

Regional chemotherapy plus or minus prophylaxis of thrombembolic events with low-dose Warfarin in the treatment of advanced pancreatic cancer – a retrospective analysis

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Background

- ✓ The overall prognosis for cancer of the exocrine pancreas remains dismal.
- ✓ For resectable disease the 5-year survival rates are approximately 5 % to 20 %.
- ✓ For metastatic and locally advanced disease median survival averages 5 and 10 months.



Aim of this study

- ✓ to determine the efficacy of different regional chemotherapeutic regimens
- ✓ to determine the efficacy of anti-hormone treatment with Octreotid
- ✓ to determine the efficacy of anti-thrombotic treatment using low-dose Warfarin



Study design

- ✔ Retrospective analysis
- ✔ 281 patients
- ✔ with inoperable or metastasized pancreatic cancer
- ✔ treated between 1/95 and 6/02 at department of surgical oncology, Carl von Hess – hospital, Hammelburg, Germany



Patient characteristics I

Gender	male / female	138 / 143
Age	Mean	59.7
	Range	26 - 84
Tumorstage		
Locally inoperable	Stage III	133
Metastasized	Stage IV	148
Localization		
Head		175
Corpus		77
Tail		36



Patient characteristics II

Karnofsky - Index	100	6.0 %
	90	15.3 %
	80	32.4 %
	70	29.5 %
	60 and less	16.7 %
Metastases		
	liver	148
	lymphnodes	106
	peritoneum	47
	Lung	23
	others	32



Patient characteristics III

Pretreatment	Pts.	%
Pretreated	203	64.1 %
Chemotherapy	75	26.7 %
Operation	92	32.7 %
Radiation	13	4.6 %
Pain - status		
Stage 0	91	32.4 %
Stage I	51	18.1 %
Stage II	21	7.5 %
Stage III	49	17.4 %
Stage IV	69	24.6 %



Treatment modalities

✓ **Cytostatic treatment**

4 different regimen of regional chemotherapy

✓ **Additive treatment**

- * antihormone treatment with Octreotid
- * anti-thrombotic treatment with Warfarin



Cytostatic treatment data

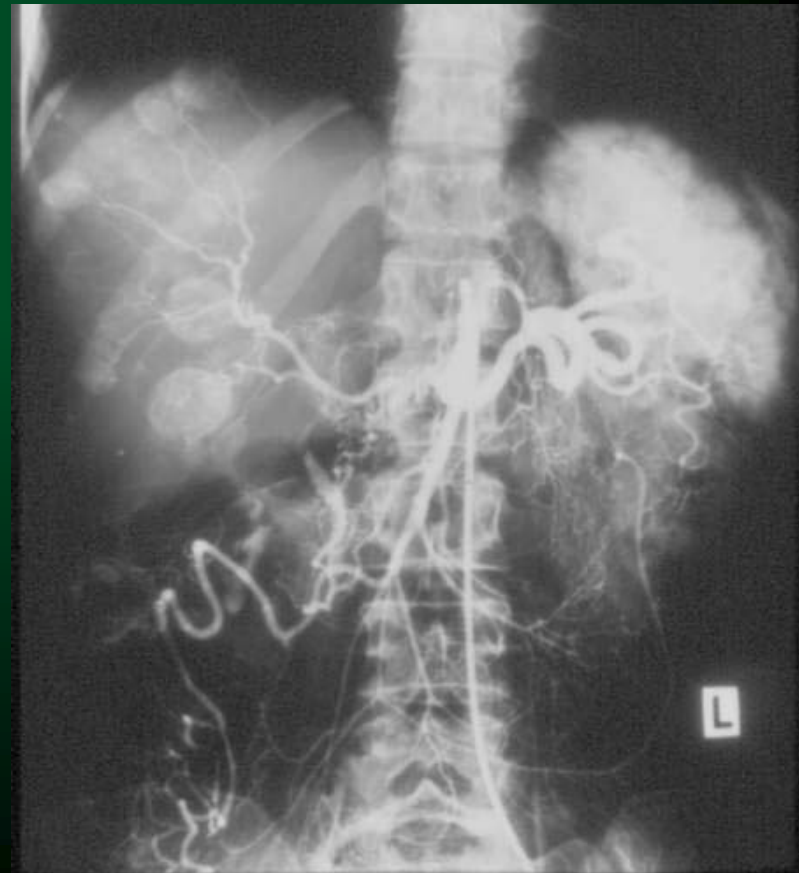
Patients treated by cytostatics	251 / 281
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Chemotherapeutic interventions

total	656
mean	2.33
range	0 - 10

Technique of application

- ✔ infusion of cytostatics via celiac axis catheter
- ✔ Catheter placed angiographically in Seldinger technique
- ✔ under x-ray guidance
- ✔ in local anaesthesia





Cytostatic treatment

▼ Regimen 1 :

Gemcitabine 1000 mg/m², Mitomycin 12 mg/m²

▼ Regimen 2 :

Bleomycin 45 mg/m², Mitomycin 12 mg/m², Venorelbine 25 mg/m²

▼ Regimen 3 :

Paclitaxel 120 mg/m², Cisplatinum 50 mg/m², Treosulfan 5000 mg/m²

▼ Regimen 4 :

Cisplatinum 50 mg/m², Mitomycin 12 mg/m², Melphalan 25 mg/m²,



Side-effects

Complications	Number
Gastrointestinal bleeding	11
Thrombosis	23
Lung embolism	14
Leucocytopenia - WHO 4	18
Thrombocytopenia - WHO 4	8
Cholangitis	14
Infection	26
Elevation of creatinin	21
Elevation of bilirubin	48



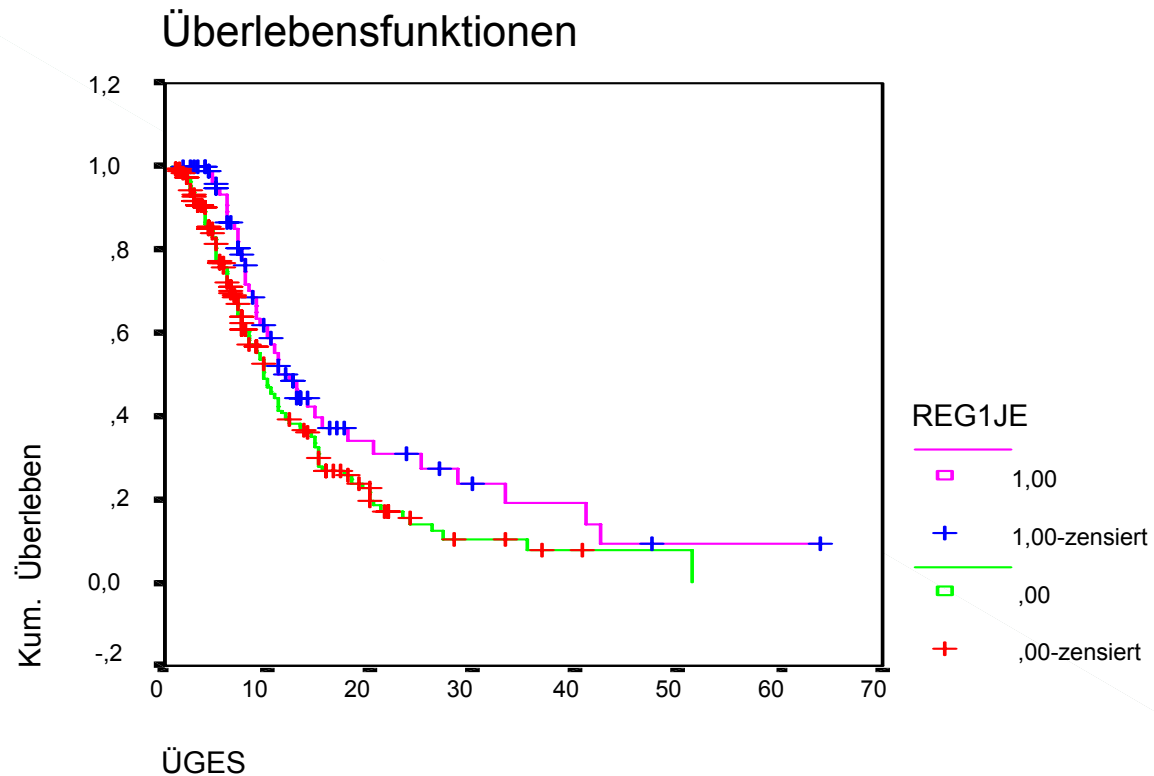
Efficacy of cytostatic treatment I

Survival data

- ✓ Regimen 1: (Gemzar, MMC) 83 pts.
 - median survival time 12.0 mon.
- ✓ Regimen 2 : (Bleo, MMC, Navelbine) 46 pts.
 - median survival time 9.6 mon.
- ✓ Regimen 3 : (Taxol, CDDP, Treo) 46 pts.
 - median survival time 9.63 mon.
- ✓ Regimen 4 : (MMC, CDDP, L-Pam, Mito) 53 pts.
 - median survival time 9.6 mon.

statistically significant $p > 0.05$

Efficacy of cytostatic treatment II



Kaplan – Meier Plot for cytostatic treatment with Gemcitabine / Mitomycin (83 pts.)
vs. other cytostatic treatments $p < 0.05$



Additive treatment I

✓ anti-thrombotic therapy

Warfarin

- Dosage : 1.25 mg / day
- Application : oral
- clotting test : none



Efficacy of Warfarin treatment I

Alterations of clotting system

▼ up front

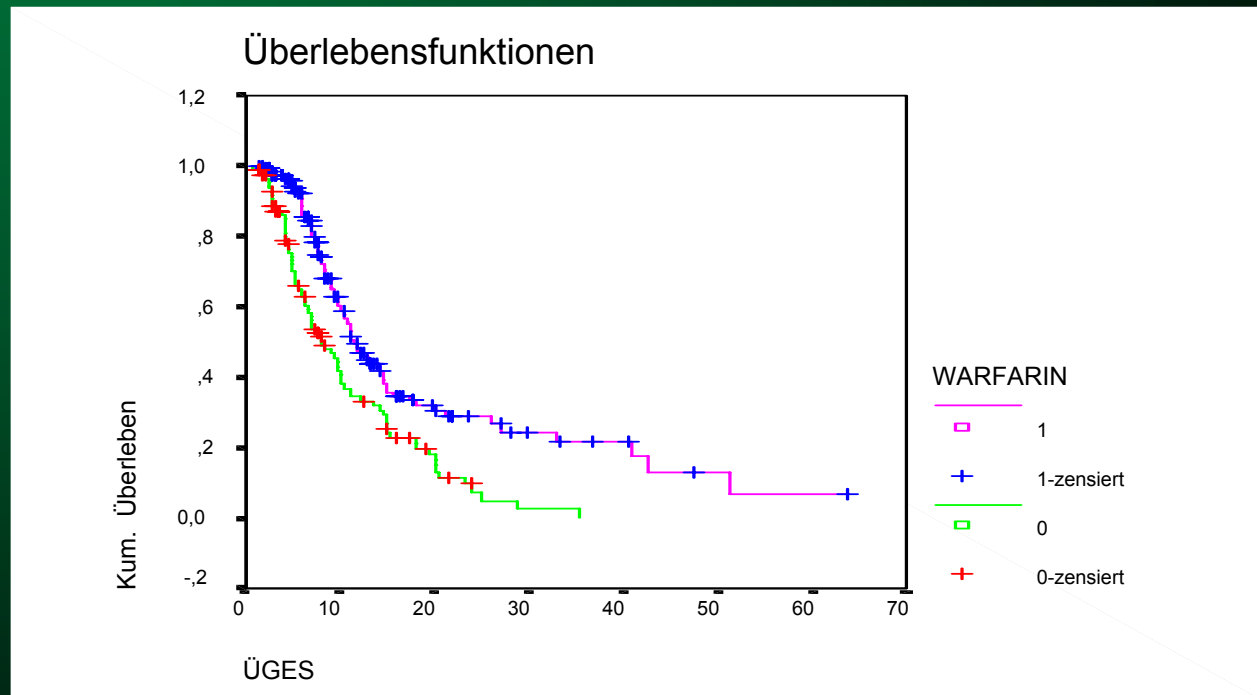
• Thrombosis	20 pts.	7.1 %
• Bleeding	10 pts.	3.5 %

▼ Warfarin treatment

Treatment in	170 / 281 pts.	
• Thrombosis	23 pts.	8.2 %
• Bleeding	11 pts.	3.9 %

No significant difference !

Efficacy of Warfarin treatment II



Kaplan – Meier Plot for regional chemotherapy plus Warfarin treatment (170 pts.)
vs. no antithrombotic intervention



Efficacy of Warfarin treatment III

survival data

✓ no anti-thrombotic treatment

- Mean survival time 10.9 mon.
- Median survival time 8.0 mon.

✓ Warfarin treatment

- Mean survival time 20.3 mon.
- Median survival time 11.3 mon.

Multi-variant analysis $p = 0.03$



Additive treatment II

✓ anti-hormon therapy

Octreotid

- Dosage : 100 mg 3 times daily
- Application : subcutaneous
- Modification: 30mg Sandostatin - LAR since 1 / 02



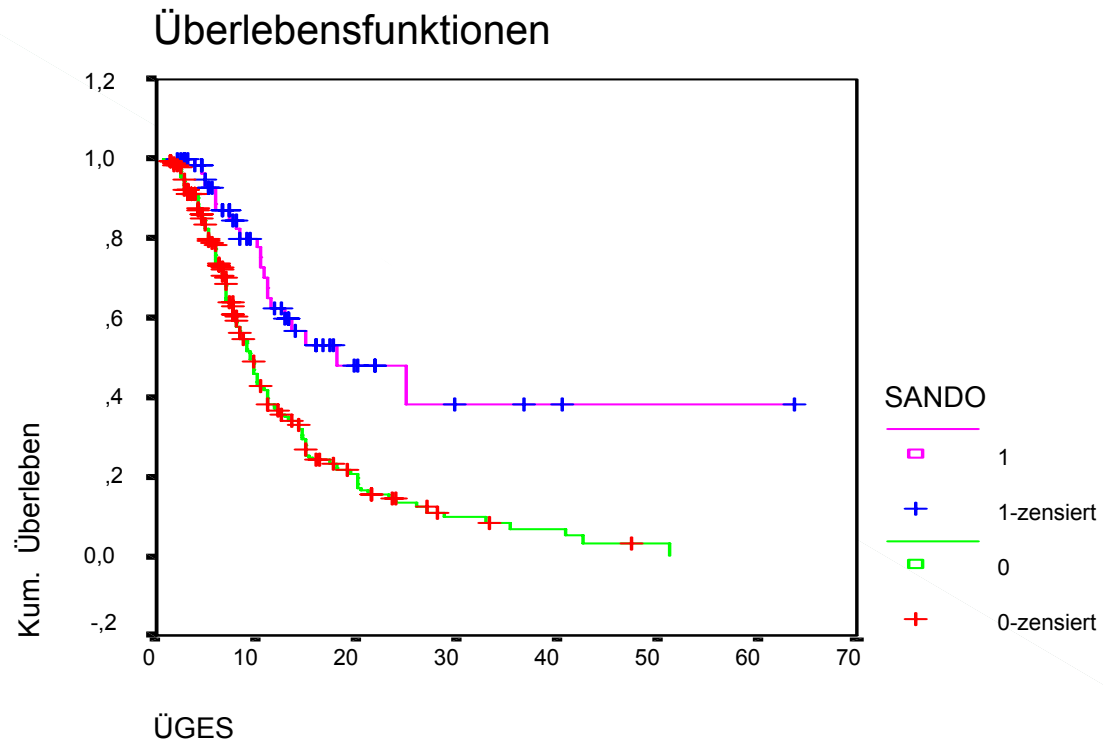
Efficacy of Sandostatin treatment I

Survival data

✓ no anti-hormone treatment	217 pts.
• Mean survival time	13.5mon.
• Median survival time	9.4 mon.
✓ Sandostatin treatment	64 pts.
• Mean survival time	32.1 mon.
• Median survival time	19.0 mon.

Multi-variant analysis $p = 0.018$

Efficacy of Sandostatin treatment II



Kaplan – Meier Plot for regional chemotherapy plus Sandostatin treatment (64 pts.)
vs. no anti-hormone treatment



Conclusion I - cytostatics

- ✓ Regional chemotherapy is feasible and safe in the treatment of pancreatic carcinoma.
- ✓ Survival difference between different cytostatic regimen for regional chemotherapy is rather small.
- ✓ Gemcitabine / Mitomycin regimen is combined with favorable outcome compared to other combinations.



Conclusion II – antithrombotic treatment

- ✔ Combination of anti-thrombotic treatment with low-dose Warfarin plus regional chemotherapy is feasible and safe in the treatment of pancreatic carcinoma.
- ✔ Low-dose Warfarin treatment does not increase the risk of bleeding events.
- ✔ Low-dose Warfarin does not reduce the rate of thrombosis, but it prolongs survival time for pancreatic cancer patients.



Conclusion III – anti-hormon treatment

- ✔ Combination of anti-hormon treatment with Sandostatin plus regional chemotherapy is feasible and safe in the treatment of pancreatic carcinoma.
- ✔ Use of anti-hormon treatment with Sandostatin seems to prolong survival time for pancreatic cancer patients.