

GI-Oncology 2010

6. Interdisziplinäres Update
Wiesbaden, 3. Juli 2010

Late breaking news:

**Gibt es einen neuen Standard beim
metastasierten Pankreaskarzinom?**

**M.P. Lutz
Saarbrücken**

ASCO, 2.-5. Juni 2010

- **Folfirinox vs. Gemcitabine**

T. Conroy et al.

ASCO 2010, LBA #4010

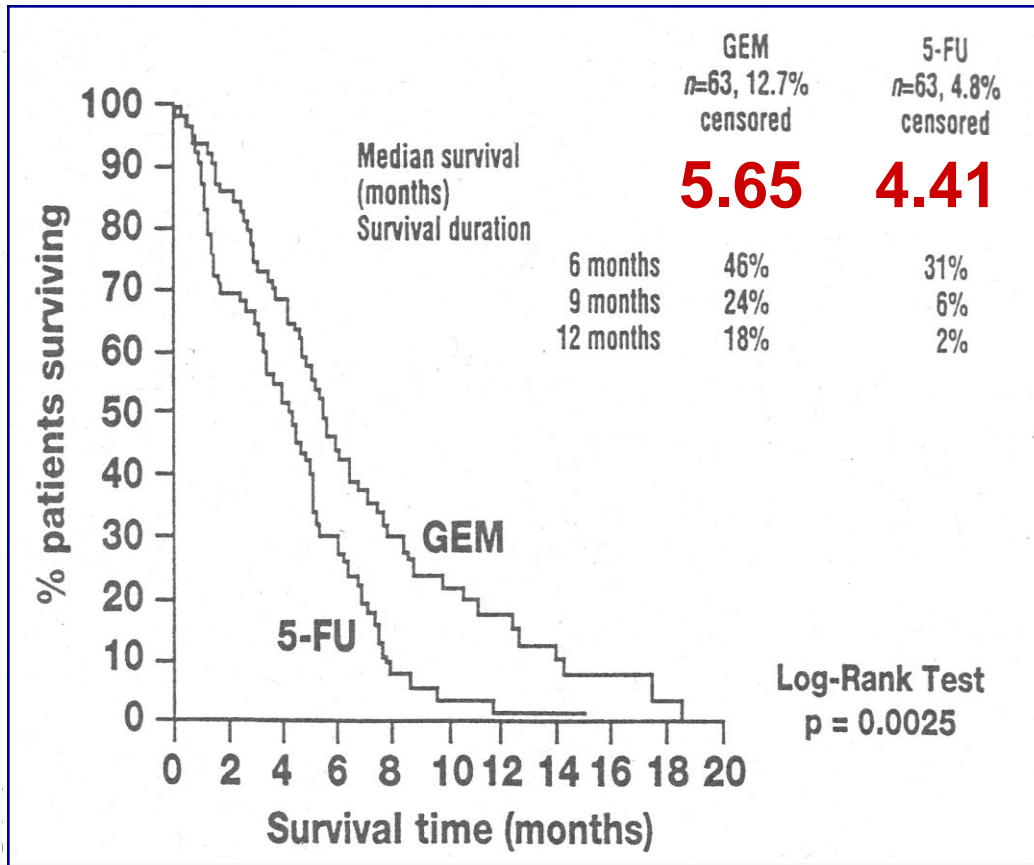
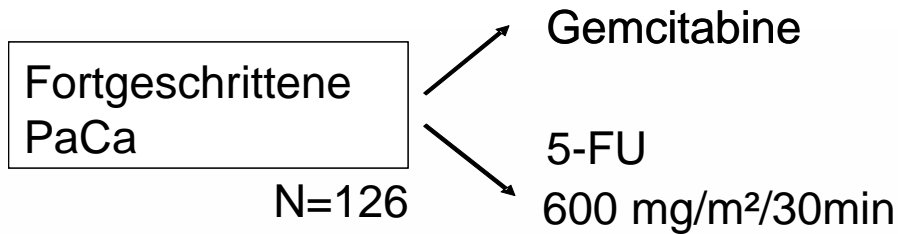
- **Gem/Erlotinib vs. Cape/Erlotinib
mit crossover (AIO-PK 0104)**

S. Boeck et al.

ASCO 2010, LBA #4011

Standard seit 1997: Gemcitabine

Burris et al. JCO 1997



Clinical benefit

Gem 23.8 %

5-FU 4.5 %

Phase III Studien (Auswahl)

Autor	Experimenteller Arm	n	ÜL (Monate)
Rocha Lima JCO 04	G + Irinotecan	360	6.3 vs. 6.6
Abou-Alfa JCO 06	G + Exatecan	349	6.7 vs. 6.2
Heinemann JCO 06	G + Cisplatin	195	7.5 vs. 6.0
Louvet JCO 05	G + Oxaliplatin	326	9.0 vs. 7.1
Poplin JCO 08/09	G fdr + Oxaliplatin	832	5.7 vs. 5.9
	G fdr		6.2 vs. 5.9
Berlin JCO 02	G + 5-FU	327	6.7 vs. 5.4
Herrmann JCO 07	G + Capecitabine	319	8.4 vs. 7.2
Cunningham JCO 11/09	G + Capecitabine	533	7.1 vs. 6.2
Moore JCO 2007	G + Erlotinib	569	6.4 vs. 5.9
Philip ASCO 07	G + Cetuximab	735	6.4 vs. 6.4
Kindler ASCO 07	G + Bevacizumab		5,8 vs. 6.1
	G + Axitinib		negativ
Van Cutsem JCO 05/09	G + Erlotinib+Bev	607	7.1 vs. 6.0



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Heinemann JCO 06	G + Cisplatin	195	7.5 vs. 6.0	} HR 0,85 p=0.01
Louvet JCO 05	G + Oxaliplatin	326	9.0 vs. 7.1	
Poplin JCO 08/09	G fdr + Oxaliplatin	832	5.7 vs. 5.9	
	G fdr		6.2 vs. 5.9	
Berlin JCO 02	G + 5-FU	327	6.7 vs. 5.4	} HR 0,86 p=0.02
Herrmann JCO 07	G + Capecitabine	319	8.4 vs. 7.2	
Cunningham JCO 11/09	G + Capecitabine	533	7.1 vs. 6.2	
Moore JCO 2007	G + Erlotinib	569	6.4 vs. 5.9	} HR 0,82 p=0.04
Philip ASCO 07	G + Cetuximab	735	6.4 vs. 6.4	
Kindler ASCO 07	G + Bevacizumab		5,8 vs. 6.1	
	G + Axitinib		negativ	
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V. Heinemann et al. BMC Cancer 03/08
D. Cunningham et al. JCO 11/09

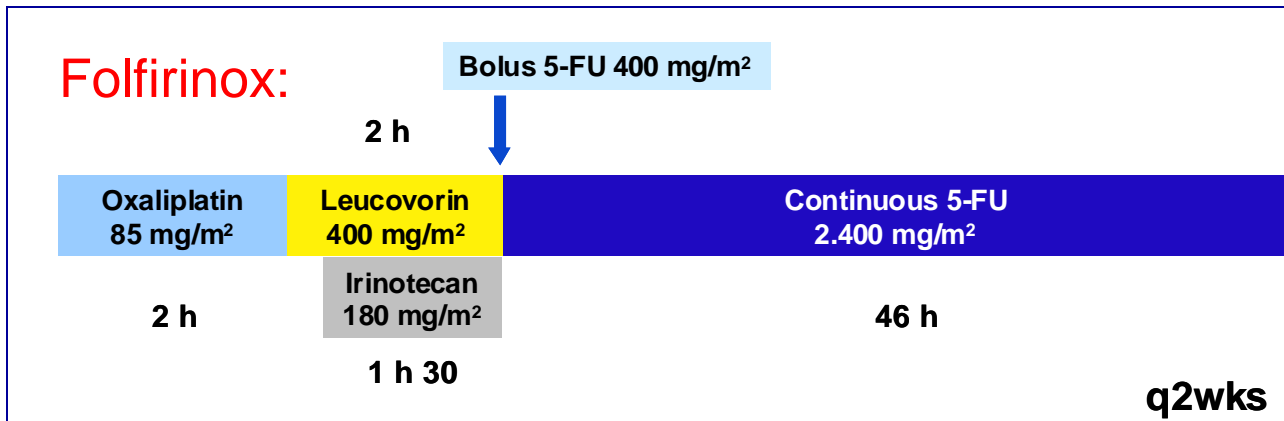
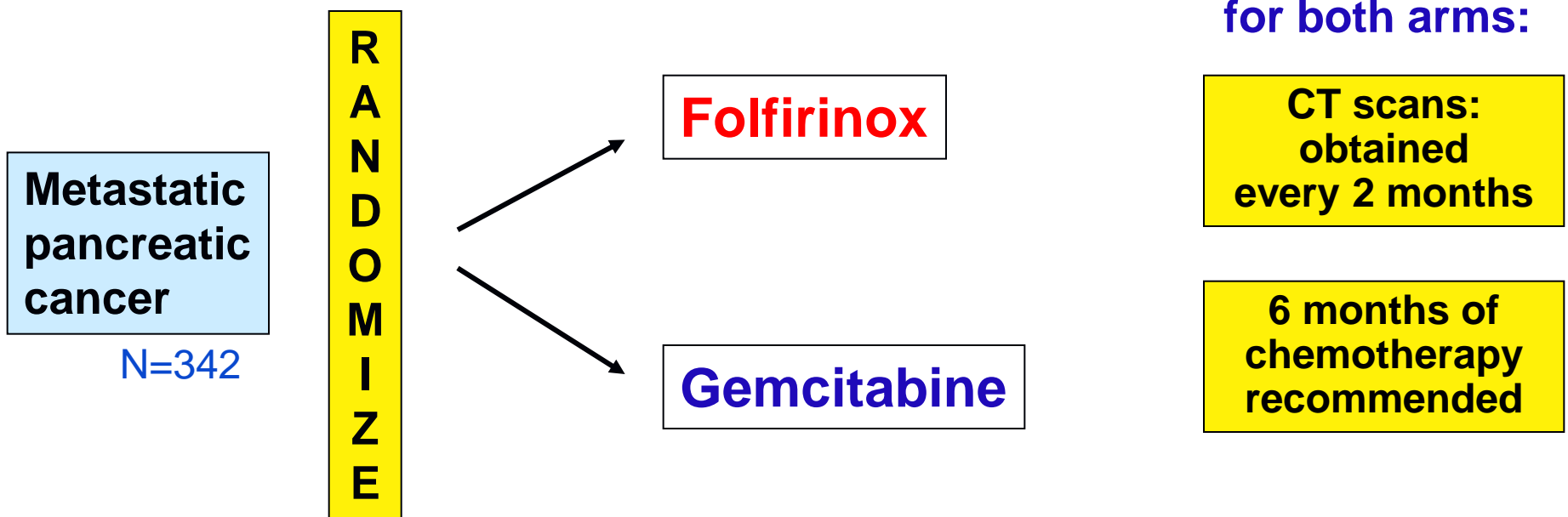
RANDOMIZED PHASE III TRIAL COMPARING FOLFIRINOX (5FU/leucovorin, irinotecan and oxaliplatin) VS GEMCITABINE AS FIRST-LINE TREATMENT FOR METASTATIC PANCREATIC ADENOCARCINOMA

Prodiges 4 - ACCORD 11/0402 trial: final results

**T. Conroy, F. Desseigne, M. Ychou, M. Ducreux, O. Bouché,
R. Guimbaud, Y. Bécouarn, C. Montoto-Grillot, S. Gourgou-Bourgade,
A. Adenis, FNCLCC-FFCD Prodiges group**

**Centre Alexis Vautrin, Nancy; Centre Léon Bérard, Lyon; Centre Val d'Aurelle, Montpellier;
Institut Gustave Roussy, Villejuif; Centre Hospitalier R. Debré, Reims;
Institut Claudius Regaud, Toulouse; Institut Bergonié, Bordeaux;
Fédération Nationale des Centres de Lutte Contre le Cancer - BECT, Paris;
Centre Oscar Lambret, Lille; FRANCE**

Prodige 4 - ACCORD 11 trial design



Modifiziert nach:
T. Conroy, ASCO 2010

Einschlusskriterien/Population

- **Messbaren Metastasen**
- **ECOG 0/1**
- **Alter < 75 Jahre**
- **Bili < 1,5N**

- **Kopf** **36%**
- **Korpus/Schwanz** **64%**

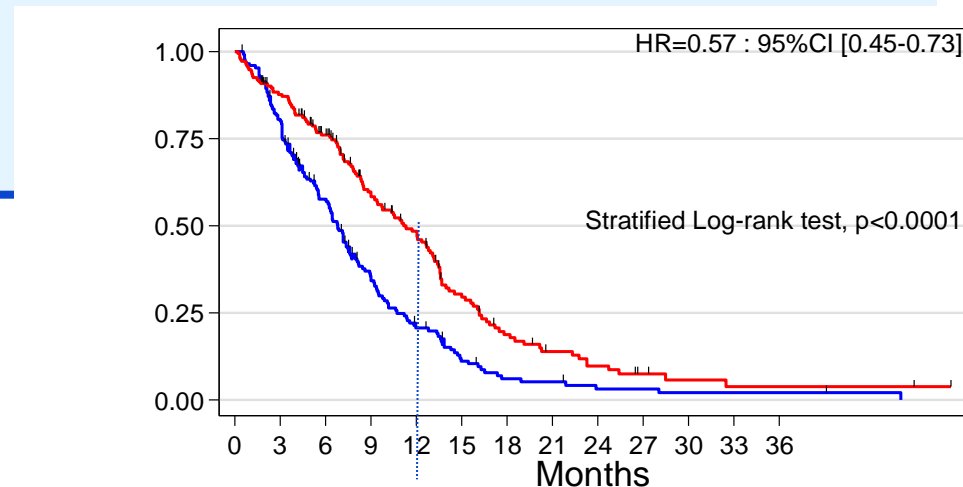
Wirksamkeit

	Folfirinox N=171	Gemcitabine N=171	p
Complete response	0.6%	0%	
Partial response	31%	9.4%	0.0001
PFS	6,4 Mo	3,3 Mo	0,0001
		HR 0,45 (0,37-0,59)	

Overall Survival

Median follow up: 26.6 months [95% CI: 20.5 – 44.9]

	Folfinrox N=171	Gemcitabine N=171	p	HR
Median survival [CI 95%]	11.1 mo. [9 - 13.1]	6.8 mo. [5.5 - 7.6]	<0.0001	0.57
1-yr. survival	48.4%	20.6%		
18-mo. survival	18.6%			



Modifiziert nach:
T. Conroy, ASCO 2010

Safety: hematological AEs

AE, % per patient	Folfinrox N=167		Gemcitabine N=169		p
	All	Grade 3/4	All	Grade 3/4	Grade 3/4
Neutropenia	79.9	45.7	54.8	18.7	0.0001
Febrile Neutropenia	7.2	5.4	2.4	0.6	0.009
Anemia	90.4	7.8	94.6	5.4	NS
Thrombocytopenia	75.2	9.1	54.8	2.4	0.008

42.5 % of the pts received G-CSF in the **F** arm vs 5.3% in the **G** arm
 One toxic death occurred in each arm

Modifiziert nach:
 T. Conroy, ASCO 2010

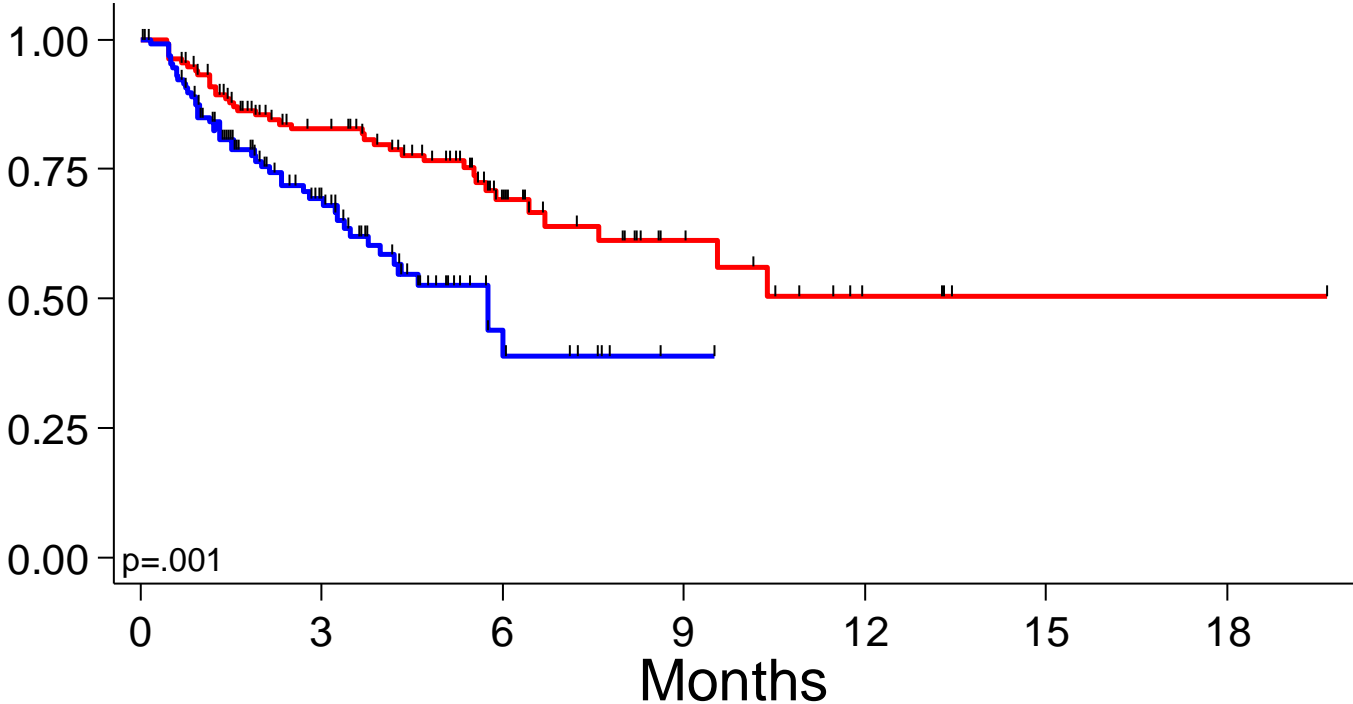
Safety: main non-hematological AEs

AE, % per patient	Folfinox N=167		Gemcitabine N=169		p
	All	Grade 3/4	All	Grade 3/4	
Infection without neutropenia	6	1.2	7.1	1.8	NS
Peripheral neuropathy	70.5	9	0.6	0	0.0001
Vomiting	61.4	14.5	43.2	4.7	0.002
Fatigue	87.3	23.2	78.7	14.2	0.036
Diarrhea	73.3	12.7	30.8	1.2	0.0001
Alopecia (grade 2)	32.5	(11.4)	3.0	(0.6)	0.0001
ALT	64.8	7.3	83.8	18.6	0.0022

Modifiziert nach:
T. Conroy, ASCO 2010

Time to definitive QoL degradation

Kaplan-Meier estimation for TUDD of Global health status/QoL (MCID 10 points)



Number at risk		0	3	6	9	12	15	18
Gemcitabine	157	53	9	1	0	0	0	0
Folfirinox	163	89	35	13	4	1	1	1

— Gemcitabine — Folfirinox

Wird Folfirinox der neue Standard?

- **Wahrscheinlich ja, aber nur für manche Patienten:**
 - in gutem AZ (ECOG 1-2)
 - eher jünger (< 75 Jahre)
 - mit normalem Bili (<1,5)
 - metastasiert (ohne Stent ???)
- **Cave !**
 - Bisläng keine zweite Studie
 - Nebenwirkungsprofil potentiell gefährlich

Kommentare

- **Folfirinox oder Folfox ?**
- **Kombinationspartner ?**

- **Adjuvante Therapie ?**
- **Lokal fortgeschrittene Tumoren ?**

- **Gemcitabine kann ersetzt werden !**

**Gemcitabine plus erlotinib followed by capecitabine versus capecitabine plus erlotinib followed by gemcitabine in advanced pancreatic cancer:
A randomized, cross-over phase III trial of the AIO**

S. Boeck*, U. Vehling-Kaiser, D. Waldschmidt, E. Kettner, A. Märten, C. Winkelmann, S. Klein, G. Kojouharoff, A. Jung, V. Heinemann*

* Dept. of Internal Medicine III, Klinikum Grosshadern, Ludwig-Maximilians-University of Munich, Germany

AIO PK-0104

Fortgeschrittene
PaCa

N=281

Gem/Erlotinib

Cape/Erlotinib

Cape

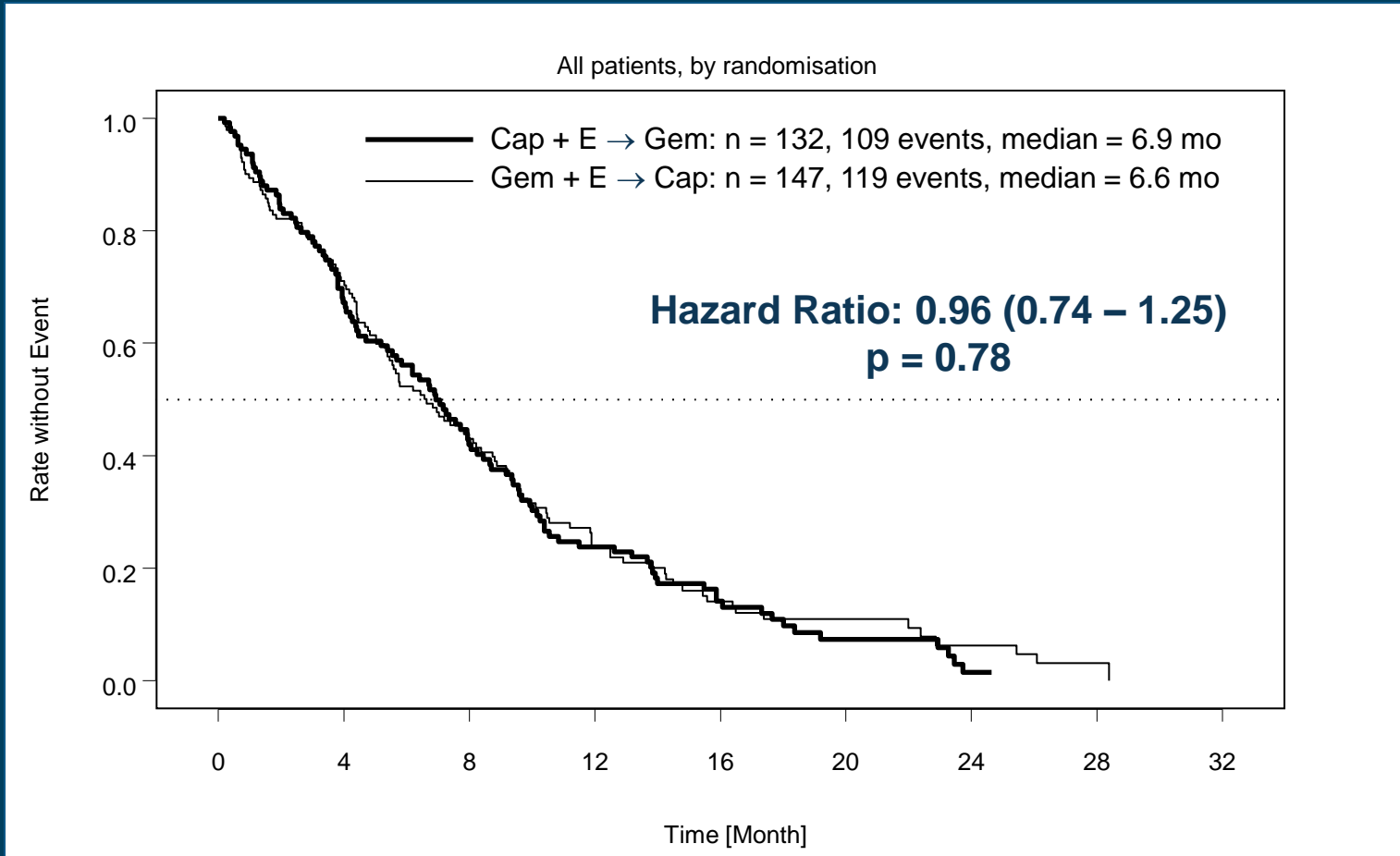
Gem

TTF1

TTFc

TTF2

Overall survival



AIO PK-0104

	Cap-E > Gem N=132	Gem-E > Cap N=147	p
OS	6.9	6.6	0.78
TTF 1	2.4	3.4	0.004
TTF c	2.5	1.9	0.002
TTF 2	4.4	4.2	0.43

Metastasiertes Pankreaskarzinom 07/10:

- **Gemcitabine ± Erlotinib**
als Standard für alle
- **Folfirinox**
für selektierte junge Patienten in gutem AZ mit
(fast) normalem Bili
- **Cape + Erlotinib** (mit cross-over zu Gem)
in Einzelfällen