

Prognosi dei pazienti con tumore

eoc

17° corso di aggiornamento per il medico di base
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Outline

- Il cancro in numeri
- Diagnosi
- Trattamento
- Sopravvivenza

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Il cancro in numeri

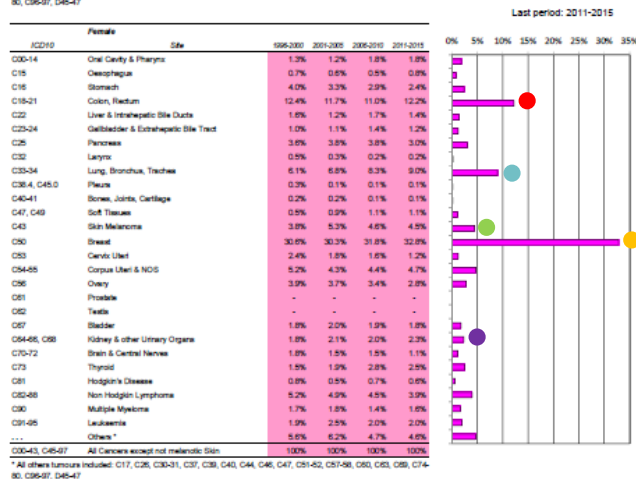
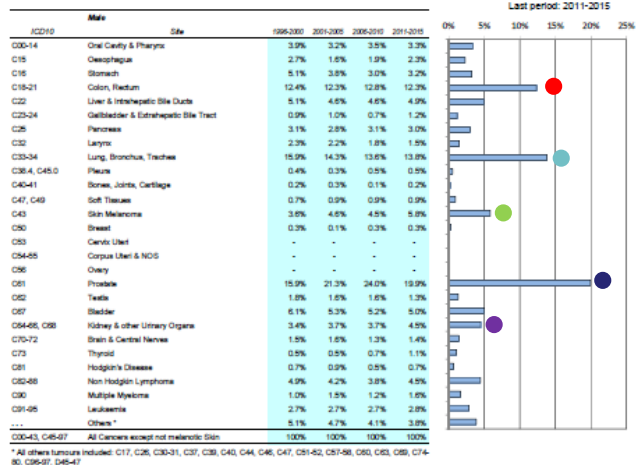
	PRIMA	DOPO
Diagnosi di tumore nel mondo	14 Mio/anno nel 2012	22 Mio/anno nel 2032
Diagnosi di tumore in USA	1.7 Mio nel 2017	2.2 Mio nel 2030
Adulti sopravvivenza a 5 anni	50% negli anni '70	70% oggi
Bambini sopravvivenza a 5 anni	60% negli anni '70	80% oggi
Diagnosi di tumore in CH *	38500 nel 2012	42000 nel 2015
Sopravvivenza a 5 anni in CH *	55% negli anni '90	65% oggi

Incidenza 2011 - 2015

Incidence

Percentage distribution by site

Summary



- ● Tumore mammario 32.8%
- ● Tumore prostatico 19.9%
- ● Tumore colon-retto 12.3% 12.2%
- ● Tumore polmonare 13.8% 9%
- ● Melanoma 5.8% 4.5%
- ● Tumore renale 4.5% 2.3%

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- Il cancro in numeri
- **Diagnosi**
- Trattamento
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Diagnosi

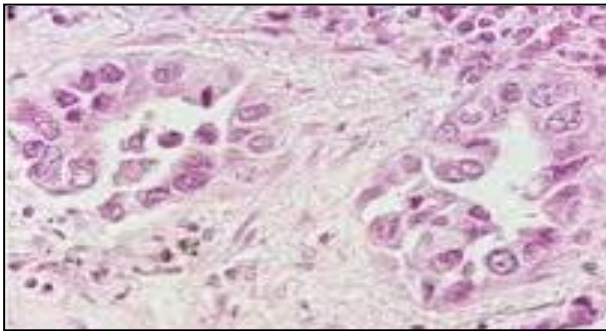
1. Diagnosi istologica
2. Immunoistochimica
3. Biologia molecolare
4. Genomica
5. Biopsie liquide

Diagnosi

1. Diagnosi istologica

→ definisce l'origine istogenetica del tumore

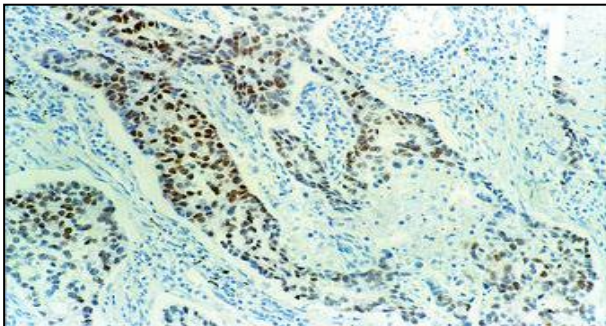
Esempio: adenocarcinoma



2. Immunoistochimica

→ determina il sito d'origine del tumore

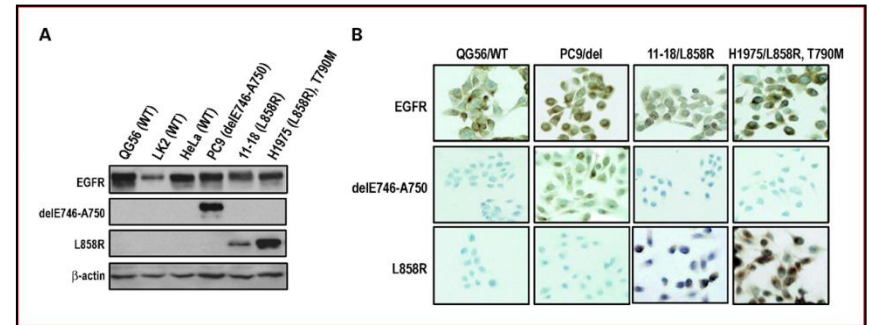
Esempio: anticorpo TTF1 per polmone



3. Biologia molecolare

→ individua il profilo molecolare del tumore

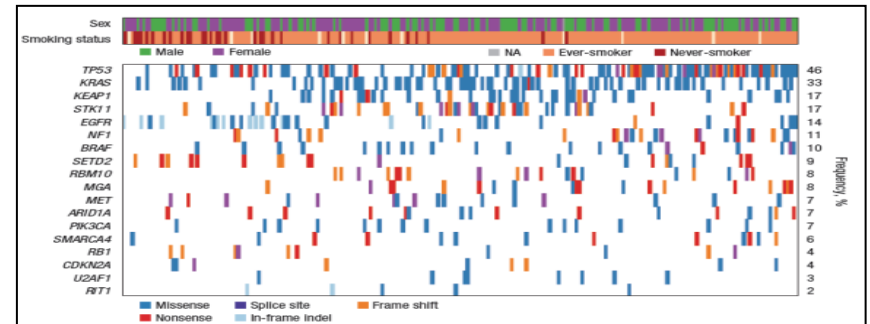
Esempio: mutazione EGFR nel tumore polmonare



4. Genomica

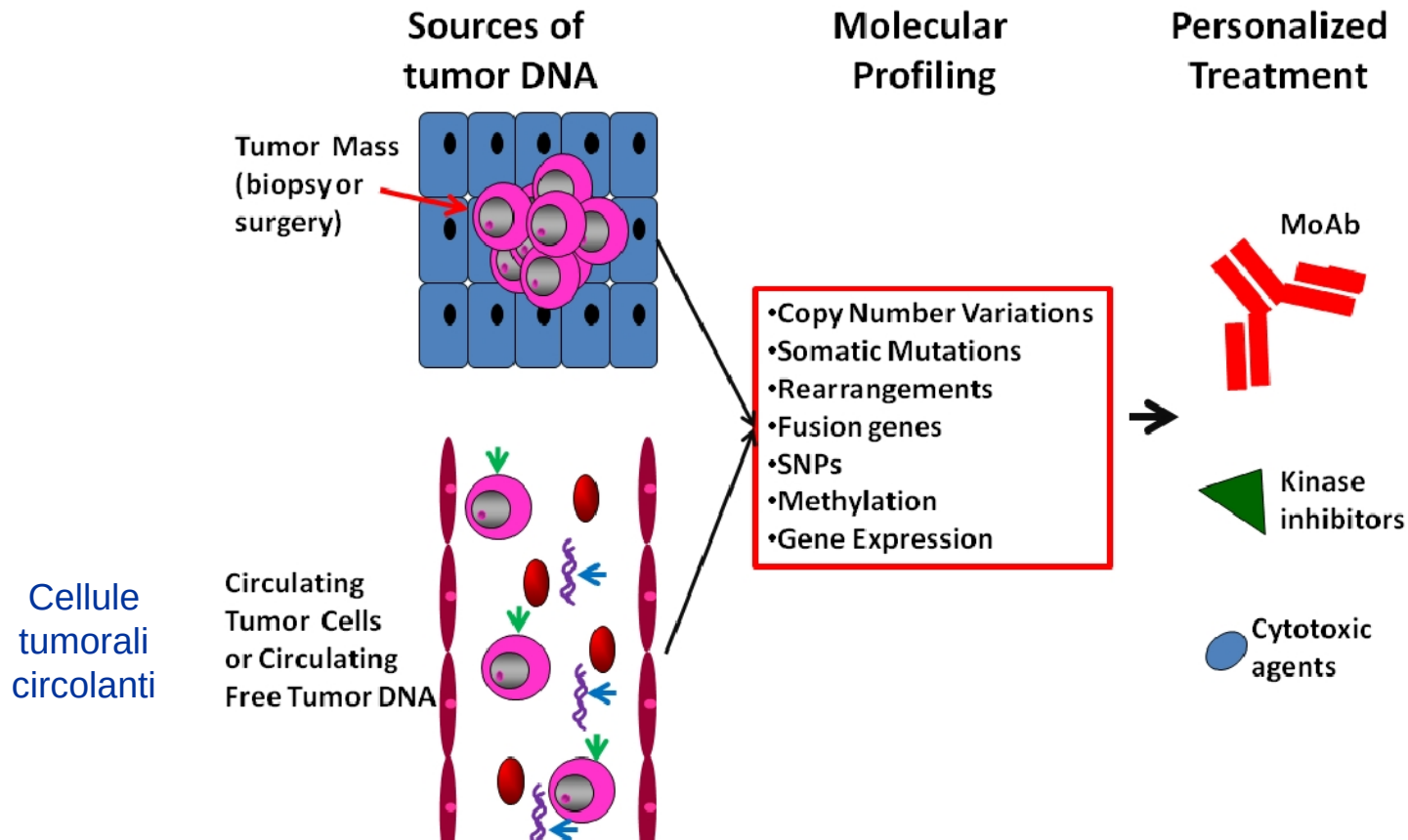
→ Individua dei pannelli di alterazioni genetiche

Esempio: sequenziamento del DNA tumorale



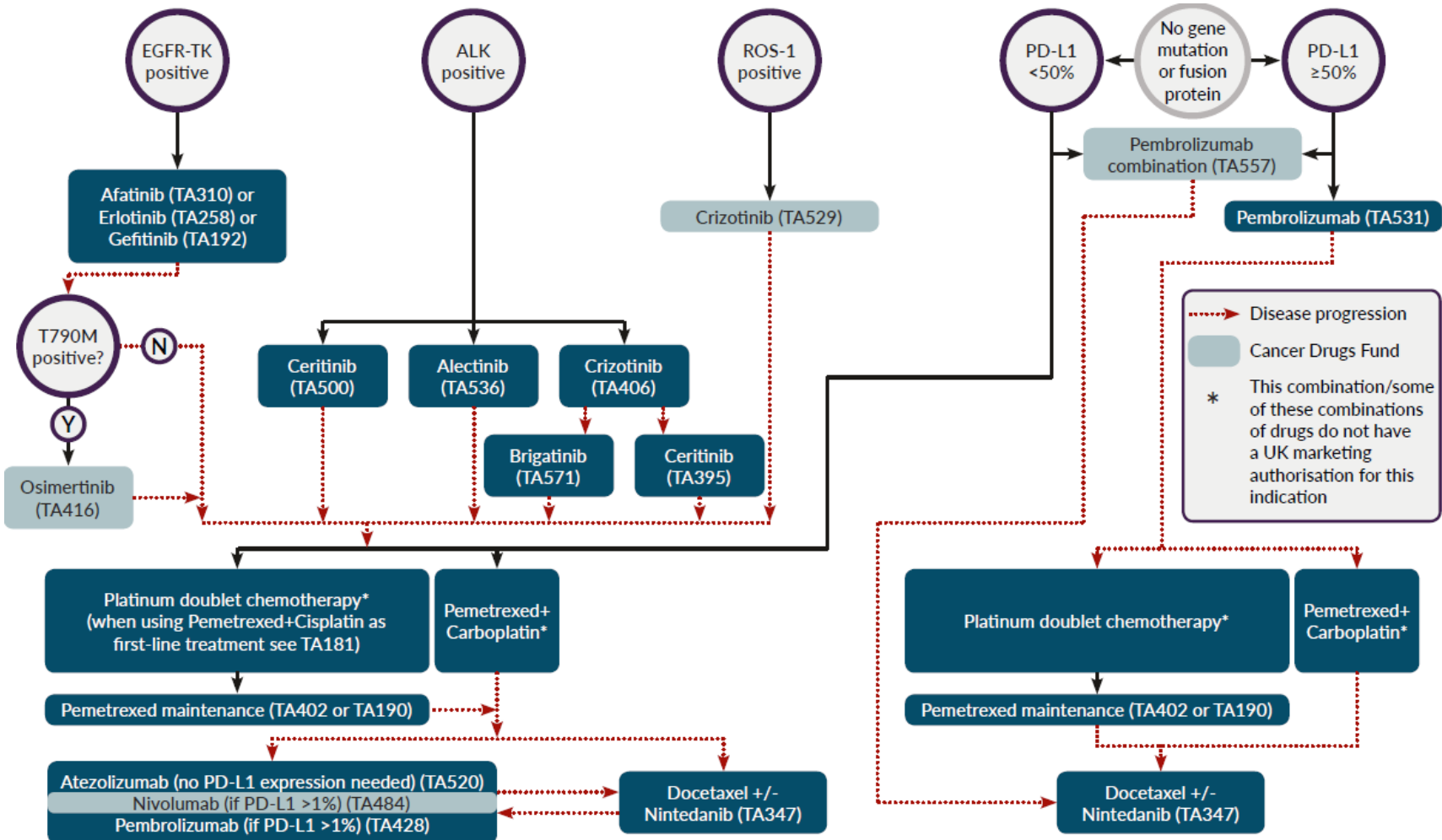
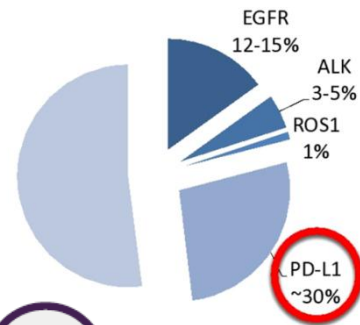
Diagnosi: «biopsie liquide»

The future of biomarker testing



Tumore al polmone

modello di medicina personalizzata



Outline

- Il cancro in numeri
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- **Trattamento**
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Table 1. FDA Approvals of Cancer Therapies From November 1, 2016, to October 31, 2017

Drug	Indication
New approval	
Rucaparib (Rubraca; Clovis Oncology, Boulder, CO)	For treatment of patients with deleterious BRCA mutation (germline and/or somatic)-associated advanced ovarian cancer who have been treated with two or more chemotherapies.
Avelumab (Bavencio; EMD Serono, Darmstadt, Germany)	For the treatment of patients ≥ 12 years of age with metastatic Merkel cell carcinoma. Avelumab is a PD-L1-blocking human immunoglobulin G1 λ monoclonal antibody. This is the first FDA-approved product to treat this type of cancer.
Niraparib (Zejula; Tesaro, Waltham, MA)	Maintenance treatment for adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to platinum-based chemotherapy.
Ribociclib (Kisqali; Novartis, Basel, Switzerland)	In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer.
Brigatinib (Alunbrig; Takeda, Osaka, Japan)	For treatment of patients with metastatic anaplastic lymphoma kinase-positive NSCLC who experienced disease progression on or who are intolerant to crizotinib.
Midostaurin (Rydapt; Novartis)	For treatment of adult patients with newly diagnosed acute myeloid leukemia with FLT3-internal tandem duplication mutation-positive, as detected by an FDA-approved test, in combination with standard cytarabine and daunorubicin induction chemotherapy.
Durvalumab (Imfinzi; AstraZeneca, London, United Kingdom)	For treatment of patients with locally advanced or recurrent squamous cell carcinoma who experience disease progression after containing chemotherapy or who experience disease progression within 12 months of neoadjuvant or adjuvant treatment with chemotherapy.
Rituximab and hyaluronidase human (Rituxan Hycela; Genentech, South San Francisco, CA)	For adult patients with follicular lymphoma, diffuse large B-cell lymphoma, or chronic lymphocytic leukemia.
Neratinib (Nerlynx; Puma Biotechnology, Los Angeles, CA)	For extended adjuvant treatment of adult patients with locally advanced or recurrent breast cancer, to follow after standard of care.
Daunorubicin and cytarabine (Vyxeos; Jazz Pharmaceuticals, Palo Alto, CA)	For treatment of adults with newly diagnosed therapy-naïve acute myeloid leukemia, two types of APL.
Enasidenib (Idhifa; Celgene, San Francisco, CA)	For treatment of adult patients with relapsed or refractory acute myeloid leukemia with IDH1 G14A mutation as detected by a validated test.
Inotuzumab ozogamicin (Besponsa; Wyeth, Madison, NJ)	For treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia.
Tisagenlecleucel (Kymriah; Novartis)	For treatment of patients ≤ 25 years of age with relapsed or refractory B-cell precursor acute lymphoblastic leukemia.
Abemaciclib (Verzenio; Eli Lilly, Indianapolis, IN)	In combination with fulvestrant for women with hormone receptor-positive, HER2-negative advanced or metastatic breast cancer with disease progression after endocrine therapy.
Bevacizumab-awwb (Mvasi; Amgen, South San Francisco, CA)	Approved as a biosimilar to bevacizumab (Avastin) for the treatment of patients with recurrent glioblastoma.
Copanlisib (Aliqopa; Bayer HealthCare, Berlin, Germany)	For treatment of adult patients with relapsed follicular lymphoma who have received at least two prior systemic therapies.
Gemtuzumab ozogamicin (Mylotarg; Pfizer, New York, NY)	Newly diagnosed CD33-positive AML in adults and pediatric patients. May be used in combination with daunorubicin or as a stand-alone therapy in pediatric patients.
Axicabtagene ciloleucel (Yescarta; Kite Pharma, Los Angeles, CA)	For treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma after two or more lines of systemic chemotherapy.

30 nuovi ttt
approvati dall'FDA

29 non chemio!

In combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy.

Recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after a platinum-based therapy.

Maintenance therapy for patients with multiple myeloma after autologous stem-cell transplantation.

For treatment of patients with locally advanced or metastatic urothelial carcinoma who experience disease progression during or after platinum-containing chemotherapy or experience disease progression within 12 months of neoadjuvant or adjuvant treatment with a platinum-containing chemotherapy.

For treatment of patients with metastatic EGFR T790M mutation-positive NSCLC, as detected by an FDA-approved test, who experienced disease progression on or after EGFR tyrosine kinase inhibitor therapy.

HR-positive, HER2-negative advanced or metastatic breast cancer in combination with an aromatase inhibitor as initial endocrine-based therapy in postmenopausal women.

For treatment of adult and pediatric patients with refractory classic Hodgkin lymphoma or those who have experienced relapse after three or more prior lines of therapy.

For treatment of patients with HCC who have been previously treated with sorafenib.

For patients with locally advanced or metastatic urothelial carcinoma who experienced disease progression during or after platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

In combination with pemetrexed and carboplatin for treatment of patients with previously untreated metastatic nonsquamous NSCLC.

For patients with locally advanced or metastatic urothelial carcinoma who experience disease progression during or after platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

For treatment of HCC in patients who have been previously treated with sorafenib.

For patients with recurrent locally advanced or metastatic, gastric, or gastroesophageal junction adenocarcinoma whose tumors express PD-L1 as determined by an FDA-approved test.

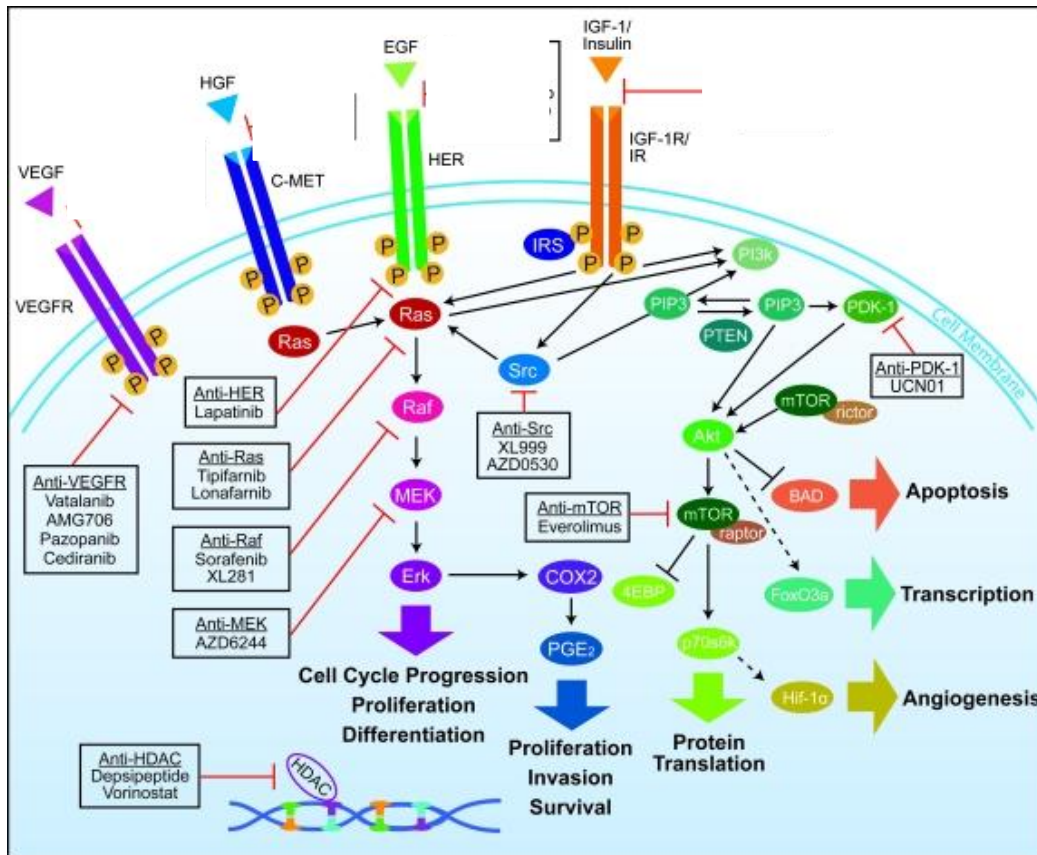
Trattamento

1. Terapie a bersaglio molecolare e anticorpi
2. Inibitori dei checkpoint immunitari
3. Immunoterapia adottiva antitumorale (car-T)
4. Terapie agnostiche

1. Terapie a bersaglio molecolare

«targeted therapy»

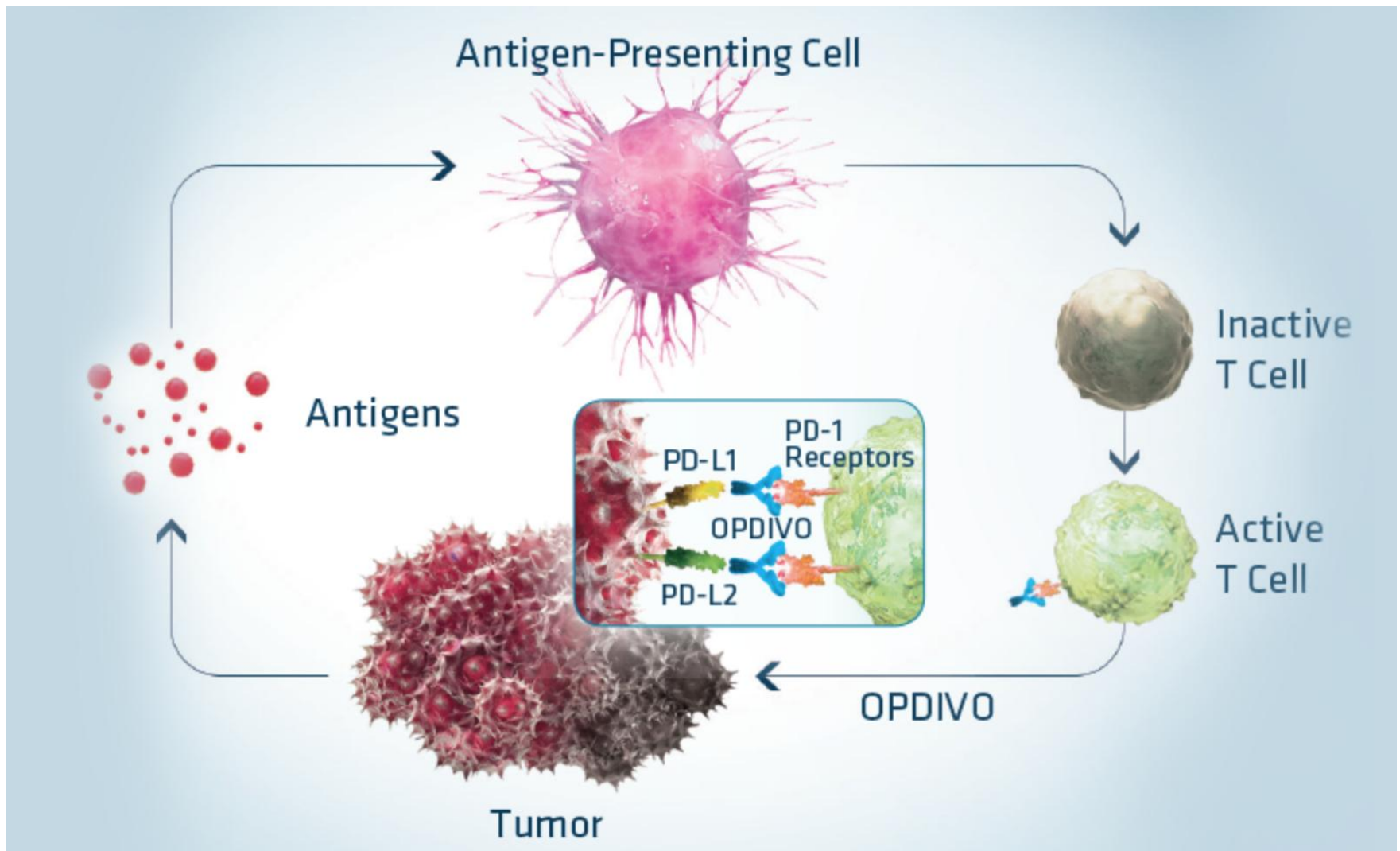
- Interferiscono con specifiche molecole necessarie per la crescita cellulare.



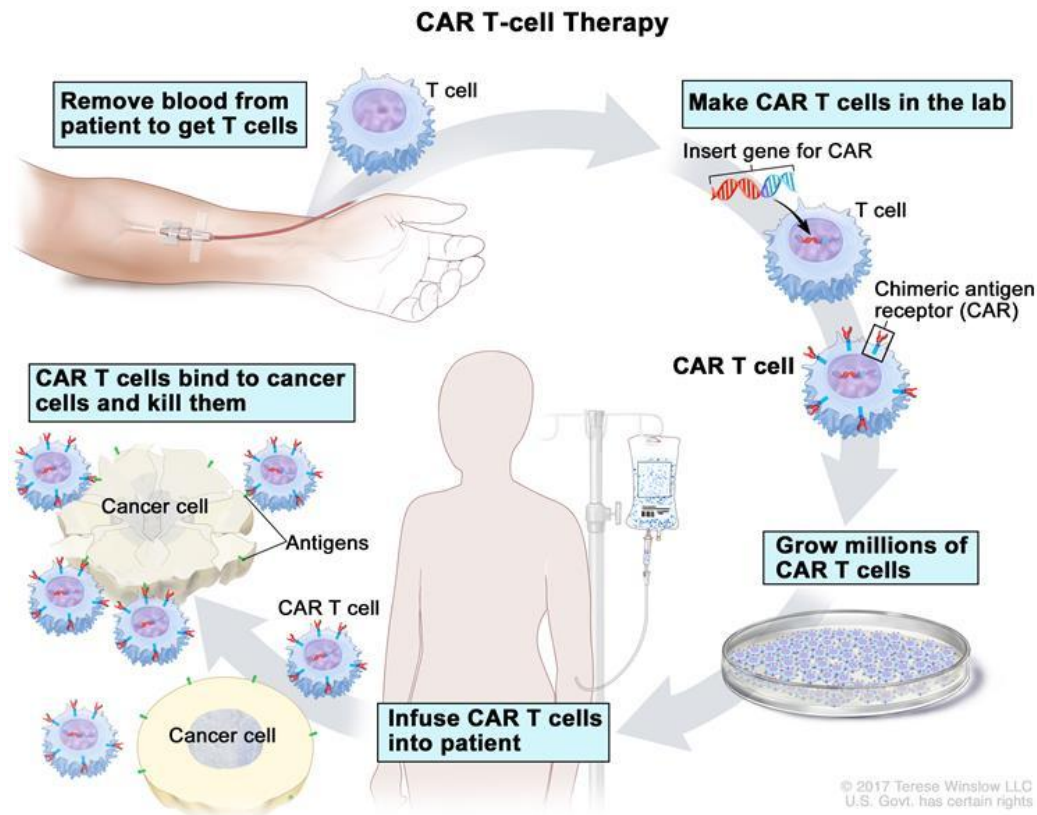
anticorpi monoclonali

piccole molecole che agiscono all'interno della cellula

2. Inibitori dei checkpoint immunitari



3. Immunoterapia adottiva antitumorale



Le **cellule T** del paziente vengono **modificate geneticamente**

Viene inserito artificialmente un gene nella cellula T

Le cellule sono moltiplicate in laboratorio

Le **cellule T modificate** esprimono recettori che **riconoscono gli antigeni tumorali**

Si iniettano una volta perché continuano a moltiplicarsi nel corpo con un effetto immunitario persistente

4. Terapie agnostiche

- Le terapie oncologiche si basano su origine e stadio del tumore
- Queste invece sono basate su alterazioni geniche non tessuto-specifiche
- 2 terapie approvate in USA:
 - Immunoterapico pembrolizumab per tumori con deficienza del meccanismo di riparazione del DNA mismatch-repair (MMR)
 - Terapia a bersaglio molecolare larotrectinib per tumori con alterazione del gene TRK

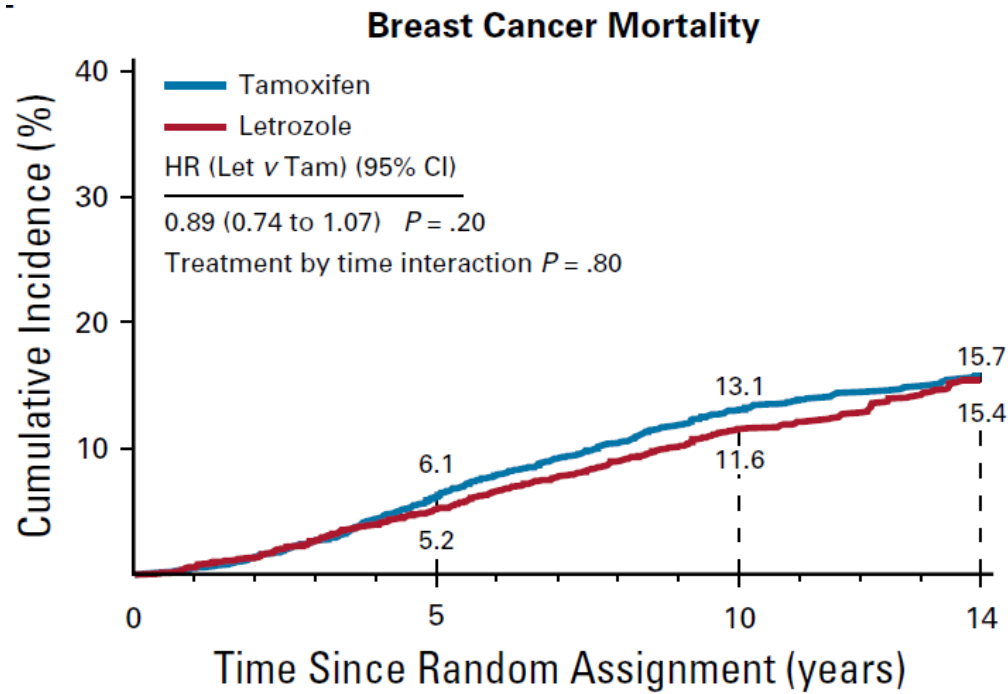
Outline

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Sopravvivenza tumore mammario Non metastatico

Terapia ormonale adiuvante

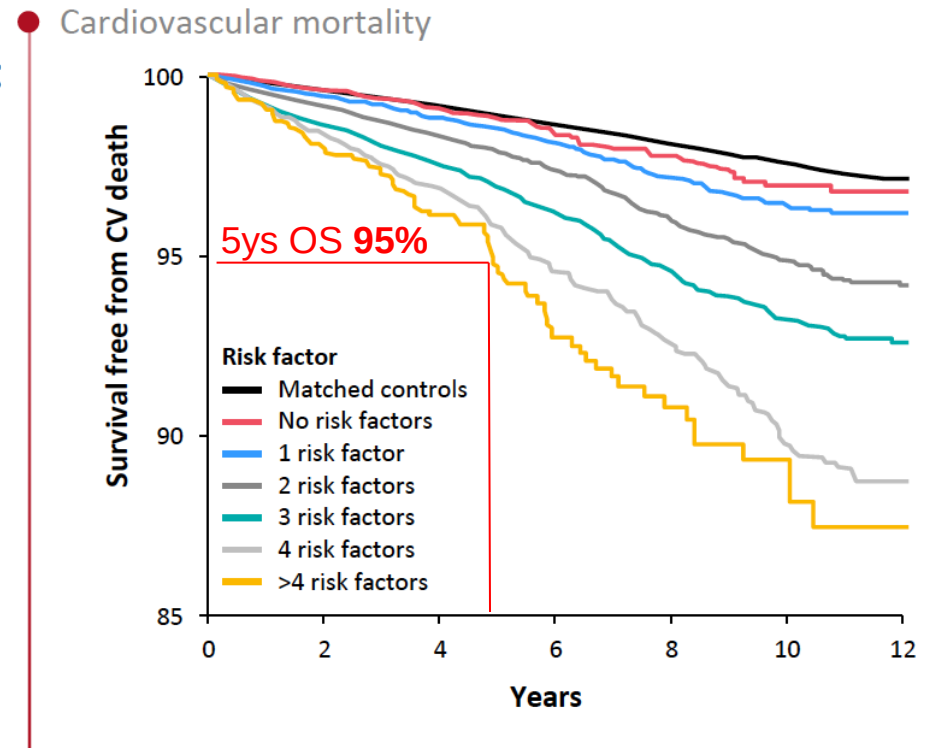
5ys OS 95%



Sopravvivenza post infarto miocardico

SWEDHEART: Risk factor control after MI and prognosis

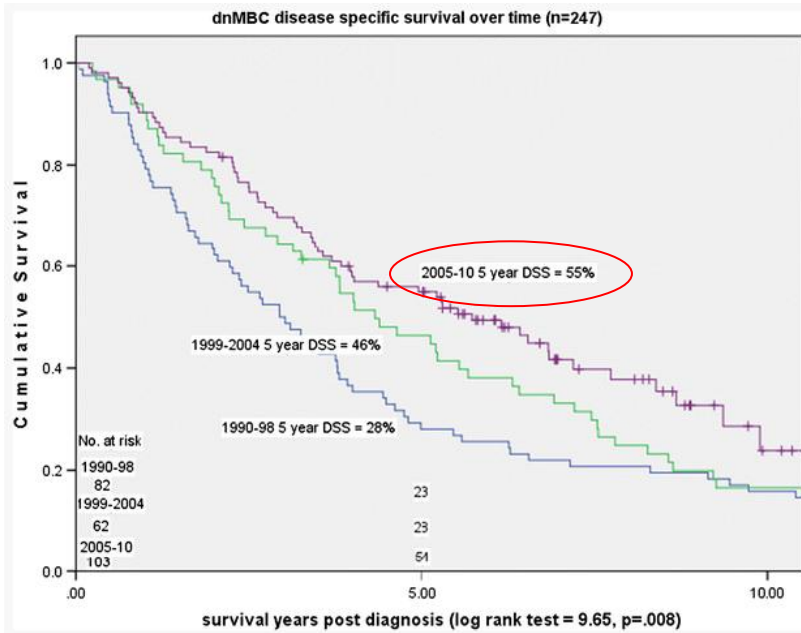
- SWEDHEART - nationwide registry of post MI patients
- 6 risk factors: physical activity, blood pressure, obesity, smoking, Hba1c and LDL
- MI patients with no risk factors had the same risk of outcome as controls
- Physical inactivity and continued smoking strongest predictors of outcomes
- **Conclusion:** lifestyle remains at the core of preventing CVD events



Sopravvivenza tumore mammario Metastatico

Secondo periodo storico

5ys OS **55%**



Antiormonale + CDK4/6

3.5ys OS **70%**

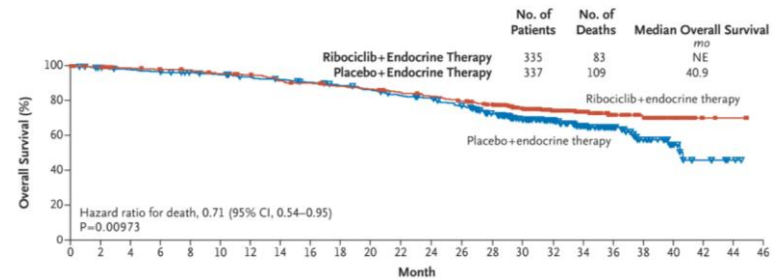
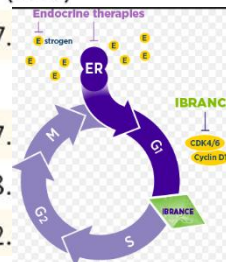


Table 1. Overall Survival

Variable	Ribociclib Group (N=335)	Placebo Group (N=337)
Deaths — no. (%)†	83 (24.8)	109 (32.3)
Data censored‡	252 (75.2)	228 (67.7)
Median overall survival – Kaplan–Meier estimated	NE	40.9 (37.7–44.1)
24 mo	82.7 (78.1–86.5)	81.8 (77.7–85.9)
36 mo	71.9 (66.0–77.0)	64.9 (58.8–71.0)
42 mo	70.2 (63.5–76.0)	46.0 (32.2–59.8)



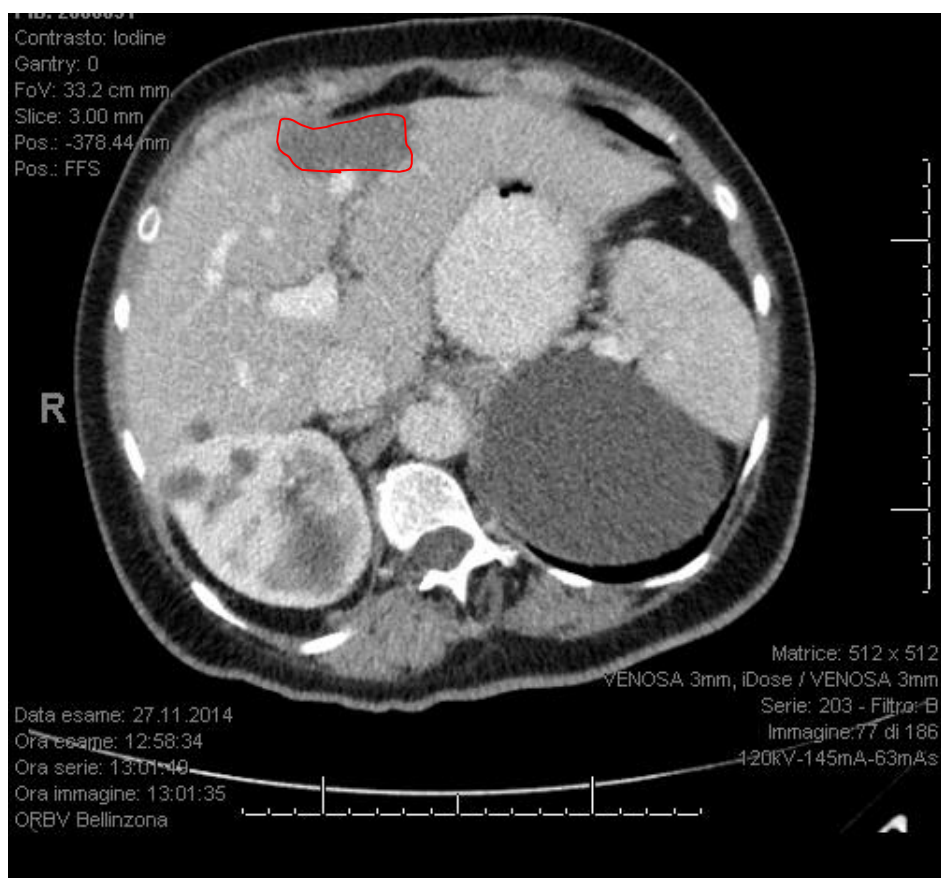
Mammario metastatico



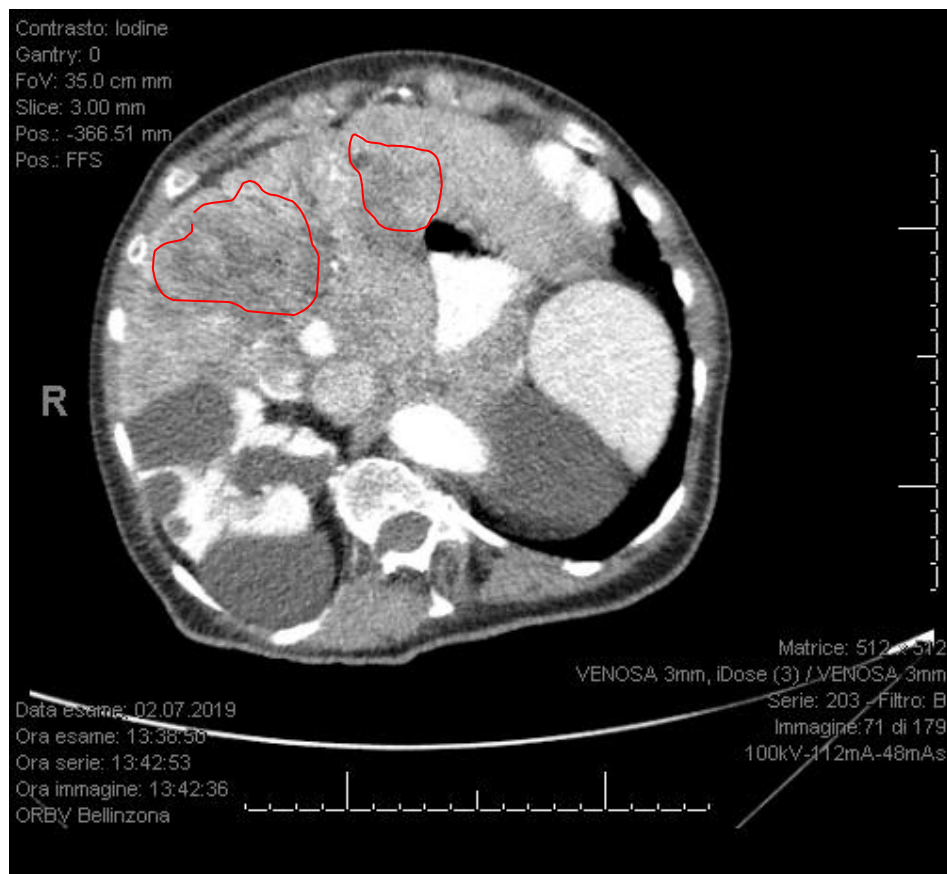
60 anni

Ormono e chemio-terapia

Controllo di malattia a 5 anni



2014



2019

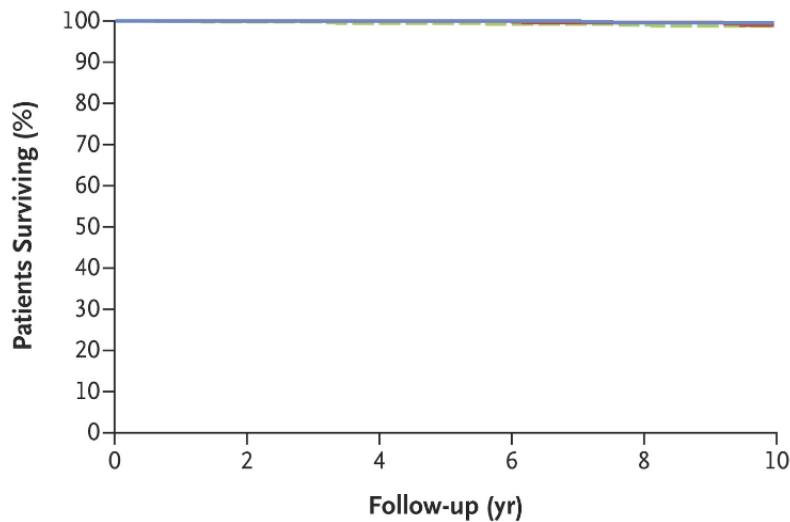
Sopravvivenza tumore prostatico

Tumore localizzato

5ys OS **98%**

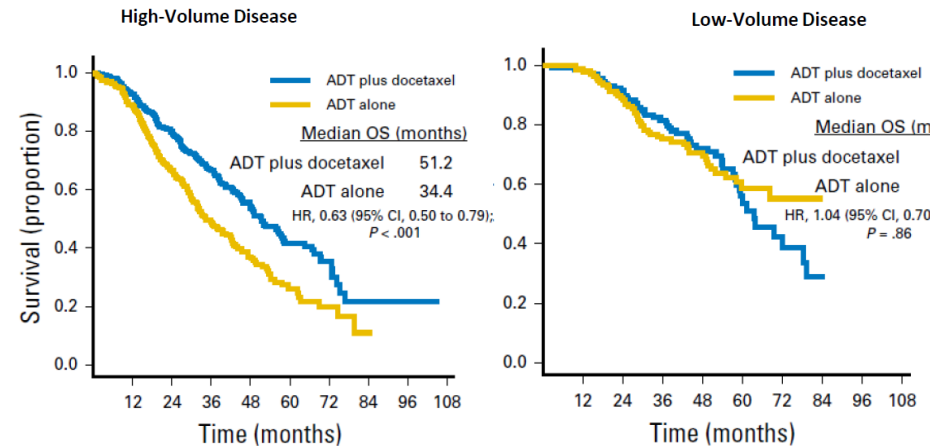
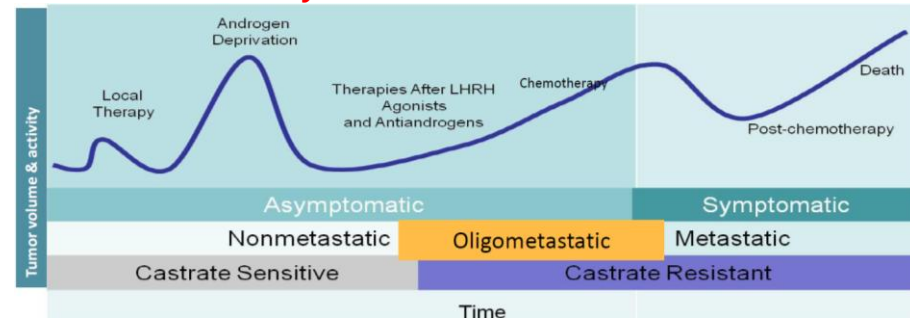
— Surgery — Radiotherapy — Active monitoring

Prostate-Cancer-Specific Survival



Tumore metastatico

5ys OS **50%-60%**





85 anni

Terapie ormonali

Denosumab

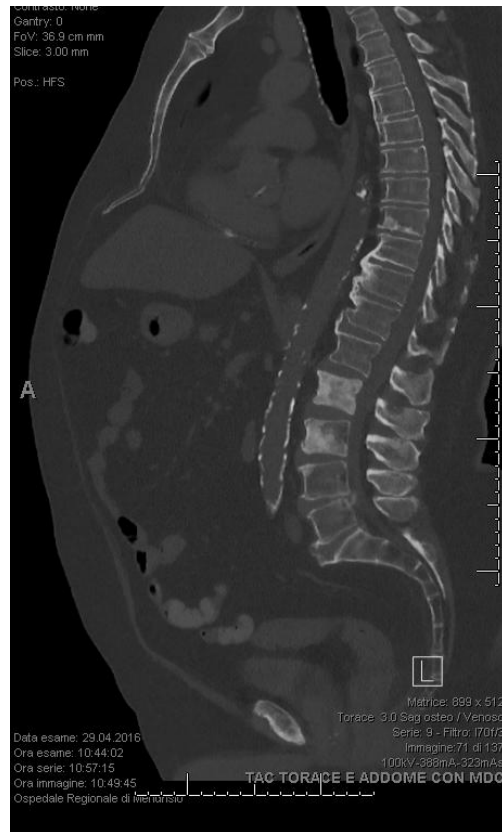
Diagnosi 20 anni fa

Prostata metastatico

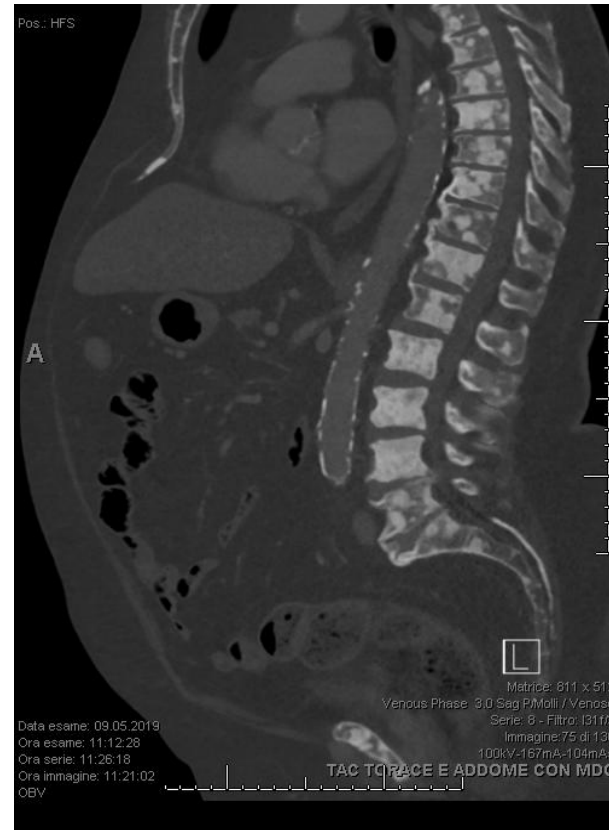
Adenocarcinoma della prostata localizzato, 1999.

Prima recidiva nel 2009.

Comparsa di metastasi ossee nel 2015.

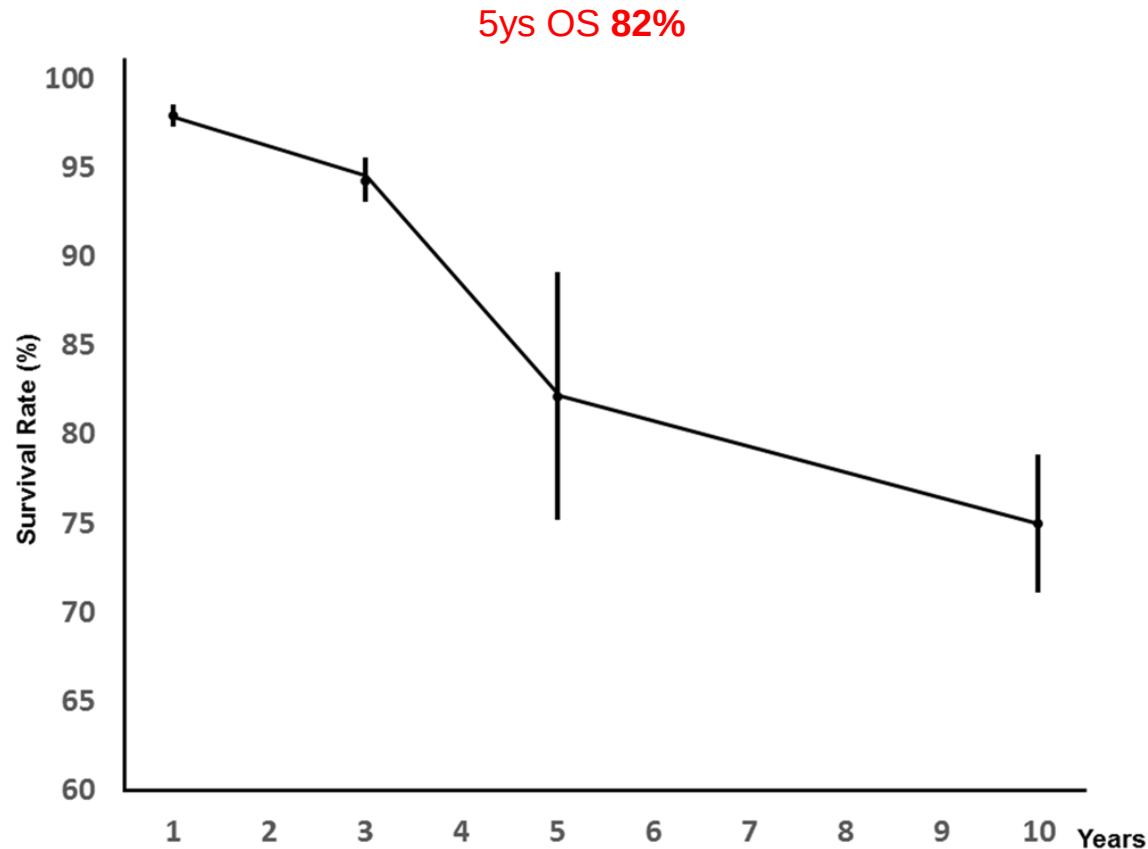


2016



2019

Sopravvivenza cardiomiopatia ipertrofica



Meta-analysis to assess pooled survival rates of patients with hypertrophic cardiomyopathy.

The pooled 1-, 3-, 5- and 10-year survival rates were 98.0%, 94.3%, 82.2% and 75.0%.

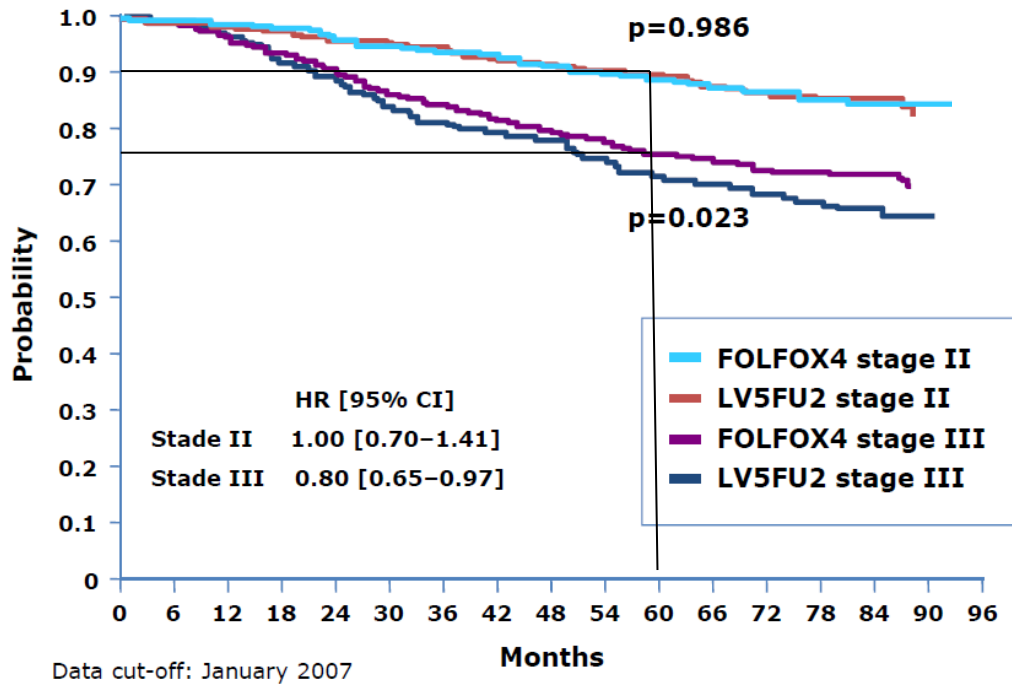
Sopravvivenza colon-retto Non metastatico

Stadio II

5ys OS **90%**

Stadio III

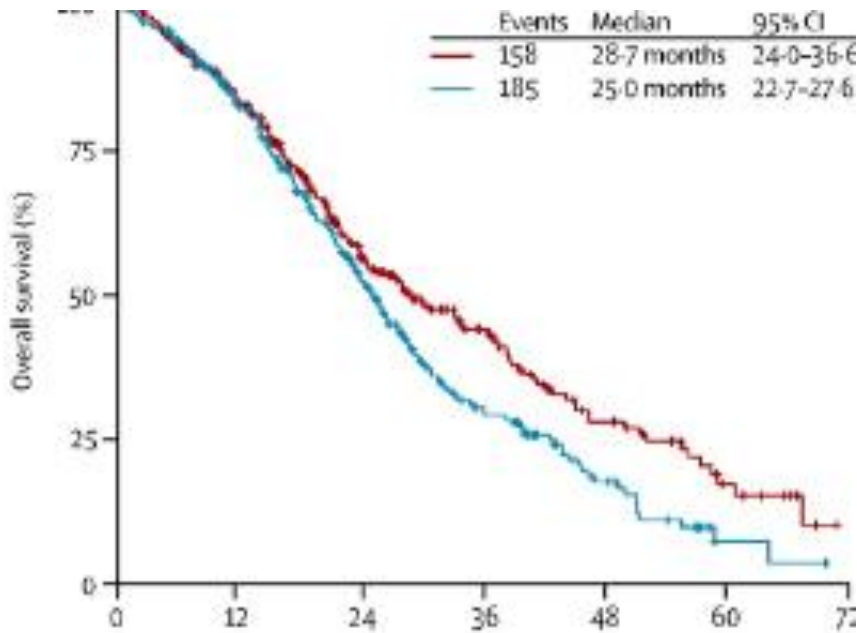
5ys OS **75%**



Sopravvivenza colon-retto Metastatico

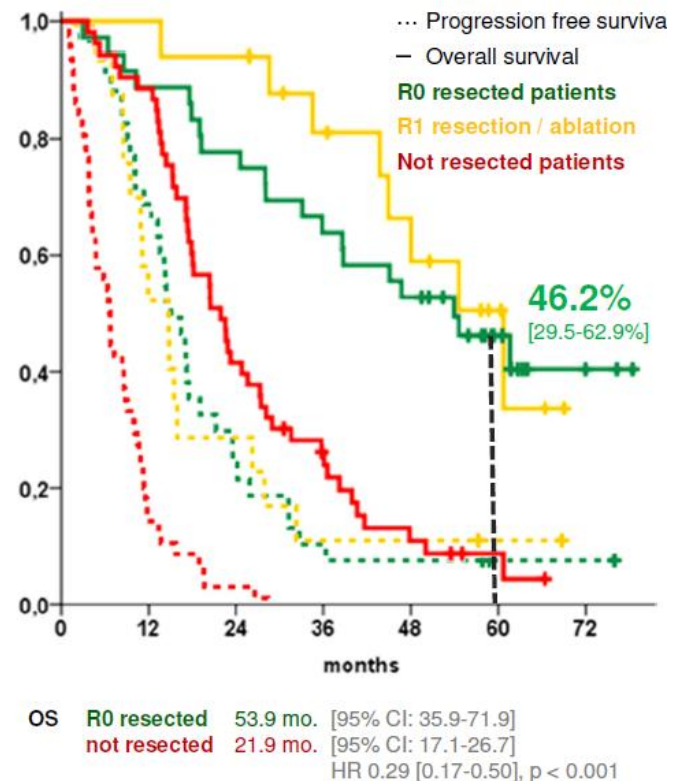
Metastasi non resecabili

5ys OS **25%**



Metastasi resecabili

5ys OS **45%**



Sopravvivenza stroke e emorragia cerebrale

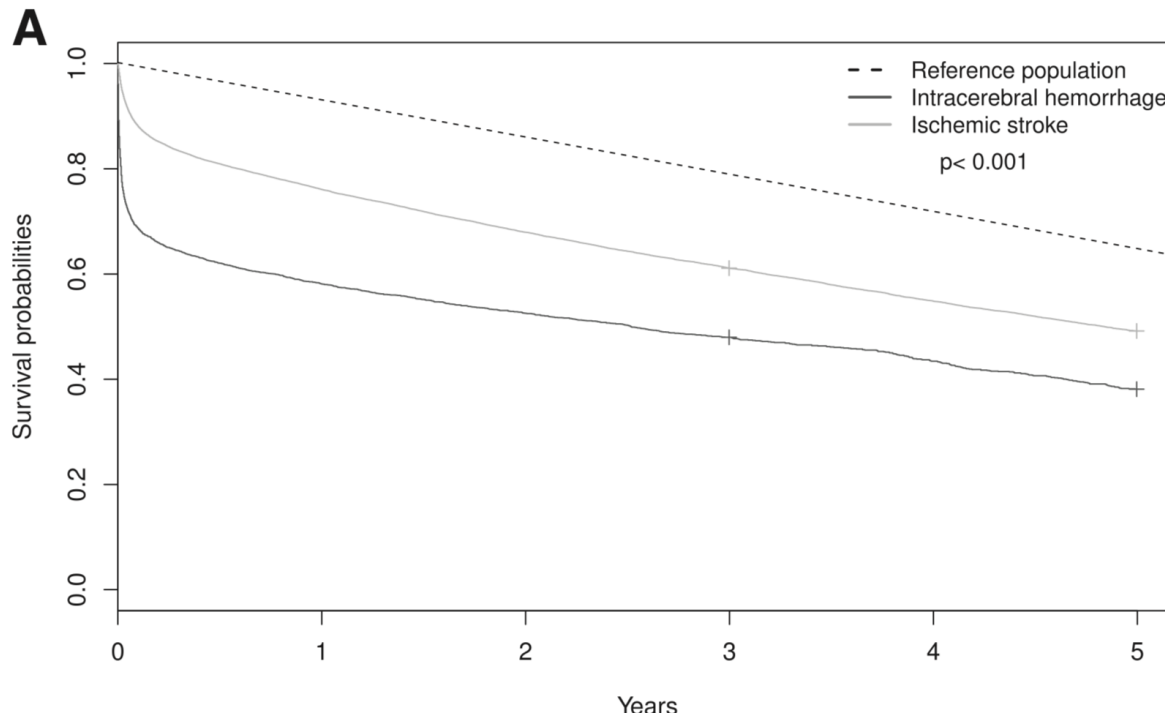
Recent survival and functional outcome data on ischemic stroke and intracerebral hemorrhage for up to 5 years poststroke from the Swedish Stroke Register (Riksstroke).

Emorragia

5ys OS **38%**

Stroke

5ys OS **50%**



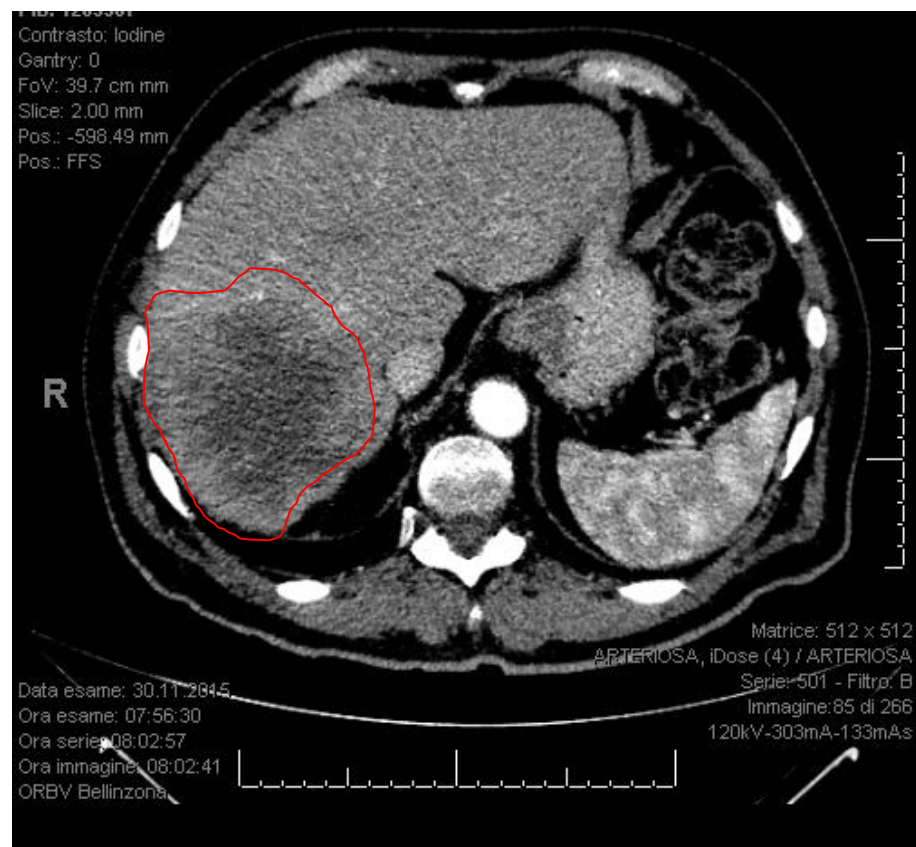
Colon metastatico



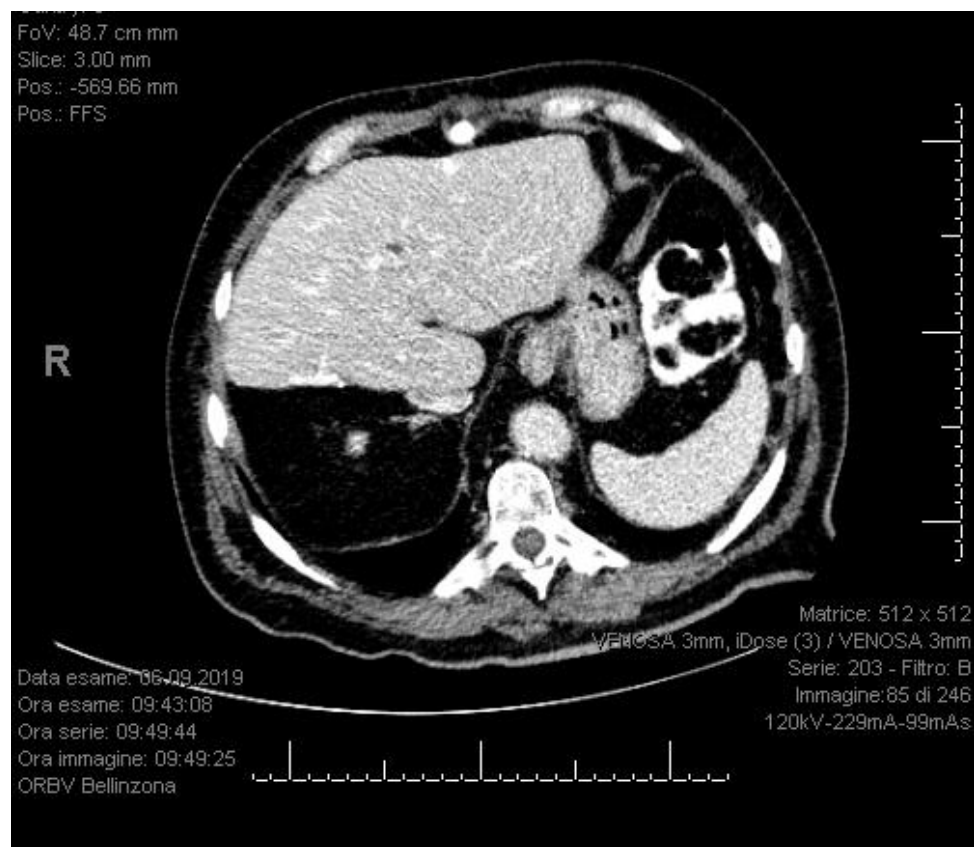
73 anni

Chirurgia e chemioterapia

Controllo di malattia 5 anni



2015

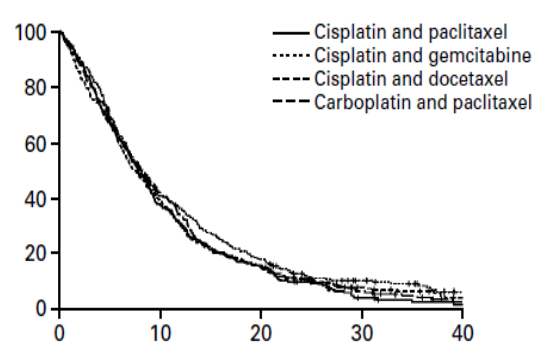


2019

Sopravvivenza tumore polmonare Metastatico

Dati storici

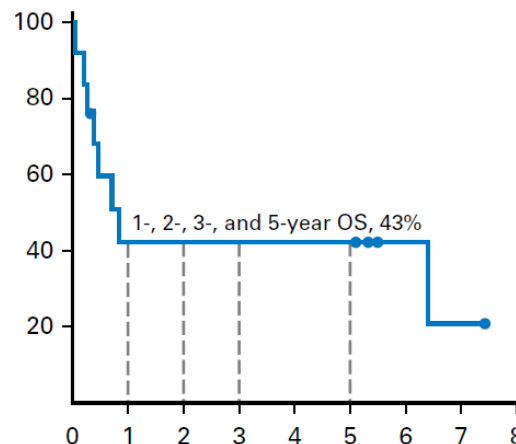
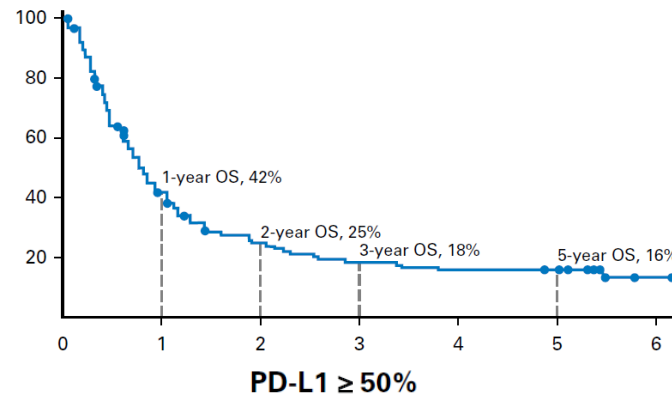
5ys OS 0%



Immunoterapia

5 ys OS 16%

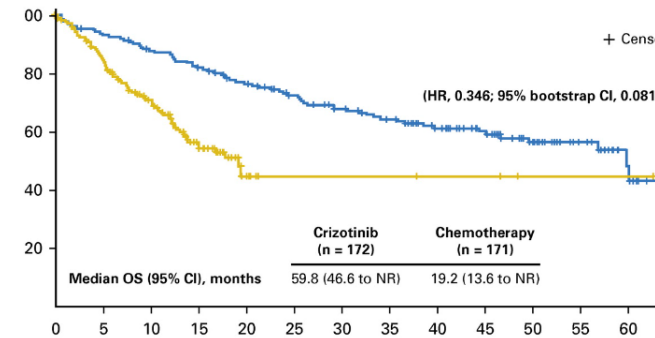
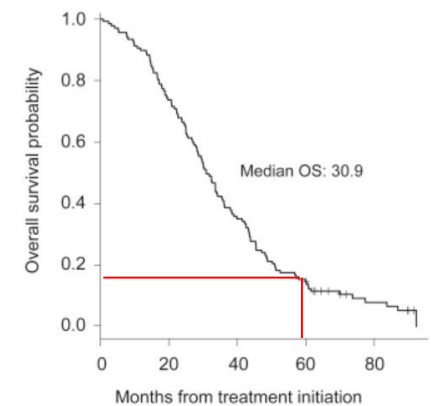
PD-L1>50% 5 ys OS **43%**



Terapie target

EGFR 5 ys OS 18%

ALK 5 ys OS **50%**



Sopravvivenza patologie polmonari

BPCO

5ys OS 65%

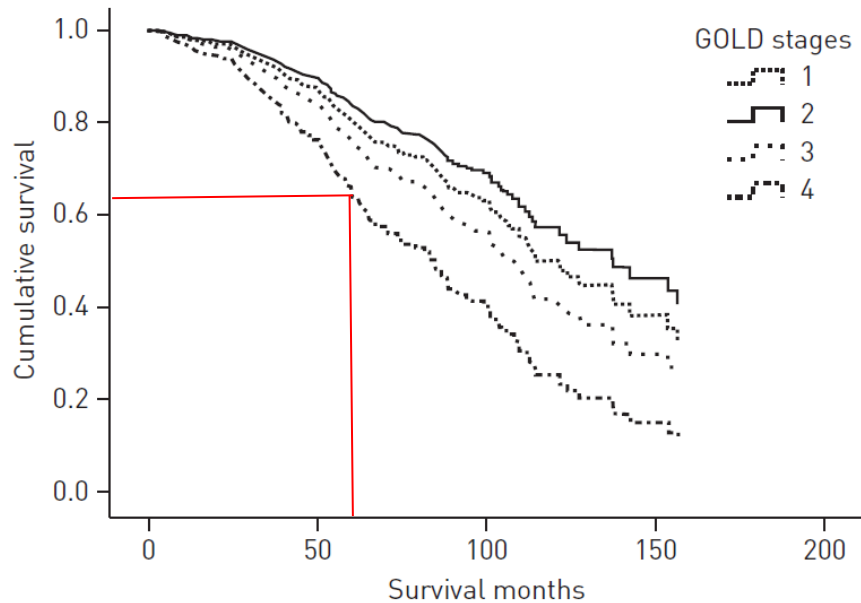


FIGURE 2 The Kaplan–Meier survival curves, adjusted for age, arterial oxygen partial pressure, carbon monoxide transfer factor % pred quartiles, forced vital capacity (FVC) % pred, forced expiratory volume in 1 s to FVC ratio, total lung capacity (TLC) % pred, functional residual capacity % pred, inspiratory capacity to TLC ratio, residual volume % pred, body mass index and arterial carbon dioxide partial pressure for the four population groups, categorised by Global Initiative for Chronic Obstructive Lung Disease (GOLD) stages. Survival only differed significantly between GOLD stage II and IV ($p=0.04$).

Fibrosi polmonare idiopatica

5 ys OS 35%

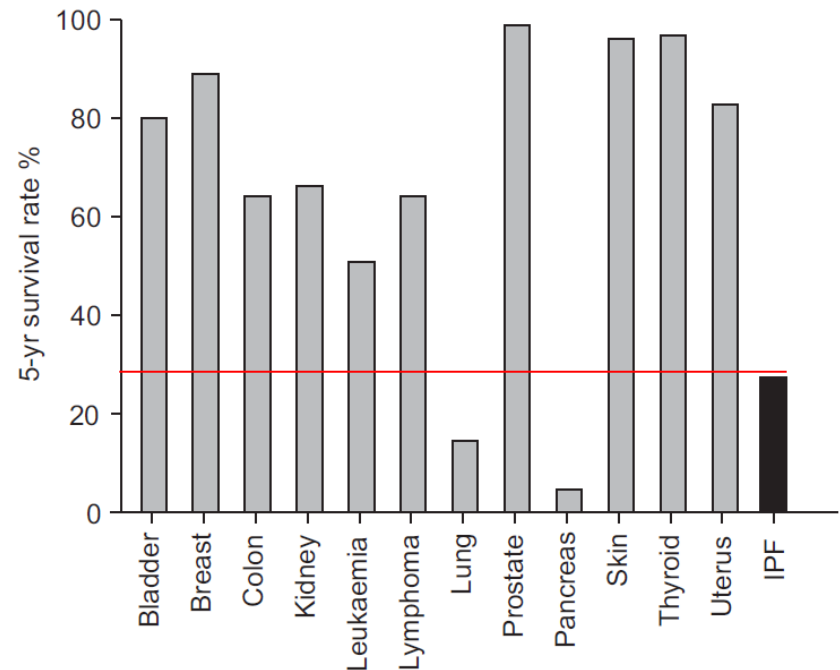


FIGURE 2. Comparison of the 5-yr survival rate for idiopathic pulmonary fibrosis (IPF) and different forms of cancer [14]. Statistics for cancer are from the US National Cancer Institute [15].

Polmone metastatico

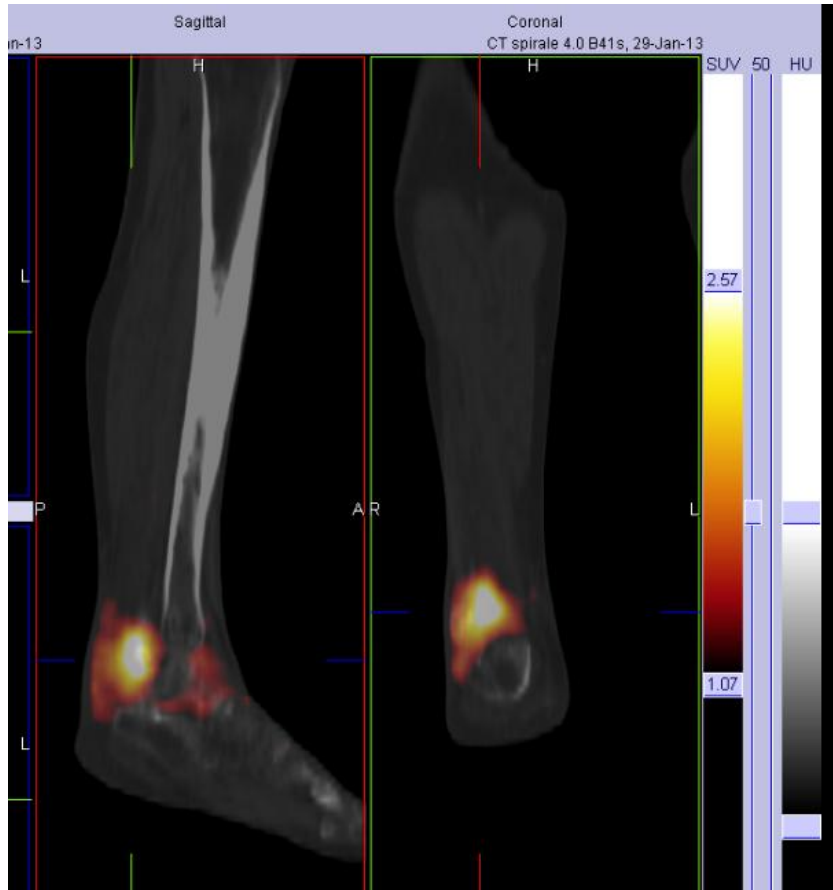


60 anni

Chemio e immunoterapia

Chirurgia e radioterapia

Controllo di malattia a 6 anni



2013



2019

Sopravvivenza tumore renale

Terapie target

5ys OS 40%

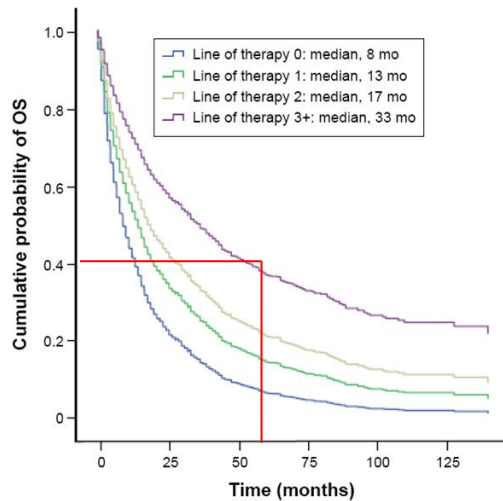
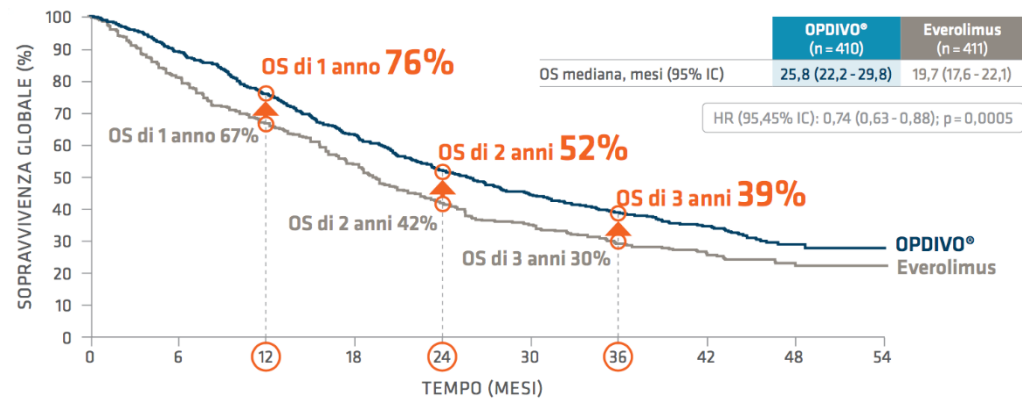


Figure S3 Kaplan-Meier estimates of OS in Norwegian patients diagnosed with mRCC by line of therapy.
Abbreviations: mo, months; mRCC, metastatic renal cell carcinoma; OS, overall survival.

Immunoterapia

3ys OS 39%

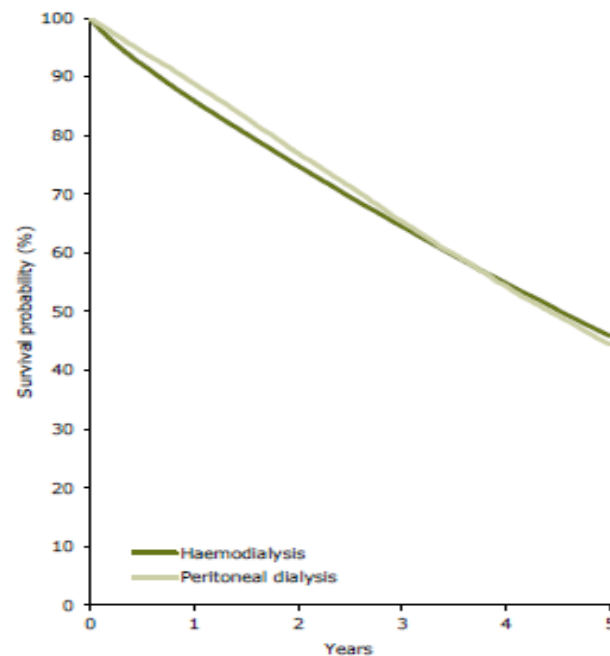


Sopravvivenza pazienti in dialisi

Dialisi

5ys OS 40%

Figure B.6.2
Adjusted patient survival by modality:
Incident dialysis patients
from day 91, adjusted for age, sex, and primary renal disease





78 anni

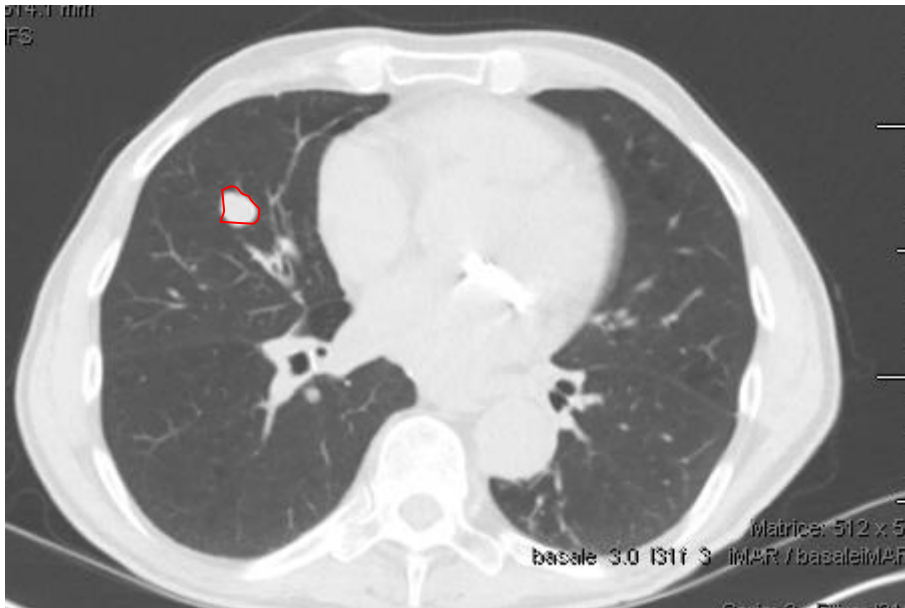
Terapia a bersaglio molecolare
sospesa per tossicità

Stabilità da un anno

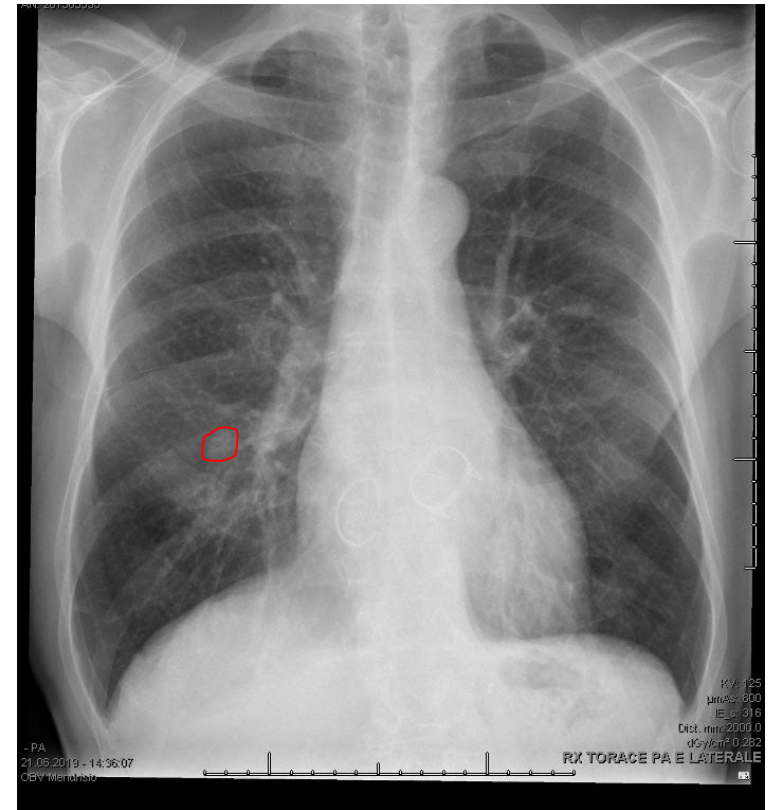
Rene metastatico

Carcinoma del rene sinistro, 2009.

Metastasi polmonari e linfonodali
mediastiniche nel 2018.



2018



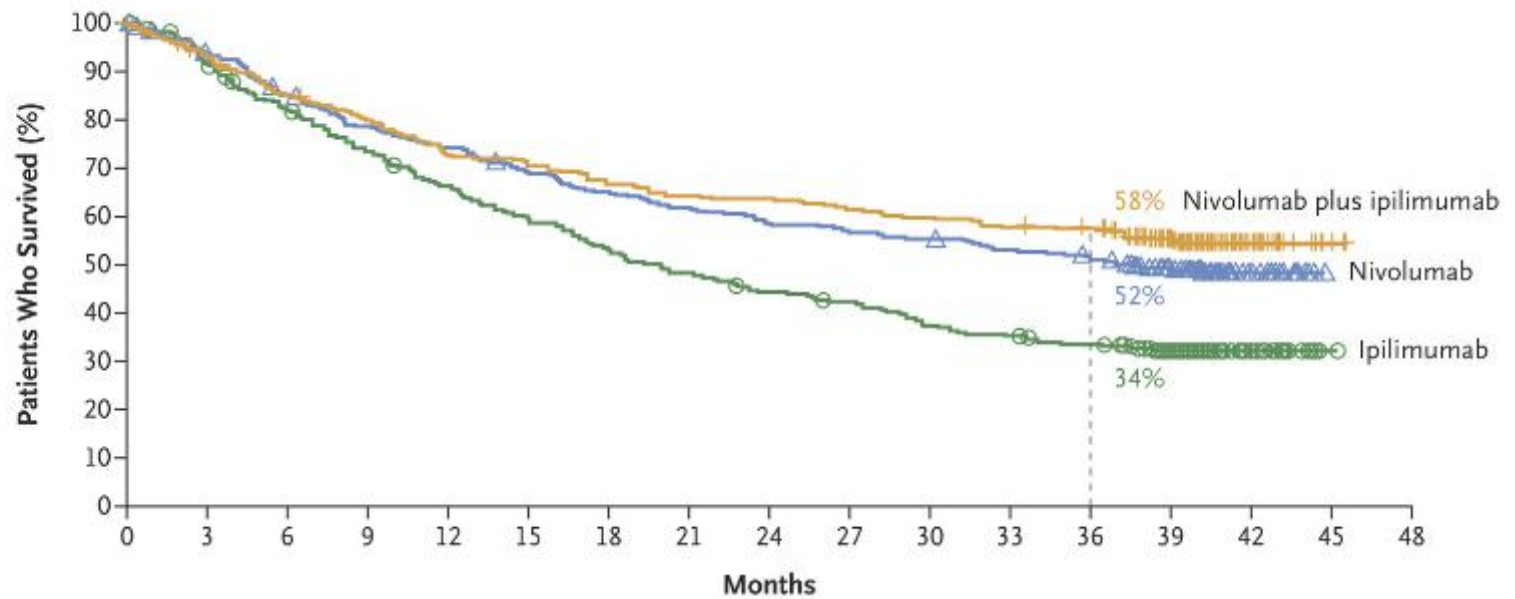
2019

Sopravvivenza melanoma Metastatico

Doppia immunoterapia

3ys OS **58%**

Overall Survival



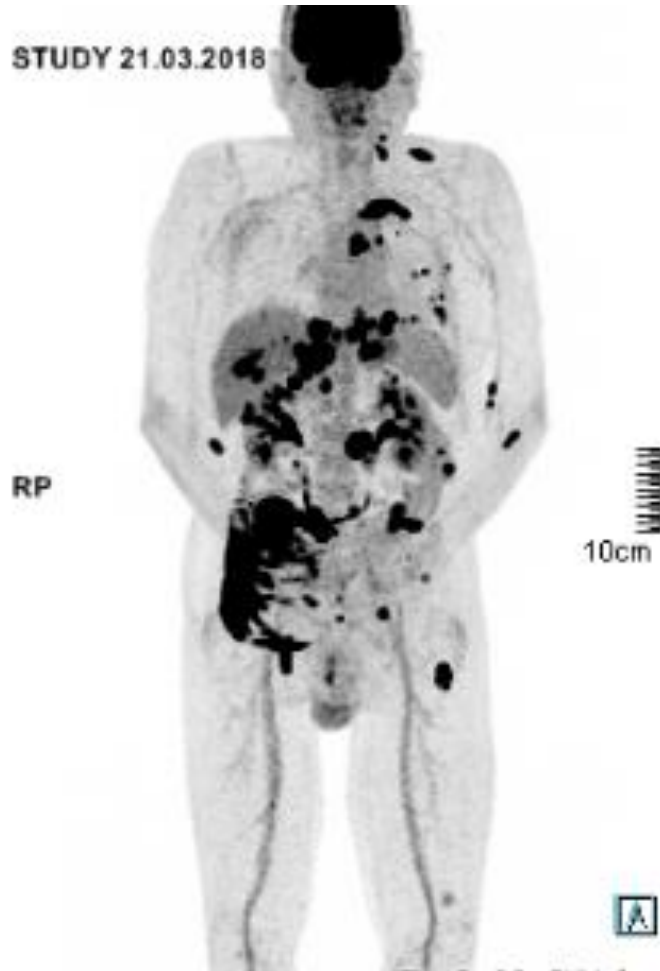
Melanoma metastatico



76 anni

Immunoterapia

Remissione completa a 1.5 anni



2018

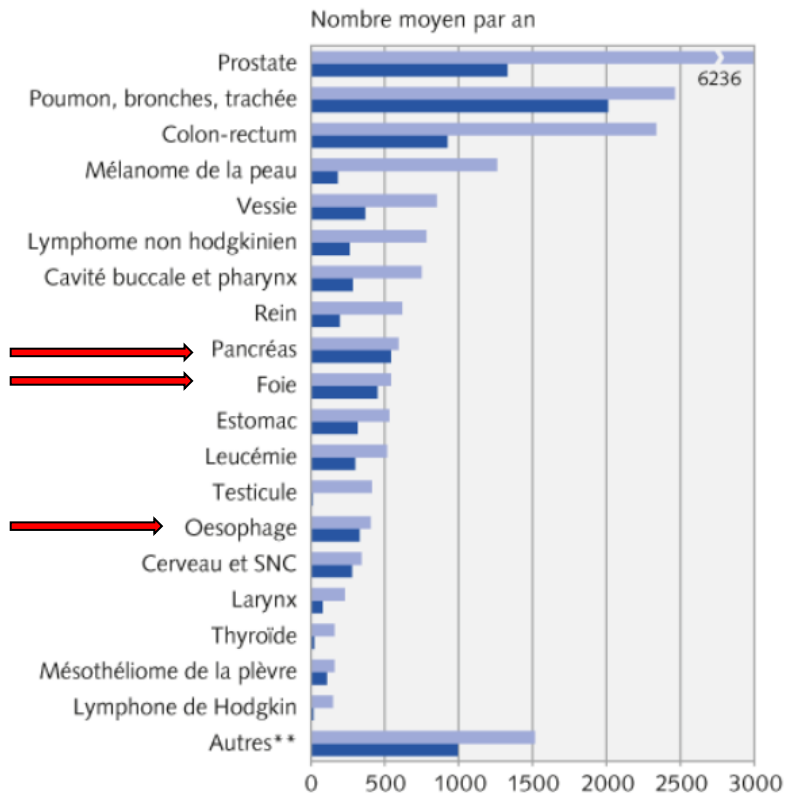


2019

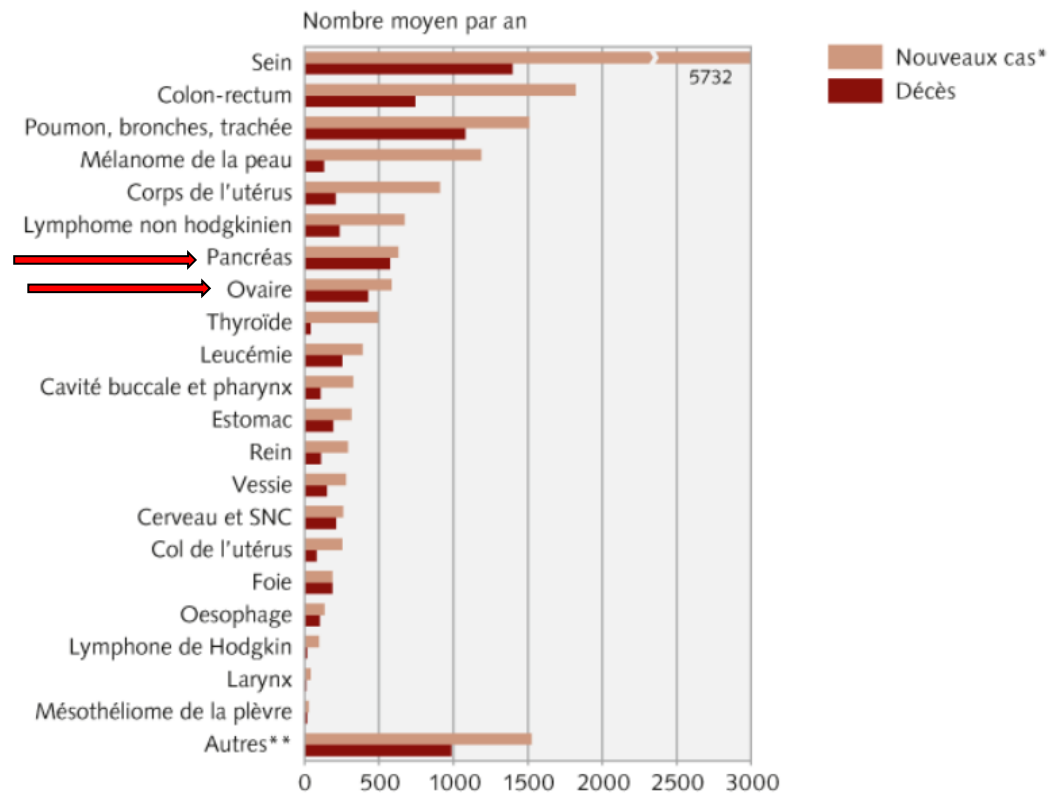
non vorreste essere anche voi Chales Bukowski?
so anche dipingere. sollevare pesi. e la mia bambina
pensa che io sia Dio.
poi, altre volte, non va così bene.

Sopravvivenza tumori aggressivi

Nouveaux cas et décès chez les hommes selon la localisation cancéreuse, 2008–2012



Nouveaux cas et décès chez les femmes selon la localisation cancéreuse, 2008–2012



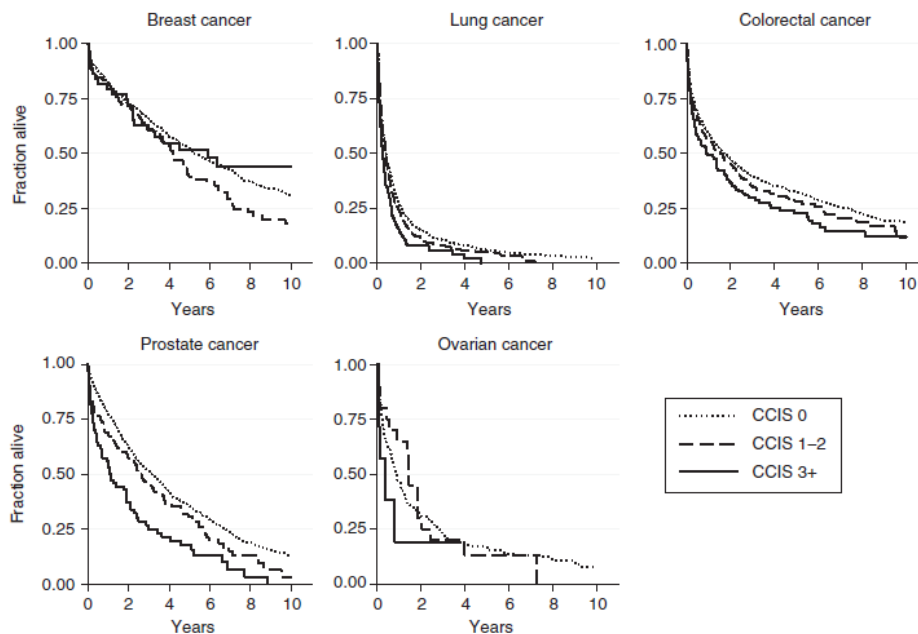
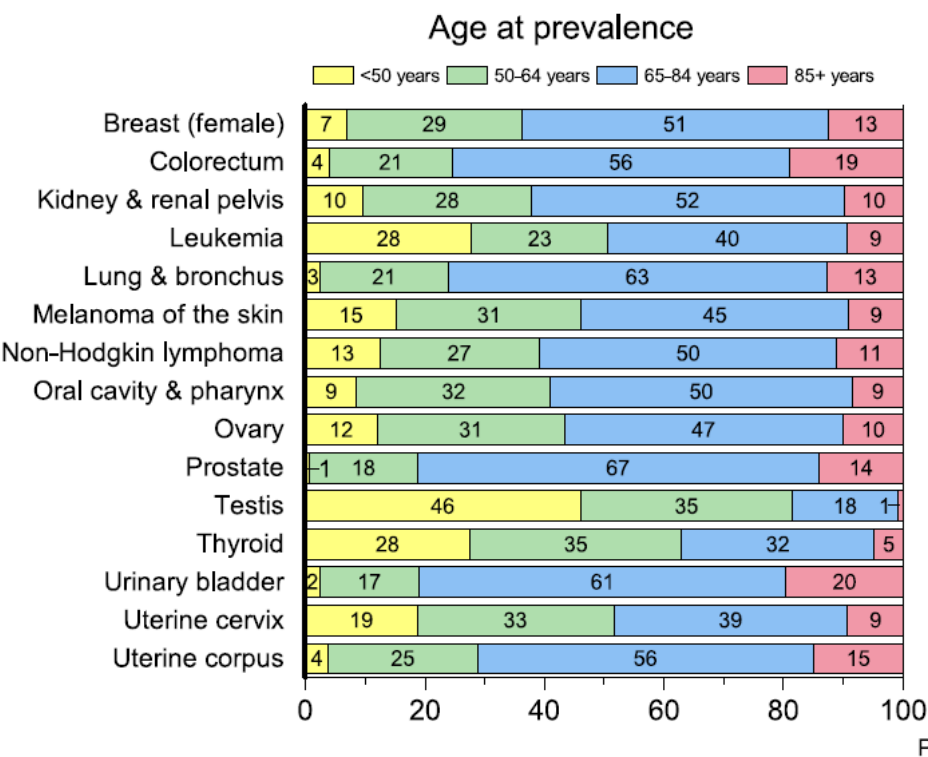
Sopravvivenza pazienti anziani

Circa il 70% dei nostri pazienti ha > 65 anni

Probabilità di sviluppare un tumore > 70 anni

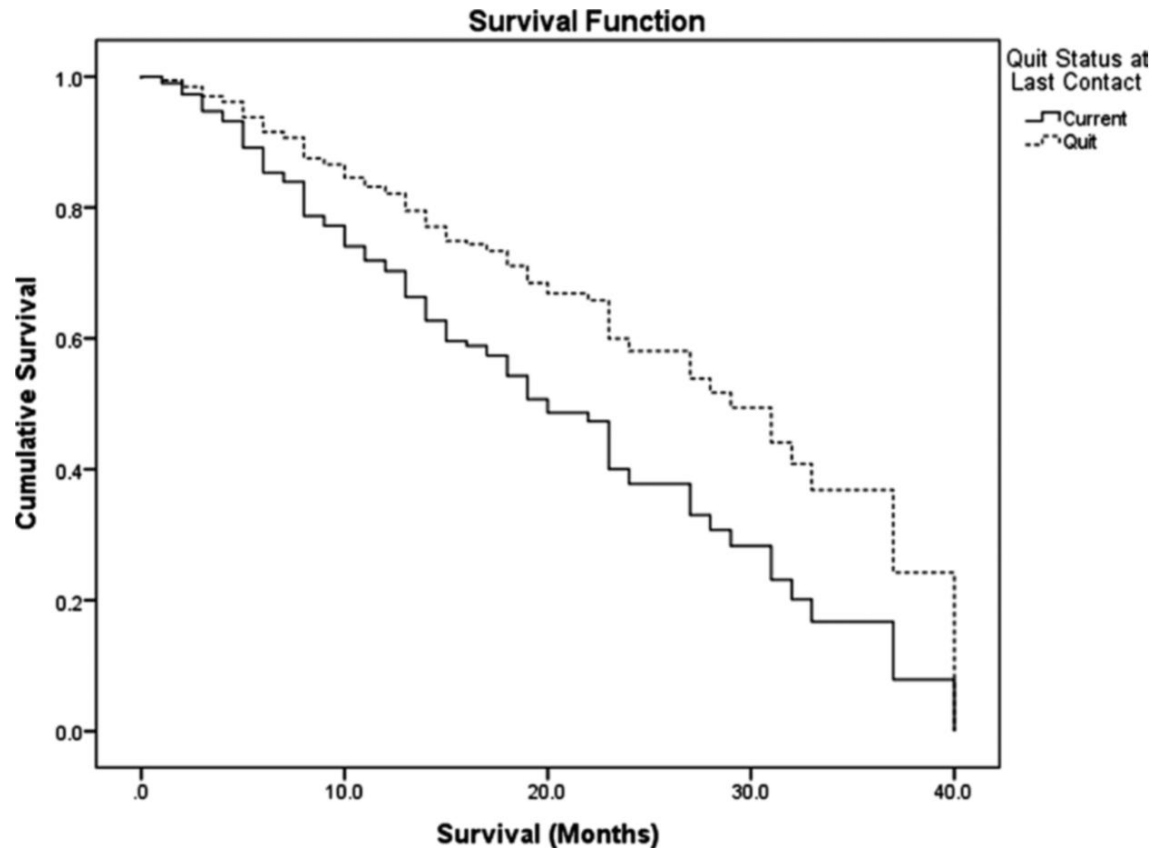
1 su 3 per gli uomini

1 su 4 per le donne



Sopravvivenza e fattori di rischio

Tumore polmonare e tabagismo



Median survival for current users at last contact was 20 months and 29 months for those who were quit at last contact.

Sopravvivenza e performance status

The Palliative Performance Scale (PPS)

Medical Care of the Dying, 4th ed.; p. 120. ©Victoria Hospice Society, 2005

Level	Ambulation	Activity & Evidence of Disease	Self-Care	Intake	Conscious Level
100%	Full	Normal activity & work. No evidence of disease	Full	Normal	Full
90%	Full	Normal activity & work. Some evidence of disease	Full	Normal	Full
80%	Full	Normal activity with Effort. Some evidence of disease	Full	Normal or reduced	Full
70%	Reduced	Unable Normal Job/Work. Significant disease	Full	Normal or reduced	Full
60%	Reduced	Unable hobby/house work. Significant disease	Occasional assistance necessary	Normal or reduced	Full or Confusion
50%	Mainly Sit/Lie	Unable to do any work. Extensive disease	Considerable assistance required	Normal or reduced	Full or Confusion
40%	Mainly in Bed	Unable to do most activity. Extensive disease	Mainly assistance	Normal or reduced	Full or Drowsy +/- Confusion
30%	Totally Bed Bound	Unable to do any activity. Extensive disease	Total Care	Normal or reduced	Full or Drowsy +/- Confusion
20%	Totally Bed Bound	Unable to do any activity. Extensive disease	Total Care	Minimal to sips	Full or Drowsy +/- Confusion
10%	Totally Bed Bound	Unable to do any activity. Extensive disease	Total Care	Mouth care only	Drowsy or Coma +/- Confusion
0%	Death	-	-	-	-

PPS Score	Average Survival in Hospice
50%	13.9 days
40%	10.3 days
30%	6.7 days
20%	2.6 days
10%	1.9 days

Palliative performance scale and survival among outpatients with advanced cancer

PPS pts OS (days)

40	38	28
50	116	71
60	208	104
70	251	173
80	109	197
90	22	226
Total	744	

Costi delle nuove cure



Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Dipartimento federale dell'interno DFI
Ufficio federale della sanità pubblica UFSP

[Home](#) > Präparatsuche nach Name

Präparate

↑ Suche ausblenden...

Suchkriterium	Suchtext
Präparat-Name	opdivo
Suchen Reset	

↑ Liste ausblenden...

	Präparat	Galen. Form / Dosierung	Packung	FAP	PP S
1.	Opdivo	conc perf 40 mg/4ml	flac 4 ml	580.45	682.75
2.	Opdivo	conc perf 100 mg/10ml	flac 10 ml	1451.14	1653.05
3.	Opdivo	conc perf 240 mg/24ml	flac 24 ml	3134.43	3458.80

Opdivo (BMS)

Dose fissa 240 mg

3134 .- costo fiala

Ogni 2 settimane

Worldwide total revenues of leading pharmaceutical companies in 2014 (in billion dollars)

Company	Total revenue (\$)	R&D costs (\$)	Sales and Marketing costs (\$)	Other activities costs* (\$)	Profit (\$)	Profit Margin (%)
1. Johnson & Johnson	71.3	8.2	17.5	31.8	13.8	19
2. Novartis	58.8	9.9	14.6	25.1	9.2	16
3. Pfizer	51.8	7.5	13.5	21.8	8.0	15
4. Merck & Co.	48.2	6.5	12.5	20.2	7.0	14
5. Amgen	44.5	6.0	11.5	19.0	6.0	13
6. Eli Lilly	41.4	5.3	9.9	17.7	8.5	21
7. GSK	41.4	5.3	9.9	17.7	8.5	21
8. AstraZeneca	25.7	4.3	7.3	11.5	2.6	10
9. AbbVie	23.1	5.5	5.7	7.2	4.7	20
10. Bristol-Myers Squibb	18.8	2.9	4.3	7.5	4.1	22
Total Top 10 global companies	429.4	65.8	98.3	175.5	89.8	20.9
Percentage of total revenue – profit		(19%)	(29%)	(52%)		

Pharma highest profit: 20%, followed by banks 10%

→ Studi costo-beneficio

Take home messages

- La sopravvivenza dei pazienti con tumore è migliorata
- Alcuni tumori vanno considerati come le malattie croniche
- Altri rimangono malattie a prognosi cattiva

→ Importanza delle scelte condivise

Grazie per l'attenzione