Payer Directions

Payers and innovation: the challenge of cancer immunotherapy

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Aetna

ICLIO 1st Annual National Conference

10.2.15

Philadelphia, Pa.

ICLIO | INSTITUTE FOR CLINICAL IMMUNO-ONCOLOGY

AN INSTITUTE OF ACCC Association of Community Cancer Centers

Aetna Values & Oncology Solutions Mission Statement

Aetna Oncology Solutions – Mission Statement:

We give our members access to high-value, personalized cancer care models. We collaborate with oncology teams that deliver best-in-class care by using evidence-based medical guidelines, clinical decision support tools and services that improve the patient's experience, increase effectiveness of care and lower costs. Our value-based approach, powered by data analytics and transparency of policy and payment, allows us to move from a fee-for-service platform to a value-driven system that rewards Oncology practices for quality care throughout the patient's care journey.

Financial Disclosures

- I currently have or have the following relevant financial relationship to disclose:
  - Employee: Aetna

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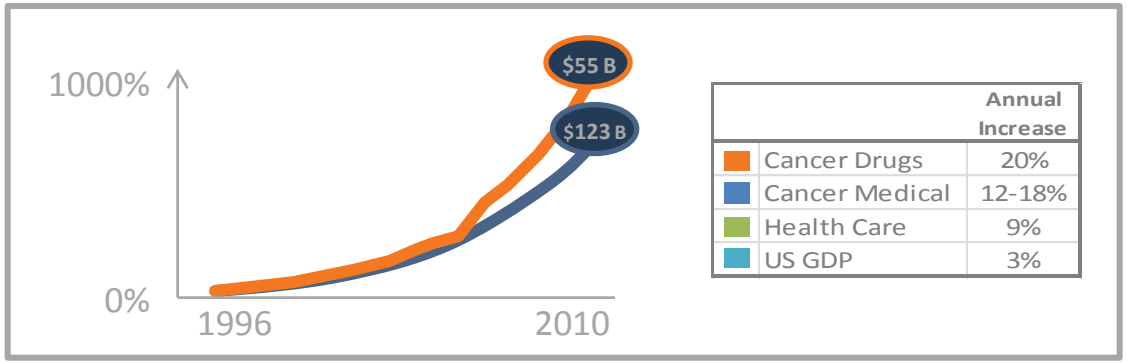
Cancer is the most costly medical item

And its cost is increasing at 2 to 3 times the rate of other costs.

Cancer care is the leading edge of medical cost trend.



	Annual Increase
Cancer Drugs	20%
Cancer Medical	12-18%
Health Care	9%
US GDP	3%

Aetna's top cost drivers in cancer care

Medical Rx	30.8%	$1.5B
Inpatient	23.3%	$1.1B
Radiology	22.4%	$1.1B
Specialist Physician	9.4%	$483M

Source: www.cancer.gov/newscenter/pressreleases/2011/CostCancer2020

Source: 2010 CY Claims; Commercial & Medicare; All Funding; Excludes AGB/SH/SRC

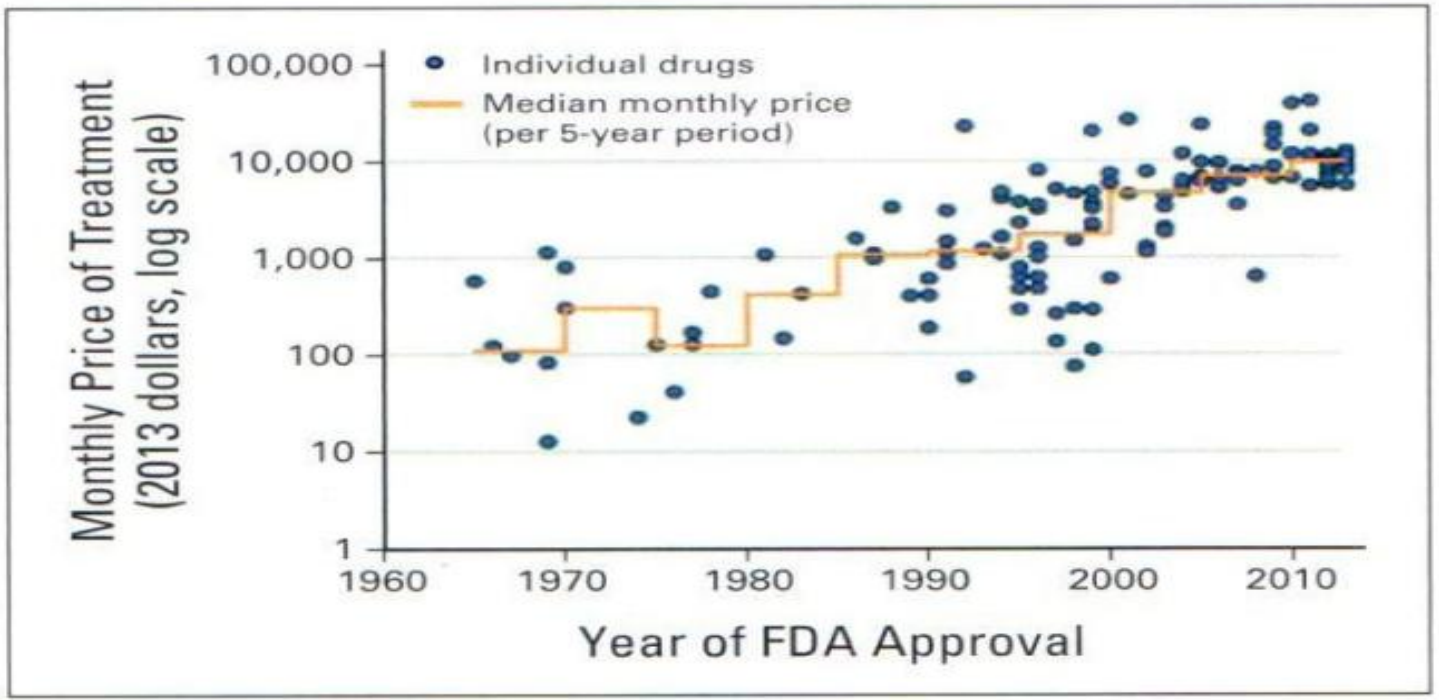
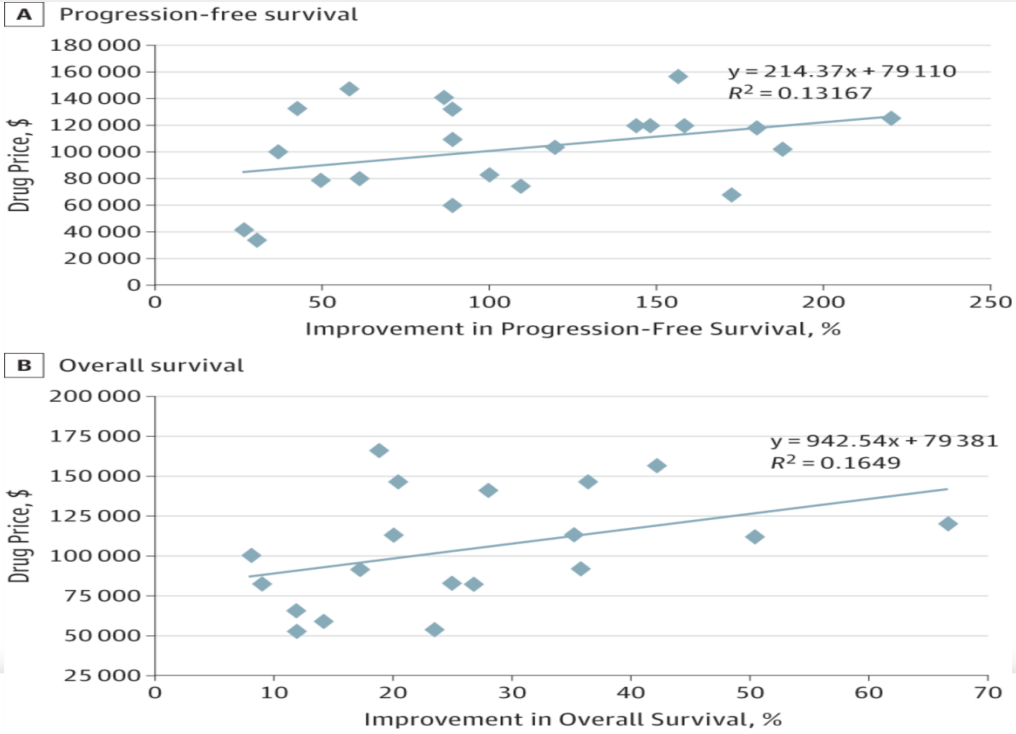


Figure 2. Monthly and median costs of cancer drugs at the time of US Food and Drug Administration (FDA) approval, 1965 to 2013. Adapted.[16]

From: **Five Years of Cancer Drug Approvals: Innovation, Efficacy, and Costs**

JAMA Oncol. Published online April 02, 2015. doi:10.1001/jamaoncol.2015.0373



EVIDENCE

cost

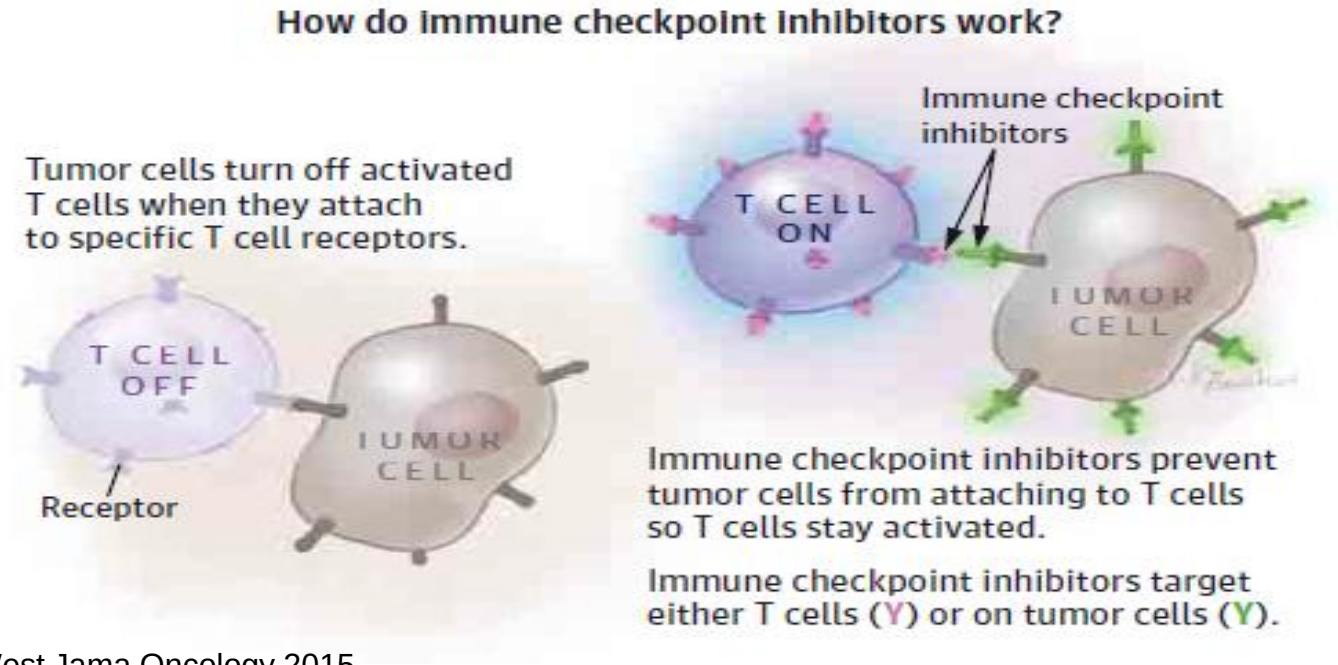
Responses to the huge and growing expense of cancer care?

- Pay less
- Manage more (prior auth)
- Narrow networks
- Shift responsibility to member (co-pay)
- Pay for performance (process measures)
- Shift risk (capitation)

Impact has been small

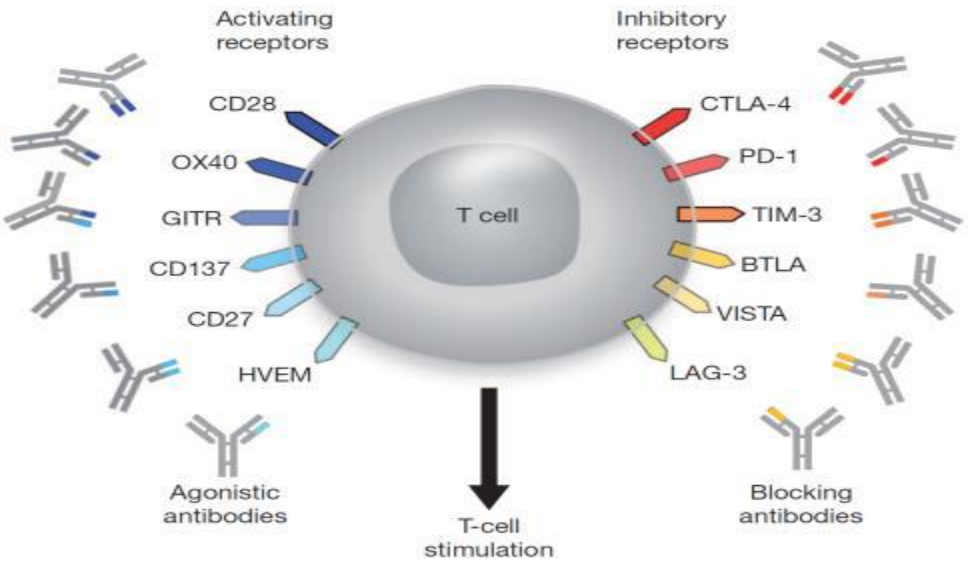
Aggravation has been large

Checkpoint inhibitors remove the “brakes” that tumor cells use to combat T cells



West Jama Oncology 2015

Immunotherapy: Multiple approaches including the approved checkpoint inhibitors CTLA-4 and PD-1



CTLA-4

YERVOY (ipilimumab) Injection for intravenous infusion

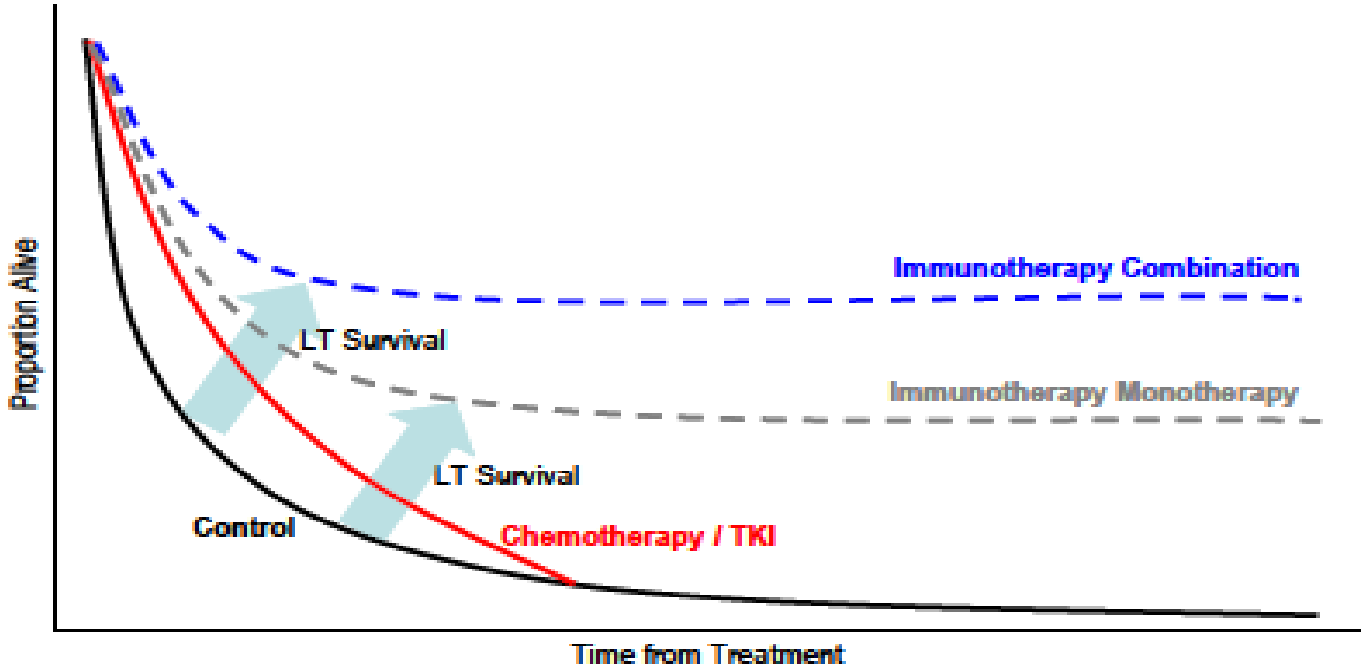
PD-1

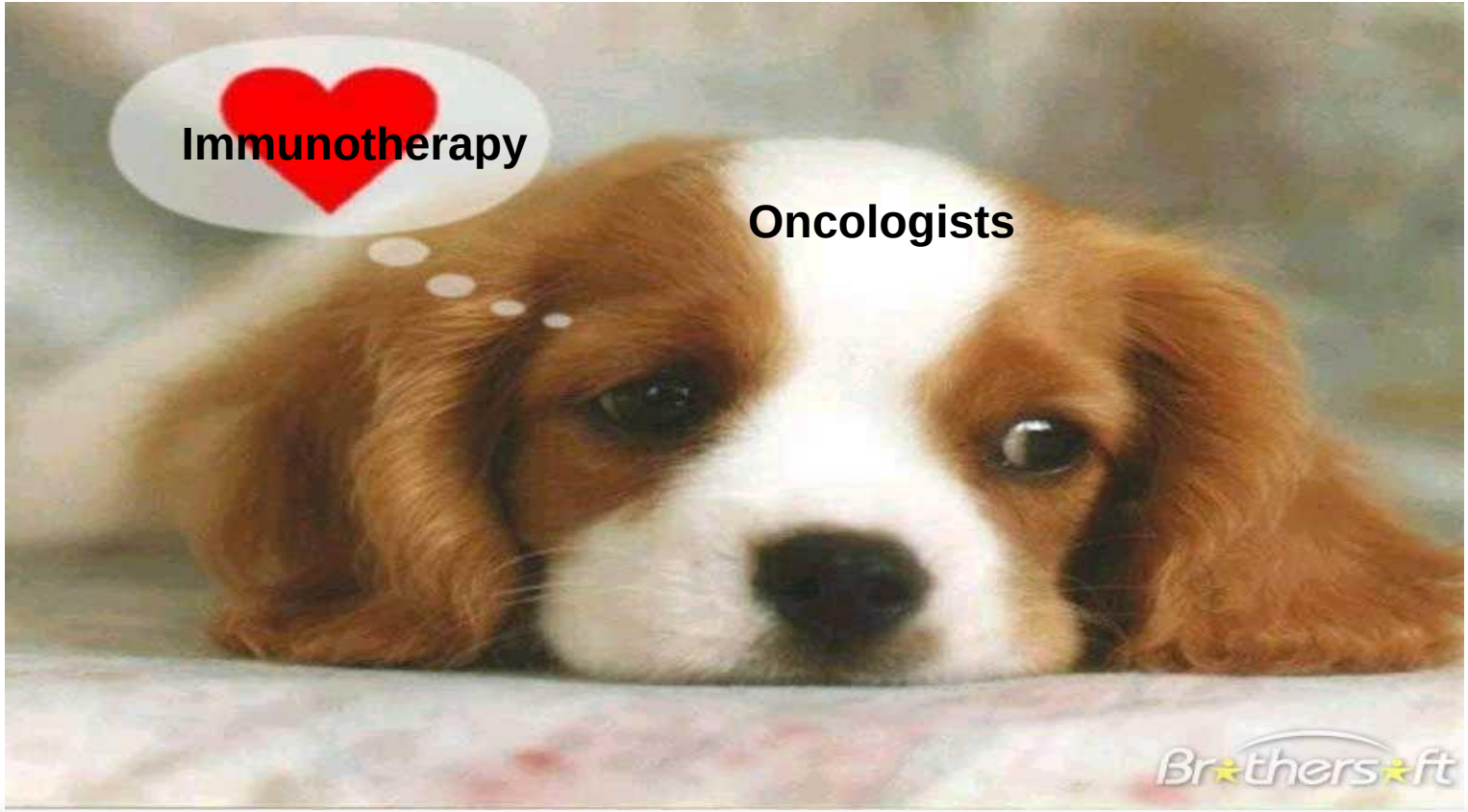
KEYTRUDA (pembrolizumab) for Injection 50 mg

NOW THERE'S OPDIVO (nivolumab) INJECTION FOR INTRAVENOUS USE 10 mg/mL

Mellman Nature 2011

The promise for immunotherapy in oncology




Immunotherapy
Oncologists

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nivolumab in Previously Untreated Melanoma without *BRAF* Mutation

Caroline Robert, M.D., Ph.D., Georgina V. Long, M.D., Ph.D., Benjamin Brady, M.D., Caroline Dutriaux, M.D., Michele Maio, M.D., Laurent Mortier, M.D., Jessica C. Hassel, M.D., Piotr Rutkowski, M.D., Ph.D., Catriona McNeil, M.D., Ph.D., Ewa Kalinka-Warzocha, M.D., Ph.D., Kerry J. Savage, M.D., Micaela M. Hernberg, M.D., Ph.D., Celeste Lebbé, M.D., Ph.D., Julie Charles, M.D., Ph.D., Catalin Mihalcioiu, M.D., Vanna Chiarion-Sileni, M.D., Cornelia Mauch, M.D., Ph.D., Francesco Cognetti, M.D., Ana Arance, M.D., Ph.D., Henrik Schmidt, M.D., D.M.Sc., Dirk Schadendorf, M.D., Helen Gogas, M.D., Lotta Lundgren-Eriksson, M.D., Christine Horak, Ph.D., Brian Sharkey, Ph.D., Ian M. Waxman, M.D., Victoria Atkinson, M.D., and Paolo A. Ascierto, M.D.

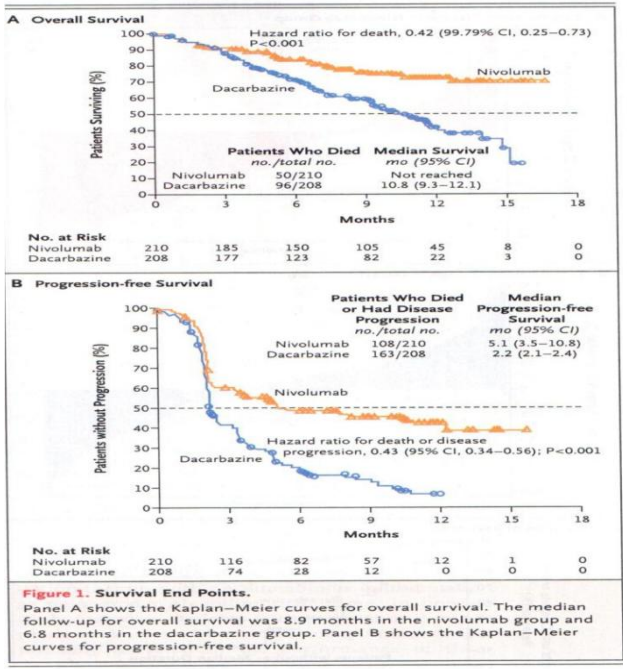


Figure 1. Survival End Points.
Panel A shows the Kaplan–Meier curves for overall survival. The median follow-up for overall survival was 8.9 months in the nivolumab group and 6.8 months in the dacarbazine group. Panel B shows the Kaplan–Meier curves for progression-free survival.

Table 2. Response to Treatment.*

Response	Nivolumab (N=210)	Dacarbazine (N=208)
Best overall response — no. (%)†		
Complete response	16 (7.6)	2 (1.0)
Partial response	68 (32.4)	27 (13.0)
Stable disease	35 (16.7)	46 (22.1)
Progressive disease	69 (32.9)	101 (48.6)
Could not be determined	22 (10.5)	32 (15.4)
Objective response‡		
No. of patients (% [95% CI])	84 (40.0 [33.3–47.0])	29 (13.9 [9.5–19.4])
Difference — percentage points (95% CI)	26.1 (18.0–34.1)	
Estimated odds ratio (95% CI)	4.06 (2.52–6.54)	
P value	<0.001	
Time to objective response — mo		
Median	2.1	2.1
Range	1.2–7.6	1.8–3.6
Mean	2.6±1.3	2.5±0.7
Duration of response — mo§		
Median (95% CI)	Not reached	6.0 (3.0–not reached)
Range	0.0–12.5	1.1–10.0

* Plus–minus values are means ±SD

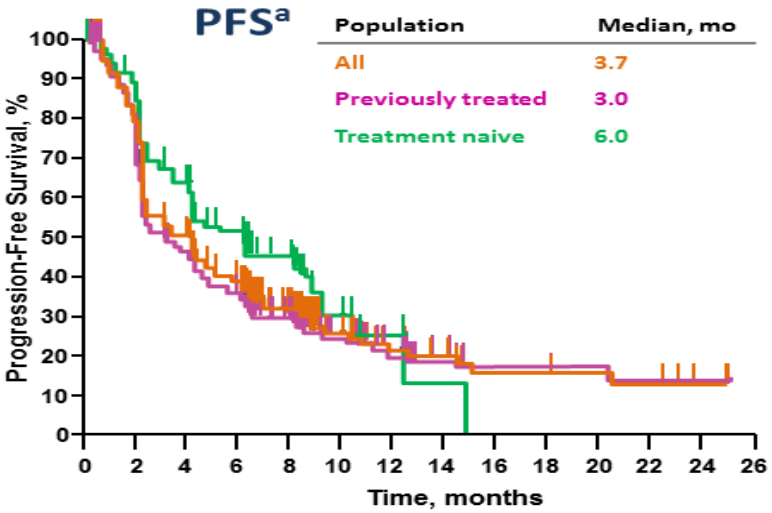
The NEW ENGLAND JOURNAL of MEDICINE

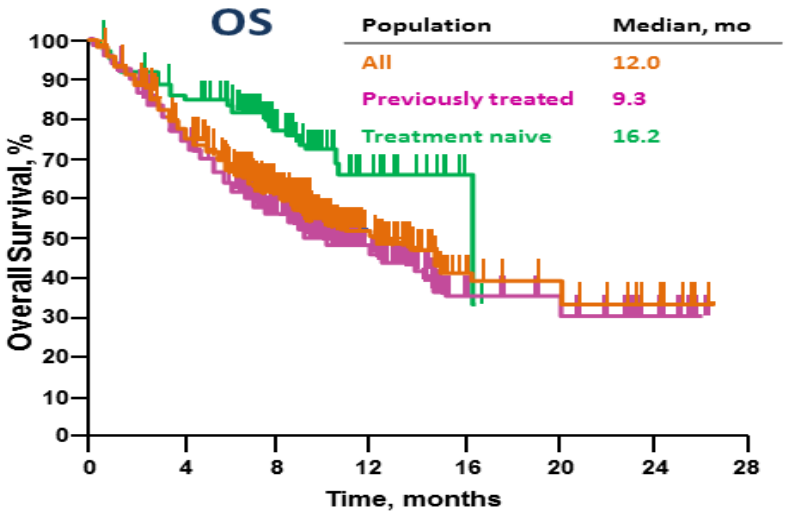
ORIGINAL ARTICLE

Pembrolizumab for the Treatment of Non–Small-Cell Lung Cancer

Edward B. Garon, M.D., Naiyer A. Rizvi, M.D., Rina Hui, M.B., B.S., Natasha Leighl, M.D., Ani S. Balmanoukian, M.D., Joseph Paul Eder, M.D., Amita Patnaik, M.D., Charu Aggarwal, M.D., Matthew Gubens, M.D., Leora Horn, M.D., Enric Carcereny, M.D., Myung-Ju Ahn, M.D., Enriqueta Felip, M.D., Jong-Seok Lee, M.D., Matthew D. Hellmann, M.D., Omid Hamid, M.D., Jonathan W. Goldman, M.D., Jean-Charles Soria, M.D., Marisa Dolled-Filhart, Ph.D., Ruth Z. Rutledge, M.B.A., Jin Zhang, Ph.D., Jared K. Lunceford, Ph.D., Reshma Rangwala, M.D., Gregory M. Lubiniecki, M.D., Charlotte Roach, B.S., Kenneth Emancipator, M.D., and Leena Gandhi, M.D., for the KEYNOTE-001 Investigators*

Longitudinal Outcomes In All Treated Patients





n at risk

495	361	230	167	97	47	26	12	7	6	6	5	2	0
394	275	173	125	75	40	23	11	7	6	6	5	2	0
101	86	57	42	22	7	3	1	0	0	0	0	0	0

495	368	209	67	18	14	7	0
394	284	165	52	16	14	7	0
101	84	44	15	2	0	0	0

[a]Assessed per RECIST v1.1 by central review.
Analysis cut-off date: August 29, 2014.

Garon_AACR 2015_19Apr15

Anti-PD1 costs: a thought experiment

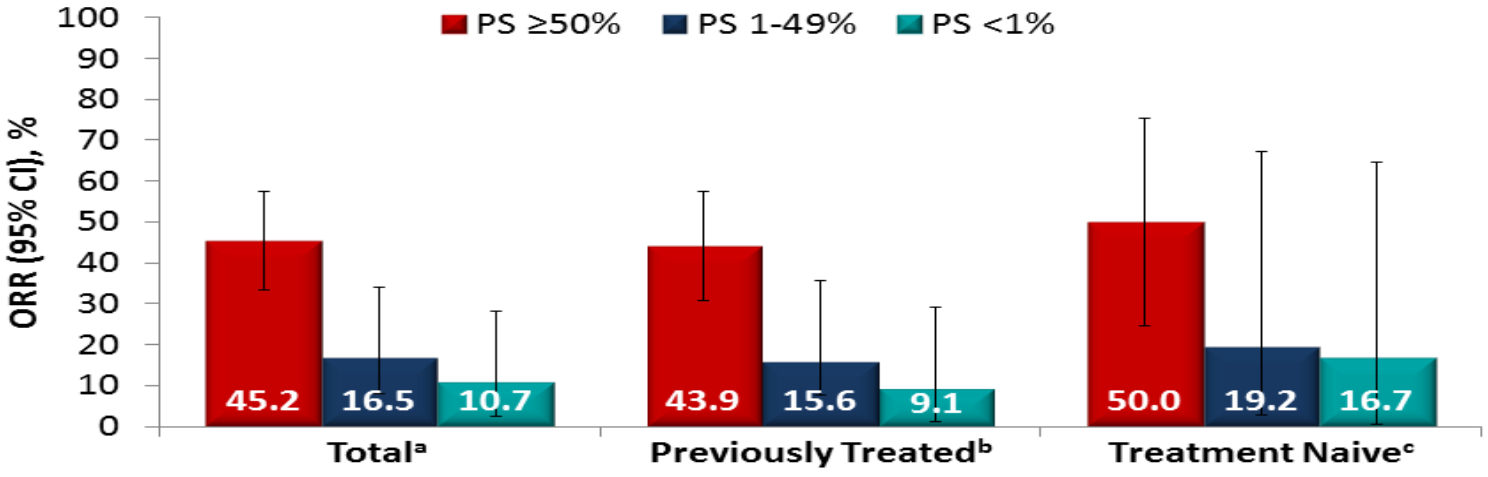
- Number of cases of lung cancer per year in the US is 220,000, and 85% are diagnosed with or develop metastatic disease.
- If anti-PD1 gets 1st line indication, the majority will be candidates for this therapy because it is non-toxic.
- Cost (ASP=150K per year of therapy) = 28 billion dollars
- Presuming 1/3 of patients are cured (this is extremely generous), 18 billion dollars are spent on futile therapy in the absence of a predictive biomarker. If only 15% are cured, then we spend 24 billion dollars on futile therapy

Depth: PD-1/PD-L1 NSCLC registration trials

25+ trials!

Line of Therapy	Opdivo nivolumab	Keytruda pembrolizumab	Atezolizumab	Durvalumab	Avelumab
Locally Advanced	Opdivo	PD-L1+	PD-L1+	Durvalumab	
				Durvalumab	
1st Line	PD-L1+	PD-L1+	NS PD-L1+	Durvalumab	
	PD-L1+	PD-L1+	NS PD-L1+	Durvalumab	
			NS PD-L1+	Durvalumab	
			Sq PD-L1+	Durvalumab EGFR+	
			Sq PD-L1+		
2nd Line	Sq	PD-L1+	PD-L1+	Durvalumab EGFR+ / T790+	PD-L1+
	NS		PD-L1+		
3rd Line	Sq			Durvalumab	

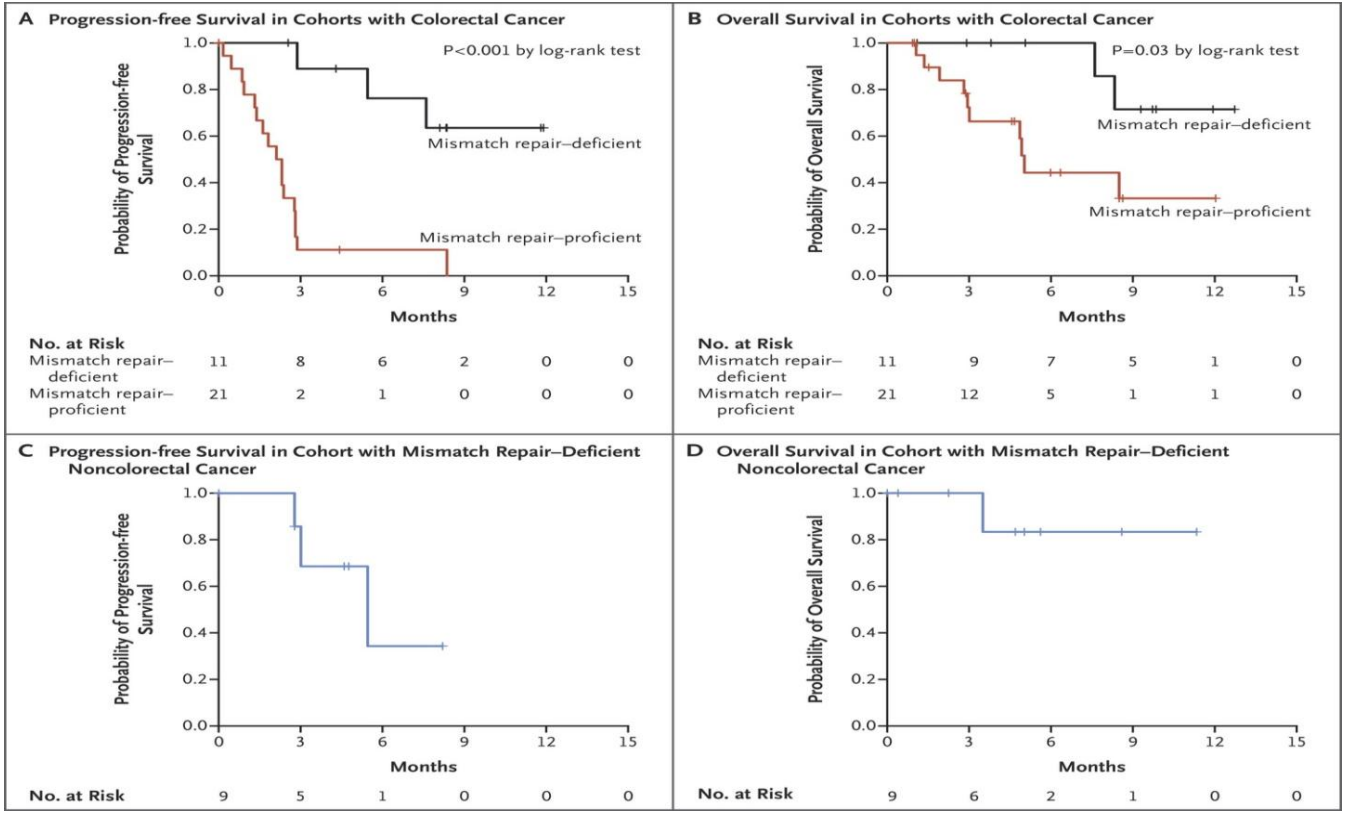
ORR by PD-L1 Proportion Score: CTA-Evaluable Validation Set Patients With Measurable Disease



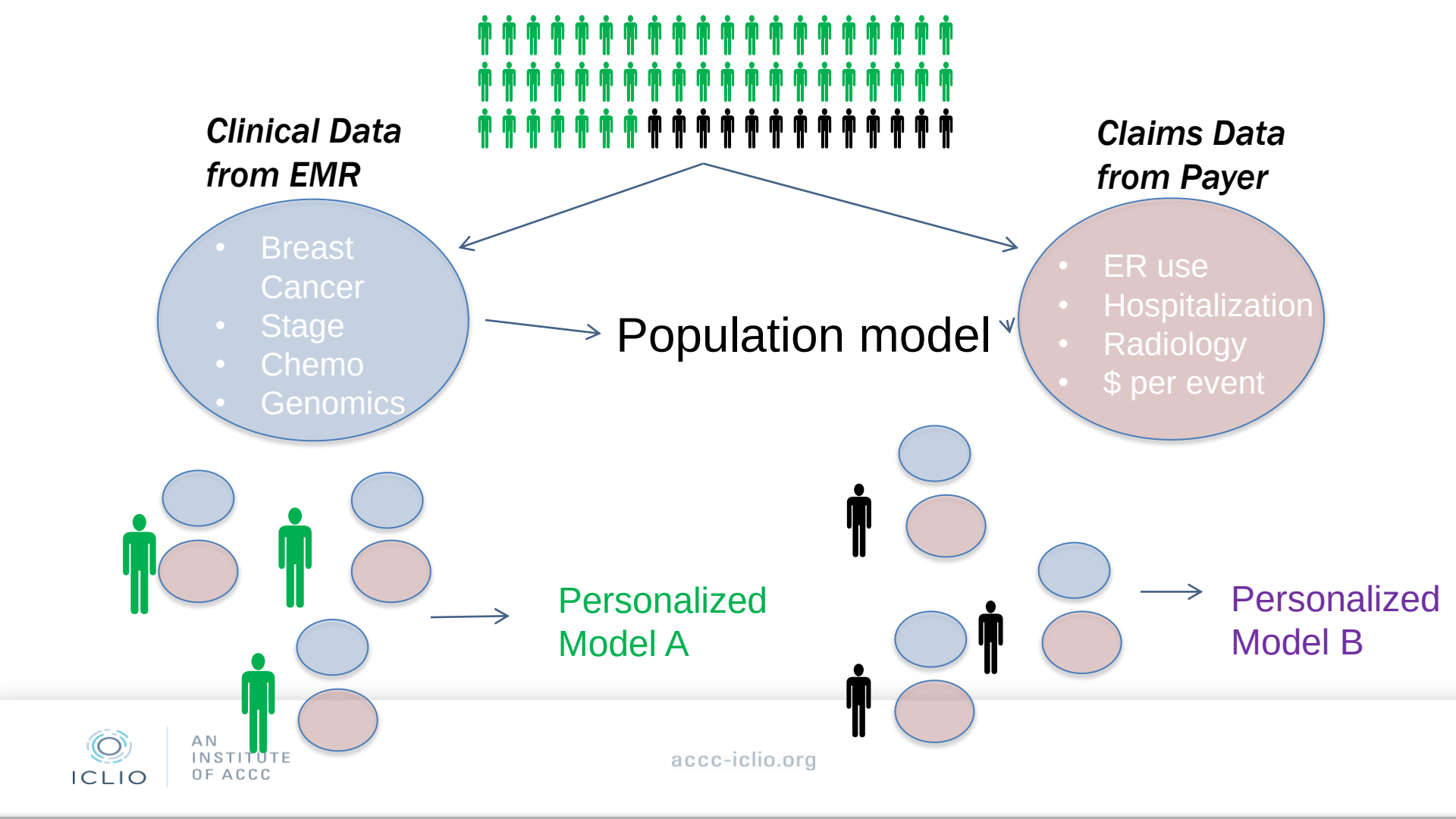
When measurable disease is NOT required, the ORR (95% CI) in the PS ≥50% subgroups are: **42.3%, 41.0%, and 47.1%** in the total, previously treated, and treatment-naive populations[d]

[a]n = 73, 103, and 28, respectively. [b]n = 57, 77, and 22, respectively. [c]n = 16, 26, and 6, respectively. [d]n = 78, 61, and 17, respectively.
ORR was assessed per RECIST v1.1 by central review in the biomarker-evaluable population (ie, patients with measurable disease per RECIST v1.1 by central review at baseline whose slides were cut within 6 months of staining and for which a proportion score could be assigned).
Analysis cut-off date: August 29, 2014.

Garon_AACR 2015_19Apr15



Le DT et al. N Engl J Med 2015;372:2509-2520.


Clinical Data from EMR
Breast Cancer
Stage
Chemo
Genomics
Claims Data from Payer
ER use
Hospitalization
Radiology
$ per event
Population model
Personalized Model A
Personalized Model B

Breadth: PD-1/PD-L1's registration trials

	Thoracic				GI						GU			Women's			Sarcoma		Skin		Other		Hem										
	NSCLC	SCCHN	SCLC	Meso	CRC	Pancreatic	Gastric	Esophageal	HCC	Biliary	Renal	Bladder	Prostate	Breast	Ovarian	Cervical	STS	GIST	Melanoma	Merkel Cell	Thyroid	GBM	CML	CLL	AML	NHL	DLBCL	FL	HD	Myeloma	MDS
Nivolumab			*						*																						
Pembrolizumab					*																										
Atezolizumab																															
Duvalumab																															
Avelumab																															

Approved	
Pre-Registration	
Ph lll	
planned	*

Verified July 20. 1015

13 cancers

The goal: value driven care

$$V = \frac{Q}{C}$$

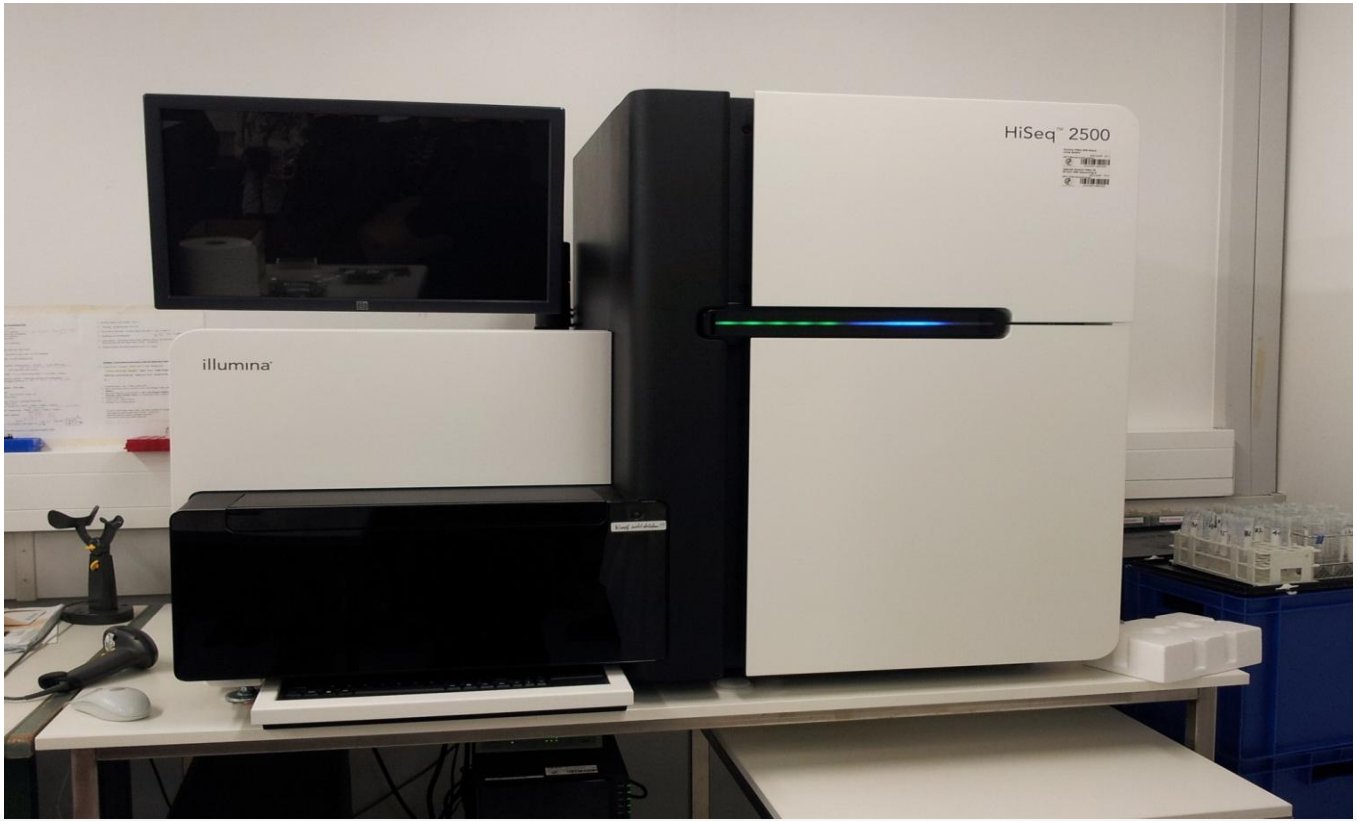
- Guideline-based therapies
- Targeted impact
- Low toxicities
- Improved survival
- Improved QOL

- Best supportive care
- Avoidance hospital days
- Avoidance ED visits
- Lower site-of-service costs
- Reduce medically unnecessary care at EOL

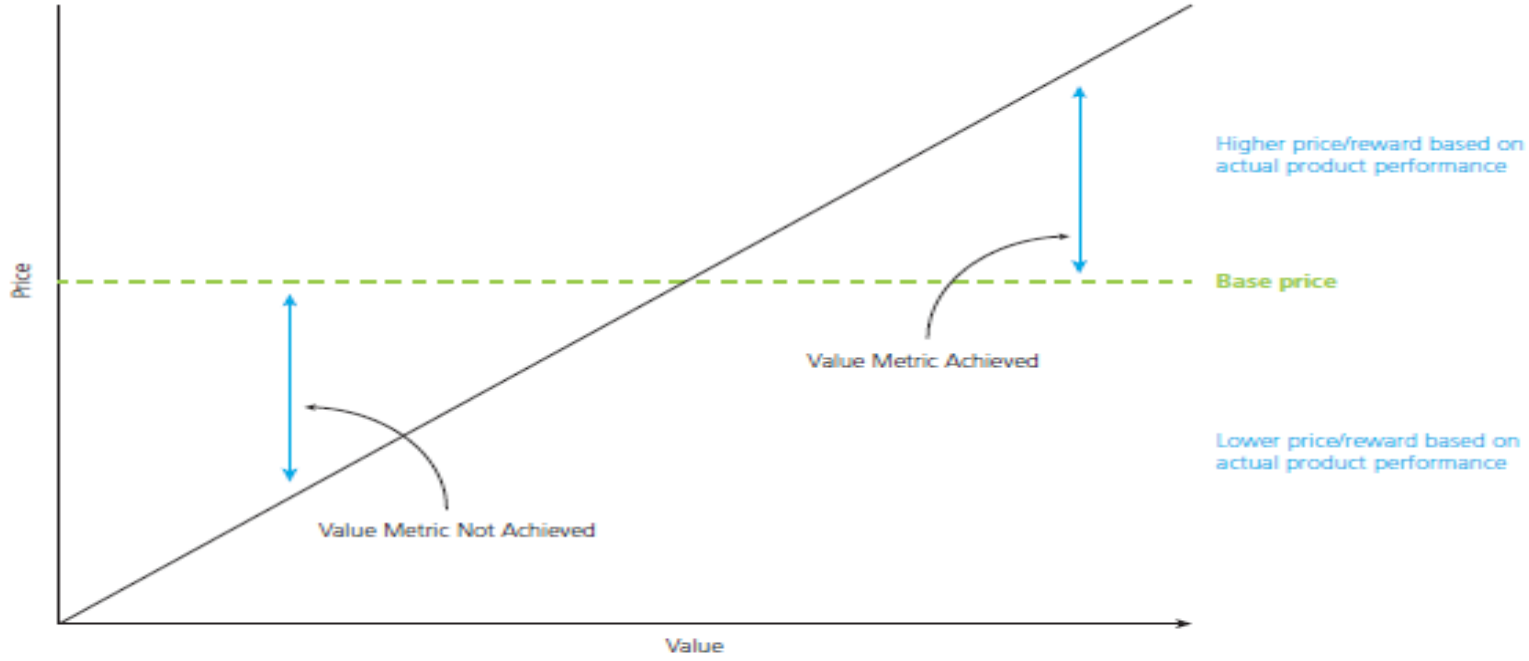
To realize value we must

Increase the size of the tail

Figure out who is in the tail

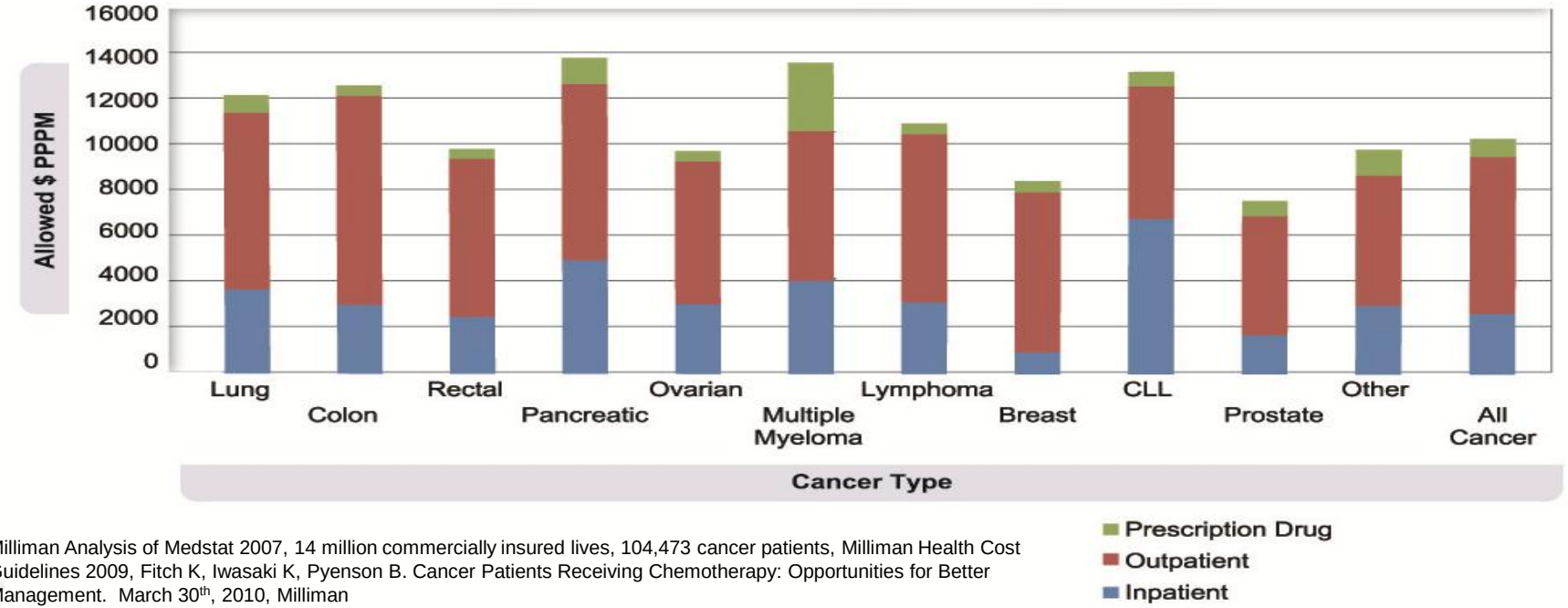

HiSeq™ 2500
illumina

Value-Based Pricing Agreements

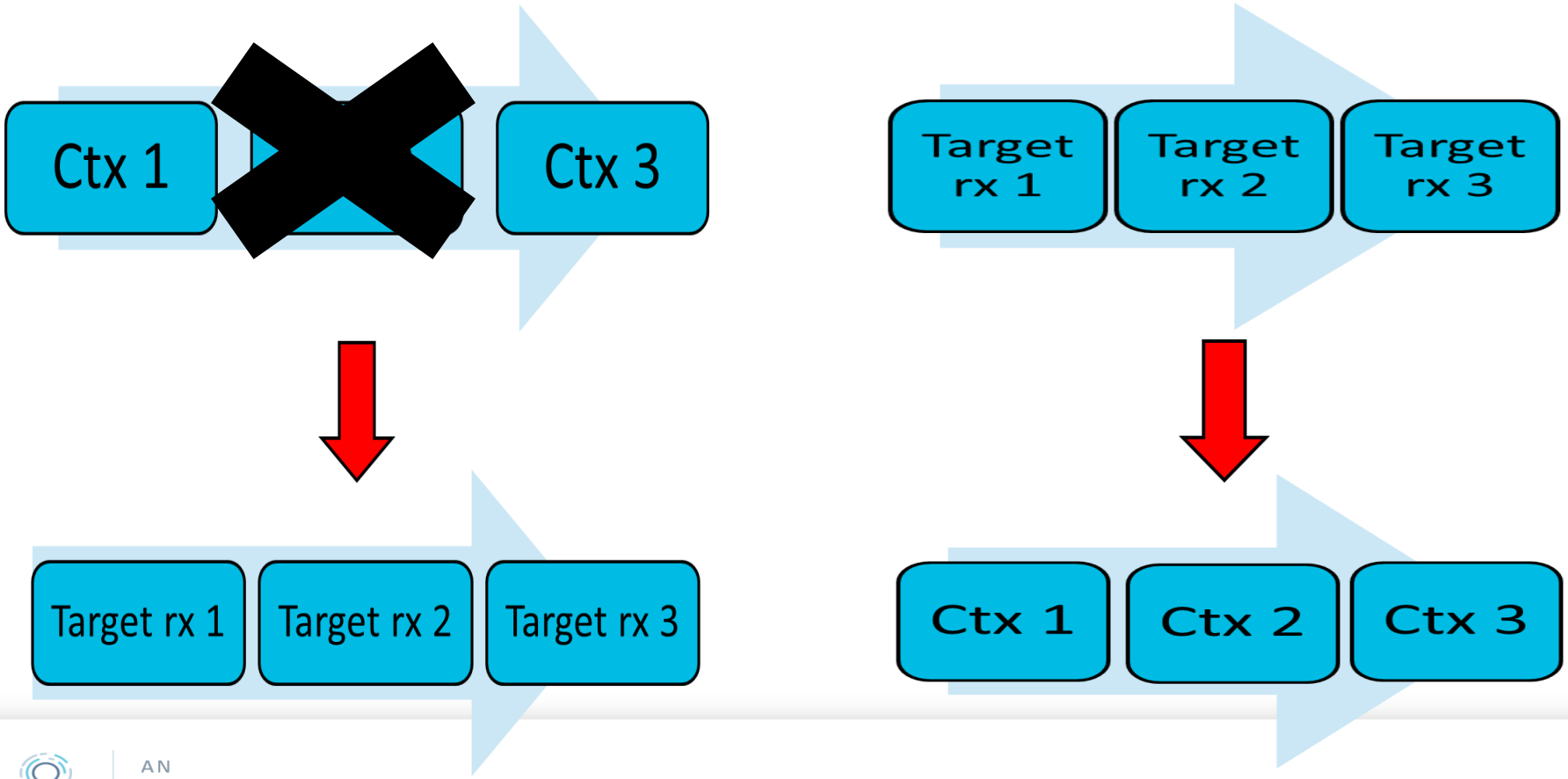


Source: U.S. Bureau of Labor Statistics, Division of Industry Employment Projections. Occupational Outlook Handbook, 2010-11 Edition.

We cannot save enough on other services to offset the drug cost



Milliman Analysis of Medstat 2007, 14 million commercially insured lives, 104,473 cancer patients, Milliman Health Cost Guidelines 2009, Fitch K, Iwasaki K, Pyenson B. Cancer Patients Receiving Chemotherapy: Opportunities for Better Management. March 30th, 2010, Milliman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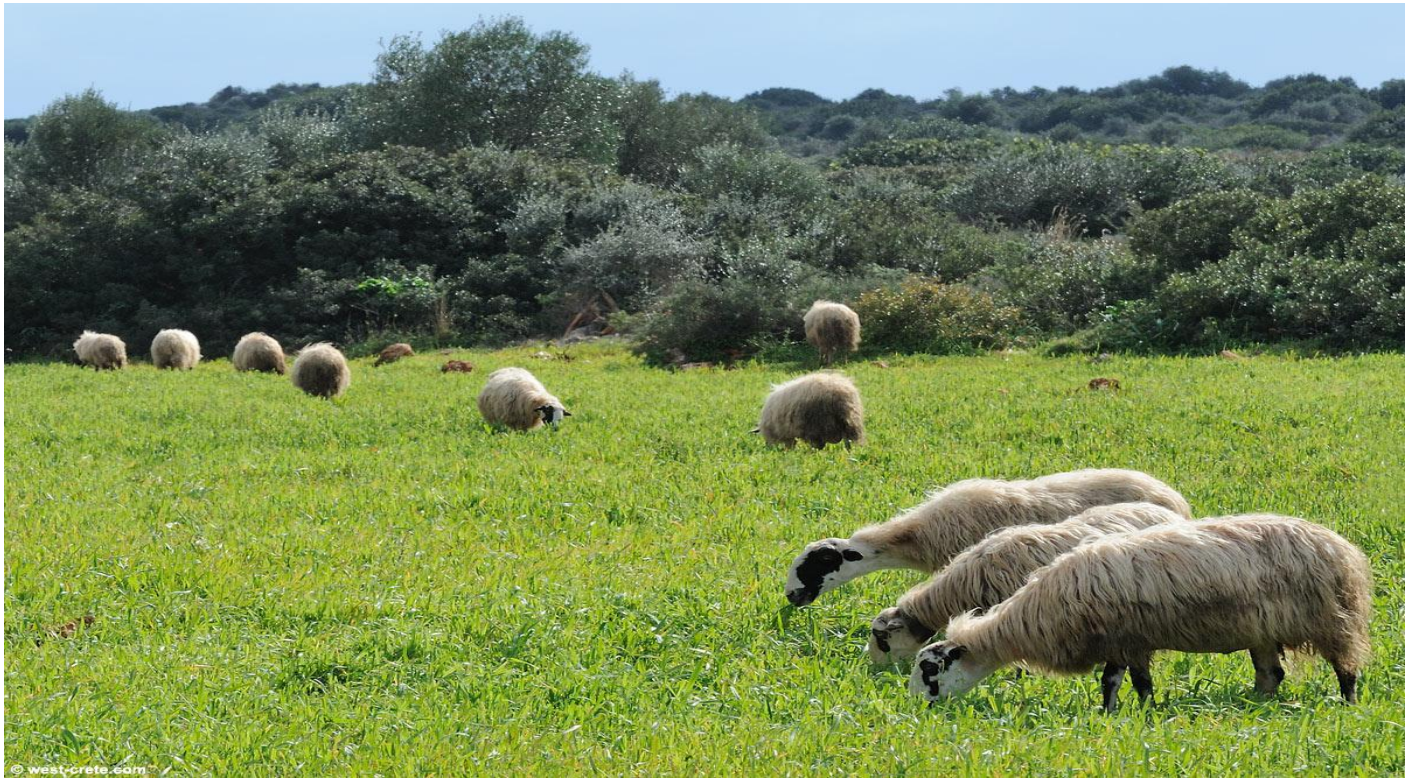
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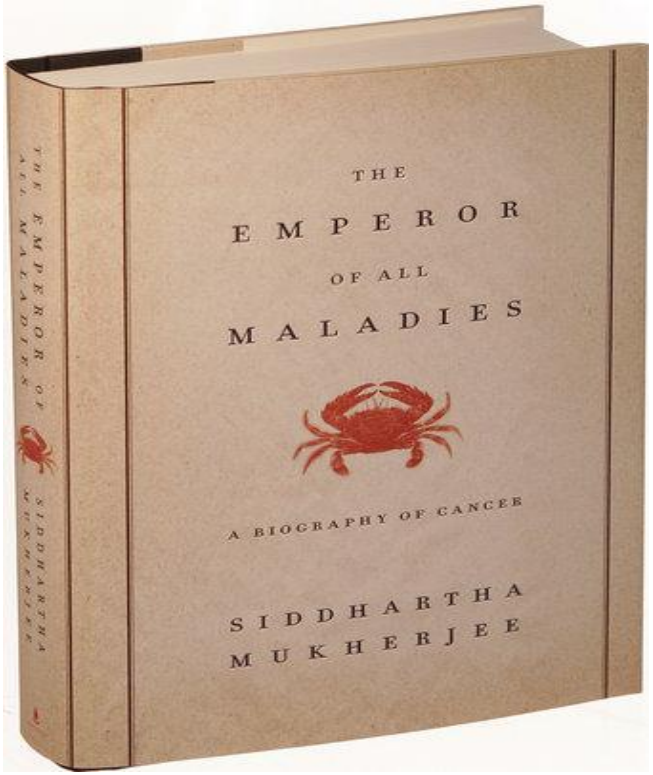
THE EMPEROR OF ALL MALADIES
SIDDHARTHA MUKHERJEE
THE
EMPEROR
OF ALL
MALADIES
A BIOGRAPHY OF CANCER
SIDDHARTHA
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Panel Discussion

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