

**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.

F. Gansauge, M. Ramadani, S. Gansauge, J. Pressmar,
B. Muehling, K. Strecker, G. Cammerer, G. Leder,
and H.G. Beger

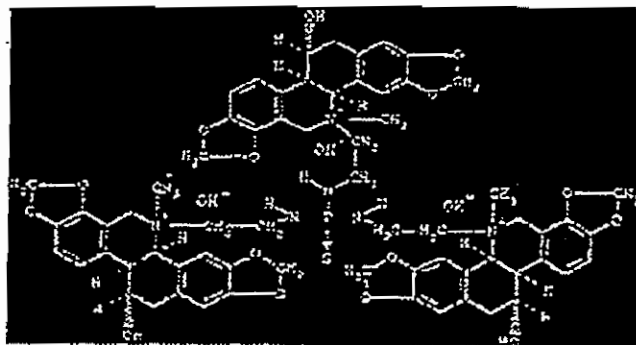


Department of General Surgery,
University of Ulm, Germany

Background

NSC-631570 (Ukrain[®]):

a semisynthetic compound of the alkaloid chelidonium 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)

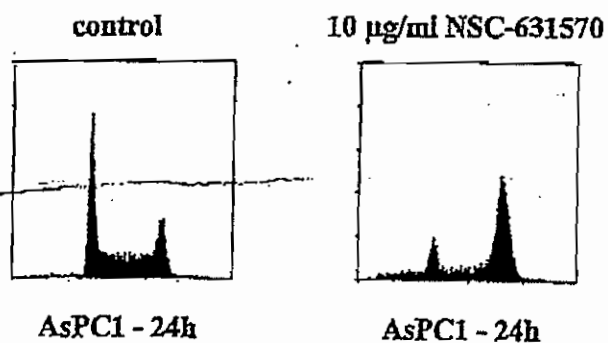
Giemsa staining and mitose sub-phase analysis

Fluorescence immunostaining

In-vitro polymerisation of monomeric tubulin

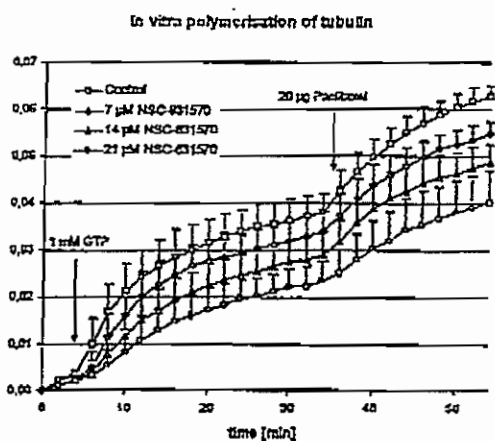
Results - in vitro

NSC-631570 leads to an accumulation of pancreatic cancer cells in the G2/M-phase of the cell cycle



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

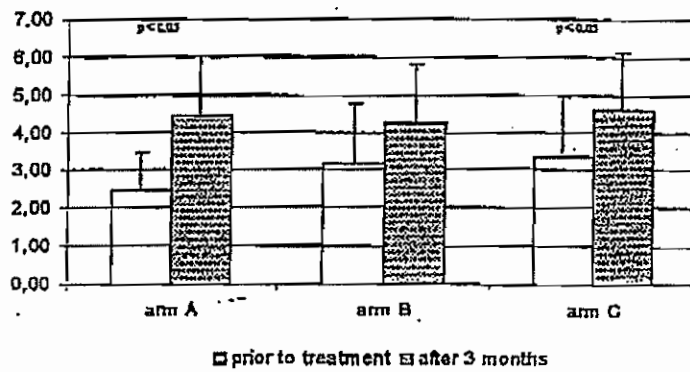
Results: clinical study

side effects

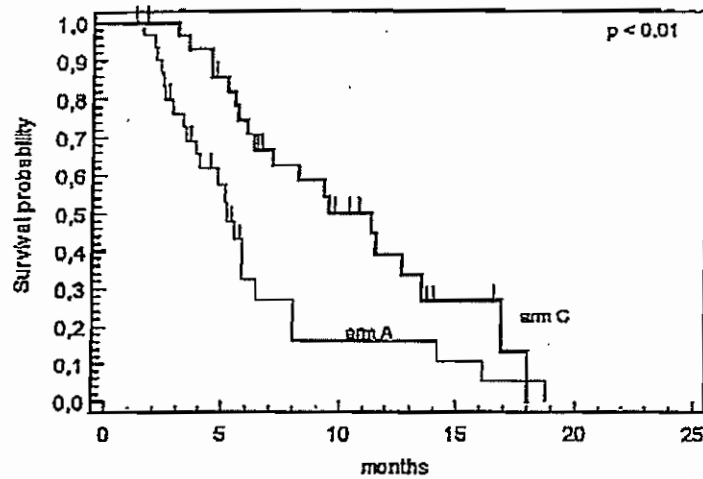
	Geostabine Arm A			NBO-G31570 Arm B			NBO-G31570/ Geostabine Arm C		
	WHO I	WHO II	WHO III	WHO I	WHO II	WHO III	WHO I	WHO II	WHO III
Hematological	40%	13%	0%	35%	5%	2%	48%	38%	4%
Obstipation	0%	27%	0%	8%	6%	0%	0%	0%	0%
Nausea	0%	33%	11%	17%	0%	0%	12%	6%	2%
Diarrhea	18%	0%	0%	7%	5%	4%	14%	4%	0%
Fever	13%	0%	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

	Gendabine Arm A			NGO-01570 Arm B			NGO-01570 / Gendabine Arm C		
	WHO I	WHO II	WHO III	WHO I	WHO II	WHO III	WHO I	WHO II	WHO III
Hematological	42%	13%	0%	33%	5%	2%	48%	36%	4%
Obstipation	0%	27%	0%	8%	8%	0%	0%	0%	0%
Nausea	9%	33%	11%	17%	8%	0%	12%	8%	2%
Diarrhea	18%	8%	0%	7%	0%	4%	14%	4%	0%
Fever	13%	8%	0%	22%	20%	0%	18%	18%	0%
Tumor Bleeding	0%			7%			7%		

Results: clinical study

Quality of life - self estimation

