

# Pancreatic Cancer

Advances in Management Strategies

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# Presenter Disclosure

- **Faculty:** Marianne Krahn
- **Relationships with commercial interests:**
  - **Grants/Research Support:** None
  - **Speakers Bureau/Honoraria:** None
  - **Consulting Fees:** None
  - **Other:** None

# Mitigating Potential Bias

- Not Applicable



# Learning Objectives

- Appropriate use of adjuvant therapy
- Identify regimens used in the treatment of advanced pancreatic cancer
- Be aware of some newer approaches in the management of pancreatic cancer

# Pancreatic Cancer

- Incidence: in MB in 2013 approximately 80 men and 80 women were diagnosed with pancreatic cancer
  - MB overall new cancer diagnoses was
    - 3200 men
    - 3200 women
- Fourth leading cause of cancer death



# Pancreatic Cancer Therapy

- Many things tried
- Many things failed
  
- Gemcitabine in combination with many many agents with disappointing results.



# Improving Outcomes after Surgery

- What do we do after a Whipple's procedure
- Adjuvant therapy has been shown to be of some value
- In Canada, we generally use chemotherapy alone
  - US generally recommend chemotherapy with RT

# Adjuvant Treatment

- Benefit to chemotherapy as adjuvant treatment has been shown in several trials
  - CONKO-001
- Basic study information
  - Trial design
  - Survival data
  - Toxicity



# Adjuvant Treatment

- Trial Design
  - Randomized phase 3 trial
    - Gemcitabine vs Observation
    - Total of 368 patients enrolled
  - Primary end point was disease free survival (DFS)
  - Secondary end point was overall survival (OS)

# Adjuvant Treatment

- Median DFS
  - Gemcitabine arm: 13.4 months
  - Observation arm: 6.7 months
- 5 year OS
  - Gemcitabine arm: 20.7%
  - Observation arm: 10.4%
  - HR 0.76 (p=0.01)

# Adjuvant Treatment

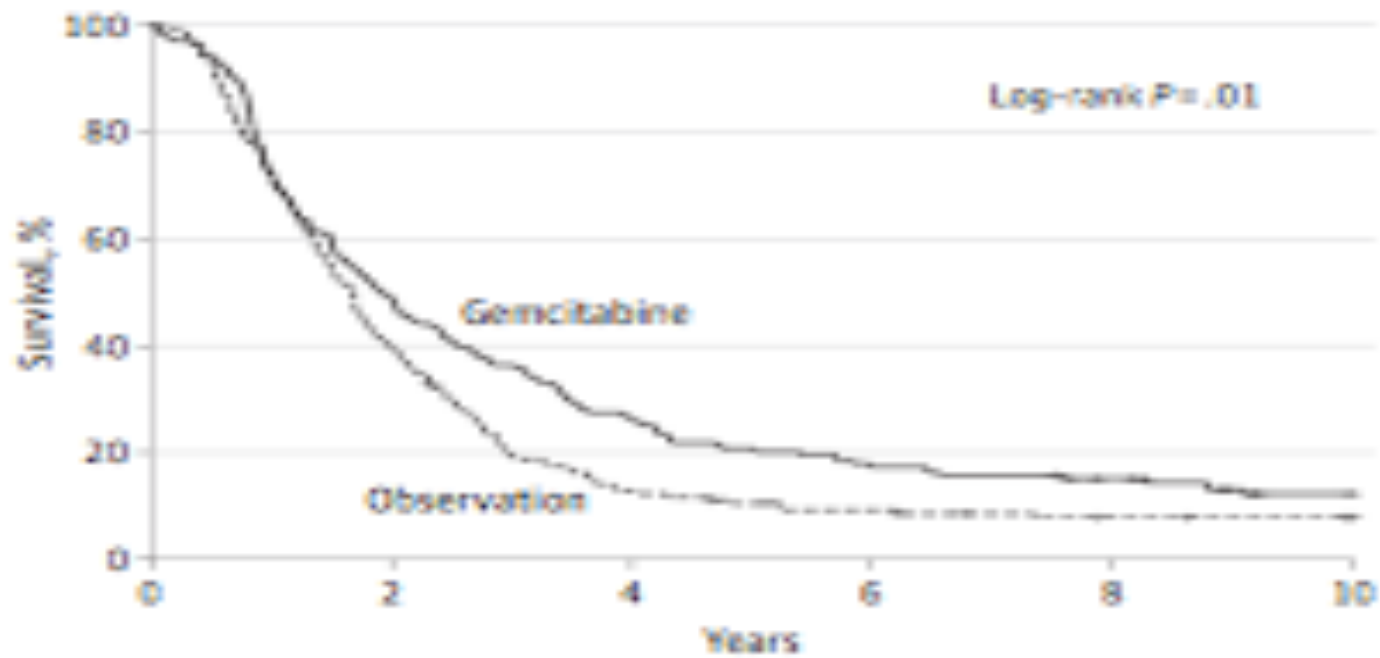
- Toxicity
  - Gemcitabine is relatively well tolerated drug
    - Neutropenia tends to be mild with few episodes of FNE
    - N/V also generally mild
- Observation associated with poorer outcome and so the effects of the disease would tend to be felt sooner

# Adjuvant Treatment

- Concluded
  - A clear benefit to adding gemcitabine
  - Results still poor
- Further study needed
  - Other regimens being studied in adjuvant setting

# Kaplan-Meier Curve

Overall survival



No. at risk

Gemcitabine	179	87	47	31	24	14
Observation	175	70	22	14	9	7

# Adjuvant Treatment

- What does this mean for our patients?
- What does this mean for us?
- Patients get 6 mo of time on chemotherapy
  - PICC line
  - But increased chance of survival



# Adjuvant Treatment

- Health Care Providers
  - More patients receiving treatment
  - More of an opportunity to ensure these patients are coping well post surgery
    - Catch weight loss sooner, note how well they are managing with diet post surgery, pain control

# Advanced Pancreatic Cancer

Realistically this is how the vast majority of the patients present!



# Metastatic Pancreatic Cancer

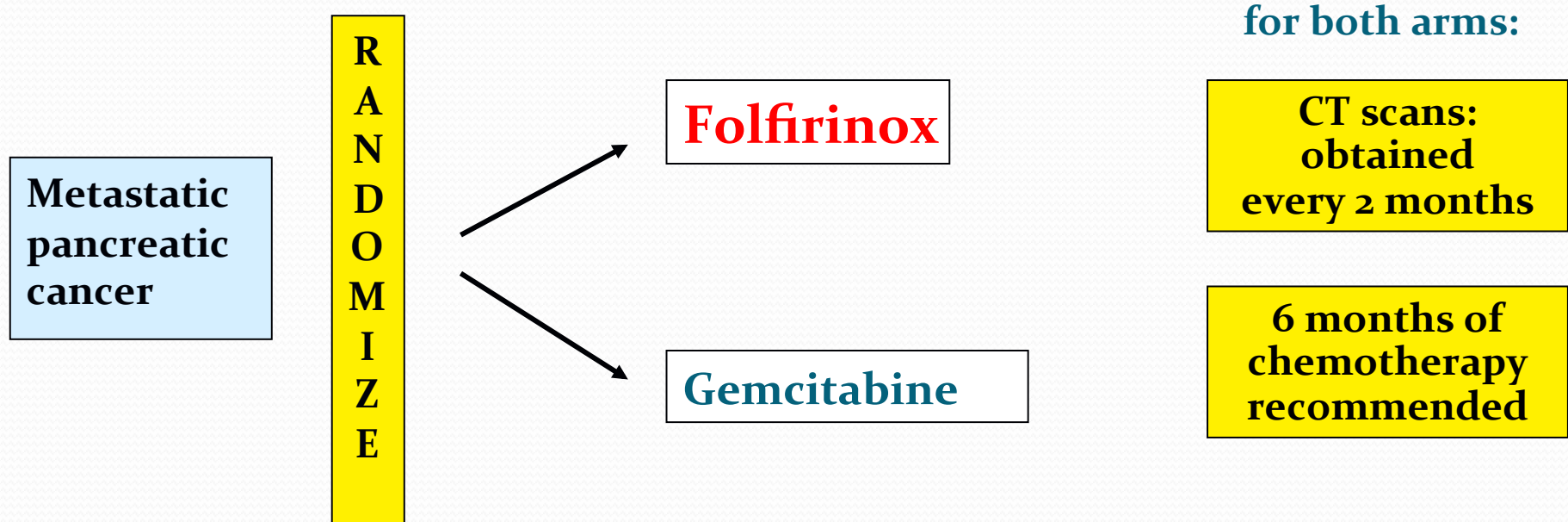
- Previous standard treatment
  - Gemcitabine
- Really, mainly useful as a palliative approach
- Left much to be desired regarding survival



# Treatment for Advanced Disease

- FOLFIRINOX
  - Study design – note the patient population
  - Outcomes
  - Toxicities
- Gemcitabine and nab-paclitaxel

# Prodige 4 - ACCORD 11 trial design



## Stratification :

- center
- performance status: 0 versus 1
- location of the tumor: head versus other location of the primary

# Safety: hematological AEs

AE, % per patient	Folfinox 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

AE, adverse event

# 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

# Objective Response Rate

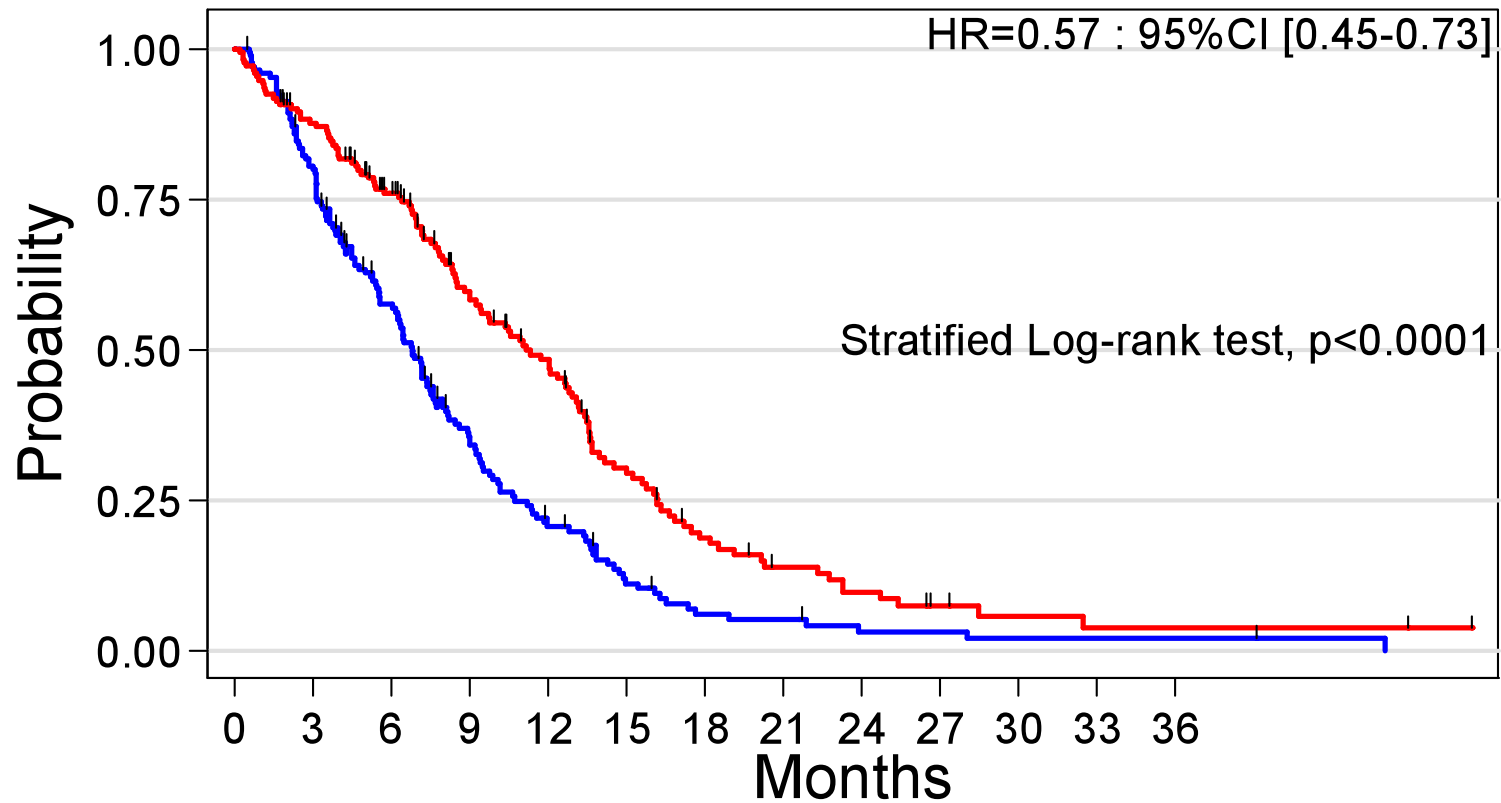
	<b>Folfirinox</b> N=171	<b>Gemcitabine</b> N=171	p
<b>Complete response</b>	<b>0.6%</b>	<b>0%</b>	
<b>Partial response</b>	<b>31%</b>	<b>9.4%</b>	<b>0.0001</b>
<b>CR/PR 95% CI</b>	<b>[24.7-39.1]</b>	<b>[5.9-15.4]</b>	
<b>Stable disease</b>	<b>38.6%</b>	<b>41.5%</b>	
<b>Disease control CR+PR+SD</b>	<b>70.2%</b>	<b>50.9%</b>	<b>0.0003</b>
<b>Progression</b>	<b>15.2%</b>	<b>34.5%</b>	
<b>Not assessed</b>	<b>14.6%</b>	<b>14.6%</b>	
<b>Median duration of response</b>	<b>5.9 mo.</b>	<b>4 mo.</b>	<b>ns</b>

# Overall Survival

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

	<b>Folfinox</b> N=171	<b>Gemcitabine</b> N=171	p	HR
<b>Median survival</b> [CI 95%]	<b>11.1 mo.</b> [ 9 - 13.1]	<b>6.8 mo.</b> [ 5.5 - 7.6]	<b>&lt;0.0001</b>	<b>0.57</b>
<b>1-yr. survival</b>	<b>48.4%</b>	<b>20.6%</b>		
<b>18-mo. survival</b>	<b>18.6%</b>	<b>6%</b>		

# Overall Survival



Number at risk

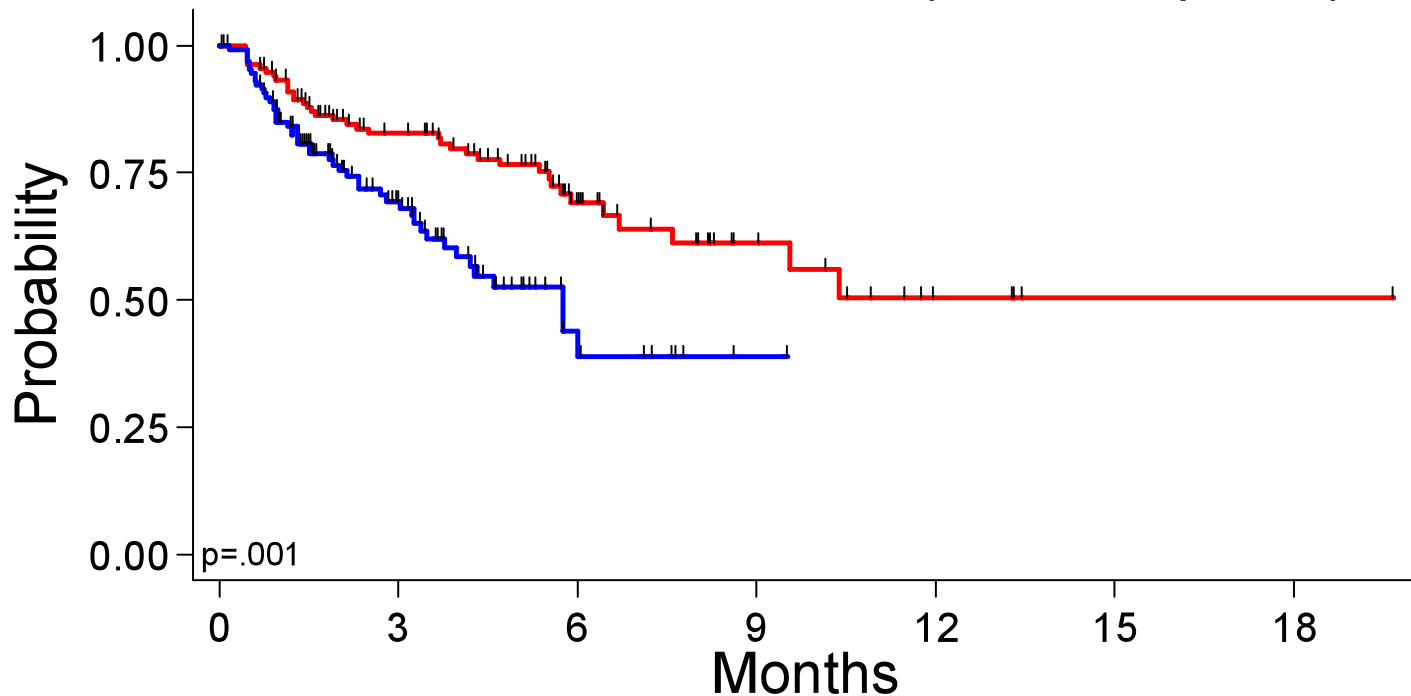
Gemcitabine	171	134	89	48	28	14	7	6	3	3	2	2	2
Folfirinnox	171	146	116	81	62	34	20	13	9	5	3	2	2

— Gemcitabine — Folfirinnox



# Time to definitive QoL degradation

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



Number at risk

Gemcitabine	157	53	9	1	0	0	0
Folfirinox	163	89	35	13	4	1	1

— Gemcitabine — Folfirinox

# FOLFIRINOX

- Much better outcomes, still much to be desired
- Again, what does this mean for our patients?
  - Intense regimen with potentially severe side effects for a non-curable disease
    - Must consider whether this is good palliation
- What does this mean for providers?
  - Considerably more clinic visits, chair time, managing symptoms
  - Rewarding when patient is doing well



# Advanced Disease

- Most recent regimen
- Nab-paclitaxel/gemcitabine
  - Study design
  - Outcomes
  - Toxicities

# Nab-paclitaxel and gemcitabine

- Published by Von Hoff et al NEJM Oct 16, 2013 p1-13
- Randomized trial comparing nab-paclitaxel/  
gemcitabine to gemcitabine alone
- Total of 861 patients randomized
- Chemotherapy given per usual protocol
  - Nab-paclitaxel and gemcitabine given days 1,8,15 every 4 weeks
  - Gemcitabine given weekly 7/8 for first cycle, then 3/4

# Outcomes

- Primary end point was OS
  - Nab-paclitaxel/gem median 8.5 months
  - Gemcitabine median 6.7 months
- HR 0.72  $p < 0.001$



# Adverse Events cont'd

- Non-hematologic events grade 3 and 4
  - Fatigue 17% vs 7%
  - Peripheral neuropathy 17% vs 1%
  - Diarrhea 6% vs 1%

# Conclusion

- A useful regimen which improves OS beyond the previous standard of care (gemcitabine)
  - Especially for those patients who do not want to take the chance of the significant side effects caused by very aggressive regimens like FOLFIRINOX



# Conclusions

- Pancreatic cancer remains deadly
- We hope that we can improve outcomes for adjuvantly treated patients
  - Problem – so few are eligible for surgery
- Improvements in treatment for advanced disease come at a price
  - Side effect profile
  - Time on chemotherapy

# Other Approaches

- Studies are being done on adjuvant treatment – trying FOLFIRINOX (modified)
- Continuing search for biologic targets
- ??SBRT
- ??intraoperative RT



# Take Home Messages

- We have made significant improvements in our management of pancreatic cancer, but we have a very long way to go
- Adjuvant treatment can increase the cure rate for resected disease
- Treatment for advanced disease is also improving, but pancreatic cancer is still quite treatment refractory and new ways of approaching this disease are required