NCCN Clinical Practice Guidelines in Oncology v.1.2009

胰腺癌的化疗

——指南及证据

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概　述

- 胰腺癌的发病率逐年升高，我国胰腺癌发病率近20年增长4倍。
- 全球每年逾20万人死于胰腺癌,死亡人数在所有癌症中居第4位。
- 胰腺癌恶性度高，早期症状隐匿，诊断困难， 生存时间短。
- 手术率低，70-15%术后5年生存率 15-20%，我国胰腺癌术后5年生存率在5%左右。

◆诊断分期及死亡情况：

转移性癌 83%

分期	I期	II期	III 期	IVA期	IVB期
比例	7.3%	3.3%	7.8%	35.9%	47.1%
5年生存率	5%-35%	2%-15%	2%-15%	1%-5%	<1%

治　疗

- 手术：
  - ✓ 手术率仅10-15%；
  - ✓ 术后2年内复发率80%-95%；
  - ✓ 术后5年生存率 15-20%。
  - ✓ 姑息切除术的3年生存率几乎为0。
- 局部治疗----放疗、介入、微波、氩氦刀
- 免疫治疗
- 内分泌治疗
- 热疗（射频、高能超声聚焦、微波、全身）
- 基因治疗
- 支持治疗、中医调理
- 化疗—几乎所有PS评分良好者

胰腺癌化疗原则–NCCN V.1.2009

Systemic therapy is used in the neoadjuvant or adjuvant setting and in the management of locally advanced unresectable and metastatic disease.

- Goals of systemic therapy should be discussed with patients prior to initiation of therapy and enrollment in a clinical trial is strongly encouraged.
- Close follow-up of patients undergoing chemotherapy is indicated.
- Gemcitabine at 1000 mg/m^2 over 30 minutes, weekly for 3 weeks every 28 days, is considered standard front-line therapy for patients with metastatic disease (category 1).
- Gemcitabine or gemcitabine-based combination therapy without RT may be considered as an alternative to 5-FU-based chemoradiation for patients with locally advanced, unresectable disease or as adjuvant therapy.
- Fixed-dose rate gemcitabine (10 mg/m^2/minute) may substitute for standard infusion of gemcitabine over 30 minutes (category 2B).
- Gemcitabine combinations have shown a favorable or potentially favorable impact on time to progression or survival (overall or 1 y) for patients with good performance status:
  - Gemcitabine + erlotinib[1]
  - Gemcitabine + cisplatin[2]
  - Gemcitabine + fluoropyrimidine[2,3]
- Second-line therapy may consist of gemcitabine for those patients not previously treated with the drug. Other options include capecitabine[4] (1000 mg/m^2 PO twice daily, days 1-14 every 21 days) or 5-FU/leucovorin[5] or CapeOx[6]. Results of the CONKO 003 trial demonstrated a significant improvement in overall survival with addition of oxaliplatin to 5-FU /leucovorin.
- The CONKO 001 trial demonstrated significant improvements in disease-free survival and overall survival with use of post-operative gemcitabine as adjuvant chemotherapy versus observation in resectable pancreatic adenocarcinoma[7]
- The use of gemcitabine based chemotherapy is frequently combined, sequentially, with 5-FU based chemoradiotherapy.
- No significant differences were observed in the RTOG 97-04 study comparing pre- and post- chemoradiation 5-FU with pre- and post-chemoradiation femcitabine for post-operative adjuvant treatment. However, overall survival was significantly increased in the gemcitabine arm compared with the 5-FU arm in the subset of patients with tumors of the pancreatic head.[8]

胰腺癌化疗

- 胰腺癌的新辅助化疗；
- 胰腺癌的辅助化疗；
- 胰腺癌一线化疗；
- 胰腺癌二线化疗；
- 胰腺癌药物治疗方向；

[1] For any tumors where there is a higher likelihood of an incomplete (R1 or R2) resection, it is suggested that chemoradiation be given prior to surgery.

胰腺癌新辅助化疗

- 适应症：
  - 临界行手术切除，无黄疸；（2B）
  - 临界行手术切除，有黄疸；（2B）
  - 可行手术切除，有黄疸—临床实验中；

任何可能不能完全R0切除的肿瘤，建议术前给予放化疗

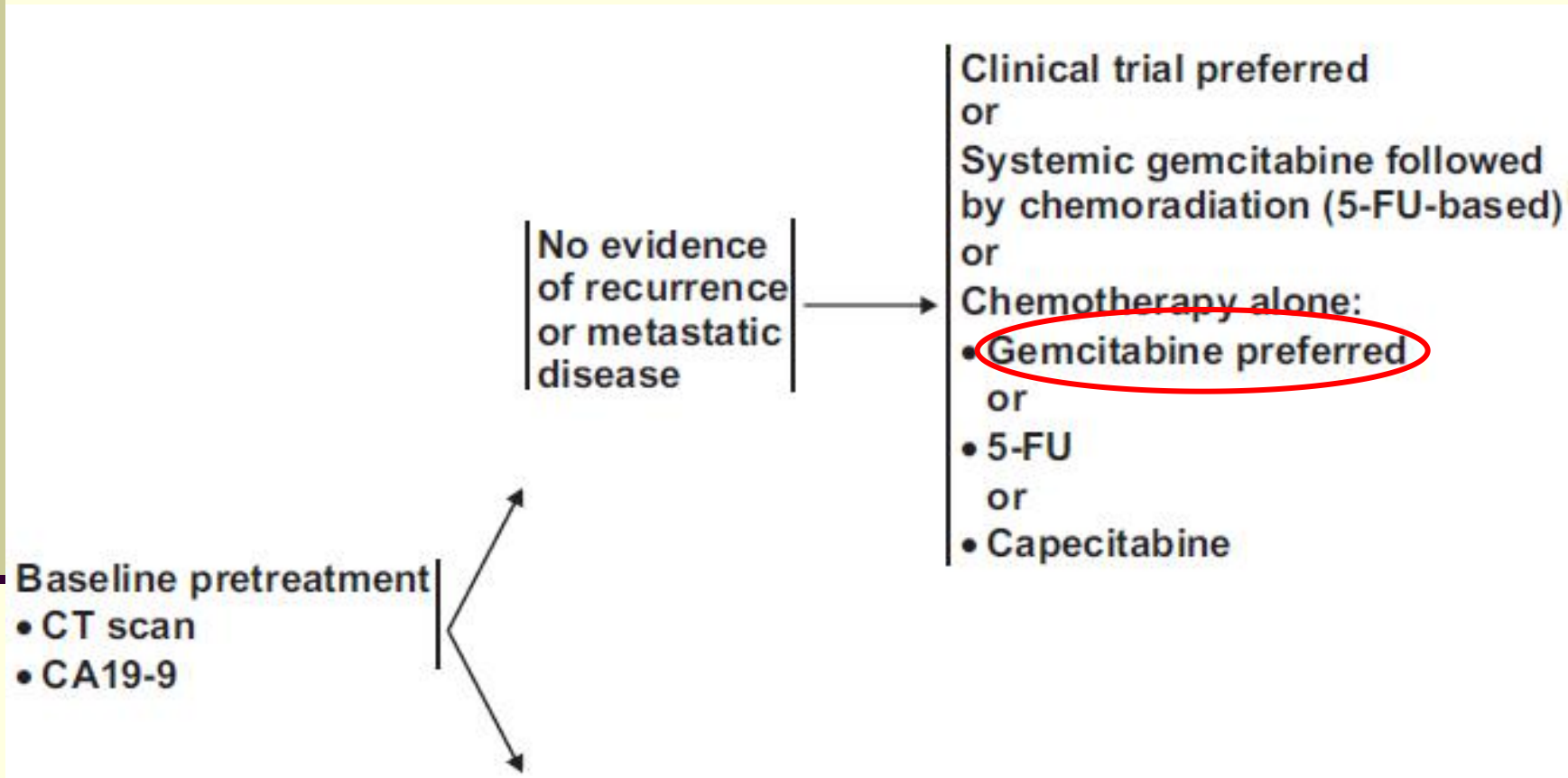
- 目的：增加切除率、提高生存期；

MD Anderson回顾术前化放疗+手术治疗132例，中位生存期21月，31%无病生存。结论：术前化放疗至少无明显害处。

Gemzar + Docetaxel 新辅助治疗局部晚期胰腺癌 II期临床研究 ASCO 2004 研究结果

- 完全切除(R0)：48/61例(79%)，无手术相关死亡
  - 1年生存率：85%
  - 3年生存率：69% (R0切除者：75%)
- 结论：
  - 胰腺癌术前GEM+Docetaxel化疗使大多数患者肿瘤降期，近80%的患者进行了根治术；
  - 生存期优于直接手术的胰腺癌患者。

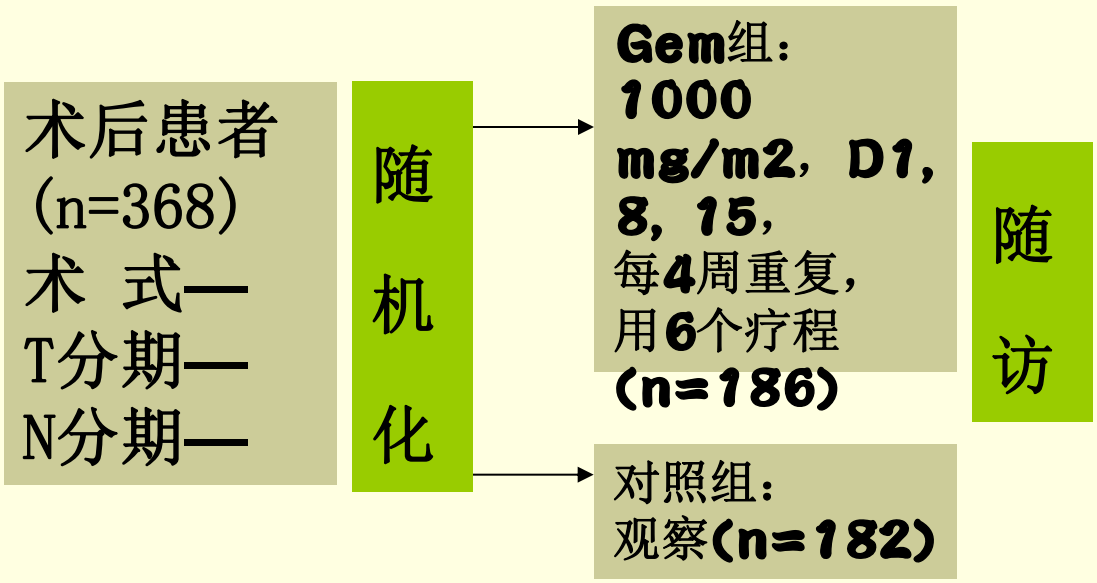
胰腺癌术后治疗-NCCN V.1.2009



CONKO-001研究

- 开放，多中心，随机对照的III期临床试验研究
- 共368例患者，R0或R1根治术后，无既往放化疗史
- 目的：验证胰腺癌术后使用Gem辅助治疗是否能延长DFS 6个月以上。

CONKO-001研究设计



◆主要研究终点：

- DFS
- 5年生存率

◆次要研究终点

- OS
- 安全性

CONKO-001研究结果

	No.of Patients		Disease-Free Survival Median(95%CI),MO			Overall Survival,Median,mo		
	Gemcitabine	Observation	Gemcitabine	Observation	P value*	Gemcitabine	Observation	P value*
All patients	179	175	13.4(11.4-15.3)	6.9(6.1-7.8)	<.001	22.1	20.2	.06
R0	145	148	13.1(11.6-14.6)	7.3(5.9-8.7)	<.001	21.7	20.8	.18
R1	34	27	15.8(7.5-24.1)	5.5(4.1-6.9)	<.001	22.1	14.1	.07
N-	52	48	24.8(6.8-42.7)	10.4(6.4-15.5)	.003	34.0	27.6	.04
N+	127	127	12.1(10.7-13.4)	6.4(5.7-7.2)	<.001	18.5	18.2	.44
T1-2	25	24	48.2(0-96.8)	10.0(4.4-15.5)	.02	50.2	27.6	.28
T3-4	154	151	12.9(11.5-14.3)	6.7(5.9-7.5)	<.001	20.5	19.1	.11

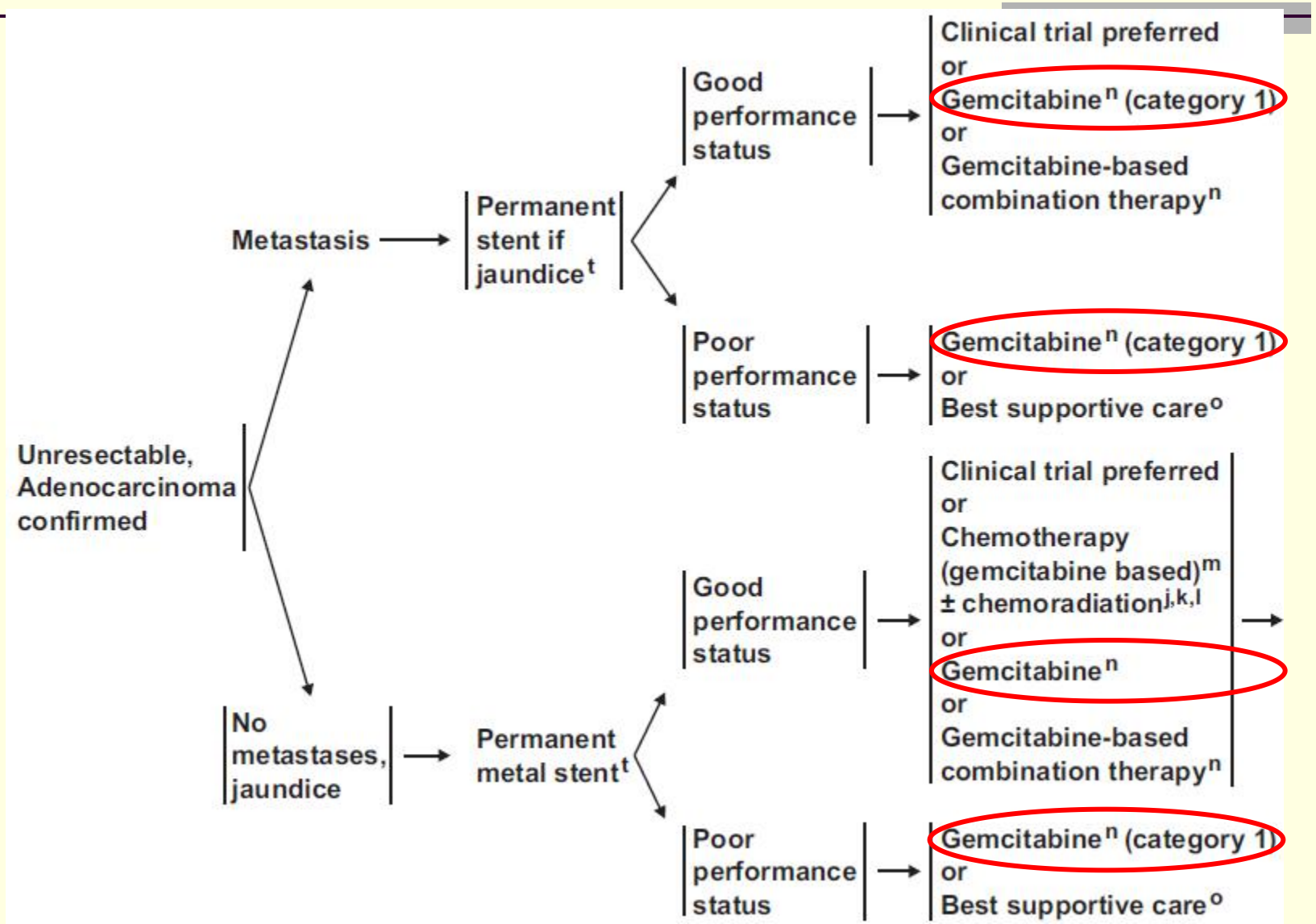
长期生存比较

OS	1 年(%)	2年(%)	3 年(%)	5 年(%)
健择组	72	48.5	36.5	21.0
观察组	72.5	40.0	19.5	9.0
两组相差	-0.5	8.5	17	12

CONKO-001研究结论

- 胰腺癌根治术后，予以健择辅助化疗，较观察组显著延长复发时间，生存期也有延长。
- 此次研究是迄今为止规模最大的胰腺癌术后辅助化疗的前瞻性随机对照临床研究。
- 基于此项研究的结果，NCCN将健择推荐为胰腺癌切除后辅助化疗的首选。

胰腺癌一线治疗-NCCN V.1.2009



胰腺癌一线化疗

人数	179	175
中位年龄（范围）	62 (34-82)	61 (36-81)
性别		
女性	74 (41%)	77 (44%)
男性	105 (59%)	98 (56%)
手术至入组中位天数	22	24
手术方式		
R0	145 (81%)	148 (85%)
R1	34 (19%)	27 (15%)

治疗现状

- 根治术后的5年生存率有提高：
  - ✓ 80年代：3.4%-7.1%
  - ✓ 90年代：10%-27%

- 手术切除的胰腺癌患者在2年内约80%-95%出现复发，包括局部和远处转移；

- 姑息切除术的3年生存率几乎为0%；

- 中位生存时间
  - ✓ 根治术：18个月
  - ✓ 局部晚期：6～10个月
  - ✓ 转移性：3～6个月

临床诊疗指南肿瘤分册，人民卫生出版社 2007.

背 景

- 胰腺癌的恶性程度高，发病率逐年上升
- 早期症状隐匿，早期诊断困难， 生存时间短
- 胰腺癌极易侵犯周围血管，手术切除率低
- 只有20%的胰腺癌病人在诊断时是局限性
- 根治性手术切除目前仍是胰腺癌治疗唯一有效方法

ESMO 胰腺癌基本临床推荐：2005

- 不同期别 胰腺癌 5年生存率
- 0期 Tis N0M0
- I期 T1-2N0M0 5%-35%
- II期 T3N0M0 2%-15%
- III期 T1-3N1M0 2%-15%
- IVA期 T4N0-1M 1%-5%

胰腺癌的特点：

- 肿瘤<2cm 就可发生转移
- 侵犯周围血管
- 淋巴转移发生早，转移率 70%
- 普遍存在微转移
- 单纯手术的疗效差
  - 局部复发率 50%~86%
  - 腹膜后种植率 40%
  - 肝转移率达 60%~90%

Wagman R , Grann A . Surg Clin N Am 2001;81(3):667-681

胰腺癌的新辅助化疗

- 适应症：可能行手术，无黄疸；或可手术，有黄疸；或可能行手术，有黄疸；

BORDERLINE RESECTABLE[1]

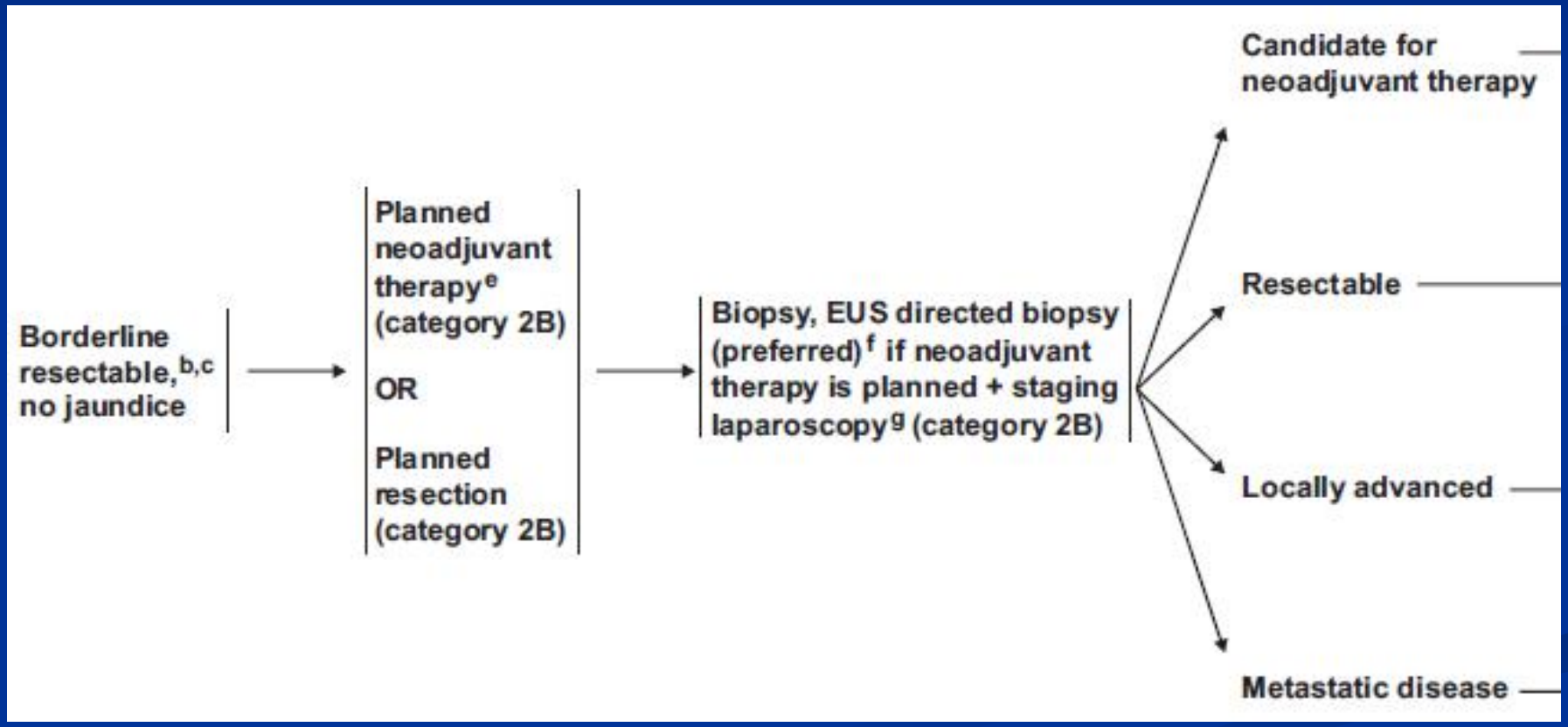
- **HEAD/BODY**
  - Severe unilateral or bilateral SMV/portal impingement
  - Less than 180 degree tumor abutment on SMA
  - Abutment or encasement of hepatic artery, if reconstructib
  - SMV occlusion, if of a short segment, and reconstructible.
- **TAIL**
  - SMA or celiac encasement less than 180 degree

Borderline resectable,[b,c] no jaundice

[1] For any tumors where there is a higher likelihood of an incomplete (R1 or R2) resection, it is suggested that chemoradiation be given prior to surgery.

方案选择：

胰腺癌的新辅助化疗


Borderline resectable,[b,c] no jaundice
Planned neoadjuvant therapy[e] (category 2B)
OR
Planned resection (category 2B)
Biopsy, EUS directed biopsy (preferred)[f] if neoadjuvant therapy is planned + staging laparoscopy[g] (category 2B)
Candidate for neoadjuvant therapy
Resectable
Locally advanced
Metastatic disease

胰腺癌的辅助化疗：

- 适应症：
- 外科根治后，基线检查无复发转移
- 方案选择：
- 化疗时机：
- 手术恢复以后，4-8周

Clinical trial preferred
or
Systemic gemcitabine followed by chemoradiation (5-FU-based)
or
Chemotherapy alone:
- Gemcitabine preferred
  or
- 5-FU
  or
- Capecitabine

胰腺癌根治术后健择辅助治疗与对照观察的多中心随机临床研究（CONKO-001）

Adjuvant chemotherapy with gemcitabine versus observation in patients undergoing curative-intent resection of pancreatic cancer. A multicenter randomized controlled trial

试验设计

- 开放，多中心，随机对照的III期临床试验研究
- 共368例患者，实行R0或R1根治术后，无既往放疗化疗史

N=368

随机对照

- ARM A:N=186
- 健择1000mg/m2，d1，8，15，Q4wks*6cycles

- ARM B:N=182
- 观察

Oettle，H.et al.JAMA 2007;297:267-277

病人基线资料（可评价病例） baseline characteristics of eligible patients		No（%）	
		Gemcitabine Group	Observation Group （control）
No，of patients		179	175
Age。Median （range），y		62（34-82）	61（36-81）
sex	Women	74（41）	77（44）
	men	105（59）	98（56）
Days from surgery to randomization	median	22	24
	Interquartile range	15-32	15-34
Days from resection to start of adjuvant Chemitherapy。median（interquartile range）		36（28-43）	
KPS，median（range）		80（60-100）	80（50-100）
Resection status	R0	145（81）	148（85）
	R1	34（19）	27（15）
Primary tumor size	T1	7（4）	7（4）
	T2	18（10）	17（10）
	T3	146（82）	146（83）
	T4	8（4）	5（3）
Nodal status	N0	52（29）	48（27）
	N1	126（70）	124（71）
	N2	1（1）	3（2）
Grading	1	10（6）	9（5）
	2	103（58）	95（54）
	3	63（35）	68（39）
	Unknown	3（2）	3（2）

结果：无病生存期和生存率

Disease-Free and Overall Survival by Intent-to-Treat Analysis in the Total Population And in Patient Subgroups

	No.of Patients		Disease-Free Survival Median(95%CI),MO			Overall Survival,Median,mo		
	Gemcitabine	Observation	Gemcitabine	Observation	P value*	Gemcitabine	Observation	P value*
All patients	179	175	13.4(11.4-15.3)	6.9(6.1-7.8)	<.001	22.1	20.2	.06
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Oettle，H.et al.JAMA 2007;297:267-277

结果：无病生存期和生存率

生存率		
	健择组	观察组
3年	34%	20.5%
5年	22.5%	11.5%

Oettle，H.et al.JAMA 2007;297:267-277

结果：不良反应

Toxicity in Percentage of Cycles by Gemcitabine Group and Control Group		Gemcitabine（n=1116cycles）			Observation（n=1092cycles）		
		Any grade	Grade 3	Grade 4	Any grade	Grade 3	Grade 4
Hematologic	Hemoglobin	27.9	0.6	0	3.3	0.1	0
	Leukocytes	30.8	2.4	0	2.1	0.1	0
	Platelets	6.4	0.5	0.3	1.0	0	0
Nonhematologic	Nausea/Vomiting	21.2	1.3	0	2.8	0.2	0
	Diarrhea	9.0	0.9	0	5.1	0.4	0
	Edema	8.9	0.4	0,1	0.4	0.1	0
	Infection	3.9	0.4	0	1.7	0.3	0
Biochemical	Alanine transaminase /aspartate transaminase	20.5	0.5	0.1	12.5	0.5	0.1

结论

- 胰腺癌根治术后，予以健择辅助化疗，较观察组显著延长复发时间，延长生存期。
- ¾级的毒性反应轻微，耐受良好。
- 基于此项研究的结果，NCCN胰腺癌指南2007年第一版胰腺癌辅助化疗部分推荐健择作为胰腺癌切除后辅助化疗的首选。

Oettle，H.et al.JAMA 2007;297:267-277

胰腺癌一线化疗

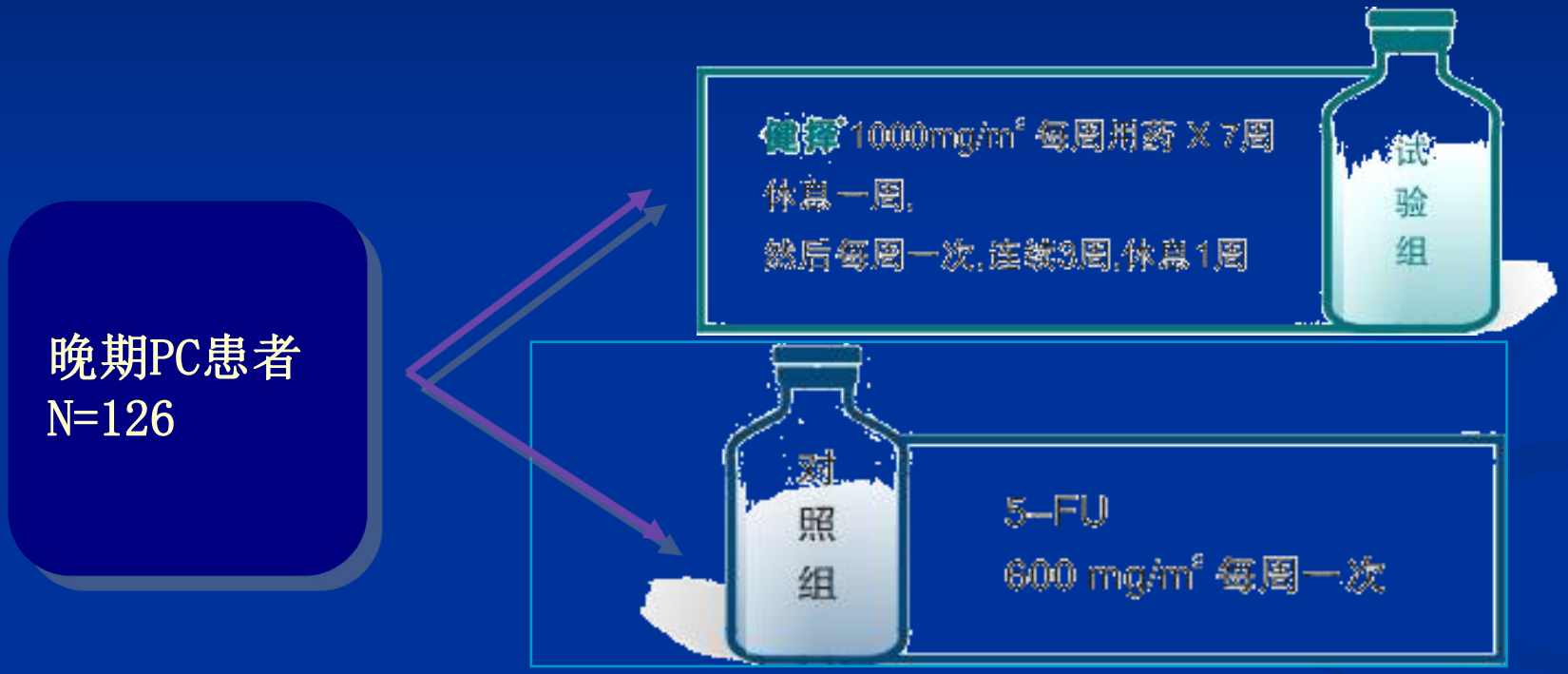
- 适应症：局部进展期不能手术
- 方案选择：
- **PS**好：

Clinical trial preferred
or
Systemic chemotherapy (gemcitabine-based)[m] ± chemoradiation[j,k,l]
or
Gemcitabine[n]
or
Gemcitabine-based combination therapy[n]

- **PS**差：

Gemcitabine[n] (category 1)
or
Best supportive care[o]

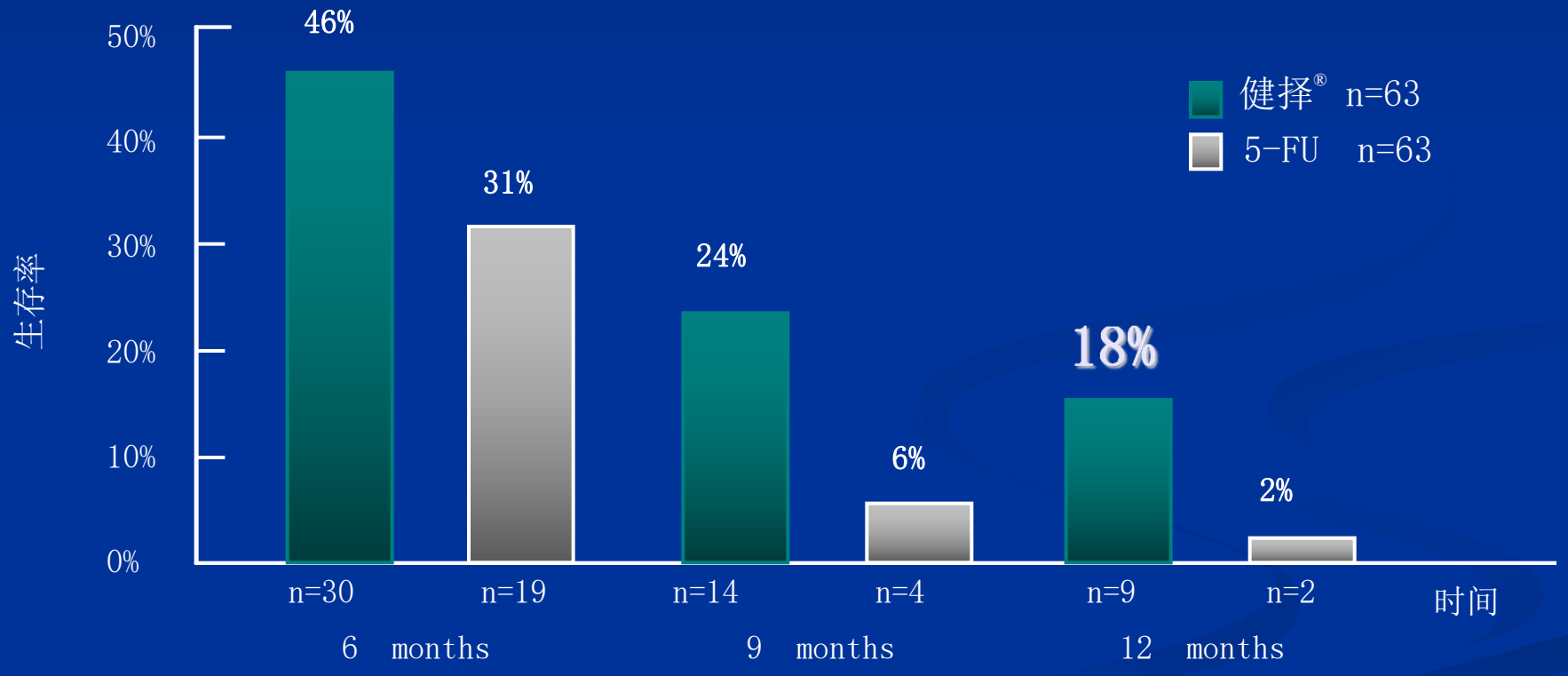
随机III期临床研究设计



主要研究终点：CBR
次要研究终点：RR、TTP、OS

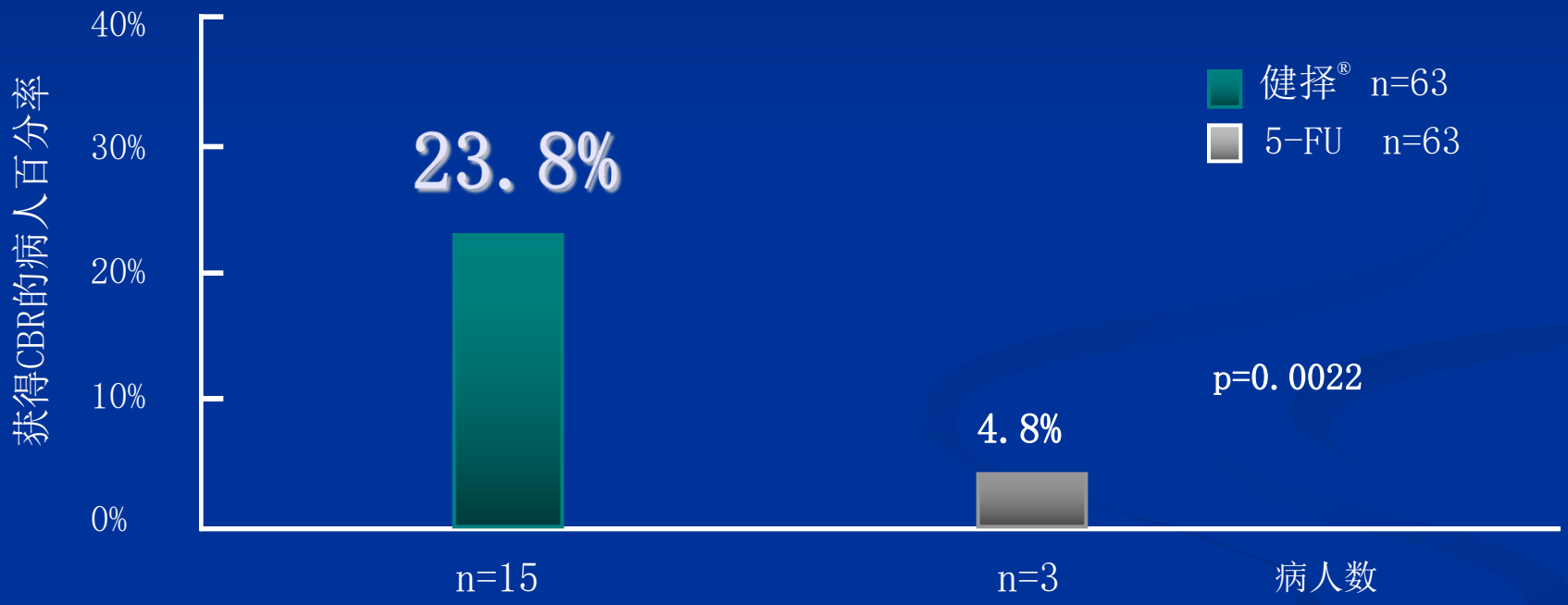
Burris Ha 3rd, Moore MJ, Anderson J, et al. Improvements in survival and clinical benefit with gemcitabine as first-line therapy for patients with advanced pancreas cancer: a randomized trial. J Clin Oncol, 1997; 15(6):2403-13

健择组的1年生存率比5-FU组提高9倍



Burris Ha 3rd, Moore MJ, Anderson J, et al. Improvements in survival and clinical benefit with gemcitabine as first-line therapy for patients with advanced pancreas cancer: a randomized trial. J Clin Oncol, 1997; 15(6):2403-13

健择®组23.8%获得临床受益反应(CBR)



Burris Ha 3rd, Moore MJ, Anderson J, et al. Improvements in survival and clinical benefit with gemcitabine as first-line therapy for patients with advanced pancreas cancer: a randomized trial. J Clin Oncol, 1997; 15(6):2403-13

临床受益反应—胰腺癌的一项新的化疗评估标准

临床受益反应(Clinical Benefit Response,CBR)定义为：

至少下列一项指标好转(持续4周或以上)，并且无任一项指标恶化：

- 镇痛药用量减少≥50% +
- 疼痛强度减轻≥50% =
- 体力状况改善≥20△分
- 体重增加≥7%无体液潴留*

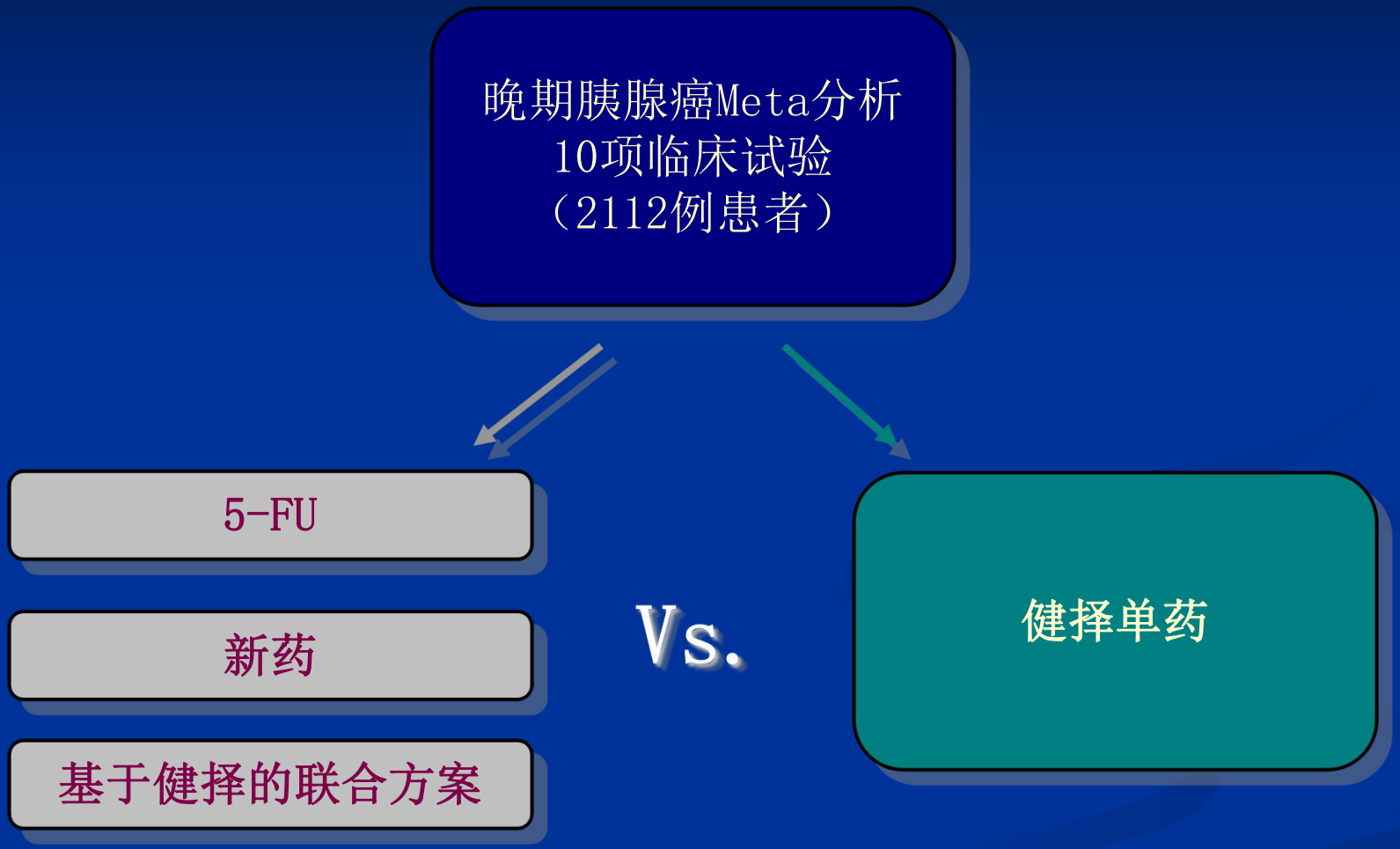
+ 每日记录，每周总结

= 每日评价，用MPAC卡每周总结

△ 每周评估，用KPS评分

* 每周称体重

胰腺癌2003年荟萃分析--研究设计



主要研究终点：中位生存期

M. C. Fung, H. Ishiguro, S. Takayama, et al. Survival benefit of chemotherapy treatment in advanced pancreatic cancer: A meta-analysis. Proceeding of the ASCO 2003; 1155a

胰腺癌2003年荟萃分析--研究结果

临床试验数	化疗方案	病例数	MST(月)	危险比(95%可信限)	P值
1	5-FU	63	4.41	0.56 (0.39-0.82)	<0.005
	慢择*	63	5.65		
2	其它新药	241	3.70	0.61 (0.50-0.74)	<0.0001
	慢择*	242	6.08		
7	慢择*	758	5.62	0.92 (0.82-1.03)	0.15
	基于慢择*的联合方案	745	6.98		

注：对照组用于危险比的计算

M. C. Fung, H. Ishiguro, S. Takayama, et al. Survival benefit of chemotherapy treatment in advanced pancreatic cancer: A meta-analysis. Proceeding of the ASCO 2003; 1155a

胰腺癌2008年荟萃分析--研究设计

- 入组
  - 18项研究；3881例晚期胰腺癌病例
- 主要研究终点
  - 6个月/12个月总生存率

方案	含健择联合组	对照组
第一组	健择+顺铂	健择单药
第二组	健择+氟尿嘧啶	
第三组	健择+伊立替康	
第四组	健择+奥沙利铂	
第五组	健择+卡培他滨	

Yang Q et al; J Clin Oncol 2008, 26: suppl. Abs. No. 15661.

胰腺癌2008年荟萃分析--研究结果

方案	含健择联合组	对照组	6个月OS风险改变*	P	12个月OS风险改变*	P
第一组	健择+顺铂	健择单药	5%	0.24	7%	0.37
第二组	健择+氟尿嘧啶		2%	0.46	4%	0.19
第三组	健择+伊立替康		-1%	0.88	0%	0.97
第四组	健择+奥沙利铂		11%	0.0007	5%	0.06
第五组	健择+卡培他滨		7%	0.03	5%	0.08

风险改变（Risk Diference）：为两组间生存率的差值

Meta分析结论：
联合方案较健择单药是否能给晚期胰腺癌患者带来生存的获益，还需要进一步的临床研究的确认。

健择单药仍然是目前治疗晚期胰腺癌的标准治疗方案，卓越疗效未被超越。

Yang Q et al; J Clin Oncol 2008, 26: suppl. Abs. No. 15661.

胰腺癌III期临床研究

	作者	III期临床试验	病人数	IV期病人(%)	PFS(TTP)	MST	ORR(%)	1-yr(%)
1	Kindler	健择/贝伐单抗	302	85	4.8	5.7	13.1	NA
		健择/安慰剂	300	84	4.3	6	11.3	
2	Philip	健择/西妥昔单抗	735	NR	3.5	6.5	12	NA
		健择			3	6	14	
3	Moore	健择/厄罗替尼	285	NR	3.75*	6.24*	8.6*	23*
		健择	284		3.55	5.91	8	17
4	Herrmann	健择/卡培他滨	160	80	4.3	8.4	15	32
		健择	159	79	3.9	7.2	12	30
6	Stathopoulos	健择/伊立替康	71	78	(2.8)	6.4	15	24.3
		健择	74	86	(2.9)	6.5	10	21.8
7	Heinemann	健择/顺铂	98	80	5.3	7.5	10.2	25.3
		健择	97	79	3.1	6.5	8.2	24.7
8	Oettle	健择/力比泰	283	90	3.9	6.2	14.8*	NA
		健择	282	91	3.3	6.3	7.1	
9	Reni	健择/顺铂/表阿霉素/5-Fu	52	71	5.4*	NA	38.5	38.50%
		健择	47	70	3.3		8.5	21.30%
10	Louvet	健择/奥沙利铂	157	68	5.8*	9	26.8*	34.7
		健择	156	70	3.7	7.1	16.3	27.8
11	Rocha-Lima	健择/伊立替康	180	82	3.5	6.3	16.1*	21
		健择	180	81	3.0	6.6	4.4	22
12	Berlin	健择/5-Fu	160	89	2.2	6.7	6.9	NA
		健择	162	90	3.4*	5.4	5.6	

自从*健择®*进入临床应用以来，已成为晚期胰腺癌的*标准化疗药物*，并成为检验所有新治疗药物的*参照标准*。

胰腺癌二线化疗

Clinical trial (preferred)
or
Fluorinated pyrimidine-based therapy ± oxaliplatin[n,p]

L-OHP/FA /5-FU (OFF) + BSC vs BSC

二线治疗 GEM 耐药的晚期胰腺癌

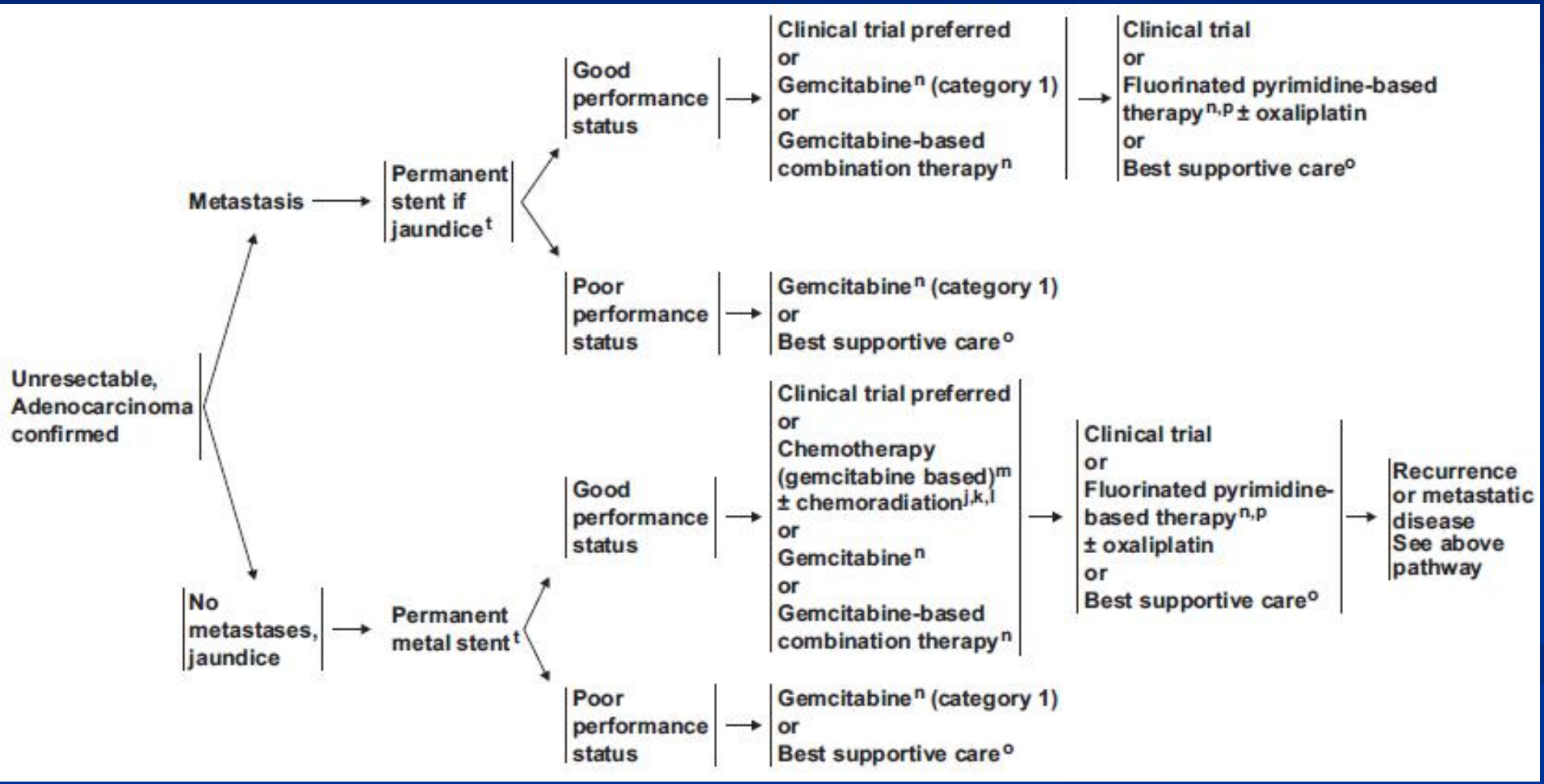
(CONKO 003) Germany (ASCO 2005)

165 例GEM一线治疗失败的晚期胰腺癌，随机接受：FU 2g/m² (24h)/FA 200 mg/m² (30min) on d1, d8, d15, d22 in + L-OHP 85mg/m² (2h) d8 and 22. 或BSC。

结果：

	OFF+BSC	BSC
MST 二线	21 周	10 周

p=0.0077


Unresectable, Adenocarcinoma confirmed
Metastasis
Permanent stent if jaundice[t]
Good performance status
Clinical trial preferred or Gemcitabine[n] (category 1) or Gemcitabine-based combination therapy[n]
Clinical trial or Fluorinated pyrimidine-based therapy[n,p] ± oxaliplatin or Best supportive care[o]
Poor performance status
Gemcitabine[n] (category 1) or Best supportive care[o]
No metastases, jaundice
Permanent metal stent[t]
Good performance status
Clinical trial preferred or Chemotherapy (gemcitabine based)[m] ± chemoradiation[j,k,l] or Gemcitabine[n] or Gemcitabine-based combination therapy[n]
Clinical trial or Fluorinated pyrimidine-based therapy[n,p] ± oxaliplatin or Best supportive care[o]
Recurrence or metastatic disease See above pathway
Poor performance status
Gemcitabine[n] (category 1) or Best supportive care[o]

Systemic therapy is used in the neoadjuvant or adjuvant setting and in the management of locally advanced unresectable and metastatic disease.

- Goals of systemic therapy should be discussed with patients prior to initiation of therapy and enrollment in a clinical trial is strongly encouraged.
- Close follow-up of patients undergoing chemotherapy is indicated.
- Gemcitabine at 1000 mg/m^2 over 30 minutes, weekly for 3 weeks every 28 days, is considered standard front-line therapy for patients with metastatic disease (category 1).
- Gemcitabine or gemcitabine-based combination therapy without RT may be considered as an alternative to 5-FU-based chemoradiation for patients with locally advanced, unresectable disease or as adjuvant therapy.
- Fixed-dose rate gemcitabine (10 mg/m^2/minute) may substitute for standard infusion of gemcitabine over 30 minutes (category 2B).
- Gemcitabine combinations have shown a favorable or potentially favorable impact on time to progression or survival (overall or 1 y) for patients with good performance status:
  - Gemcitabine + erlotinib[1]
  - Gemcitabine + cisplatin[2]
  - Gemcitabine + fluoropyrimidine[2,3]
- Second-line therapy may consist of gemcitabine for those patients not previously treated with the drug. Other options include capecitabine[4] (1000 mg/m^2 PO twice daily, days 1-14 every 21 days) or 5-FU/leucovorin[5] or CapeOx[6]. Results of the CONKO 003 trial demonstrated a significant improvement in overall survival with addition of oxaliplatin to 5-FU /leucovorin.
- The CONKO 001 trial demonstrated significant improvements in disease-free survival and overall survival with use of post-operative gemcitabine as adjuvant chemotherapy versus observation in resectable pancreatic adenocarcinoma[7]
- The use of gemcitabine based chemotherapy is frequently combined, sequentially, with 5-FU based chemoradiotherapy.
- No significant differences were observed in the RTOG 97-04 study comparing pre- and post- chemoradiation 5-FU with pre- and post-chemoradiation femcitabine for post-operative adjuvant treatment. However, overall survival was significantly increased in the gemcitabine arm compared with the 5-FU arm in the subset of patients with tumors of the pancreatic head.[8]

全球每年逾20万人死于胰腺癌
我国胰腺癌发病率近20年增长4倍

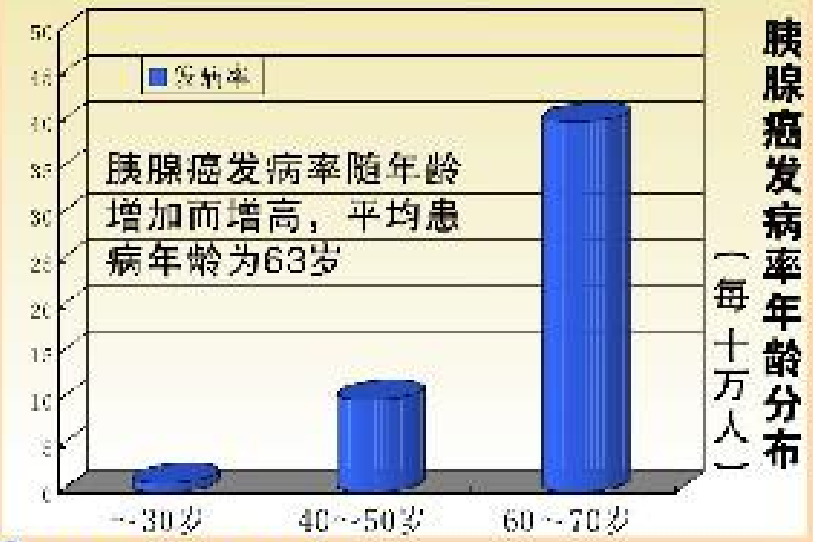
中国健康知识传播激励计划（癌症·2006）　　胰腺癌警示月

种类

胰腺癌
- **外分泌型**：占胰腺癌总数的90%，肿瘤发生于生产消化酶（外分泌）的细胞
- **内分泌型及壶腹部癌**：这两种肿瘤类型比例较小

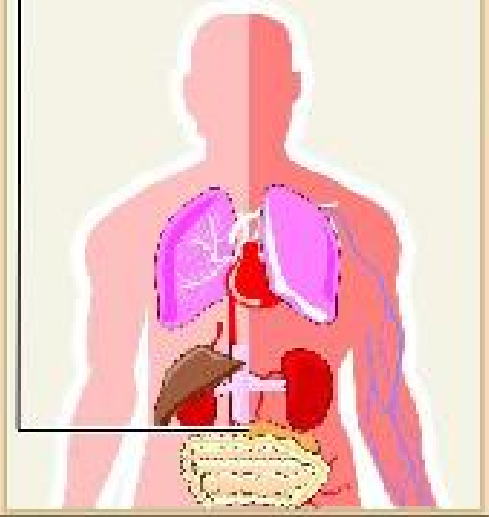
胰腺癌流行病学

- 胰腺癌是引起人口死亡的十大恶性肿瘤之一
- 死亡人数在所有癌症中居第 4 位
- 全世界每年 20 多万人死于胰腺癌
- 我国胰腺癌发病率近 20 年增加了 4 倍
- 我国胰腺癌术后 5 年生存率在 5% 左右



胰　腺

- 位于中上腹部，呈扁平的斜卧状，长约6-10英寸，同小肠相通，是重要的消化器官之一
- 可以分泌胰岛素控制血糖，并分泌各种消化酶帮助消化脂肪、碳水化合物以及蛋白质



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