AND GI-TRACT SURGERY**

**GASTROINTESTINAL SURGERY TODAY  
- THE ULM SURGICAL SCHOOL**

**SATURDAY, SEPTEMBER 8TH, 2001**

**ORAL PRESENTATIONS**



# Pancreatic cancer and chemotherapy. New developments from bench to bedside.

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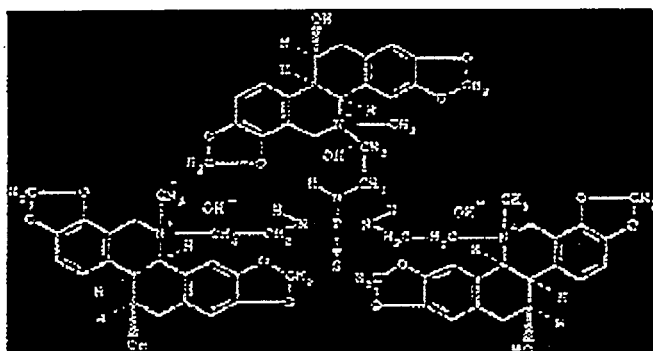


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## Background

### NSC-631570 (Ukrain<sup>®</sup>):

a semisynthetic compound of the alkaloid chelidonine from the plant *Chelidonium majus* L. and thiotepa.



## Material & Methods - in-vitro

### Material

pancreatic cancer cell lines: AsPC1, BxPC3, Capan 1, MiaPaca2, Panc1

### Methods

cell cycle analysis

proliferation assays (BrdU-incorporation)

Western blotting (whole cell lysates from serial experiments)

Giemsa staining and mitose sub-phase analysis

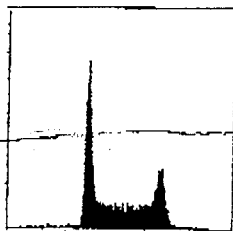
Fluorescence immunostaining

In-vitro polymerisation of monomeric tubulin

## Results - in vitro

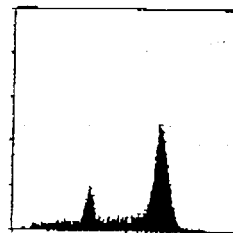
NSC-631570 leads to an accumulation of pancreatic cancer cells in the G<sub>2</sub>/M-phase of the cell cycle

control



AsPC1 - 24h

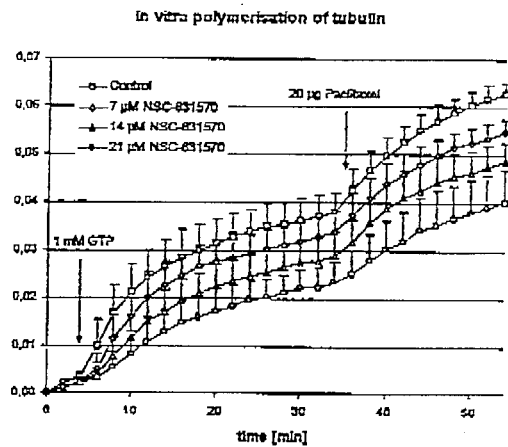
10 µg/ml NSC-631570



AsPC1 - 24h

## Results - in vitro

### NSC-631570 inhibits polymerisation of monomeric tubulin in-vitro



## Material & Methods: clinical study

Monocentric, prospective, controlled,  
randomized study:

inclusion criteria:

histologically proven unresectable  
adenocarcinoma of the pancreas

exclusion criteria:

age below 18 years  
pregnancy or no contraception  
other cancer diseases  
viral infection with hepatitis B or C or HIV  
immunosuppressive therapy  
diseases of the central nervous system

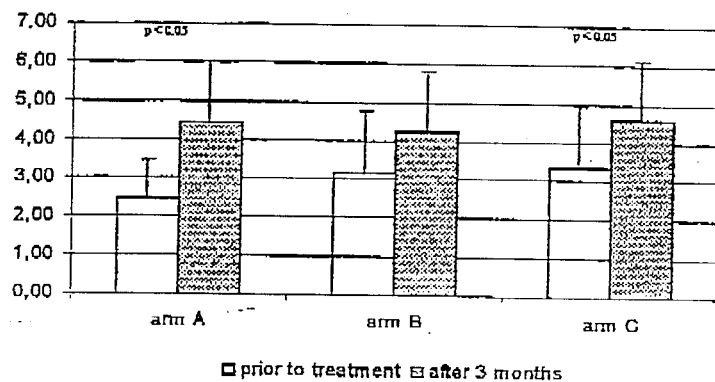
## Results: clinical study

### side effects

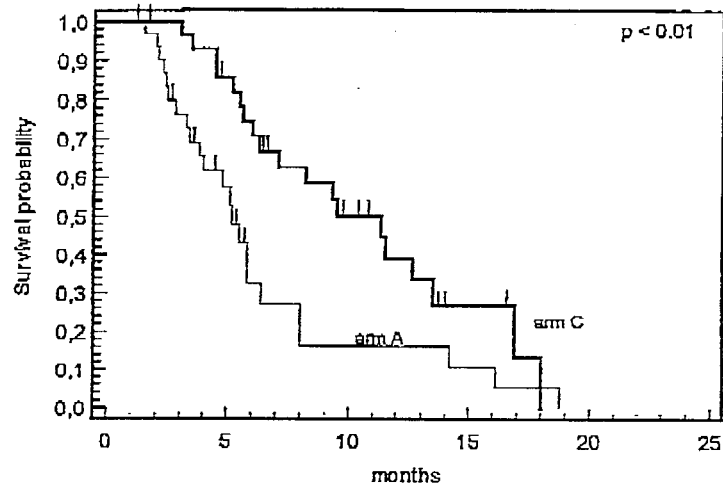
	Gemcitabine Arm A			NSC-631670 Arm B			NSC-631670 / Gemcitabine Arm C		
	WHO I	WHO II	WHO III	WHO I	WHO II	WHO III	WHO I	WHO II	WHO III
Hematological	46%	13%	0%	25%	5%	2%	48%	38%	4%
Obstipation	0%	27%	0%	8%	8%	0%	0%	0%	0%
Nausea	9%	33%	11%	17%	9%	0%	12%	8%	2%
Diarrhea	18%	9%	0%	7%	5%	4%	14%	4%	0%
Fever	15%	9%	0%	22%	20%	0%	18%	15%	0%
Tumor Bleeding	0%			7%			7%		

## Results: clinical study

### Quality of life - self estimation



## Results: clinical study



## Summary

**NSC-631570 arrests pancreatic cancer cells in prophase via inhibition of tubulin polymerisation**

**NSC-631570 reduces proliferation rate and induces apoptosis in pancreatic cancer cells**

**NSC-631570 shows non-understimating side effects in clinical application and should be administered under medical control**

**NSC-631570 in combination with gemcitabine prolongs overall survival in patients with advanced pancreatic cancer**

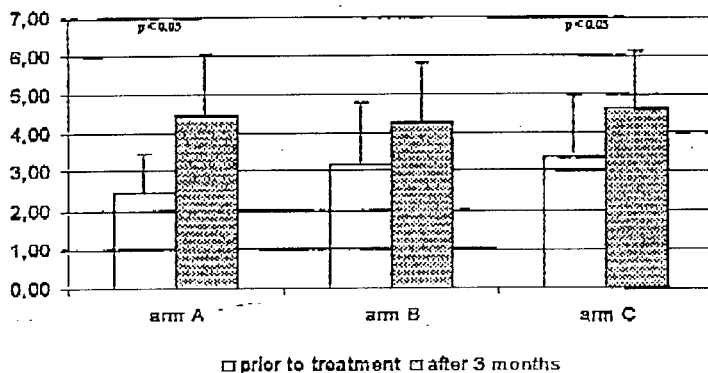
## Results: clinical study

### side effects

	Gencicabine Arm A			NGC-631570 Arm B			NGC-631570 / Gencicabine Arm C		
	WHO I	WHO II	WHO III	WHO I	WHO II	WHO III	WHO I	WHO II	WHO III
Hematological	48%	13%	0%	39%	5%	2%	48%	38%	4%
Obstipation	0%	27%	0%	8%	6%	0%	0%	0%	0%
Nausea	8%	33%	11%	17%	8%	0%	12%	8%	2%
Diarrhea	18%	8%	0%	7%	3%	4%	14%	4%	0%
Fever	13%	5%	0%	22%	20%	0%	18%	18%	0%
Tumor Bleeding	0%			7%			7%		

## Results: clinical study

### Quality of life - self estimation



## **Conclusion**

**NSC-631570 is a new potential cytostatic drug for the treatment of advanced pancreatic cancer in combination with gemcitabine.**

**Administration should be performed under medical control.**

**These results warrant further studies.**