

# Rational and Irrational Use of Aggressive Interventions at the End of Life

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CARE + RESEARCH



# Disclosures

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This lecture is a combination of my thoughts from my experience as a practicing oncologist treating GI cancers; mixed with the writings of others.

I went to a first-rate medical school but we never had any instruction in palliative care or discussing end-of-life issues. What I have learned was on the job training.

I thought when Gary asked me to do this he wanted me to do a 10 minute talk and participate in a panel.

Its an honor to give the Jeremy Oliver lecture. Jeremy was a patient of mine.

# What does Gary think the problem is?

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- ❑ Doctors, and patients, and families use a focus on treatment as a substitute for dealing with the fear and anxiety around end of life issues.
- ❑ These treatments may hurt more than help.
- ❑ More importantly, they may preclude conversations and actions that would make end-of-life more meaningful and comforting for the patient, their friends and family.
- ❑ Assisted dying is not of itself the solution to this problem.

# Definitions

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- ❑ Rational: based on or in accordance with reason or logic.
- ❑ Irrational: without or deprived of normal mental clarity or sound judgment.
- ❑ End-of-life: there is no exact definition of what is the interval referred to as end of life or what end-of-life care is.

# Definitions

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- ❑ End-of-life care: health care, not only of patients in the final hours or days of their lives, but more broadly care of all those with a terminal illness or terminal condition that has become advanced, progressive and incurable.
- ❑ End-of-life care requires a range of decisions, including questions of palliative care, patients' right to self-determination, the ethics and efficacy of extraordinary or hazardous medical interventions, and the ethics and efficacy even of continued routine medical interventions.
- ❑ End-of-life treatments are subject to considerations of patient autonomy. "Ultimately, it is still up to patients and their families to determine when to pursue aggressive treatment or withdraw life support.

# Definitions

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- ❑ A Good Death:
  - ❑ Free of pain and discomfort
  - ❑ Surrounded by loved ones.
  - ❑ In a supported and dignified setting.
  - ❑ Affairs are in order.
  - ❑ Receiving mindful care and support.
  - ❑ Be protected from needless procedures.

# Case #1

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- ❑ A 62 year old physician is diagnosed with advanced pancreatic cancer (PDAC). She is troubled with pain, tiredness and problems around biliary obstruction.
- ❑ She has always felt that if she were diagnosed with advanced cancer she would not take chemotherapy.
- ❑ The data around chemotherapy for advanced PDAC are reviewed. She chooses Gemcitabine + Abraxane to see if it will help with the pain and tiredness.
- ❑ After a transient improvement the tiredness worsens and treatment is stopped.
- ❑ Patient dies at home 2 months later well supported by family and palliative care.

# Case #2

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- ❑ A 42 year old salesman from Peterborough is diagnosed with advanced colon cancer. He is married with 2 children aged 8 & 10. He is referred to a local oncologist and is given an app't in 14 days.
- ❑ The patient travels to a well-known cancer centre in the US and is seen within 2 days. He starts chemotherapy.
- ❑ He initially does well but eventually fails standard therapies. He is having difficulty paying the medical bills. His oncologist recommends a different treatment approach – the patient is unable to pay the costs – so the US oncologist recommends Princess Margaret Cancer Centre and arranges a referral.



# Case #2 continues

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- ❑ When seen at PMH the patient is highly anxious; his wife is quiet and defers to her husband.
- ❑ The patient requests that PMH administer the treatment recommended by the US oncologist. It is explained to him that there is little to no evidence of benefit; the drugs are expensive and would not be covered. He is not interested in a referral to Psychosocial Oncology or in a referral to his local oncologist in Peterborough.
- ❑ We agree on a treatment that contains some elements of what was recommended in the US to start in 10 days.
- ❑ The next day he returns to the US and starts treatment – he mortgages his house in order to raise the cash.

# Case #2 continues

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- ❑ He continues for the next 6 weeks getting treatment both in Toronto and in the US. A follow-up scan shows worsening disease.
- ❑ He goes elsewhere seeking further treatment.
- ❑ He presents to ED in Peterborough and dies in the emergency department.
- ❑ About 4 weeks after death the wife writes us a letter.

# Question #1

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- The percentage of patients who receive chemotherapy within 2 weeks of end-of-life in Ontario is?
- A. 2%
  - B. 4%
  - C. 10%
  - D. 20%
  - E. 40%

# Question #1

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- The percentage of patients who receive chemotherapy within 2 weeks of end-of-life in Ontario is?
- A. 2%
  - B. 4%**
  - C. 10%
  - D. 20%
  - E. 40%

## Question #2

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- The percentage of patients with advanced lung cancer who receive chemotherapy in the last month of life in Ontario is?
- A. 2%
- B. 4%
- C. 7.5%
- D. 15%
- E. 25%

## Question #2

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- The percentage of patients with advanced lung cancer who receive chemotherapy in the last month of life in Ontario is?
- A. 2%
  - B. 4%
  - C. 7.5%**
  - D. 15%
  - E. 25%

## Question #3

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- The percentage of patients with advanced lung cancer who receive chemotherapy in the last month of life in United States is?
- A. 2%
  - B. 5%
  - C. 7.5%
  - D. 15%
  - E. 25%

## Question #3

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- The percentage of patients with advanced lung cancer who receive chemotherapy in the last month of life in United States is?
- A. 2%
  - B. 5%
  - C. 7.5%
  - D. 15%**
  - E. 25%



# Question #4

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- The percentage of patients who visit an Emergency Department within 2 weeks of end-of-life in Ontario is?
  - A. 2%
  - B. 5%
  - C. 10%
  - D. 20%
  - E. 40%

# Question #4

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- The percentage of patients who visit an Emergency Department within 2 weeks of end-of-life in Ontario is?
- A. 2%
  - B. 5%
  - C. 10%
  - D. 20%
  - E. 40%**

# Question #5

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- The percentage of patients who visit an ICU within 2 weeks of end-of-life in Ontario is?
- A. 2%
  - B. 5%
  - C. 10%
  - D. 20%
  - E. 40%

# Question #5

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The percentage of patients who visit an ICU within 2 weeks of end-of-life in Ontario is?

A. 2%

B. 5%

**C. 10%**

D. 20%

E. 40%

# Question #6

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- The percentage of advanced cancer patients who die in an acute care hospital in Ontario is?
- A. 5%
  - B. 15%
  - C. 30%
  - D. 60%
  - E. 90%

# Question #6

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- The percentage of advanced cancer patients who die in an acute care hospital in Ontario is?
- A. 5%
  - B. 15%
  - C. 30%
  - D. 60%**
  - E. 90%

# Question #7

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- The percentage of advanced cancer patients who die at home in Ontario is?
- A. 5%
  - B. 10%
  - C. 20%
  - D. 40%
  - E. 60%

# Question #7

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The percentage of advanced cancer patients who die at home in Ontario is?

- A. 5%
- B. 10%**
- C. 20%
- D. 40%
- E. 60%



# Question #8

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- The percentage of advanced cancer patients who in Ontario who do not receive any palliative assessment in last year of life is?
- A. 5%
  - B. 10%
  - C. 20%
  - D. 40%
  - E. 60%

## Question #8

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- The percentage of advanced cancer patients who in Ontario who do not receive any palliative assessment in last year of life is?
- A. 5%
  - B. 10%
  - C. 20%
  - D. 40%**
  - E. 60%

# Question #9

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- The highest rate of patients dying in hospice care is in ?
- A. Canada
- B. England
- C. Netherlands
- D. South Korea
- E. United States

## Question #9

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- The highest rate of patients dying in hospice care is in ?
- A. Canada
  - B. England
  - C. Netherlands
  - D. South Korea
  - E. United States***

## National trends (US) in selected measures of the care of cancer patients near the end of life

	2003-2007	2010
# Cancer Deaths	235,000	212,000
Deaths in Hospital	29%	25%
Admitted ICU in final month	24%	29%
ICU days	1.3	1.6
Receiving chemotherapy last 2 weeks	6%	6%
Enrolled in Hospice Care final month	54%	61%
Hospice Days-last month	9	9
Sees 10 or more MD's – final 6 months	46%	59%

# So what have we learned so far

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In the last month of life in Canada...

- ❑ Chemotherapy is given infrequently.
- ❑ Emergency visits are very common.
- ❑ Visits to the ICU are around 10%
- ❑ Most Canadians die in acute care hospitals.
- ❑ While most Canadians say they would like to die at home – very few actually do.

# So what have we learned so far

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When comparing Canada to the US

- ❑ Chemotherapy is given less frequently at EOL
- ❑ Less visits to the ICU
- ❑ Emergency visits are more common.
- ❑ More Canadians die in acute care hospitals.
- ❑ Fewer Canadians have hospice care or die at home.

# Acute Care Hospitals and End-of-Life care

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- ❑ Not well suited to dealing with the palliative patient.
- ❑ Before advent of acute care hospitals. Care of dying was mainly at home.
- ❑ Availability of alternatives is critical.
- ❑ Experience of insurers in US
  - ❑ Availability of hospice – reduces ED visits, chemotherapy usage, costs of care and...
  - ❑ In some studies also improves survival.



# Intensive Care Units and End-of-Life care

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- ❑ Occurs due to absence of an advance directive or the lack of the ‘difficult conversation’ and a care team and patient who have never met.
- ❑ Evidence shows worsened quality of life for patient and higher incidence of subsequent depression for their caregivers.
- ❑ “Spending ones final days in an ICU with a terminal illness is a failure...You lie attached to a ventilator, your mind teetering on delirium and beyond realizing you will never leave this place. The end comes with no chance to say – Good Bye, It’s OK, I’m sorry or I love you”

# Estimated Cancer Deaths in 2013



Males  
**39,400**  
Deaths



Females  
**36,100**  
Deaths

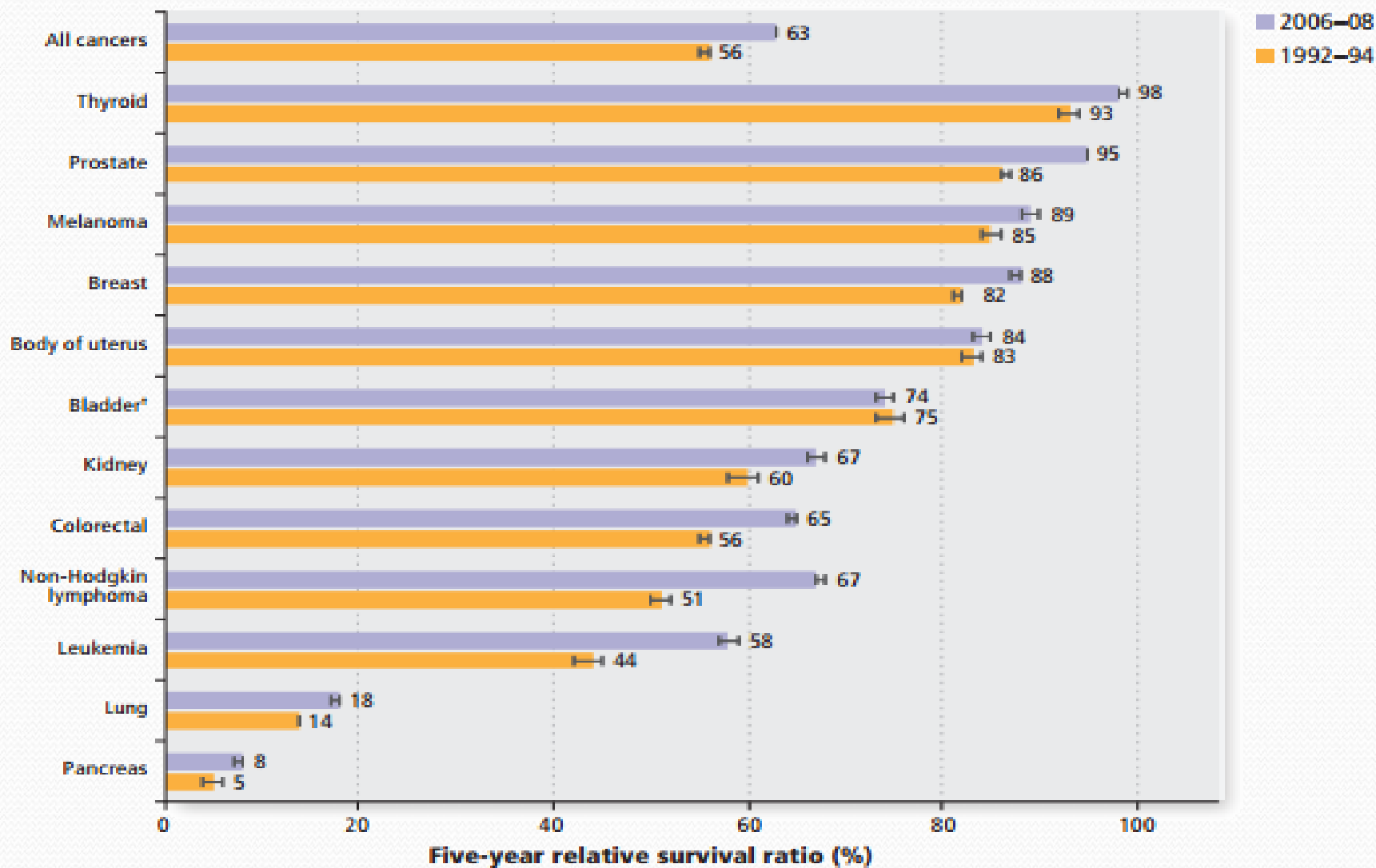
Site	Percent	Deaths
Lung	27.2%	10,700
Colorectal	12.7%	5,000
Prostate	10.0%	3,900
<b>Pancreas</b>	<b>5.5%</b>	<b>2,200</b>
Leukemia	3.8%	1,500
Bladder	3.8%	1,500
Esophagus	3.8%	1,500
Non-Hodgkin lymphoma	3.6%	1,450
Stomach	3.2%	1,250
Brain	2.9%	1,150

Site	Percent	Deaths
Lung	26.3%	9,500
Breast	13.9%	5,000
Colorectal	11.6%	4,200
<b>Pancreas</b>	<b>6.0%</b>	<b>2,200</b>
Ovary	4.7%	1,700
Non-Hodgkin lymphoma	3.3%	1,200
Leukemia	3.1%	1,100
Body of uterus	2.5%	890
Brain	2.2%	790
Stomach	2.2%	780

*Every hour 10 Canadians will die from cancer.*

*There will be a period of months to years before death occurs.*

# Five-Year Relative Survival Ratios



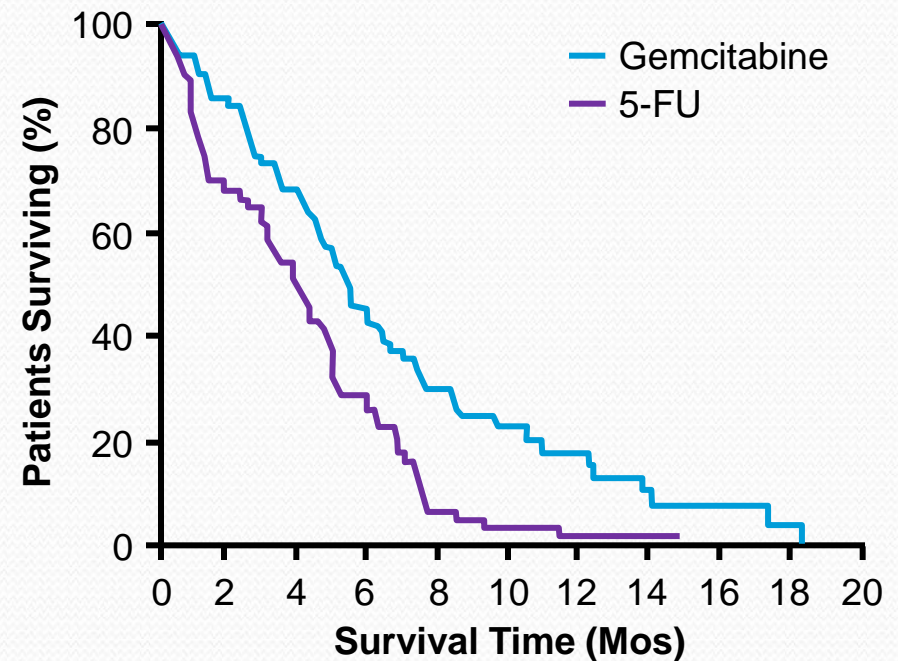
# Clinical Problems in Pancreatic Cancer

<b>Problem</b>	<b>Treatments</b>
Pain	Analgesia, XRT, nerve block
Pancreatic Insufficiency	Pancreatic enzymes
Biliary Tract Obstruction	Stent, Bypass
Cachexia	Challenging
Fatigue and Tiredness	Challenging
Gastric Outlet Obstruction	Stent, Bypass
Depression	Psychosocial care
Bowel Dysfunction	Motility agents
Venous Thromboembolism	LMWH

*Patients with advanced cancer often don't feel well at all.*

# Metastatic Pancreatic Cancer: The Basis of Gemcitabine as the Mainstay of Treatment

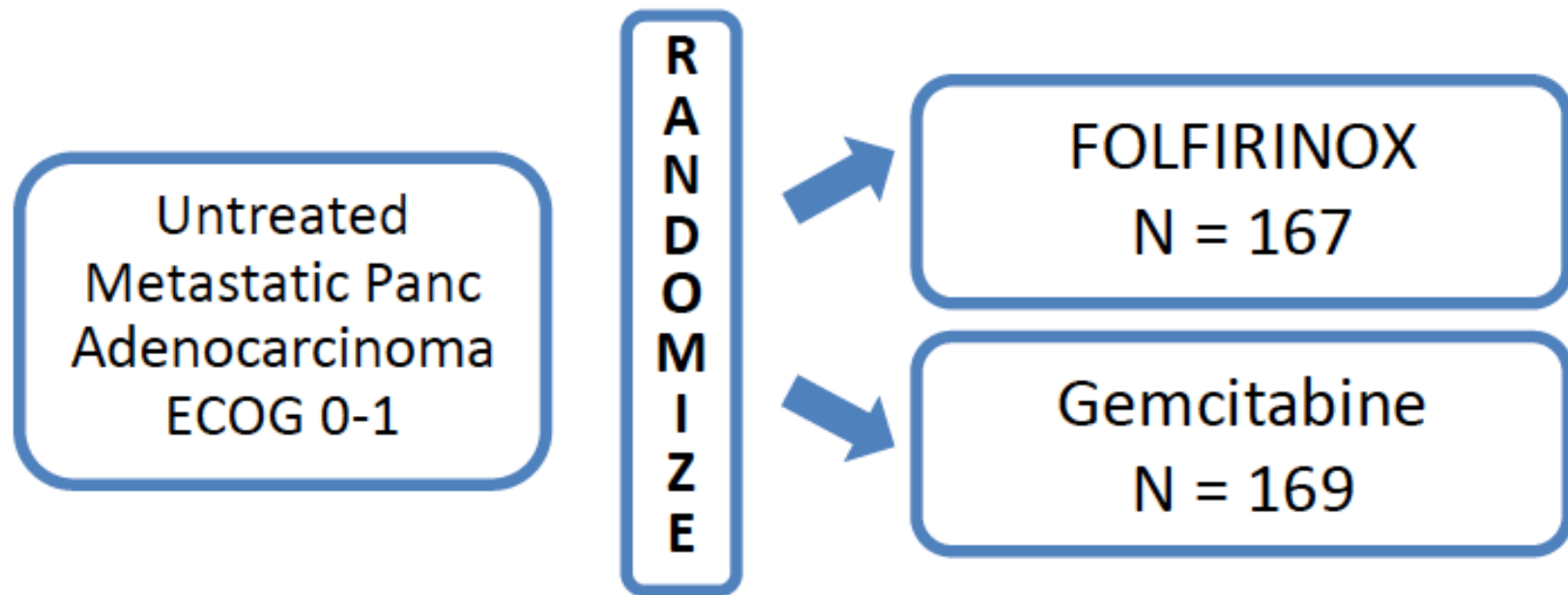
- Pivotal study defining role for gemcitabine as first-line treatment for patients with advanced pancreatic cancer
  - Median survival (vs bolus 5-FU): 5.65 vs 4.41 mos. ( $P = .0025$ )
  - **1-year survival: 18% vs 2%**
  - Clinical benefit\*: 23.8% vs 4.8% ( $P = .0022$ )
  - Response rate: 5.4% vs 0% ( $P = NS$ )



\*A composite of measurements of pain (analgesic consumption and pain intensity), Karnofsky performance status, and weight.

# FOLFIRINOX vs Gemcitabine

Prodige 4- ACCORD 11



Randomization 1: 1

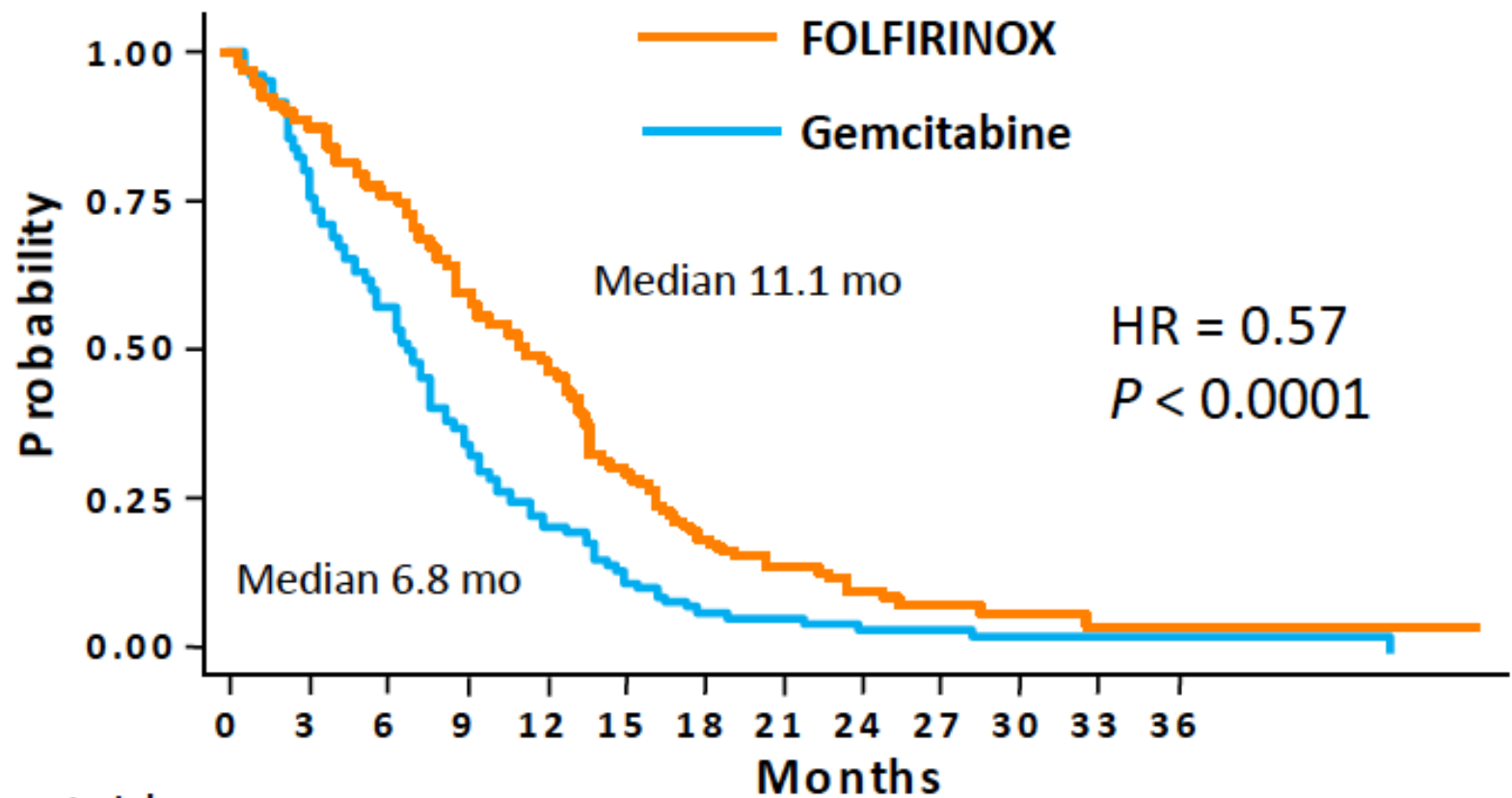
Stratification

- PS: 0-1 vs 2; Primary tumor location, Center

Primary Endpoint: Overall Survival



# FOLFIRINOX vs Gemcitabine Overall Survival



## Number at risk

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

# FOLFIRINOX vs Gemcitabine

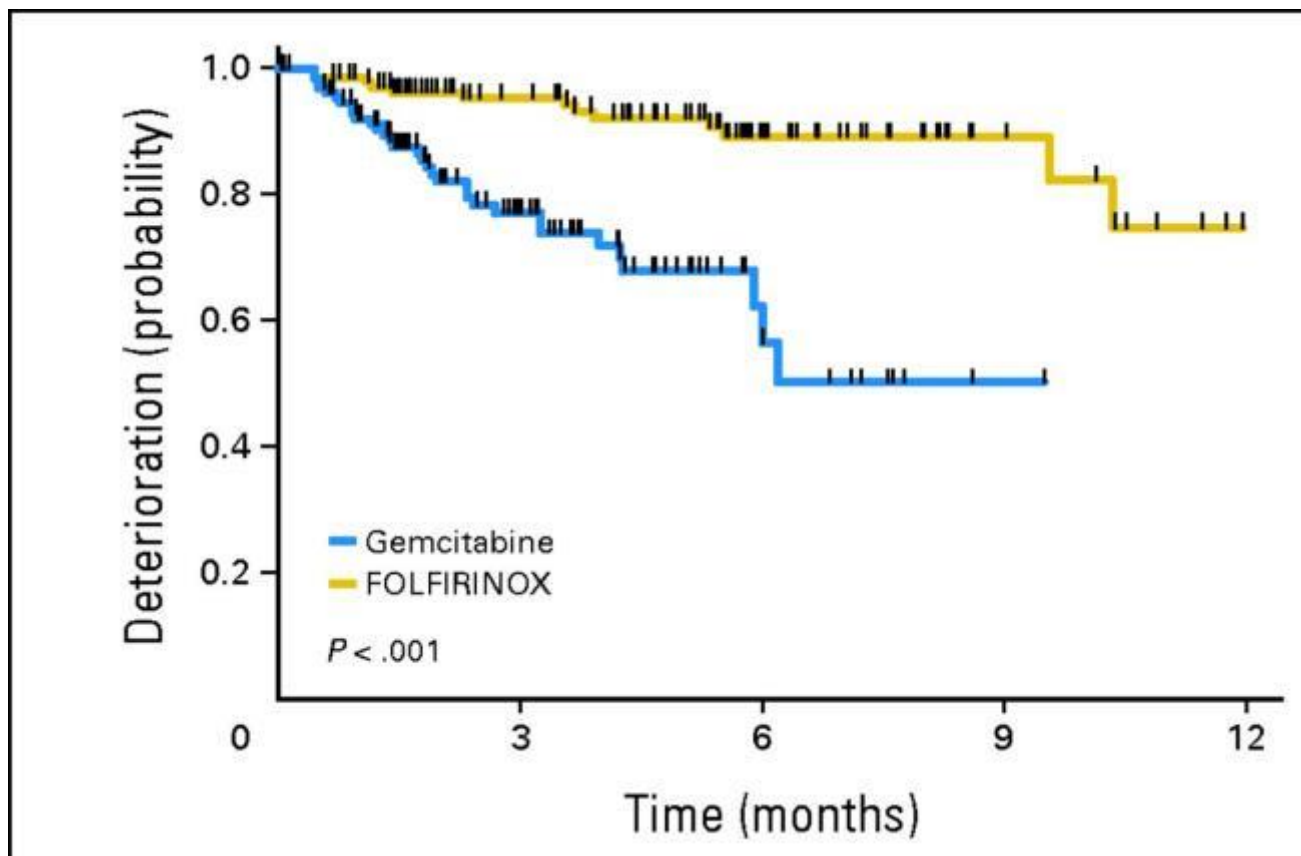
## Secondary Endpoints and Safety

	FOLFIRINOX N= 167	Gemcitabine N= 169	P-Value
Overall response rate	31.6%	9.4%	0.0001
Median PFS	6.4 m	3.3 m	0.0001 HR = 0.47
Toxicity	FOLFIRINOX	Gemcitabine	
Febrile neutropenia	5.4%	0.6%	0.009
Thrombocytopenia	9.1%	2.4%	0.008
Peripheral neuropathy	9%	—	0.001
Vomiting	14.5%	4.7%	0.002
Diarrhea	12.7%	1.2%	0.0001
Elevated LFT's	7.3	20.8%	< 0.001
Thromboembolic events	6.6%	4.1%	
Growth factor support	42.5%	5%	



# FOLFIRINOX vs. Gemcitabine: Quality of Life

## Time Until Definitive Deterioration



# Survival in Advanced Pancreatic Cancer

## First line chemotherapy – ECOG 0/1

	Pre-Gemcitabine	Gemcitabine	Gemcitabine +Abraxane	FOLFIRINOX
Median (mos)	4.5	6.5	8.7	11.1
1-year	2%	20%	35%	48%
2-year	<1%	5%	10%	10%
3-year	<1%	<1%	4%	4%

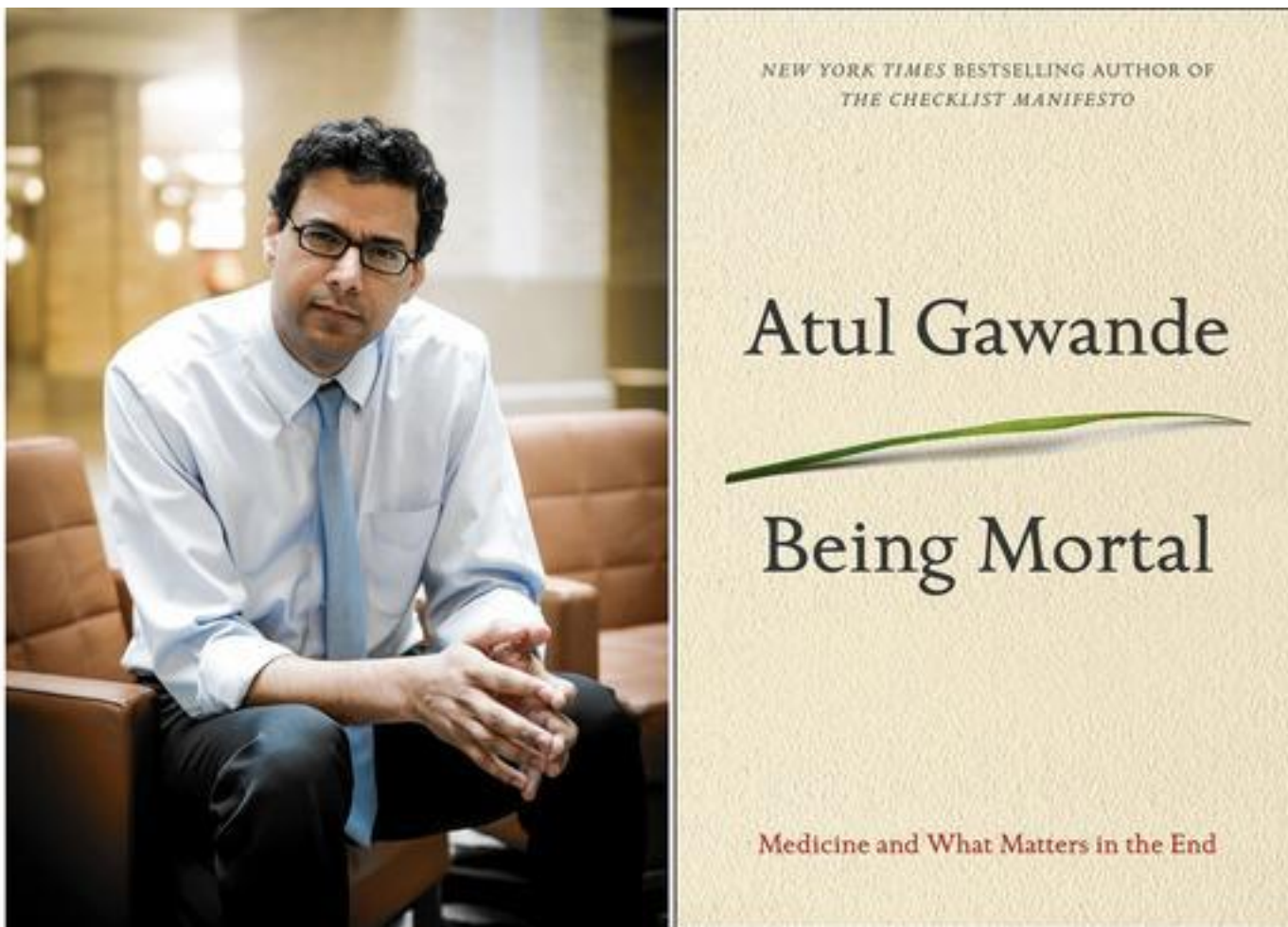
# Pancreatic Cancer – Survival by KPS Score

KPS Subgroup	ABRAXANE/Gemcitabine		Gemcitabine		Hazard Ratio HR <sub>A+G/G</sub> 95% CI	P-value
	Death/n (%)	Median OS 95% CI (months)	Death/n (%)	Median OS 95% CI (months)		
100	49/69 (71)	12.6 (9.6, 14.9)	43/69 (62)	10.9 (7.5, 13.5)	0.92 (0.60, 1.41)	0.697
90	138/179 (77)	8.9 (7.9, 10.1)	169/199 (85)	7.1 (6.5, 8.7)	0.72 (0.57, 0.91)	0.006
80	114/149 (77)	8.1 (7.4, 9.6)	115/128 (90)	5.6 (4.2, 6.6)	0.55 (0.41, 0.72)	<0.001
<b>70</b>	<b>28/30 (93)</b>	<b>3.9 (2.3, 5.5)</b>	<b>31/33 (94)</b>	<b>2.8 (1.8, 4.0)</b>	<b>0.99 (0.57, 1.72)</b>	<b>0.963</b>

# Sara

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- ❑ 34, pregnant with first child (39 weeks) develops cough and chest pain.
- ❑ Diagnosed with advanced lung cancer.
- ❑ Baby is delivered.
- ❑ Starts treatment with Erlotinib.
- ❑ Sara and husband don't want to focus on survival statistics. They want to aggressively manage the cancer. The oncologist states "some responses to erlotinib can be long-term".
- ❑ Erlotinib doesn't work (no mutation), pulmonary embolus, starts on carboplatin, paclitaxel



“The story of Sara”

# The Value of not taking chemotherapy

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- ❑ Patients don't have to plan their life around their treatment and dealing with the toxicities of treatment.
- ❑ They can spend the remaining time that they have living their life, doing the things they found meaningful
  - ❑ Visiting grandchildren, playing bridge...
  - ❑ Completing things
- ❑ Patients often become more narrowly focussed.
- ❑ These patients are 'easier' to look after.

# The Doctor-Patient Relationship

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- ❑ It is essential to ask patients (and family) at the initial appointment, about what they understand about their illness, why they are coming to see you and what are their expectations.
- ❑ It is also useful to ask patients how much information they want and at the conclusion of the interview to ask if there is anything additional they wish to ask or discuss.
- ❑ Once a therapeutic relationship is built it becomes easier to have those difficult conversations.

# Talking to patients

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- ❑ Oncologists tend to focus discussion around therapeutic decisions and practicalities
- ❑ Better Oncologists will discuss the bigger picture
  - ❑ Limitations of therapy
  - ❑ Options for therapy
  - ❑ The realities of the disease and the patients circumstances.
- ❑ Finding the 'sweet spot' between paternalistic and informative- to guide and counsel patients
- ❑ To do that we need to talk about their fears, what matters most.
- ❑ How do we engage a patient/family who does not want to have such a conversation?



# End-of-Life Discussions and aggressive care.

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- ❑ Study by Mack, JCO 2012. 1231 patients with advanced lung and colorectal cancer.
- ❑ Patients who had EOL discussions with their physicians before the last 30 days of life were less likely to receive aggressive measures
  - ❑ Chemotherapy ( $p < 0.003$ ),
  - ❑ Acute care ( $P .001$ )
  - ❑ Patients were also more likely to receive hospice care ( $P .001$ ) and to have hospice initiated earlier ( $P .001$ ).

# Chemotherapy in Advanced Cancer

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- ❑ You don't know what you will do when faced with advanced cancer, until you have advanced cancer.
- ❑ There is good evidence that chemotherapy improves quality of life in many/most types of advanced cancer.
- ❑ But
  - ❑ ...you need to understand what is happening in the individual patient not what happens on average.
  - ❑ ...you also need to understand what is important to the patient, their fears and wishes.
  - ❑ ...our failure is perhaps more in knowing when to stop.

# Chemotherapy in Advanced Cancer

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- ❑ Many studies have shown that oncologists are overly optimistic in their prediction of survival.
- ❑ Studies also show that oncologists generally do discuss whether a treatment is for cure or palliation.
- ❑ Patients have an optimistic understanding of the benefits of chemotherapy (Weeks).
  - ❑ More than half of patients being treated with advanced lung and colon cancer felt there was a chance of a cure.
  - ❑ Association between inaccurate beliefs about the likelihood of cure and higher ratings of physician communication

# Other challenges

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- ❑ Oncologists are busy.
  - ❑ They may have 15-25 patients with advanced cancer in a half-day clinic.
- ❑ Oncologists work reasonably regular hours in cancer centres. Patients get sick at all hours and may require care in different places.
- ❑ Cancer is a progressive illness. Bad things can happen suddenly and the reality will change.
- ❑ Families don't always agree.

# Dying

- ❑ Ben Hur: Death of Masala. Provision of comfort both physical and psychological.



# Another way of putting it.

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- “You don’t have to spend much time with those with terminal illness to see how often medicine fails the people it is supposed to help. The waning days of our lives are given over to treatments that addle our brains and sap our bodies for a sliver’s chance of benefit. They are spent in institutions where regimented, anonymous routines cut us off from all the things that matter to us in life. Our reluctance to honestly examine the experience of dying has increased the harm we inflict on people and denied them the basic comforts they most need ... we have allowed our fates to be controlled by the imperatives of medicine, technology and strangers.”

# Patient-centred Care

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- ❑ Patient centred care – Institute of Medicine definition
- ❑ "Providing **care** that is respectful of and responsive to individual **patient** preferences, needs, and values, and ensuring that **patient** values guide all clinical decisions."
- ❑ Shared decision making with patients and families.
  - ❑ What if consensus cant be found – the “Slow” Code.
  - ❑ The 'value' of life- patient/family perspective.

# Points

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- ❑ When dealing with decisions around whether to undertake treatments of modest benefit there is no single right answer.
- ❑ Patient choice and values need to drive care...
  - ❑ ...but fear can drive medically inappropriate decisions.
  - ❑ ...most patients and families have a limited understanding of what it is like to die of advanced cancer.



# Conclusions

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- ❑ We can do better with end-of-life care.
- ❑ There is good data that chemotherapy can improve both survival and quality of life ... to a point.
- ❑ Aggressive interventions (chemotherapy) occur relatively infrequently in last month of life in Ontario.
- ❑ There is too much reliance on ED visits and acute care.
- ❑ Being able to have those difficult conversations: and the availability of appropriate support (e.g. hospice, home palliative services) will reduce aggressive care.
- ❑ One size does not fit all. Patient preferences can drive different approaches.

T<sub>1</sub> H<sub>4</sub> A<sub>1</sub> N<sub>1</sub> K<sub>5</sub>

Y<sub>4</sub> O<sub>1</sub> U<sub>1</sub>