ACT TOGETHER AGAINST
LUNG CANCER

CENTRAL AND EASTERN EUROPE FORUM
OF CANCER PATIENT ORGANIZATIONS

Immuno-Oncology

The Power of the immune system in treating Cancer

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President, Central European Cooperative Oncology Group (CECOG)

Chairman, Clinical Division of Oncology and Department of Medicine I

Chairman, Comprehensive Cancer Center Medical University Vienna

COMPREHENSIVE
CANCER
CENTER VIENNA

ONCHQ15NP06215, 09-15

Oncology is a branch of medicine that deals with tumors. The name's etymological origin is the Greek word ὄγκος (*ónkos*), meaning "tumor", "volume" or "mass".

Cancer has existed for all of human history.

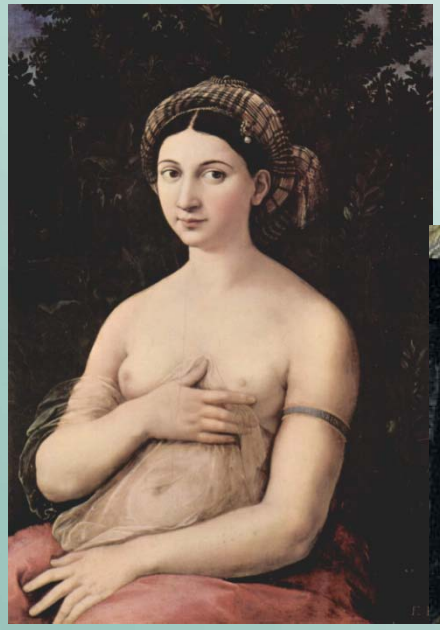
The earliest written record regarding cancer is from circa 1600 BC in the Egyptian Edwin Smith Papyrus and describes cancer of the breast.

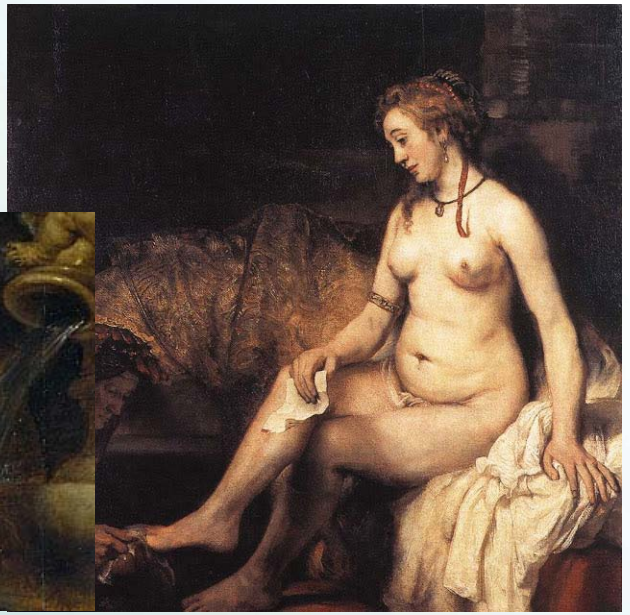
Hippocrates (ca. 460 BC – ca. 370 BC) described several kinds of cancer, referring to them with the Greek word καρκίνος karkinos (crab or crayfish). This name comes from the appearance of the cut surface of a solid malignant tumor, with "the veins stretched on all sides as the animal the crab has its feet, whence it derives its name.

www.wikipedia.com

Breast Cancer Survival in the Arts

R. Gross, Breast Cancer Res Treat 84: 293, 2004





Rafael: La Fornarina Margherita Luti

Rubens: The Three Graces Helene Fourment

Rembrandt: Bathsheba Hendrickje Stoeffels

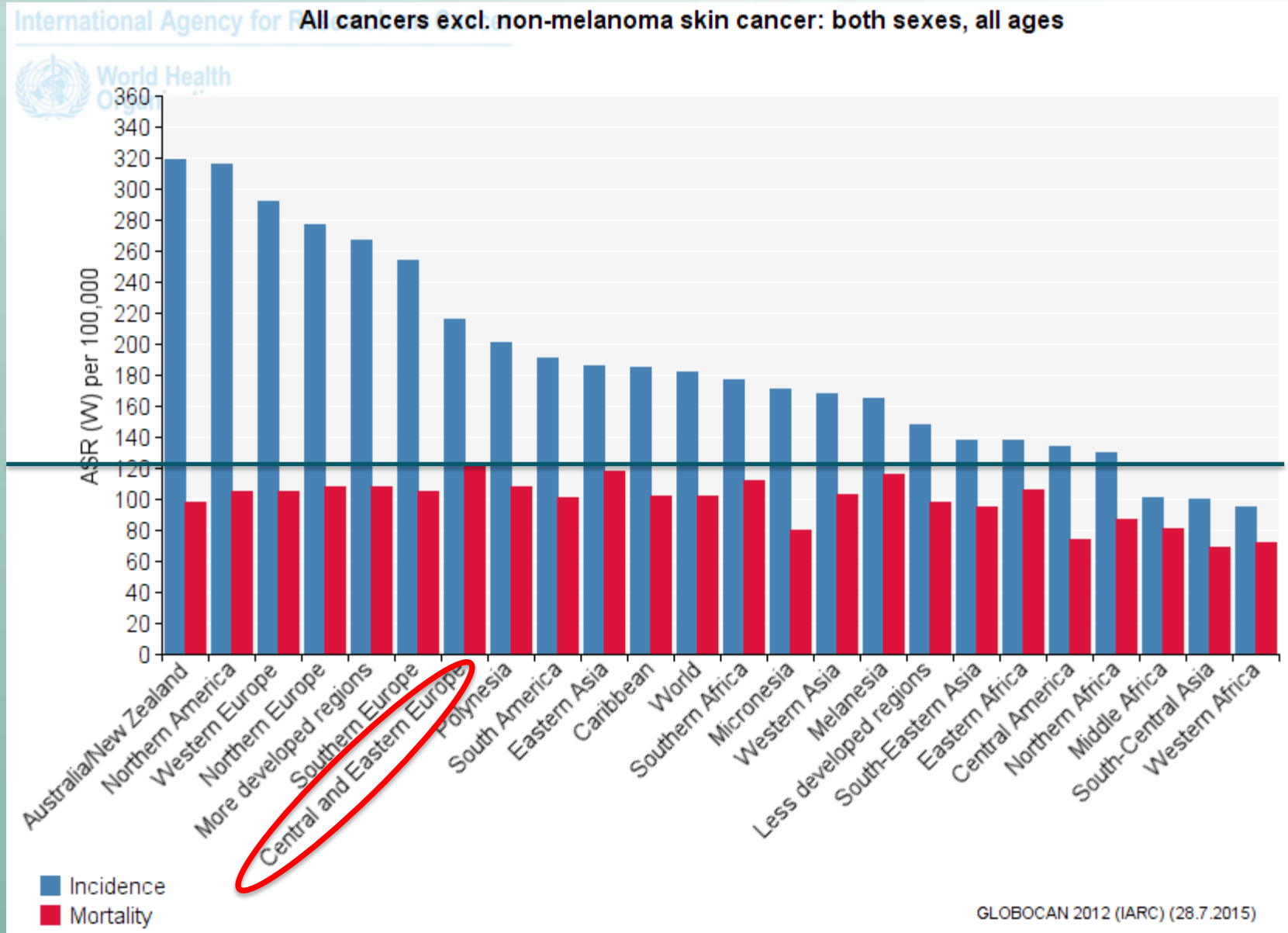
Survival after the Painting:

at least >2yrs.

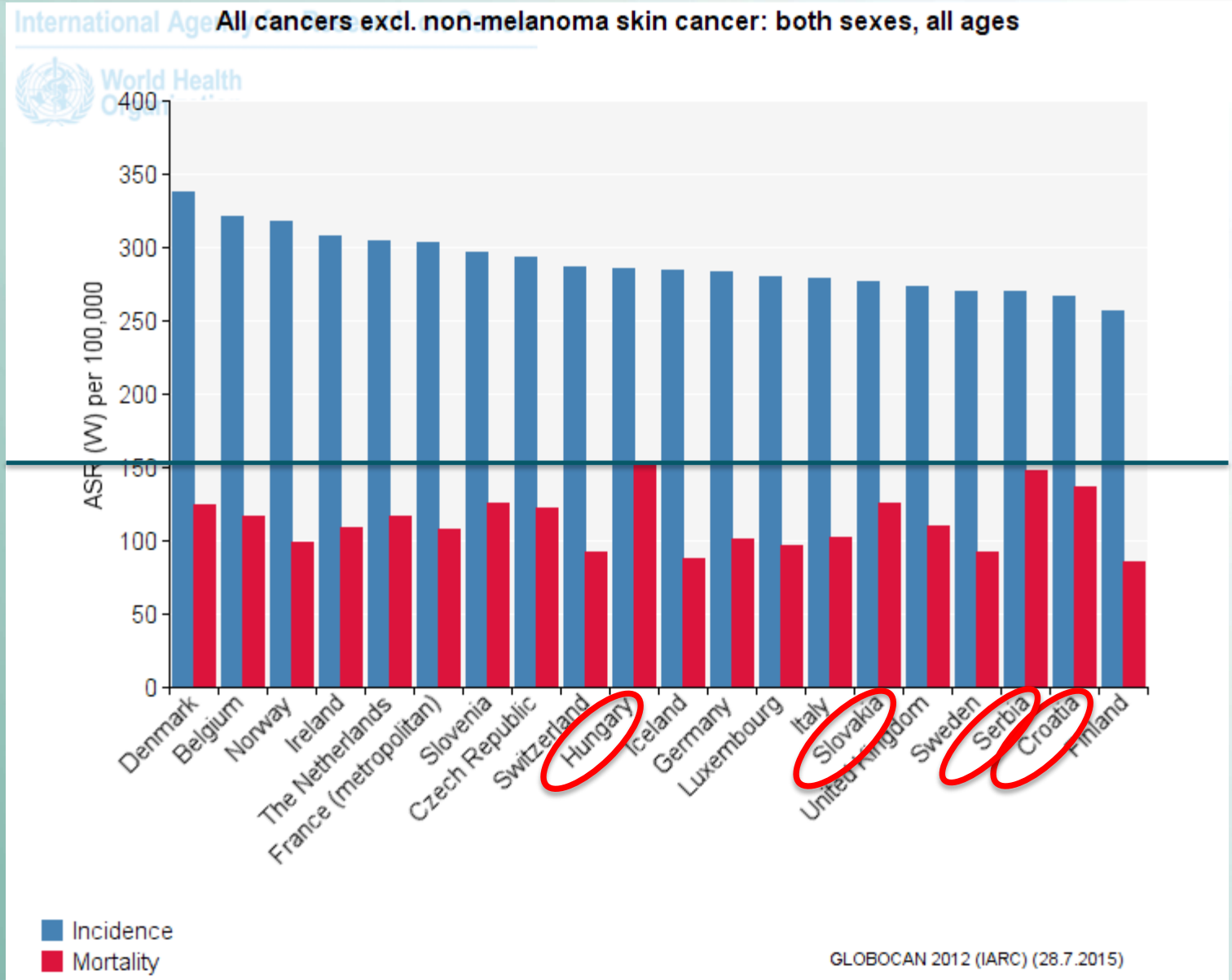
>30 yrs.

9 yrs.

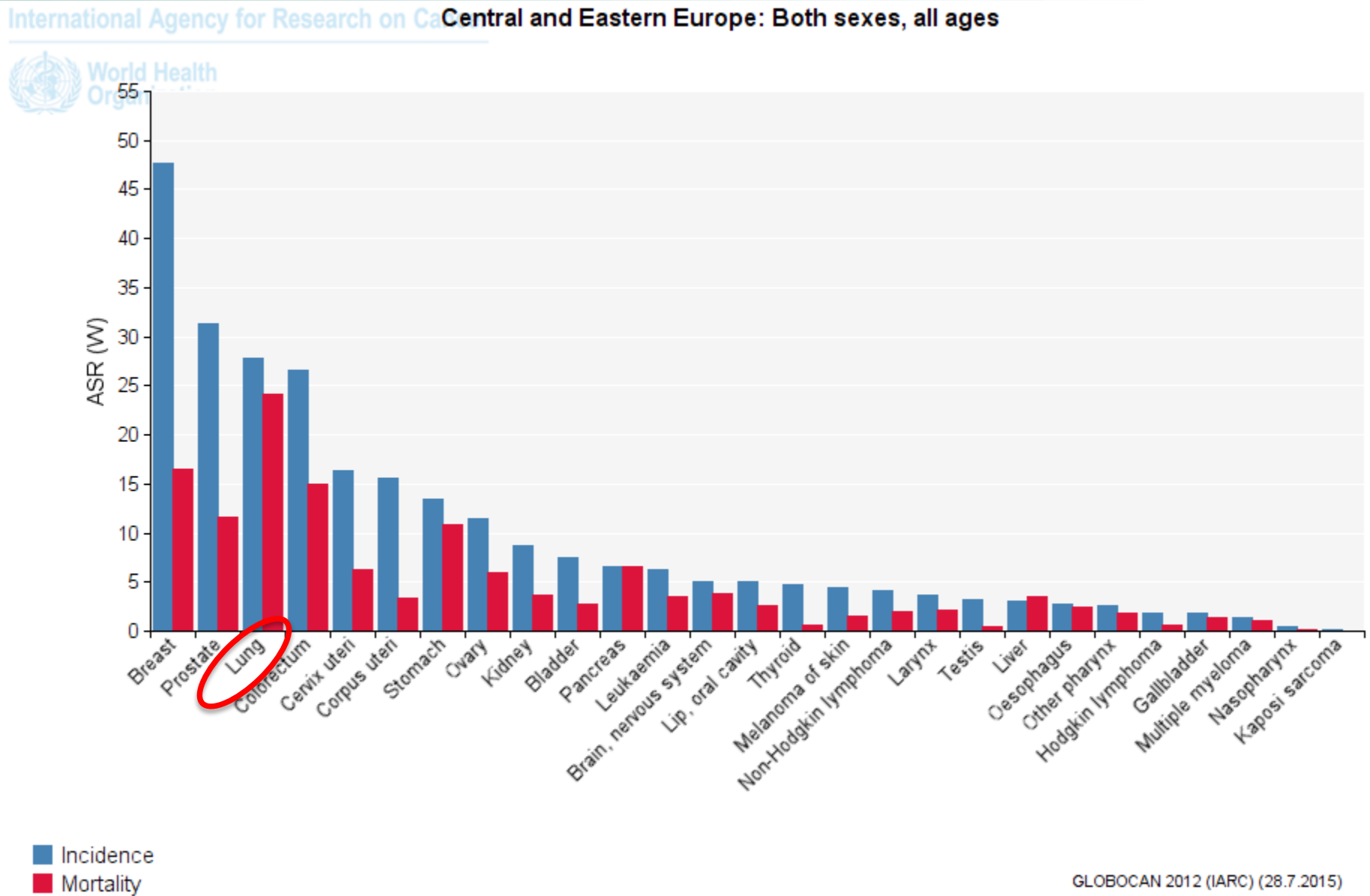
All cancers incidence & mortality by region
Higher relative mortality in CEE! Why?



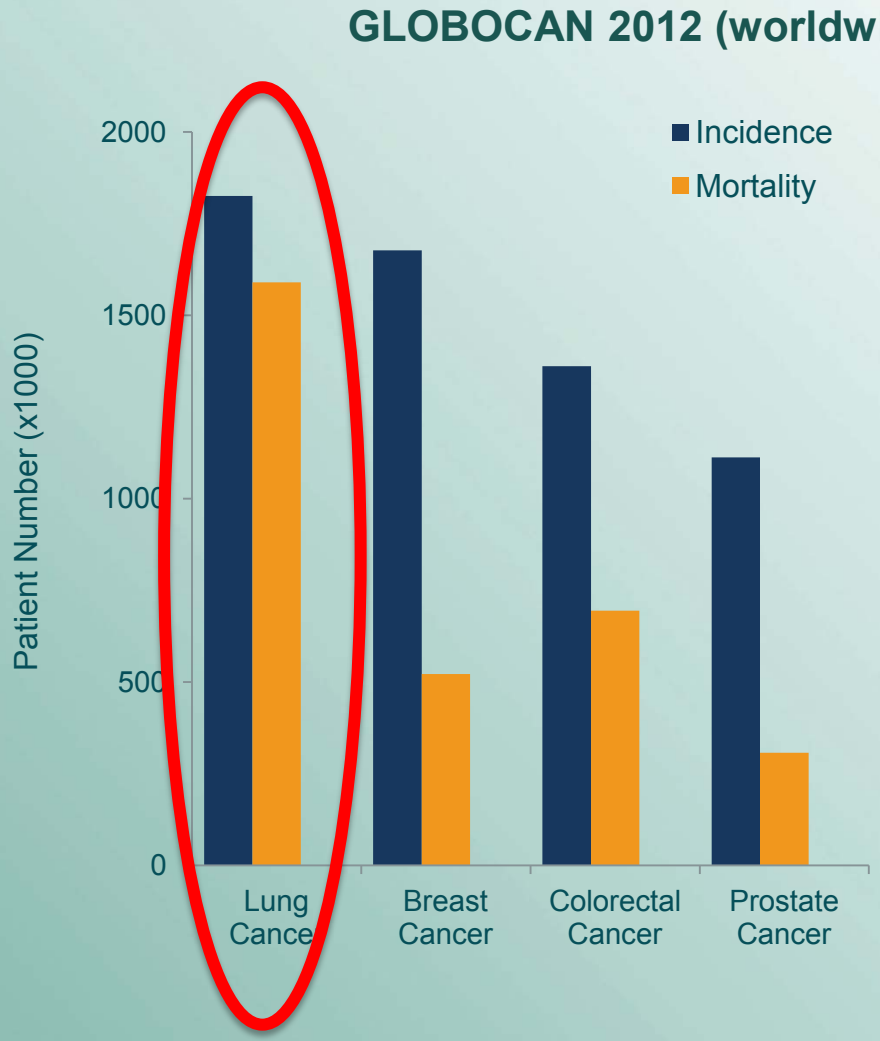
All cancers incidence & mortality in EU
Significant differences in mortality. Why?



CEE incidence & mortality by cancer
Mortality is driven mostly by lung cancer!



Lung cancer: the most common and the leading cause of cancer-related mortality worldwide



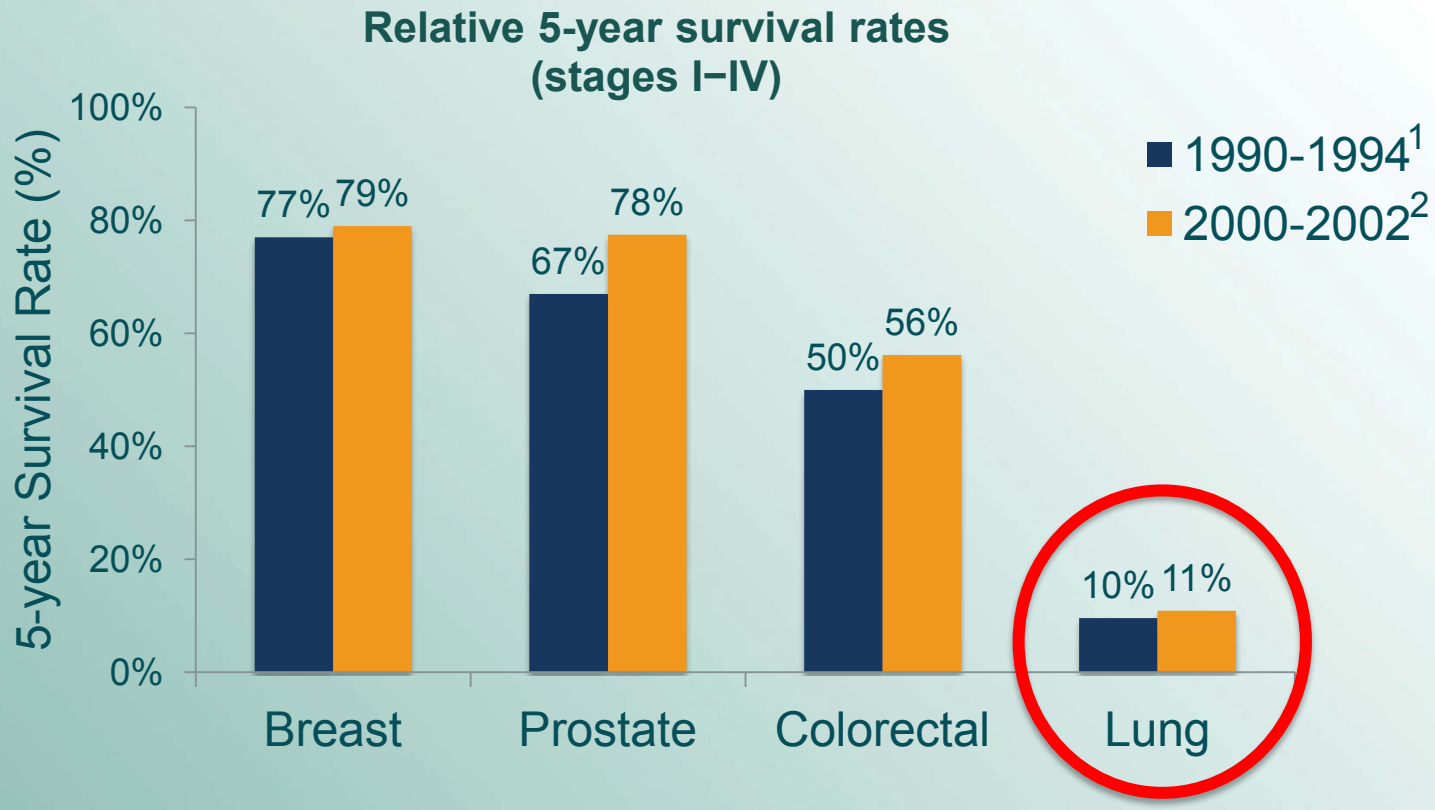
More people die from lung cancer than breast, colorectal and prostate cancers combined

1.82 million
estimated new cases worldwide

1.59 million
estimated deaths worldwide (20% of all cancer deaths)

WHO GLOBOCAN 2012. Population fact sheets; World. Available at: http://globocan.iarc.fr/Pages/fact_sheets_population.aspx. Accessed June 2014.

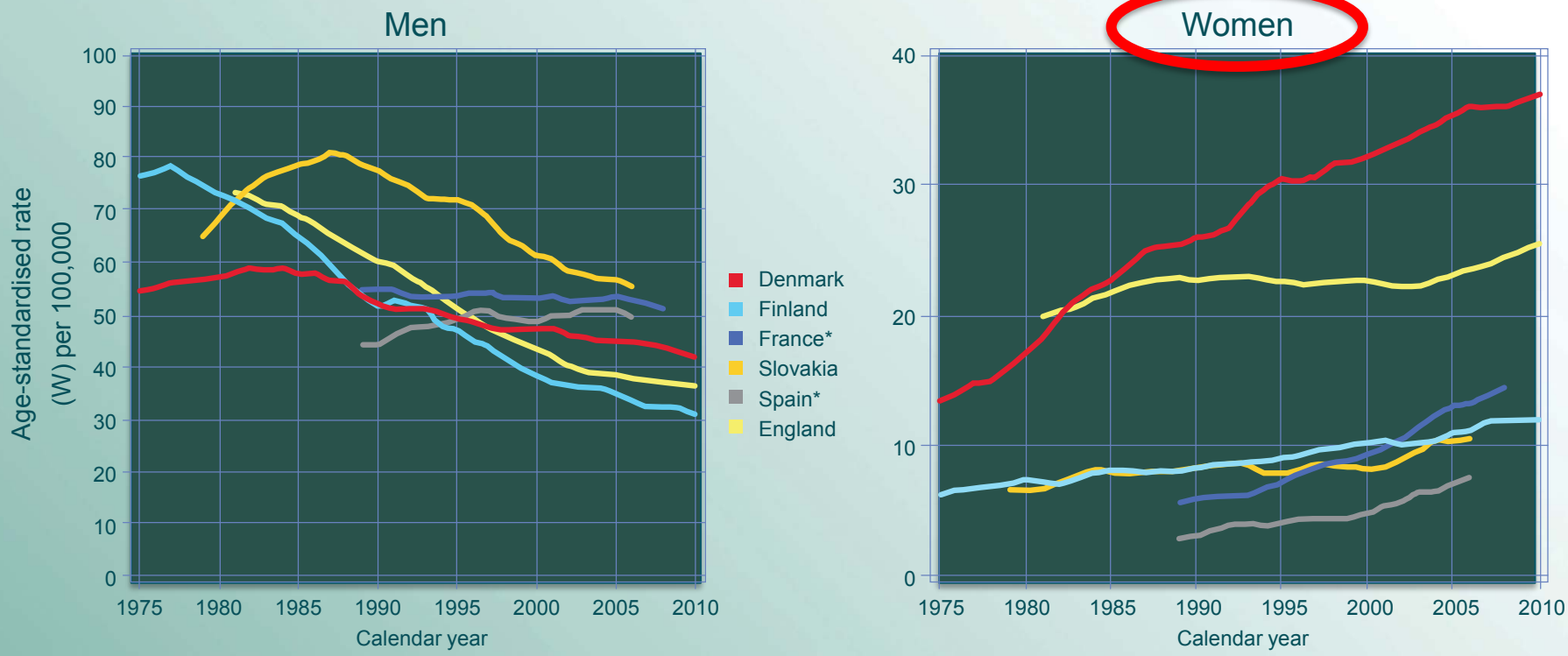
5-year survival improvements in lung cancer lag behind the next 3 most common cancers



1. Sant M, et al. *Ann Oncol.* 2003;14(suppl. 5):v61−v118; 2. Verdecchia A, et al. *Lancet Oncol.* 2007;8:784−796.

Historical exposure to tobacco smoke reflects the incidence of lung cancer in Europe

GLOBOCAN 2012 (selected European countries):
lung cancer incidence, age-standardised rate per 100,000

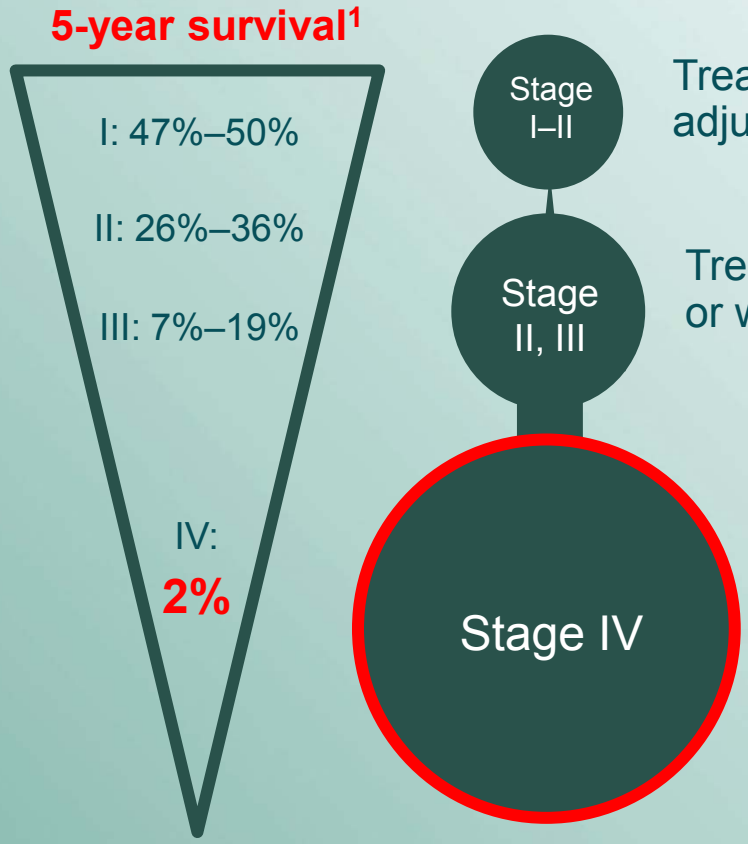


- Incidence rates are decreasing in men due to reduced smoking
- Incidence rates are increasing in women as started smoking later

*Regional data.

WHO GLOBOCAN 2012. Cancer fact sheets; Lung cancer. Available at: http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx. Accessed June 2014; Ferlay J, et al. *Eur J Cancer.* 2013;49:1374–1403.

5-year survival is only 2% for patients with stage IV NSCLC



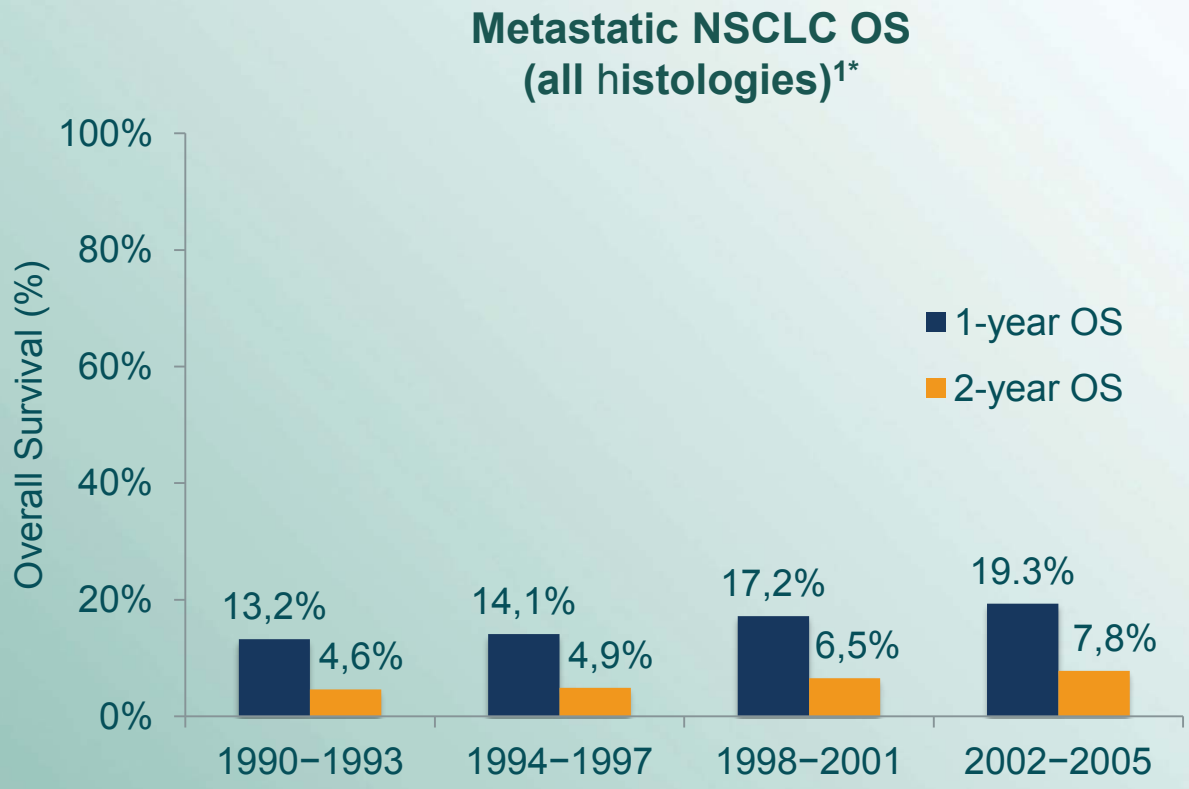
Treatment: surgery or radiotherapy, with or without adjuvant chemotherapy[2]

Treatment: chemoradiation or chemotherapy (with or without surgery or radiotherapy)[2,3]

Treatment: platinum-based doublet chemotherapy, anti-angiogenic therapy, targeted treatment, multiple lines of therapy due to treatment failure, best supportive care, palliative therapy[2,4]

1. Detterbeck FC, et al. *Chest*. 2009;136:260–271; 2. NCCN Guidelines. Non-small cell lung cancer. v3.2014;
3. Vansteenkiste J, et al. *Ann Oncol*. 2013;24:vi89–vi98.

Despite modest survival gains, 80% of patients with metastatic NSCLC still die within 1 year of diagnosis



- During 2002−2005, ~4/5 patients (~80%) were dead at 1 year (survival rate: 19.4%)
- During 2002−2005, >9/10 patients were dead at 2 years (survival rate: 7.8%)

1. Morgensztern D, et al. *J Thorac Oncol*. 2009;4:1524−1529.

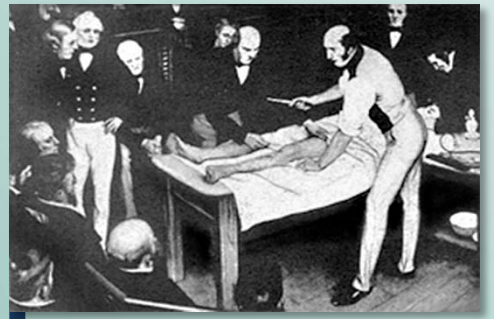
New Therapies are Needed to Improve the Survival of Patients with Advanced Disease

- 5-year survival rates are poor for many patients with advanced cancer*

Tumor Type	5-Year Survival Rate	
	Overall	Advanced Disease
Prostate	99.2%	27.9%
Melanoma	91.3%	16.0%
Breast	89.2%	24.3%
Kidney/renal pelvis	71.8%	12.3%
Colorectal	64.9%	12.5%
Ovarian	44.2%	27.3%
Stomach	27.7%	3.9%
Lung	16.6%	3.9%
Pancreatic	6.0%	2.0%

*Based on patients diagnosed in the United States between 2003 and 2009.
Surveillance, Epidemiology and End Results (SEER) Program. http://seer.cancer.gov.

Evolution of Cancer Therapy: Core Treatment Modalities

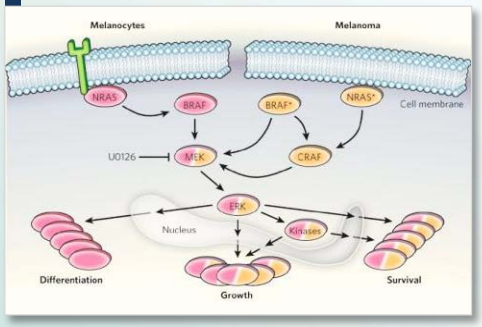


Surgery
1846

Chemotherapy
1946

Radiation Therapy
1901

Targeted Therapy
1997



DeVita VT Jr, et al. *Cancer Res*. 2008;68:8643–8653; American Cancer Society. http://www.cancer.org/cancer/cancerbasics/thehistoryofcancer/; Ross JS, et al. *Am J Clin Pathol*. 2004;122:598–609.

Singular Discoveries and Major Events in the Cancer Field and Changing Relative Survival Rates for Patients with Cancer in the United States, 1863–2006.

Table 1. Singular Discoveries and Major Events in the Cancer Field and Changing Relative Survival Rates for Patients with Cancer in the United States, 1863–2006.*

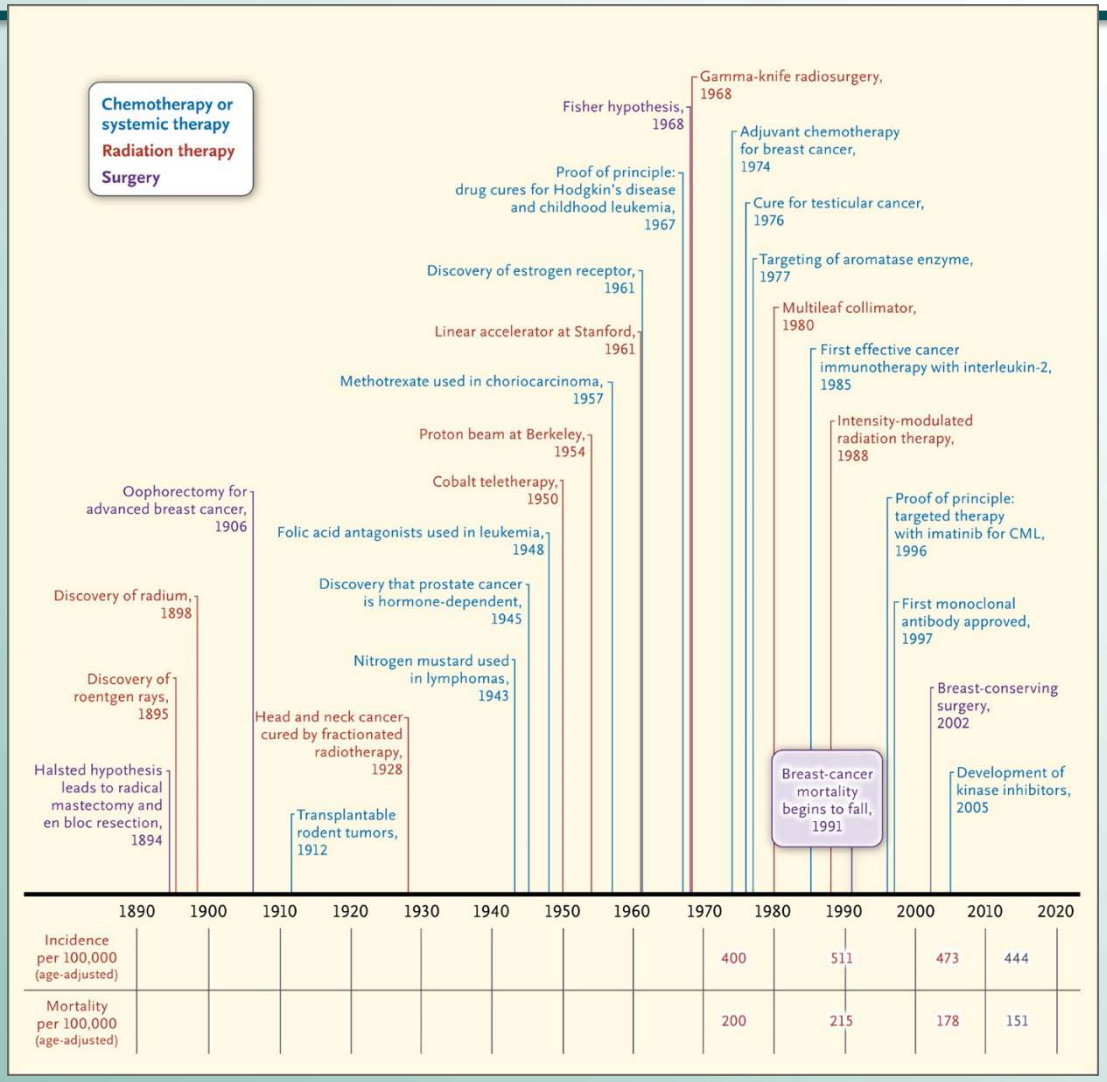
Year	Discovery or Event	Relative Survival Rate
1863	Cellular origin of cancer (Virchow)	
1889	Seed-and-soil hypothesis (Paget)	
1914	Chromosomal mutations in cancer (Boveri)	
1937	Founding of NCI	
1944	Transmission of cellular information by DNA (Avery)	
1950	Availability of cancer drugs through Cancer Chemotherapy National Service Center	
1953	Report on structure of DNA	35%
1961	Breaking of the genetic code	
1970	Reverse transcriptase	
1971	Restriction enzymes Passage of National Cancer Act	
1975	Hybridomas and monoclonal antibodies Tracking of cancer statistics by SEER program	50%
1976	Cellular origin of retroviral oncogenes	
1979	Epidermal growth factor and receptor	
1981	Suppression of tumor growth by p53	
1984	G proteins and cell signaling	
1986	Retinoblastoma gene	
1990	First decrease in cancer incidence and mortality	
1991	Association between mutation in APC gene and colorectal cancer	
1994	Genetic cancer syndromes Association between *BRCA1* and breast cancer	
2000	Sequencing of the human genome	
2002	Epigenetics in cancer MicroRNAs in cancer	
2005	First decrease in total number of deaths from cancer	68%
2006	Tumor stromal interaction	

* Data are from the National Cancer Institute (NCI) Survival, Epidemiology, and End Results (SEER) program. APC denotes adenomatous polyposis coli.

DeVita VT Jr, Rosenberg SA. N Engl J Med 2012;366:2207-2214.

The NEW ENGLAND JOURNAL of MEDICINE

Timeline of Pivotal Events in Cancer Treatment.

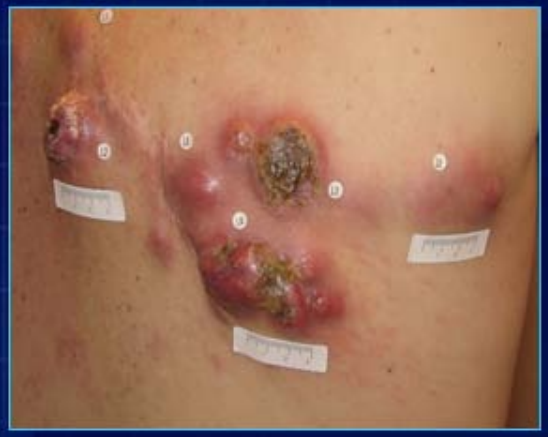


DeVita VT Jr, Rosenberg SA. N Engl J Med 2012;366:2207-2214.

The NEW ENGLAND JOURNAL of MEDICINE

Immuno-oncology: new treatment modality
First use in metastatic malignant melanoma

Screening (Nov,2007)



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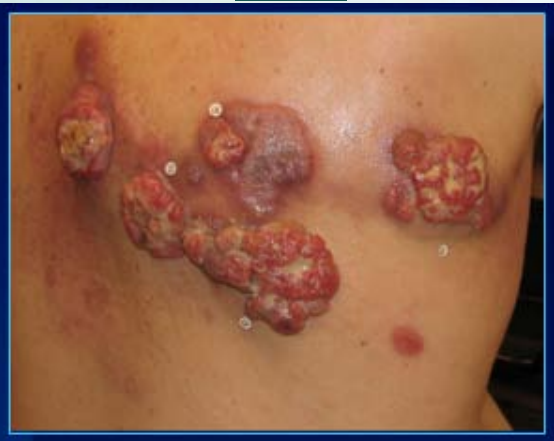

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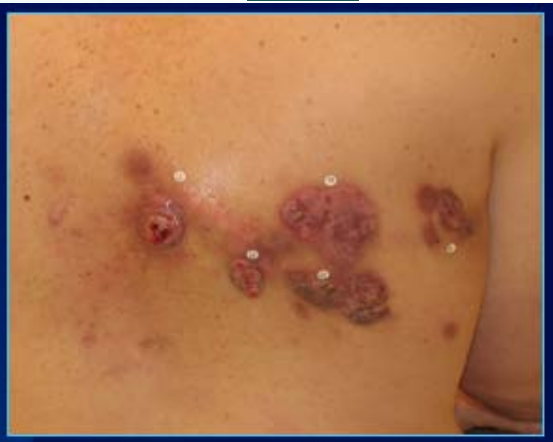

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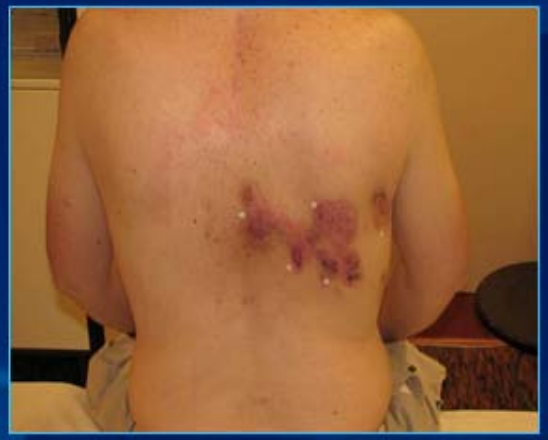
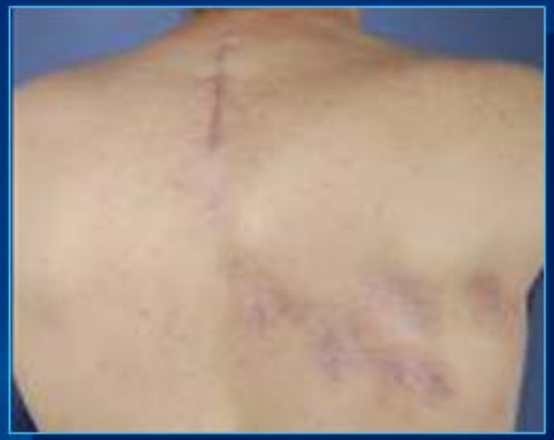


72 W



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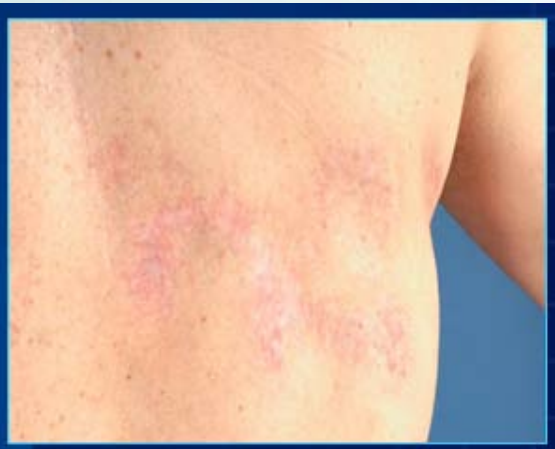
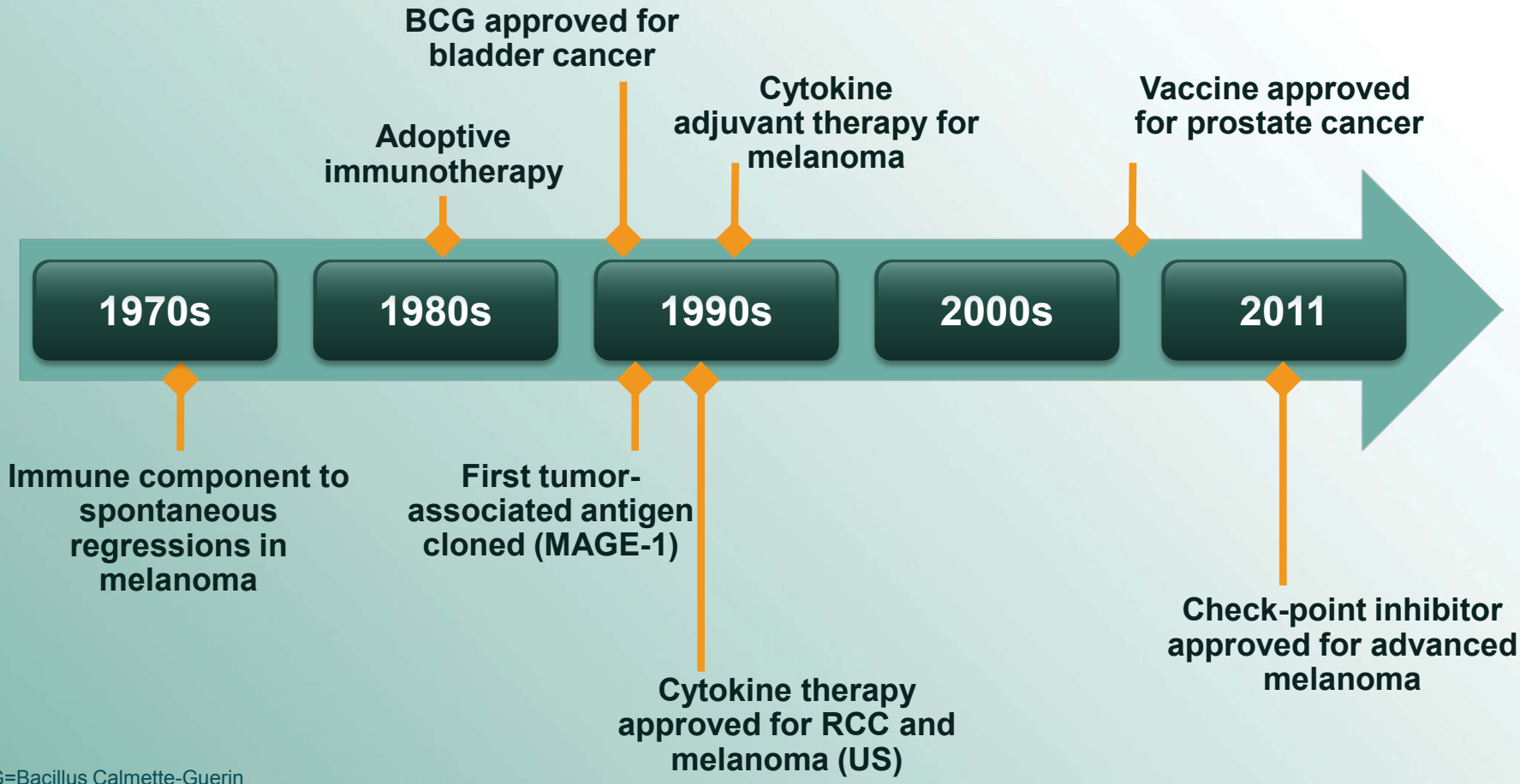


Courtesy of Dr. Harmankaya

The History of Cancer Immunotherapy

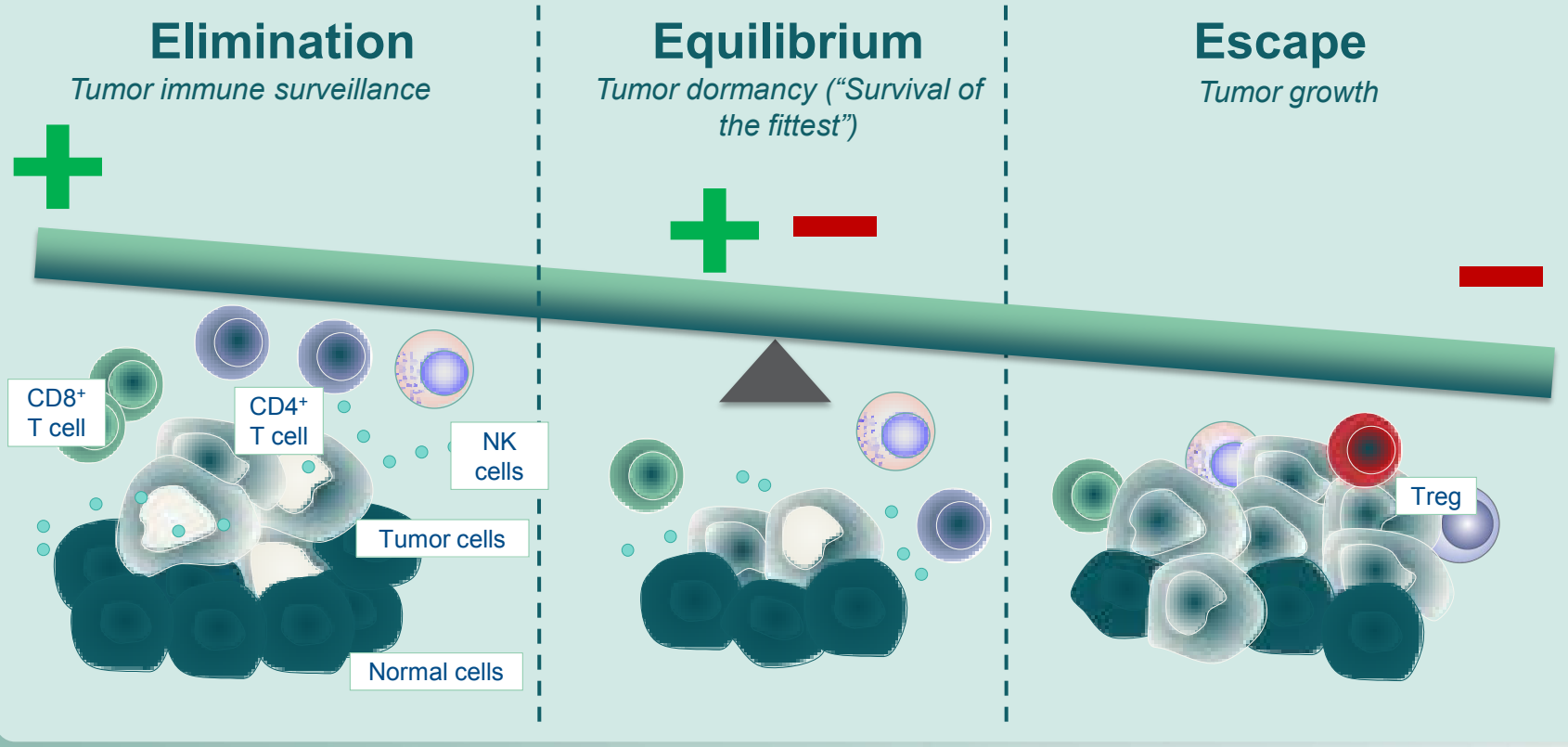


BCG=Bacillus Calmette-Guerin

Adapted from Kirkwood JM, *Ca J Clin.* 2012;62:309–335; George S, et al. *JNCCN.* 2011;9:1011–1018; Garbe C, et al. *The Oncologist.* 2011;16:2–24; Cheever MA, et al. *Clin Cancer Res.* 2011;17:3520–3526; Kantoff PW, et al. *N Engl J Med.* 2010;363:411–422; Mansh M. *Yale J Biol Med.* 2011;84:381–389; Hodi FS, et al. *N Engl J Med.* 2010;363:711–723; Aldousari S, et al. *CUAJ.* 2010;4:56–64.

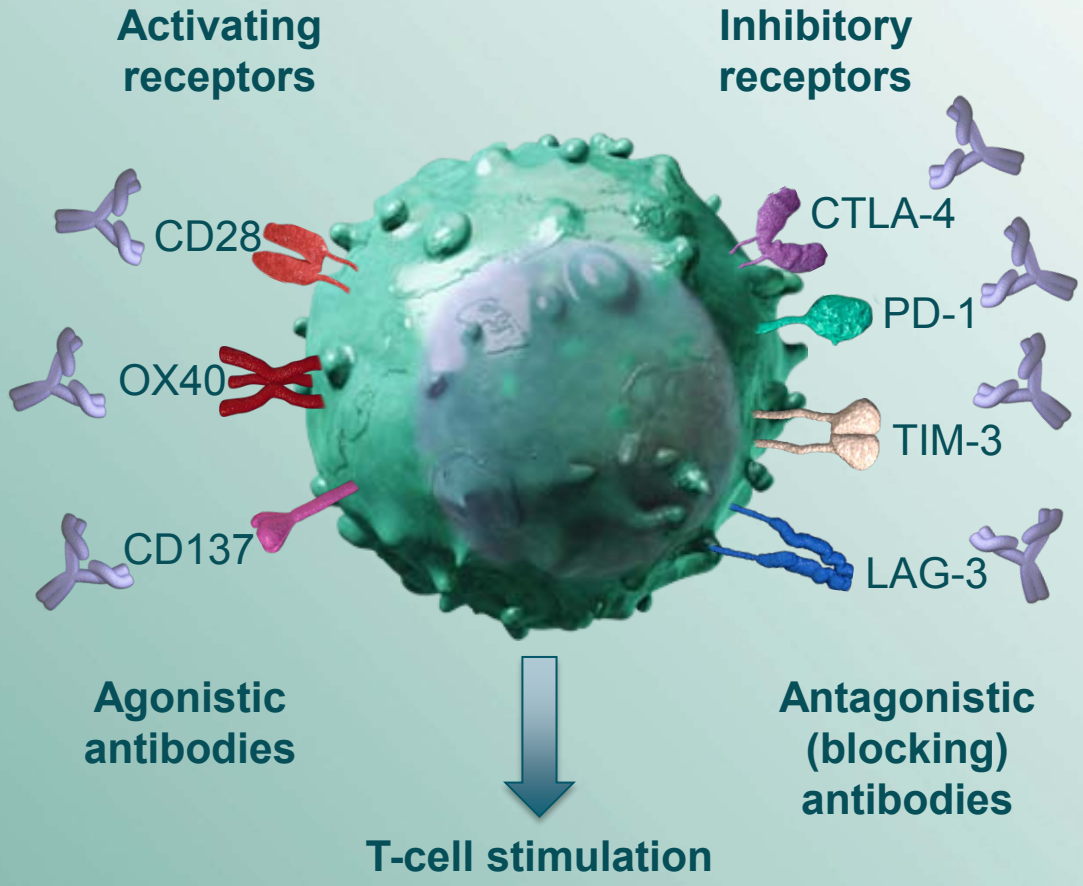
Cancer can develop immune system escape mechanism

The three "E's" of immunoediting describe the processes of tumor control by the immune system and how the tumor escapes this control.



Vesely et al, Ann Rev Immunol 2011, 29: 235

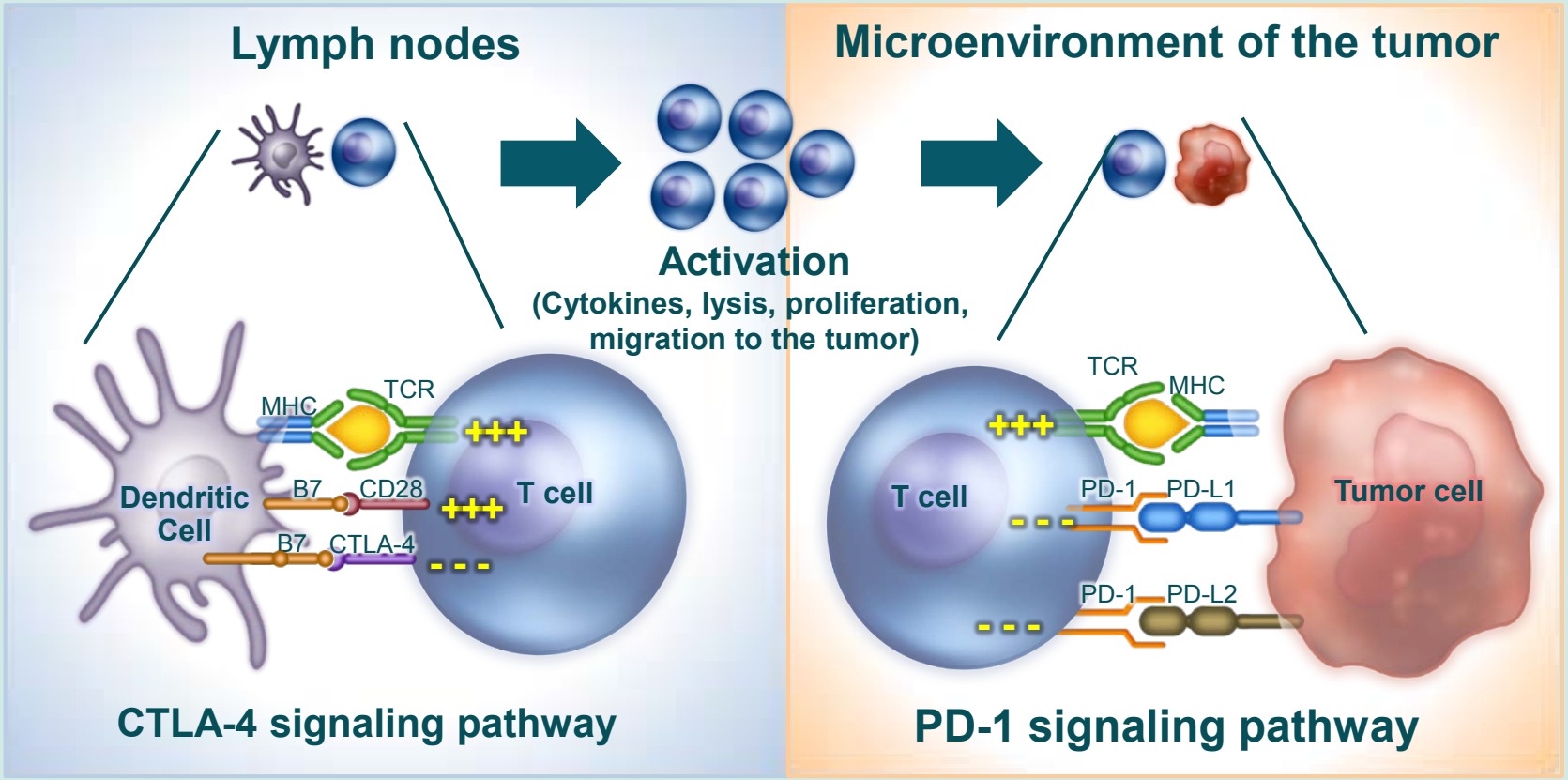
Discovery of T-Cell Checkpoint Regulation explain tumor escape mechanisms



- T-cell responses are regulated though a complex balance of inhibitory ("checkpoint") and activating signals
- Tumors can dysregulate checkpoint and activating pathways, and consequently the immune response
- Targeting checkpoint and activating pathways is an evolving approach to cancer therapy, designed to promote an immune response

Adapted from Mellman I, et al. *Nature.* 2011:480;481–489; Pardoll DM. *Nat Rev Cancer.* 2012;12:252–264.

Targeting checkpoints became hypothetical therapeutic option



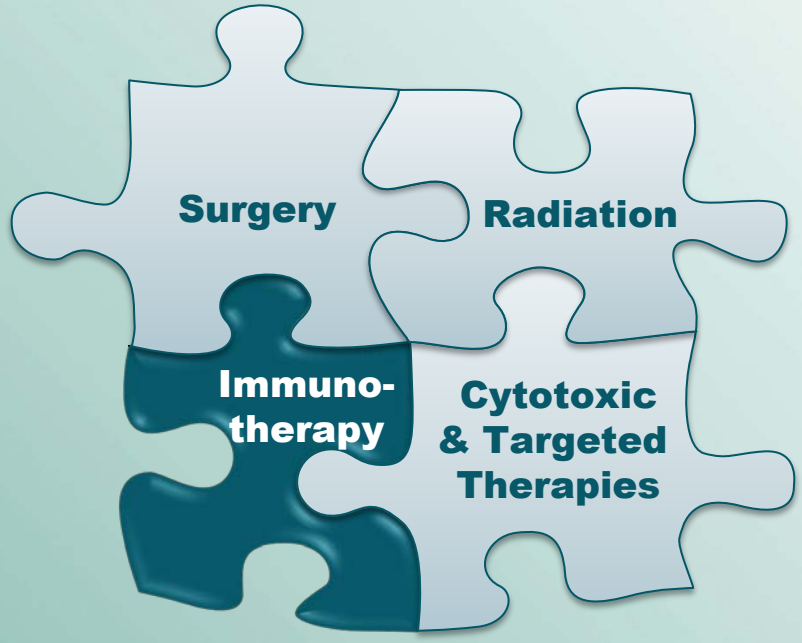
CTLA-4 regulates the **amplitude of the earlier activation** of naive and memory T cells.

PD-1 limits the **T-cell activation** in the **periphery** during an inflammatory reaction.

Wolchock et al, J Clin Oncol 2013 ASCO Annual Meeting Abstracts 31:15_suppl

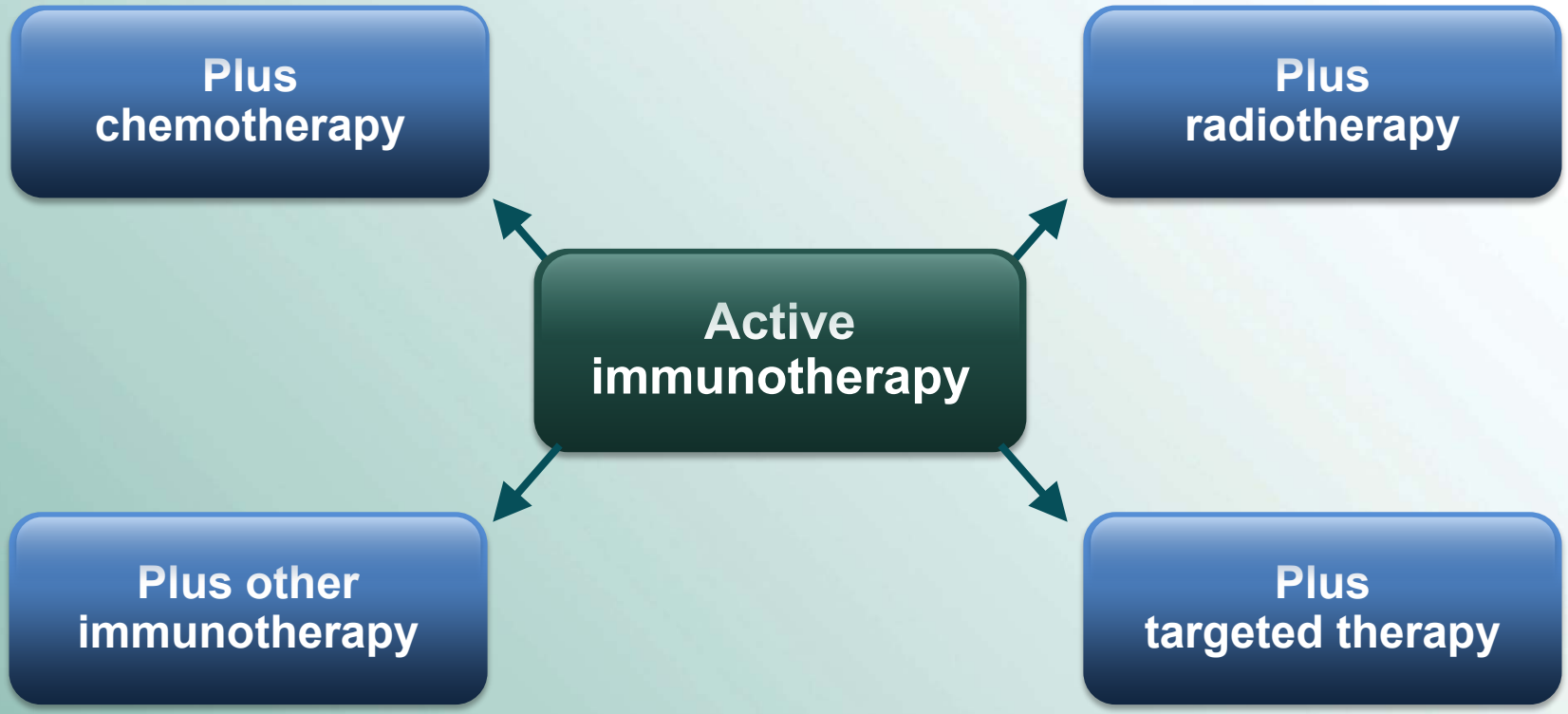
Immuno-Oncology Is an Emerging Therapeutic Modality[1]

- **Immuno-Oncology** treatment is different from other treatment modalities because it **uses the natural capability of the patient's own immune system to fight cancer**[2]
- Immuno-Oncology treatment works with the body's immune system to fight cancer rather than working directly on the tumor[2]



1. DeVita VT, Rosenberg SA. *N Eng J Med*. 2012:366:2207-2214.
2. Borghaei H, Smith MR, Campbell KS. *Eur J Pharmacol*. 2009;625:41-54.

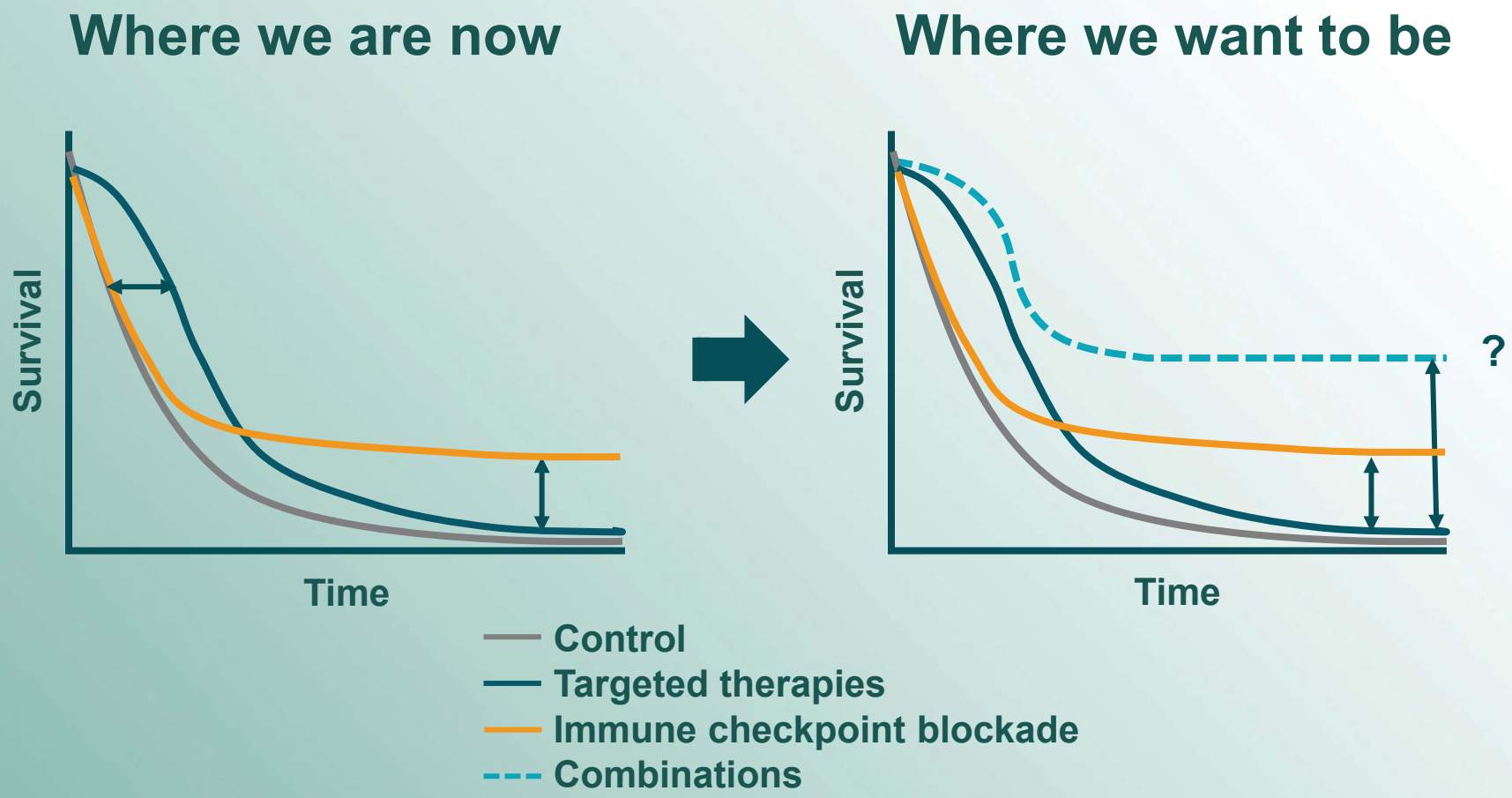
New Approaches to Build on Active Immunotherapies to Maximize Clinical Benefit



Immuno-Oncology research and development will continue to inform future strategies, including new targets and rationale drug combinations and sequencing

Drake CG. *Ann Oncol*. 2012;23(suppl 8):viii41–viii46; Hannani D, et al. *Cancer J*. 2011;17:351–358; Ménard C, et al. *Cancer Immunol Immunother*. 2008;57:1579–1587; Ribas A, et al. *Curr Opin Immunol*. 2013:25:291–296.

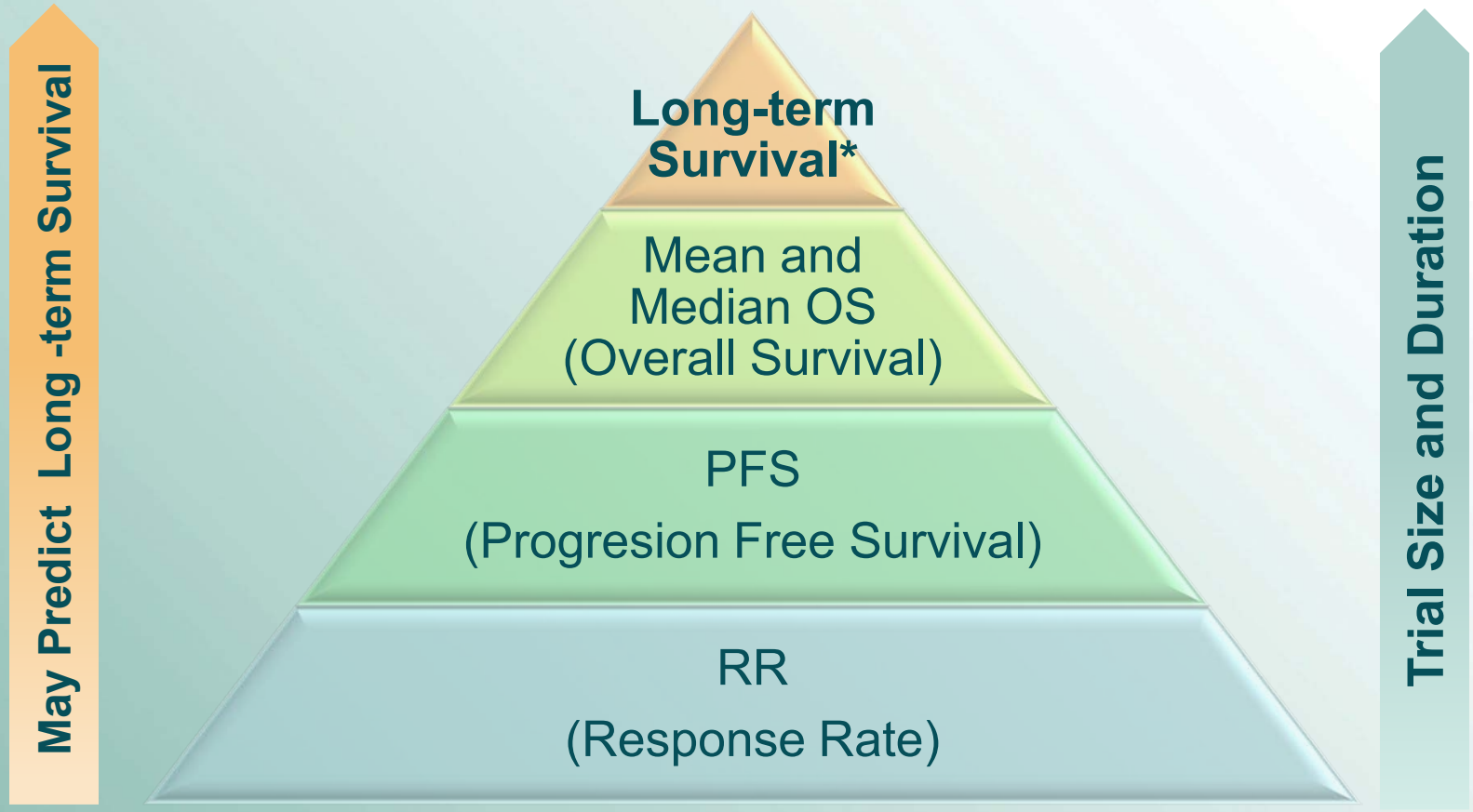
Hypothetical Effect of Targeting Distinct and Potentially Complementary Immune Evasion Pathways



Adapted from Ribas A, presented at WCM, 2013; Ribas A, et al. *Clin Cancer Res.* 2012;18:336–341; Drake CG. *Ann Oncol*. 2012;23(suppl 8):viii41–viii46.

Hypothetical slide illustrating a scientific concept, and is beyond data available to date.
These charts are not intended to predict what may actually be observed in clinical studies.

Immuno-oncology increase expectation to achieve long-term survival



*Long-term survival as measured by landmarks such as 1 yr, 2yr, 5 yr, etc

1. Cancer Drug Approval Endpoints. www.fda.gov/About/CentersOfficeofMedicalProductsandtobacco/CDER/ucm117709.htm#lung
2. Workshop Summary on Endpoints for Approval of Cancer Drugs for Lung Cancer. www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/ DevelopmentResources/CancerDrugs/ucm094744.pdf. 3. Lee ME, Berstein D, Voest E, et al. Defining clinically meaningful outcomes: ASCO Recommendations to Raise the Bar for Clinical Trials [draft for public comment]. www.asco.org/sites/asco.org/files_asco_meaningful+outcomes_draft_for_comment_april_2013.pdf.

Availability of new treatments is key to achieve success in anti-cancer interventions

Average time elapsing between the date of EU market authorisation and the "accessibility" date (i.e. date of completion of pricing / reimbursement procedures) in 20 European countries will vary from 116 to 550 days (Not considering Estonia with an average of 848 days, based on 3 observations only.)

Country *Latest update*	Number of medicines included % rates of total number within scope *100% = 66 new medicines*		**Average time elapsed between date of EU MA and "accessibility" date** ***In number of days***
Estonia *May 2011*	15	23%	**848** Average for 3
Czech Republic *April 2011*	23	35%	**550**
Romania *April 2011*	25	38%	**458** Average for 11
Slovakia *May 2011*	4	5%	**426**
Portugal *May 2011*	23	35%	**412**
Belgium *April 2011*	31	43%	**371**
Spain *May 2011*	25	38%	**352**
Italy *May 2011*	33	50%	**347**
France *May 2010*	23	35%	**316**

www.efpia.eu - Patients W.A.I.T. indicator 2011 report – based on EFPIA's database (first EU marketing authorisation in the period 2008-'10)

CECOG
Central European Cooperative Oncology Group

CECOG News

SPLENDOUR Trial included the 1st patient in Austria

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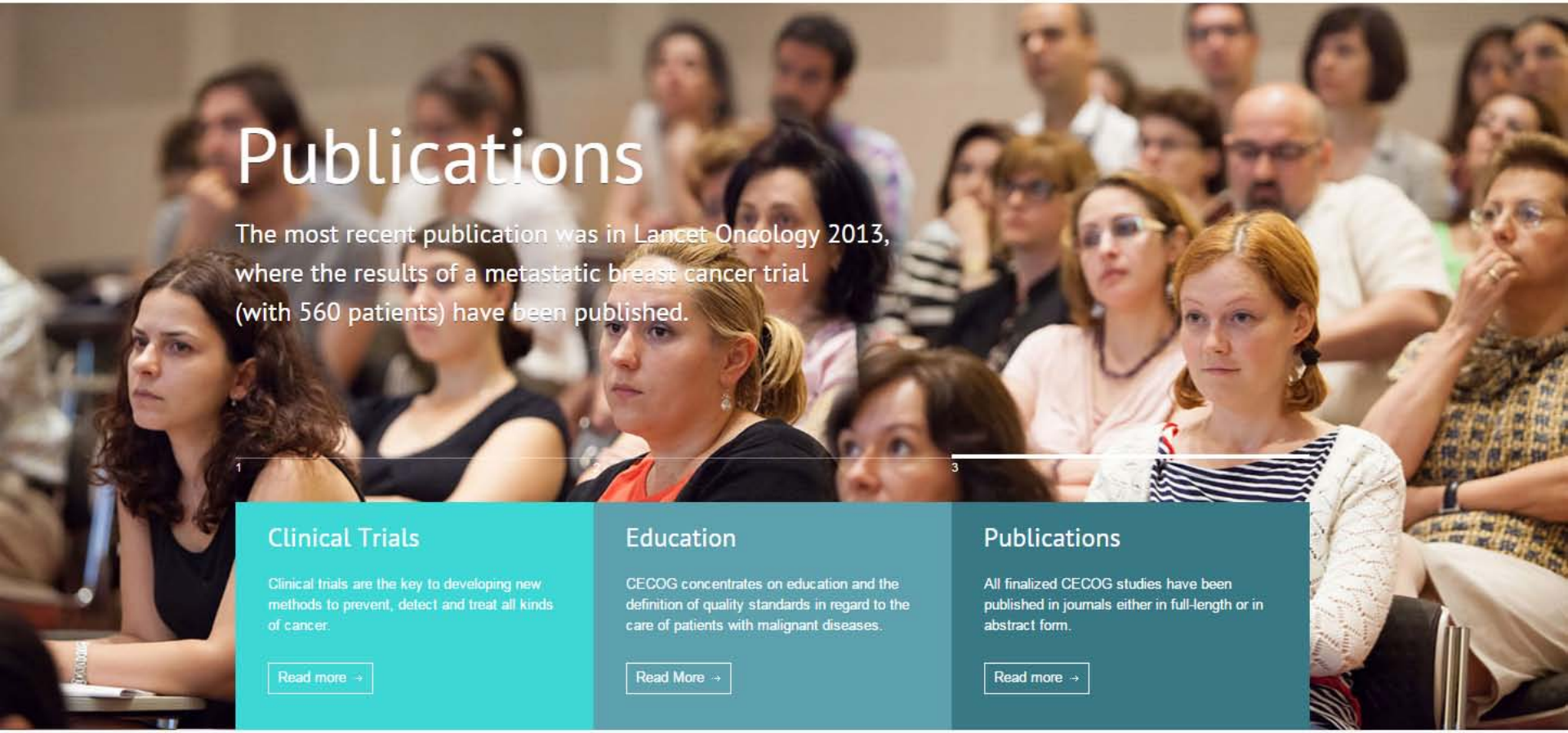

Publications

The most recent publication was in Lancet Oncology 2013, where the results of a metastatic breast cancer trial (with 560 patients) have been published.

1 2 3

Clinical Trials

Clinical trials are the key to developing new methods to prevent, detect and treat all kinds of cancer.

Read more →

Education

CECOG concentrates on education and the definition of quality standards in regard to the care of patients with malignant diseases.

Read More →

Publications

All finalized CECOG studies have been published in journals either in full-length or in abstract form.

Read more →

Conclusion

- **5-year survival remains poor for many patients with advanced solid tumors**
- **Lung cancer is leading cause of death in oncology**
- **Immuno-Oncology is designed to harness the patient's own immune system to fight cancer with the goal to provide long-term survival**
- **Patient advocates play an important role providing patient and caregiver perspectives:**
  - to scientific community to ensure it captures endpoints which are meaningful to patient
  - to healthcare providers, to ensure their patient voice is considered in regulatory and access decisions