Cost and Value of Chemotherapy and Biologic Cancer Treatments:

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Obstacles and Solutions to Maximizing Value of Oncology Drugs

- The Goal: Use biologics/chemotherapy to:
  - Save, Extend and Improve Lives
  - Cut costs
  - Drive Innovation
  - Maximize Value
- What strategies should we pursue to help control the costs of chemotherapy and biologics?
- How?
  - Ongoing investment in better evidence base/research
  - More communication, education, teamwork, coordination
  - Better align incentives—value based benefit design
  - Insurance reform

Cancer Drugs FDA Approved: 2012

Drug	Indication	Effect
Axitinib	Met Kidney CA	Median OS=2m>Sorafenib (6.7 vs. 4.7m)
Pertuzumab	Met BrCA	Median PFS=6m> placebo (18.5 vs. 12.4)
Ziv-Aflibercept	Met CRC	Median OS=1m> placebo (13 vs. 12)
Vismodegib	Basal Cell CA	Objective RR% in 104 patients In single arm trial (30%)
Carfilzomib	Refractory M. Myeloma	22% RR
Enzalutamide	Met Prostate	Median OS =6m>placebo (18.4 vs. 13.6)
Bosotinib	Refractory PH+ CML	33% cytogenetic RR
Regorafinib	Met CRC	Median OS=1.4m>placebo (6.4 vs. 5)

Cancer Drugs FDA Approved: 2012

Drug	Indication	Effect	Approximate Cost 1 month of Rx
Axitinib	Met Kidney CA	Median OS=2m> Sorafenib (6.7 vs. 4.7m)	$9800
Pertuzumab	Met BrCA	Median PFS=6m> placebo (18.5 vs. 12.4)	$5900
Ziv-Aflibercept	Met CRC	Median OS=1m> placebo (13 vs. 12)	~$11,000
Vismodegib	Basal Cell CA	Objective RR% in 104 patients In single arm trial (30%)	$7500
Carfilzomib	Refractory M. Myeloma	22% RR	$9,950
Enzalutamide	Met Prostate	Median OS =6m>placebo (18.4 vs. 13.6)	$7,450
Bosotinib	Refractory PH+ CML	33% cytogenetic RR	N/A
Regorafinib	Met CRC	Median OS>1.4m>placebo (6.4 vs. 5)	$~10,000

Onyx Stock Price and Regorafinib Development Time Line

Sellers Set and Maintain Drug Prices

- Limited # of products for any single indication
- Patent protection
- Cross subsidization –global market
- Biggest payer (CMS) can't negotiate
- Oncology drugs are in a protected "Special class"—can't not cover them

A More Competitive Marketplace is Emerging

- 7 drugs have been FDA approved for kidney cancer since 2005
  - Sorafenib: 2005
  - Sunitinib: 2006
  - Temsirolimus: 2007
  - Everolimus: 2009
  - Bevaciumab: 2009
  - Pazopanib: 2009
  - Axitinib: 2012

Clinical Trials Remain the Linchpin

- We must do better at accrual
- Design studies with meaningful endpoints/effect sizes
- Embed molecular correlatives to specify mechanisms
- Distinguish little benefit for many vs. big benefit for few
  - crizotinib for alk mutated lung cancer
- Invest in publicly funded clinical trial system
  - “Can we do less?” not just “Can we do more?”
- Align CMS/FDA/CDC/AHRQ and NCI

Align Incentives to Maximize Value

- Pharma-MDs-Patients vs. Payors/Taxpayers
  - Strange bedfellows and conflicts….
- Oncologists still paid at ASP+6%
- Oncologists still earn a lot
- Moral hazard of health insurance
  - Vast majority of patients have “no skin in the game”
  - Generous policies, Medigap, Medicaid, caps
  - Limited role of patient assistance plans
  - Cost passed on to employers/taxpayers

States Seek Curb on Patient Bills for Costly Drugs

The New York Times By ANDREW POLLACK April 12, 2012

- The hemophilia drug that saves 7-year-old William Addison from uncontrolled bleeding costs $100,000 a year. His family's insurance pays virtually all of it. A collection of empty bottles from William's medicine, which costs $100,000 a year at his home in Falmouth, Me. (picture of 100s of vials)

- But his mother, Victoria Kuhn, says she is terrified that the insurance company may start requiring patients to pay as much as a third of the cost of the drug.

- Spurred by patients and patient advocates like Ms. Kuhn, lawmakers in at least 20 states, from Maine to Hawaii, have introduced bills that would limit out-of-pocket payments by consumers for expensive drugs used to treat diseases like cancer, rheumatoid arthritis, multiple sclerosis and inherited disorders.

- Pharmaceutical companies would also benefit from such legislation because high co-payments discourage patients from taking their medicines. The pharmaceutical giant Pfizer has been helping the legislative drive behind the scenes, even drafting some of the bills, according to legislators and patient advocates.

Align Incentives to Promote Teamwork and Coordination

- If you give chemotherapy, you need a plan to minimize ED/hospitalization use afterwards
- Value based design: reward good behavior
- Incentivize accessibility outside routine hours
- Incentivize communication strategies
  - Patient to Clinician
  - Clinician to Clinician/Hospital/Home Care/Pcare
  - Waiting room/group education
  - Across systems

Fostering Accountability: Value Based Design

- What is each oncologist were profiled based on panel of all health care service utilization within 30 days of chemotherapy treatment?
- How to make this win/win for pt/MD?
  Benefit/Design
- How to avoid ED visits/hospitalizations
  - Don't treat people who shouldn't be treated
  - Communicate honestly about risk/benefits
  - Don't postpone difficult discussions
  - Be available off hours/remote communication
  - Communicate, educate, reinforce
  - Partner with home care

Existing Strategies to Limit Costs of Oncology Drugs

- More choices within therapeutic class
- Shift from Medical to Pharmacy Benefit

- Tiered formularies
- Step edits
- Prior authorization
- Quantity limits
- Cost transparency

Treatment Pathways/Guidelines

- Work best when there is menu of choices
- If similar efficacy choose least $$ option
- Resource intensive to develop and curate
- Challenging to keep free from commercialism
- Chemo order entry systems are helping
- Need tracking systems for molecular profiling
- Need interoperable IT systems
- Proprietary vs. open access

Comparative Effectiveness Research One Strategy, but not a Solution

- Leverage day to day experience and abundant unused data, system capacity
- Better Health IT facilitates CER
- Standard setting/linked/de-identified data sets
- Examine patients left out of trials
- Examine gap between how:
  - Rx can work
  - Rx does work
- Better data sets and methods
- Actively engage patients
- Conflict management

Challenges of Informed Decision Making About Advanced CA Rx

- Life threatening
- Framing matters
- Information about Rx benefits difficult to obtain
- Customizing info is challenging
  - How do these results apply to me?
- Doctors want to provide comfort, be humane, be liked, therapeutic rapport

What Do Patients Expect from Chemotherapy?

- CANCORS multisite population based study across US
- Comprehensive survey/record abstraction 2005-2011
- Telephone interviews ~4 months from diagnosis

- What do patients with metastatic cancer expect from chemotherapy?

- Are expectations in line with reality?

- What factors are associated with realistic expectations?

Cohort Selection for Survey about Chemo Effectiveness

CanCORS enrollees with baseline survey

Lung	Colorectal
5,015	4,725

Excluded	**Lung**	**CRC**
Stage I-III or unknown stage	3,138	3,931

Enrolled patients with baseline survey and Stage IV cancer

Lung	Colorectal
1,877	794

Excluded	**Lung**	**CRC**
Item on effectiveness of chemotherapy not asked		
Survey type (surrogate of deceased patient or brief version omitting the item)	986	238
Patient/surrogate reported that no physician discussed chemotherapy	113	51
Physician told patient not to have chemotherapy	7	2

Patients with Stage IV cancer who were surveyed regarding their beliefs about the effectiveness of chemotherapy

Lung	**Colorectal**
771	**503**

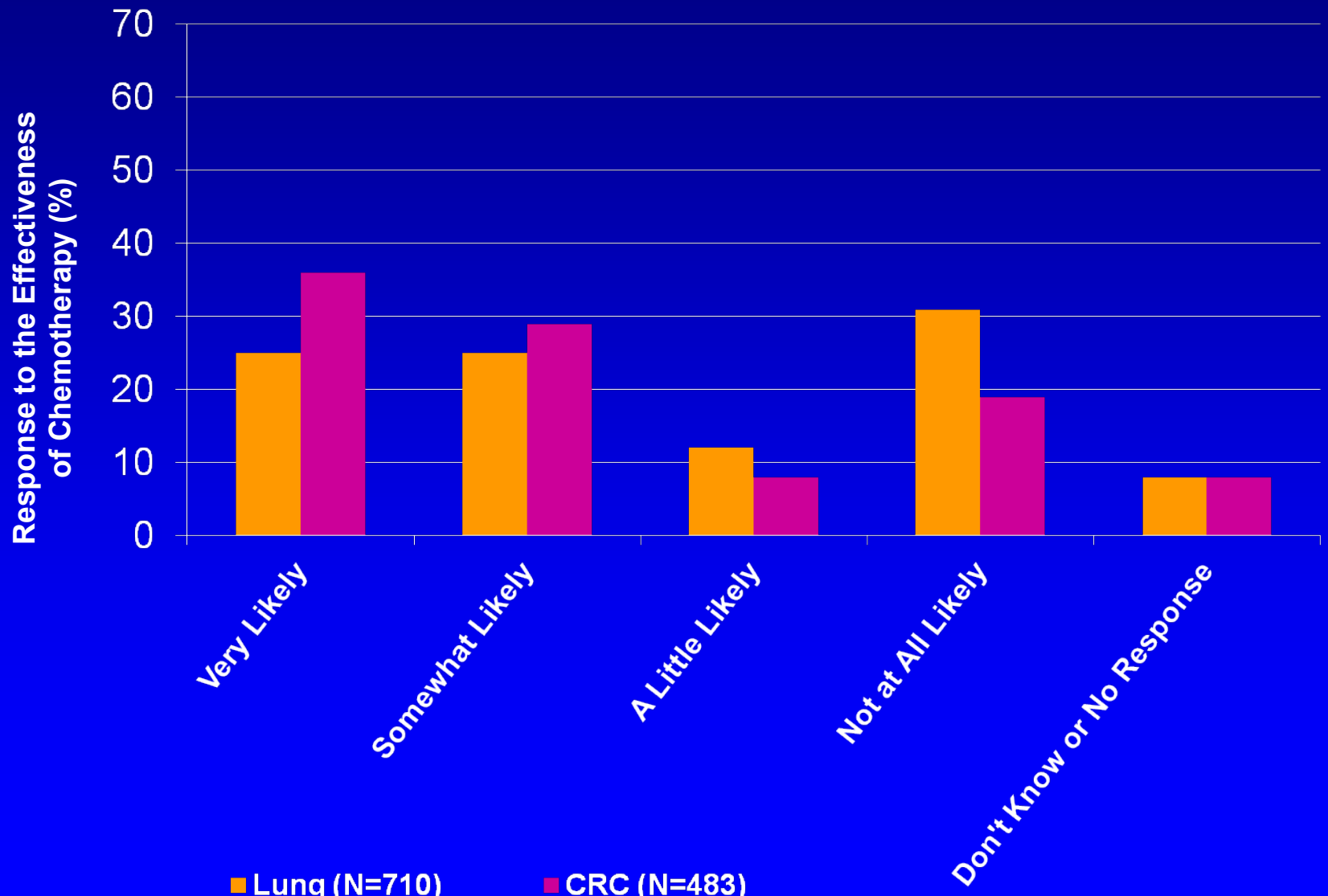
Excluded	**Lung**	**CRC**
No chemotherapy	61	20

Patients with Stage IV cancer who were surveyed regarding their beliefs about the effectiveness of chemotherapy and opted to receive chemotherapy

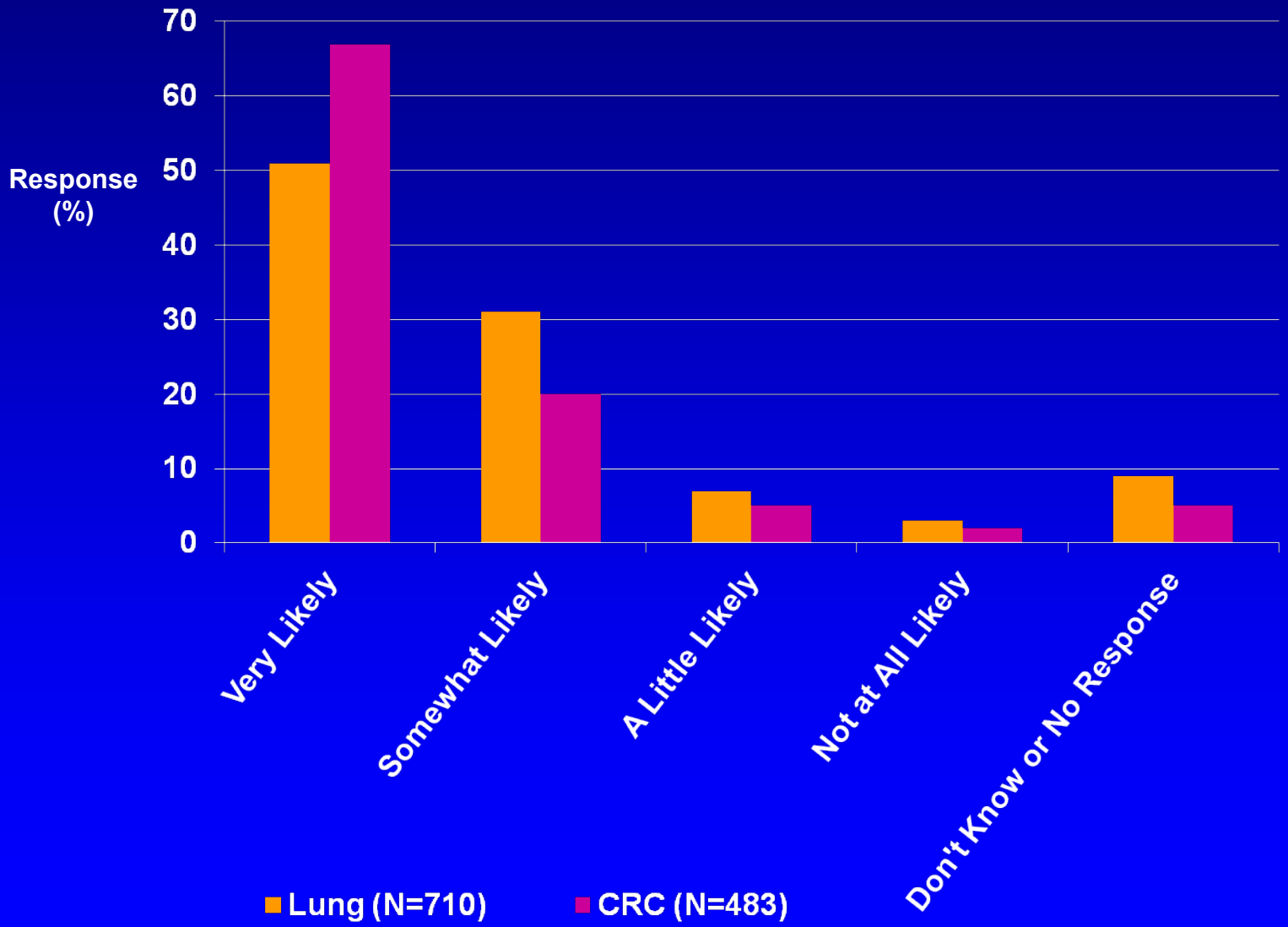
Lung	**Colorectal**
710	**483**

Weeks et al in press 10/12
CanCORS Study

Patients' Expectations of Likelihood that Chemotherapy will *Cure Cancer: CanCORS Study*



Expectations about Likelihood that Chemotherapy will *Extend Life: CanCORS Study*



Factors Associated with Inaccurate Response to Question about the Likelihood of Cure from Chemotherapy

		Odds Ratio (95% CI)	P Value
Cancer type			<0.001
	Lung	Reference	
	Colorectal	1.75 (1.29, 2.37)	
Age			0.06
	21 to 54	Reference	
	55 to 69	1.10 (0.77, 1.57)	
	70 to 79	1.68 (1.10, 2.57)	
	80+	1.47 (0.77, 2.80)	
Race			<0.001
	White	Reference	
	Hispanic/Latino	2.82 (1.51, 5.27)	
	African-American	2.93 (1.80, 4.78)	
	Asian/Pacific Islander	4.32 (2.19, 8.49)	
	Other	3.07 (1.50, 6.27)	
Integrated health care network			0.02
	No	Reference	
	Yes	0.70 (0.52, 0.94)	
Physician communication rating			0.002
	0 to 79	Reference	
	80 to 99	1.37 (0.93, 2.02)	
	100 (perfect score)	1.90 (1.33, 2.72)	

Odds ratios > 1 represent greater likelihood of an inaccurate belief about effects of chemotherapy
Factors with $p<0.10$ in univariate analyses retained in multivariable model

Factors NOT Associated with Inaccurate Response to Question about the Likelihood of Cure from Chemotherapy

	Odds Ratio (95% CI)	P Value
Gender		0.29
Male	Reference	
Female	0.85 (0.63, 1.15)	
Marital status		0.68
Married/living as married	Reference	
Non-married	1.07 (0.77, 1.49)	
Education		0.32
Less than high school	Reference	
High school/some college	0.86 (0.57, 1.29)	
College degree or higher	0.68 (0.41, 1.14)	
Household income ($)		0.39
< 20,000	Reference	
20,000-39,999	1.12 (0.76, 1.66)	
40,000-59,999	1.51 (0.94, 2.41)	
≥ 60,000	1.18 (0.73, 1.91)	
Good physical function (EQ5D based)		0.18
No	Reference	
Yes	1.22 (0.91, 1.64)	
Patient-physician role in decision making		0.31
Patient controlled	Reference	
Shared control	1.07 (0.79, 1.45)	
Physician controlled	1.45 (0.90, 2.35)	
Patient-family role in decision making		0.86
Patient controlled	Reference	
Shared control	1.04 (0.77, 1.39)	
Family controlled	0.80 (0.30, 2.12)	

Odds ratios > 1 represent greater likelihood of an inaccurate belief about effects of chemotherapy
Factors with $p<0.10$ in univariate analyses retained in multivariable model

What Is Missing from ChemoRx Labels and Consent Forms

- Clear simple statement of magnitude of benefit
- Not RR, HR, 95% CI.
- Clear, simple, transparent
- Median survival
- Better still:
  - % alive at 1 year with treatment XYZ
  - % alive at 2 years with treatment XYZ

Personal View: Low Yield Strategies

- Incorporate costs into discussions about advanced cancer treatment
- Eliminate patient accountability for cost sharing
- Individual provider profiling
- Invest scarce NCI $$ in prognostic models that don’t get used
- Cost-effectiveness analyses/NICE-UK approach

Potential Leverage Points to Maximize Value in Oncology Therapeutics

- Get Federal/state agencies to row together
- Curate/modernize/sustain cancer registries
- Invest in NCI sponsored clinical trials
- Require pharma to conduct follow on trials
- Coverage with evidence development
- Engage patients. Really Really. PCOR/CER
- Incentivize clinicians to build evidence base
- Simplify research/data collection enterprise

Potential Leverage Points for Maximizing Value in Oncology Rx

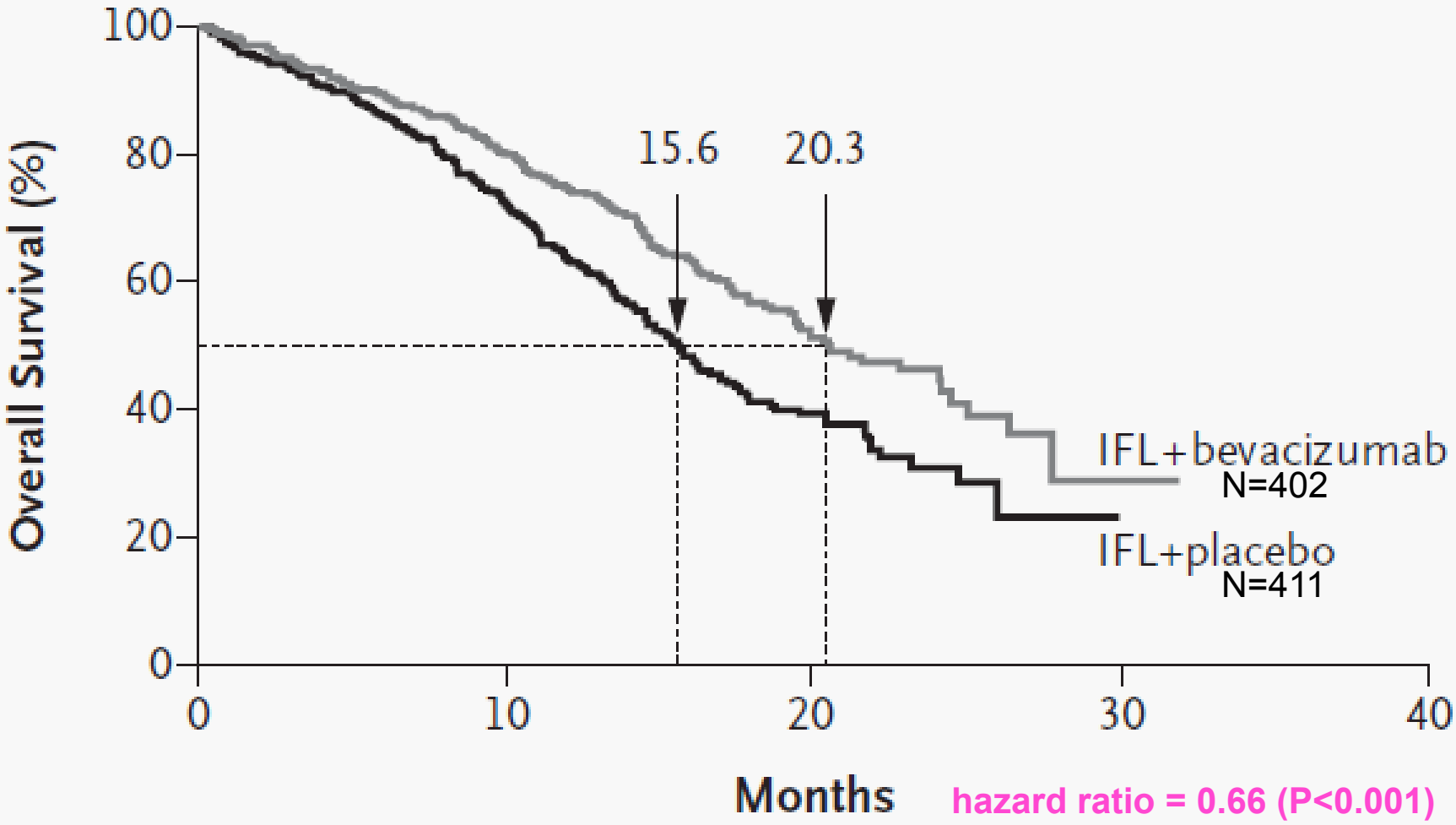
- Transparency in communicating benefits
- Standard interpretable labels
- Two weeks of oral chemo at a time
- Build/curate better pathways/guidelines
- Strategic value-based benefit design to incent patients/providers to choose wisely
- Recognize that hospitalization remains the biggest cost driver of oncology care—need to foster accountability for downstream consequences of chemorx
- Incentivize ($$$) good performance

Shared Accountability and Responsibility

- Pharma/Biotech
- Government
- Physicians/Providers
- Health Insurers
- Employers
- Patients
- Taxpayers

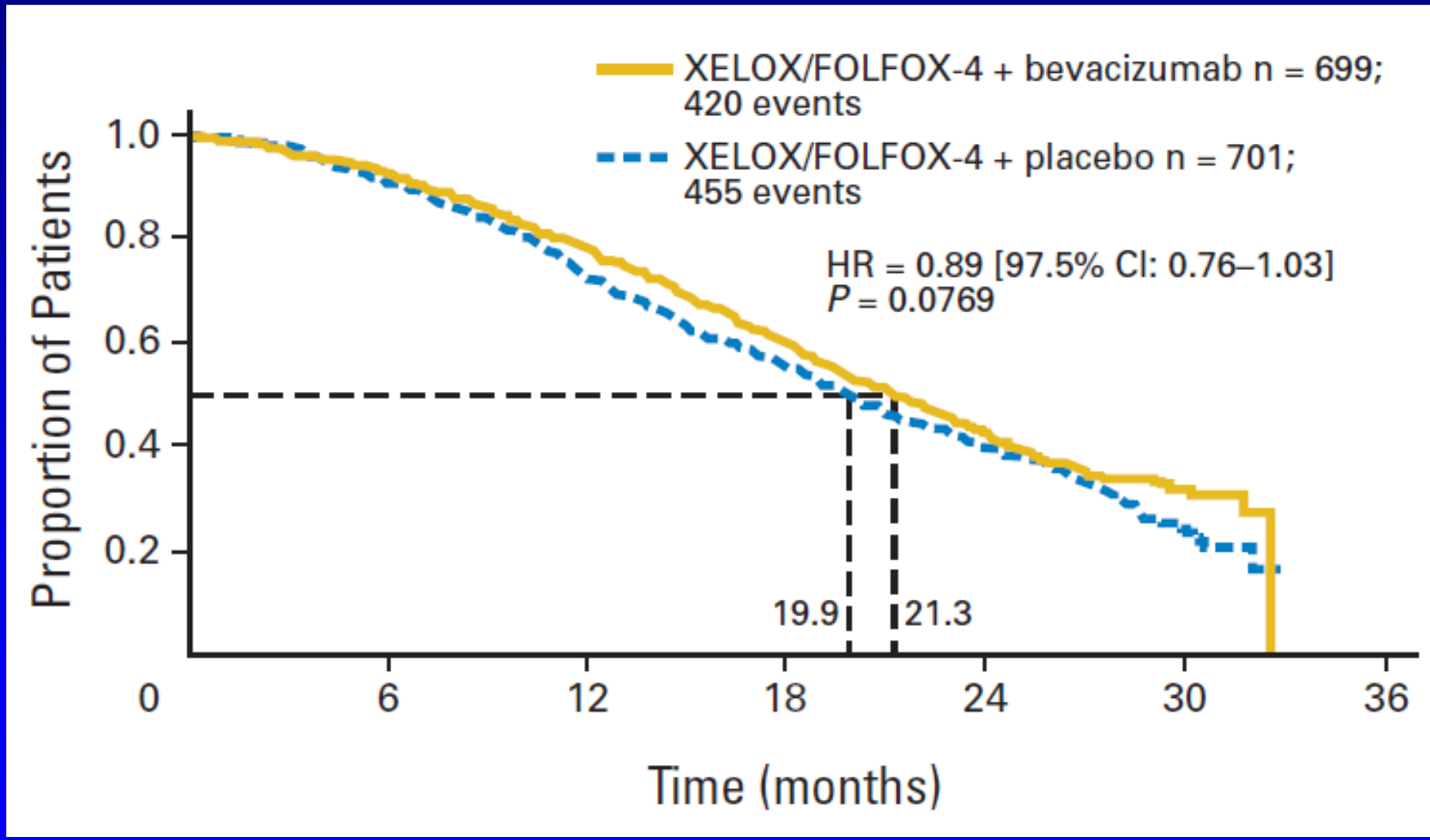
THANK YOU!

The Efficacy Study
Randomized Controlled Trial: IFL +/- BEV



Hurwitz H, N Engl J Med. 2004 Jun 3;350(23):2335-42.

Does Bev Work with FOLFOX?
First line treatment of MCRC



Saltz LB, J Clin Oncol. 2008 Apr 20;26(12):2013-9.

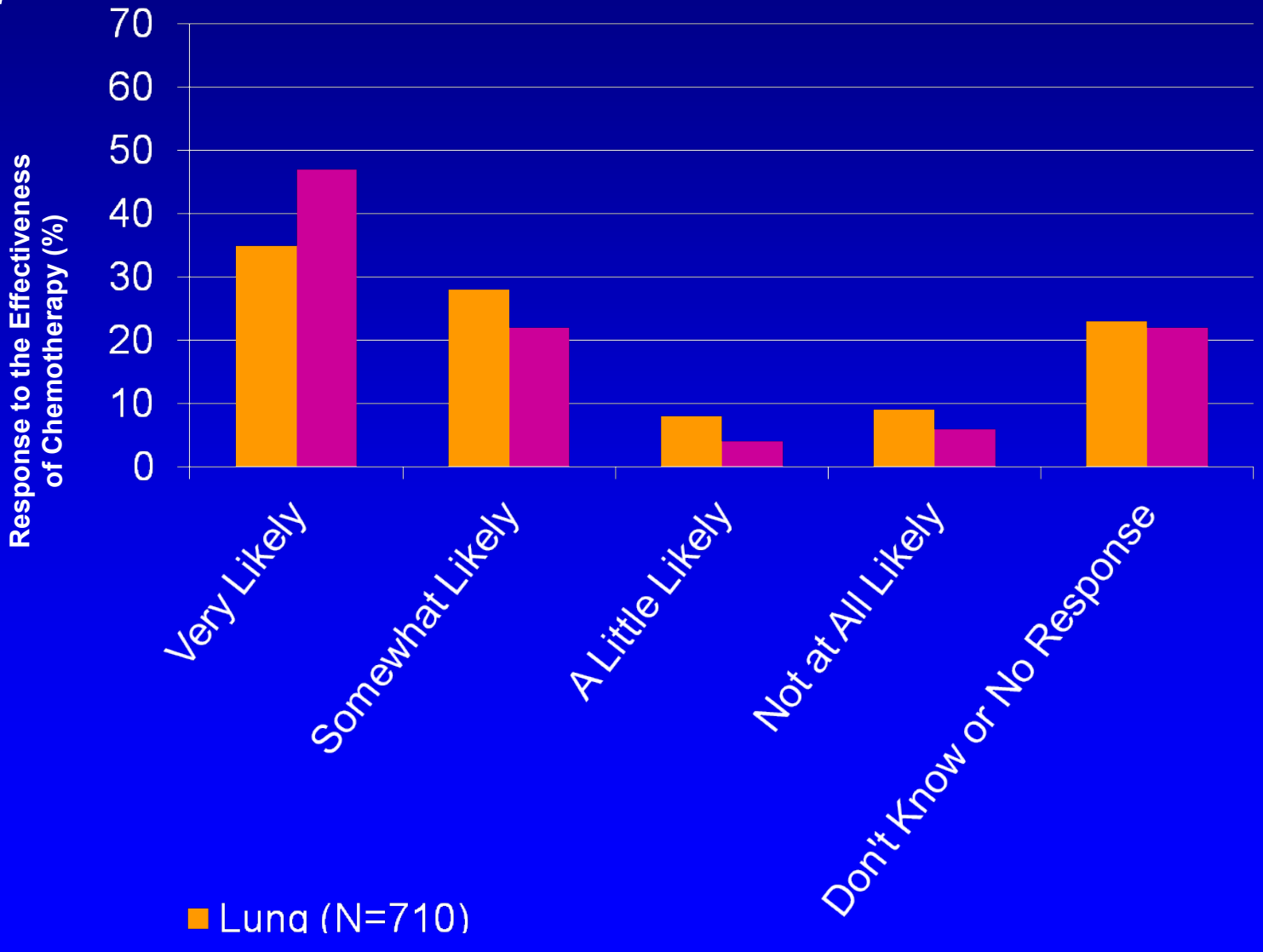
Patient characteristics by cancer type

Characteristic	Lung N = 710 %	Colorectal N = 482 %
Age		
21 to 54	18	34
55 to 69	47	43
70 to 79	29	17
80+	6	6
Gender		
Male	62	60
Female	38	40
Race and ethnicity		
White	69	59
Hispanic/Latino	6	12
African-American	12	17
Asian/Pacific Islander	7	8
Other	6	4
Marital status		
Married/living as married	63	64
Non-married	37	36
Education		
Less than high school	20	17
High school/some college	60	57
College degree or higher	20	25
Household income ($)		
< 20,000	28	27
20,000-39,999	27	24
40,000-59,999	13	14
≥ 60,000	19	23
Missing	14	12
Integrated health care network		
No	63	66
Yes	37	34

Patient Characteristics by Cancer Type

Characteristic	Lung N = 710 %	Colorectal N = 482 %
Baseline interview type		
Full	76	84
Brief	5	4
Surrogate for ill patient	19	12
Physical function (EQ5D based)		
Bad	38	27
Good	38	56
Missing	25	17
Physician communication rating		
0 to 79	20	16
80 to 99	25	28
100 (perfect score)	48	50
Missing	7	6
Patient-physician role in chemotherapy decision making		
Patient controlled	36	38
Shared control	47	45
Physician controlled	12	13
Missing	4	3
Patient-family role in treatment decision making		
Patient controlled	46	43
Shared control	46	50
Family controlled	1	3
Missing	7	4
Survey after end of first-line chemotherapy		
No	41	61
Yes	59	39

Figure 1C. Shown are the responses of patients with advanced lung cancer or colorectal cancer to questions regarding whether chemotherapy will *provide relief of symptoms*



% Responding that Chemotherapy Might Be Curative

	Lung Cancer (N = 710)	Colorectal Cancer (N = 483)
Overall	69	81
Age		
21 to 54	69	79
55 to 69	66	80
70 to 79	76	83
80+	66	89
Gender		
Male	71	80
Female	67	82
Race		
White	63	74
Hispanic/Latino	79	91
African-American	82	91
Asian/Pacific Islander	88	88
Other	81	90
Marital status		
Married/living as married	71	78
Non-married	67	84
Education		
Less than high school	75	86
High school/some college	68	82
College degree or higher	68	75
Household income ($)		
< 20,000	66	82
20,000-39,999	67	81
40,000-59,999	73	81
≥ 60,000	66	78
Integrated health care network		
No	70	85
Yes	69	72

% Responding that Chemotherapy Might Be Curative

	Lung Cancer (N = 710)	Colorectal Cancer (N = 483)
Overall	69	81
Baseline interview type		
Full	70	80
Brief	76	88
Surrogate for ill patient	66	85
Good physical function (EQ5D based)		
No	68	74
Yes	71	82
Physician communication rating		
0 to 79	61	72
80 to 99	69	77
100 (perfect score)	74	85
Patient-physician role in decision making		
Patient controlled	67	80
Shared control	70	79
Physician controlled	72	86
Patient-family role in decision making		
Patient controlled	67	79
Shared control	71	81
Family controlled	56	80
Survey done after end of 1st line chemotherapy+		
No	71	84
Yes	65	74

+ Restricted to the 885 patients for whom data on the timing of chemotherapy were available