International CME webinar

GOOD PRACTICES FOR IMPROVING THE EFFICIENCY OF CANCER TREATMENT IN EUROPE

Pierfranco Conte
Coordinator, Rete Oncologica Veneta
Chairman, Fondazione Periplo

From Clinical Trials to Real World Evidence: the role of Veneto Oncology Network

Scientific Coordination: euregha

Under the auspices of: ARESS Puglia

Provider and Organisation: SANITANOVA matching your needs

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PierFranco Conte

Disclosure of potential conflicts of interests

- Consultant:
  Novartis, EliLilly, Astra Zeneca, Tesaro, Daiichi-Sankyo, Gilead, Reveal Genomics
- Honoraria:
  BMS,Roche, EliLilly, Novartis, AstraZeneca
- Research Funding from profit organizations:
  Novartis, Roche, EliLilly, BMS, Merck-KGa
- Funding from non profit organizations:
  National Research Council, Ministry of Education and Research, Italian Association for Cancer Research, Italian Drug Agency (AIFA), EmiliaRomagna Secretary of Health, Veneto Secretary of Health, University of Padova, Ministry of Health
- Founder & Chairman:
  Periplo Foundation

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From Clinical Trials to Real World Evidence: Role of Cancer Networks

- Efficacy vs Effectiveness
- Pathway-related and procedure-related outcomes
- A paradigm change:
  from histology to biomarker, from efficacy to effectiveness

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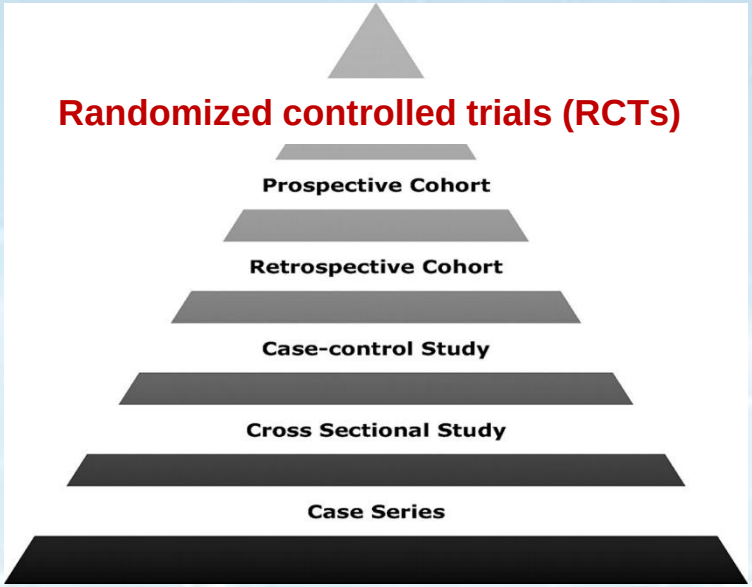
Evidence-based Medicine vs Real World Evidence

EBM



Randomized clinical trials are the backbone of an application for marketing authorization. However they operate in an idealised experimental environment (estimate of efficacy rather than a true measure of effectiveness):

- may lack external validity
- include selected patients (~2-4% of cancer patients participate in clinical trials):
  - not entirely representative of real-life population: elderly, poor PS patients or those with comorbidities are under-represented or excluded from clinical trials
  - differences in ethnic/racial composition
  - lacking data on budget impact

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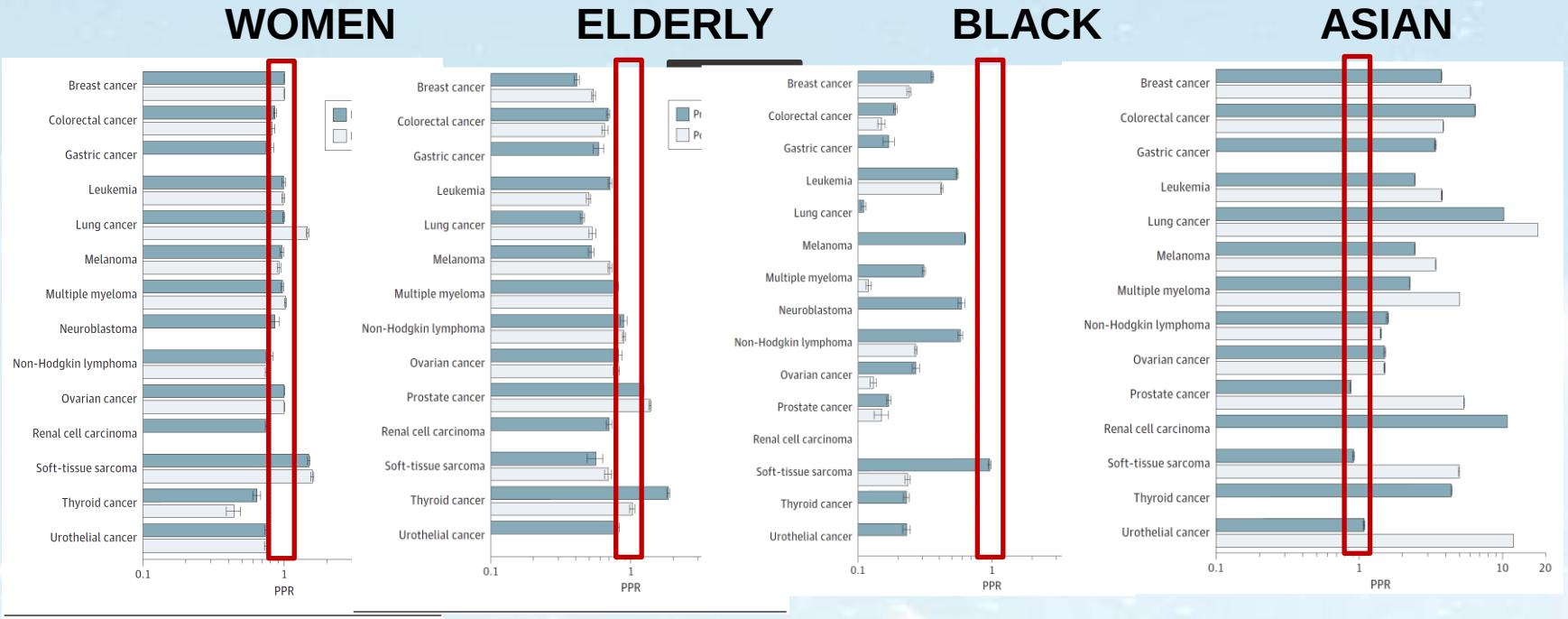
JAMA Network Open. April 20, 2021

JAMA Network Open. 2021;4(4):e217063. doi:10.1001/jamanetworkopen.2021.7063



The PPR is calculated by dividing the proportion of study patients in the subgroup by the proportion of US cancer patients who are in the subgroup

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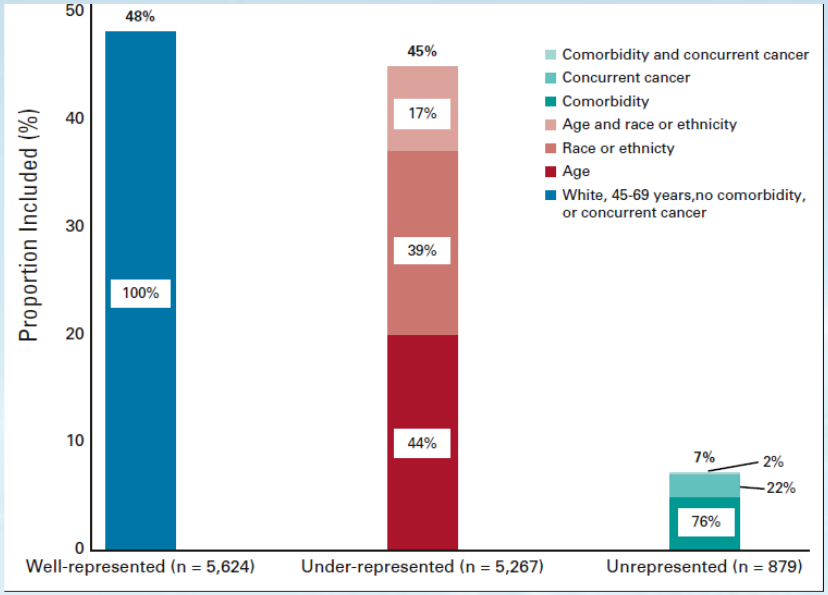
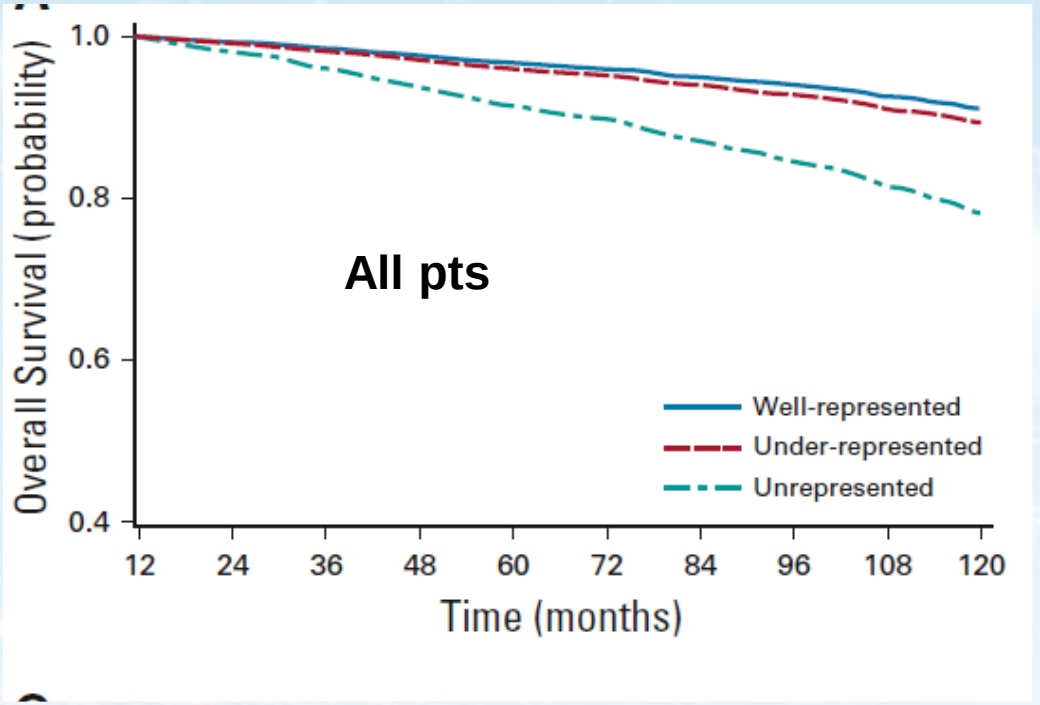
Survival of eBC in Real World: CancerLinQ Discovery 2005-2015





R Gidwani et al, JCO Oncol Pract 2021

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The Oncologist®
Commentary

Real-World Evidence in Oncology: Opportunities and Limitations

Massimo Di Maio.[a] Francesco Perrone.[b] Pierfranco Conte[c]

Trial patient

Real life patient

Large proportion of new treatments only show a globally modest efficacy within RCTs

↓

Effect in clinical practice might be further diluted

↓

Real value of results may fall under an acceptable threshold of relevance

↓

Post marketing studies could be useful to **confirm or refute the drug's benefit** on survival in real-world populations

↓

RWE analysis may challenge the magnitude of the efficacy previously shown in RCTs

Di Maio, Perrone, Conte; The Oncologist *2020*

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The NEW ENGLAND JOURNAL of MEDICINE

SOUNDING BOARD

The Magic of Randomization versus the Myth of Real-World Evidence

Rory Collins, F.R.S., Louise Bowman, M.D., F.R.C.P., Martin Landray, Ph.D., F.R.C.P., and Richard Peto, F.R.S.

Observational studies cannot be trusted when the effect of treatment is moderate (i.e. less than a two-fold difference in the incidence of the health outcome).
Replacement of randomized trials with non randomized observational studies is a false solution to a serious problem.

Examples quoted:
«false effect» of statins and aspirin in the reduction of cancer incidence

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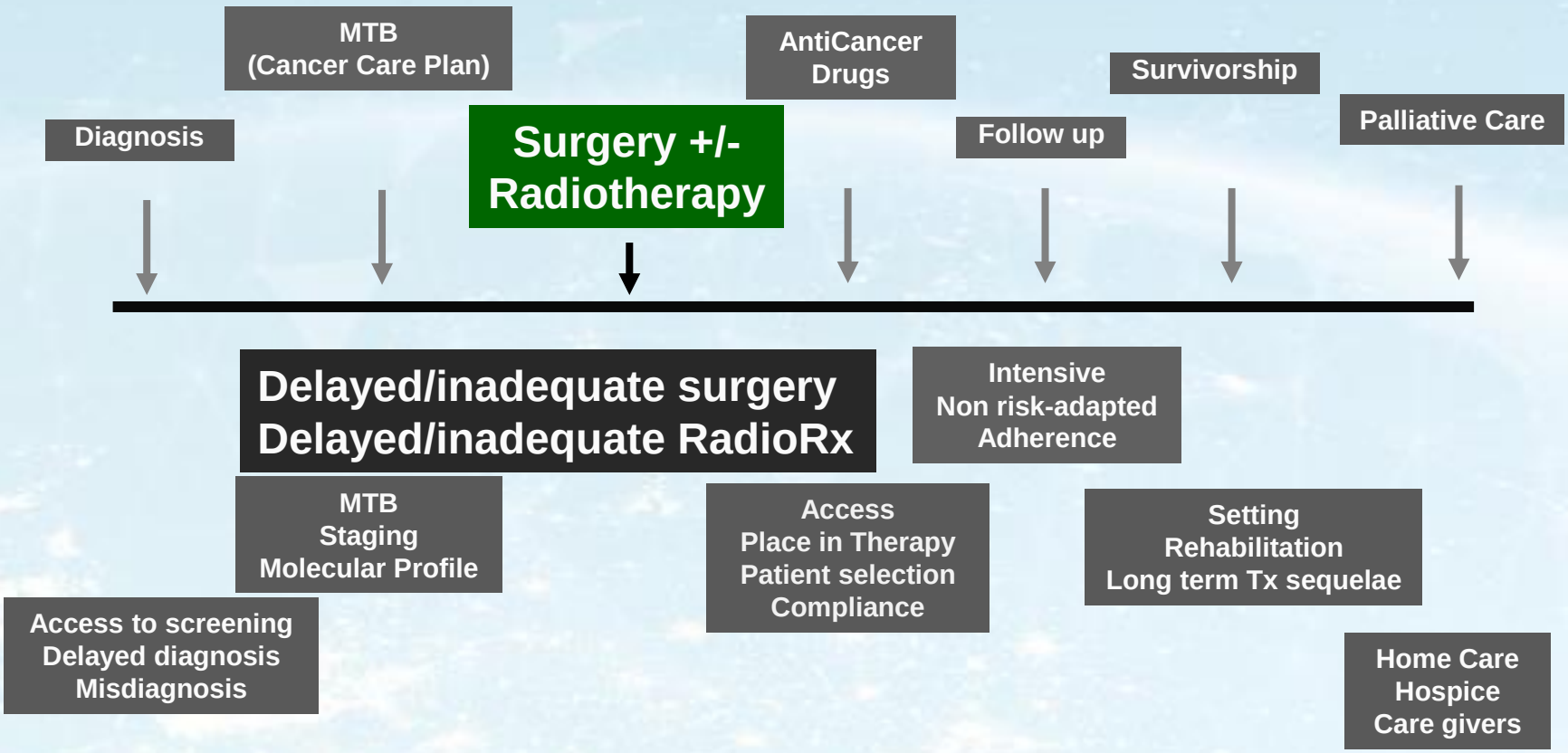
Patients' Journey in Oncology



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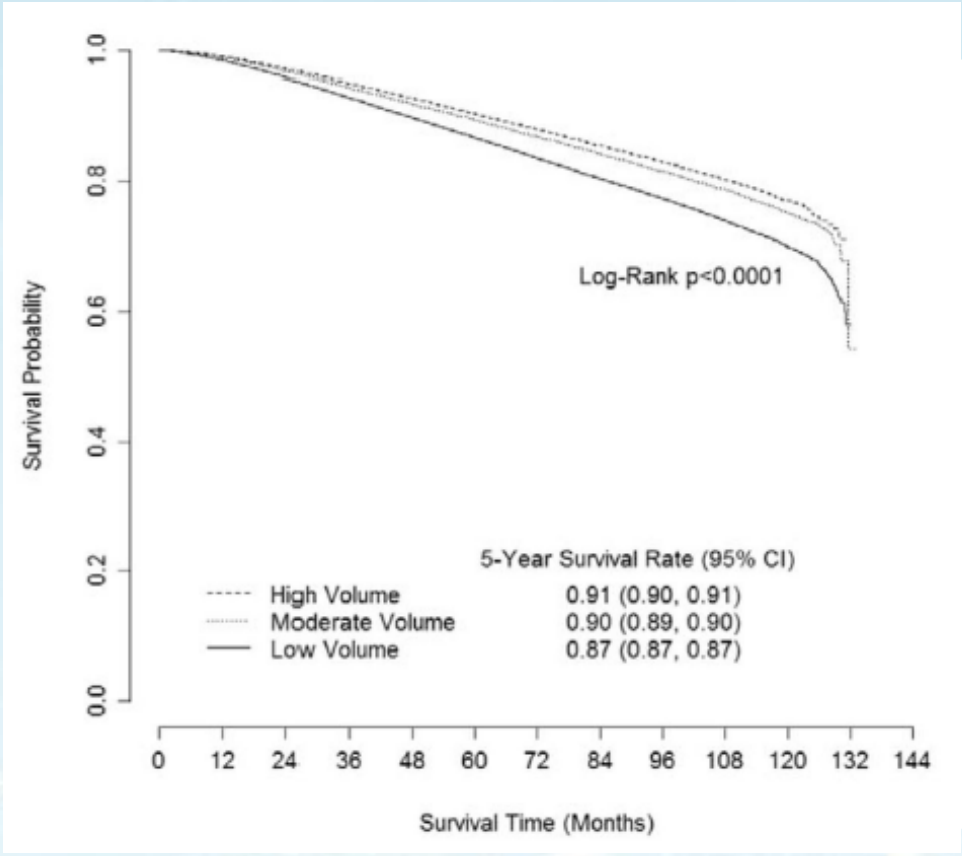
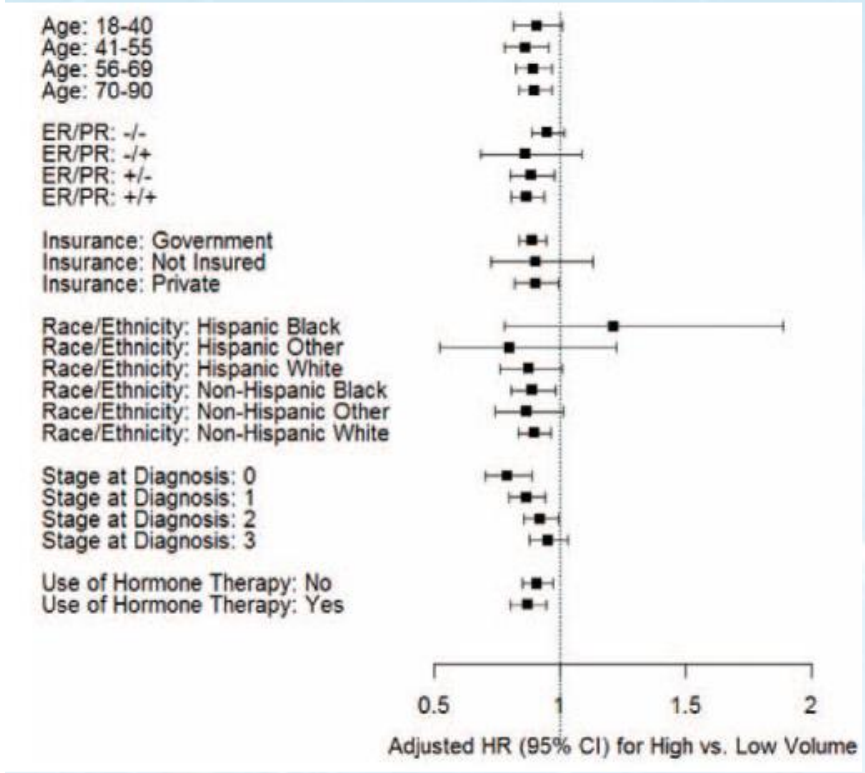
Patients' Journey in Oncology : Hospital volume & Breast Cancer Mortality

1,058,198 breast cancers in the NCDB treated in low (< 148 cases/yr), moderate (148-298 cases/yr) and high volume hospitals (> 298 cases/yr)





Greenup NA et al, Ann Surg 2018

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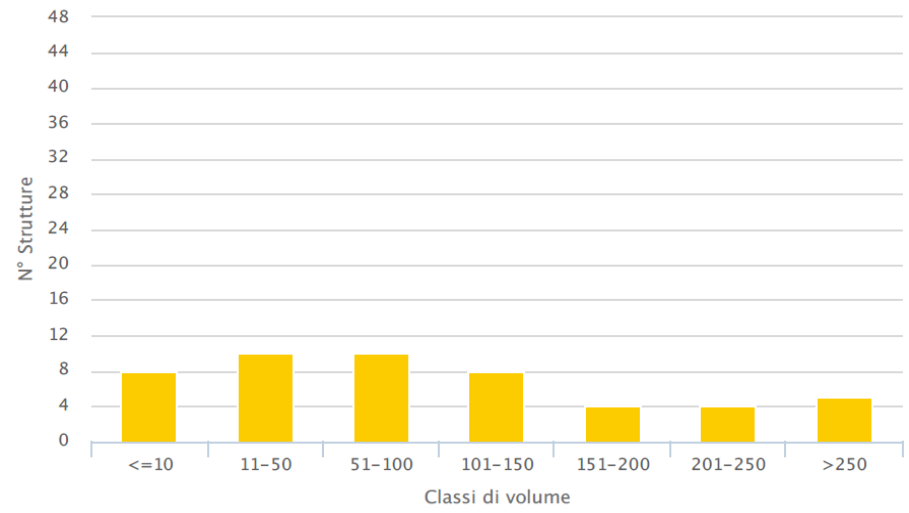
IL MODELLO ORGANIZZATIVO INTEGRATO

Prevenzione-diagnosi precoce- trattamento del carcinoma della mammella

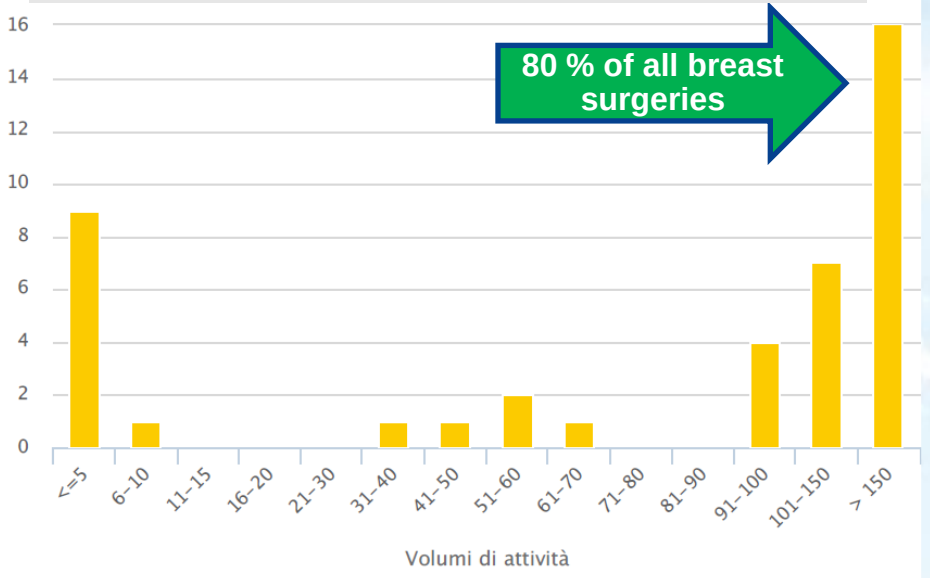
DGR n.1693/2017

21 centers (instead of 40) :
- **5 hub centers**
- **16 spoke centers**

Nb of breast surgeries/hospital - 2015



Nb of breast surgeries/hospital - 2019



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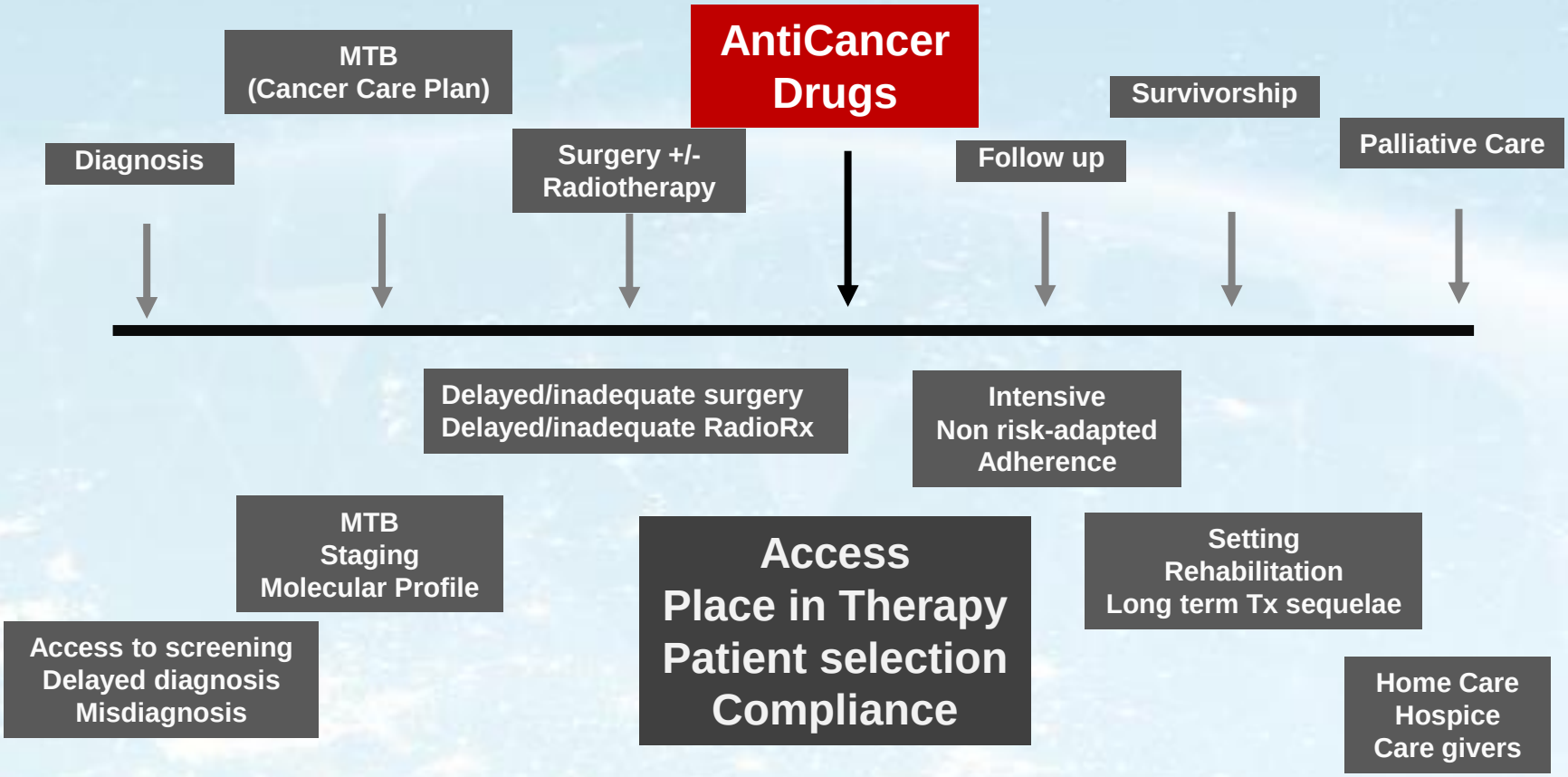
Patients' Journey in Oncology



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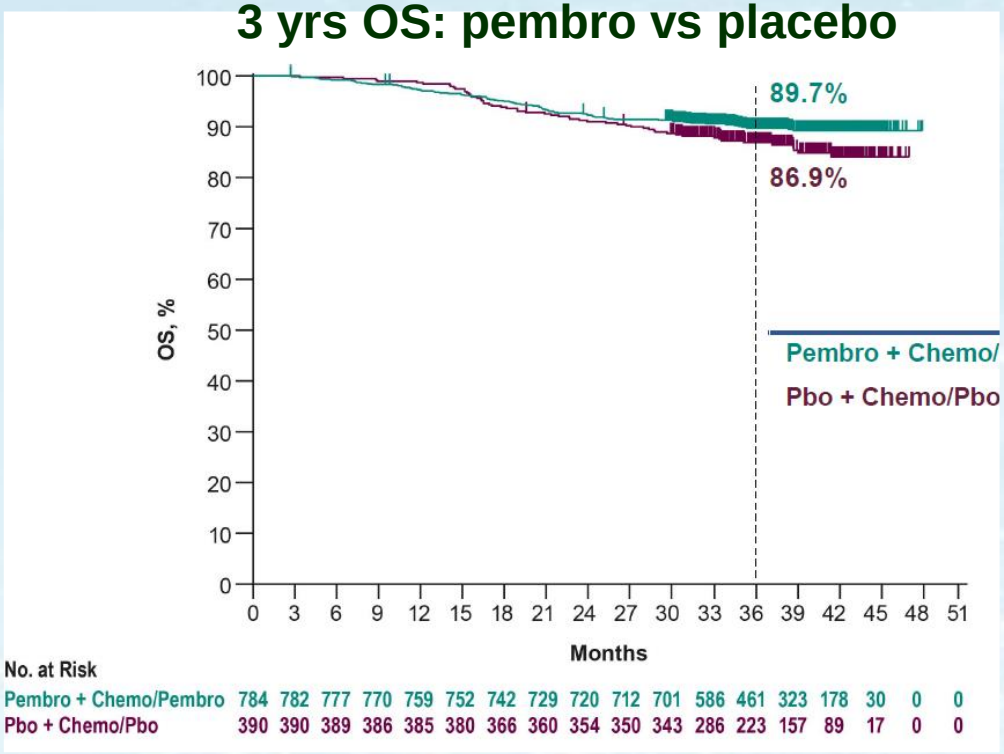
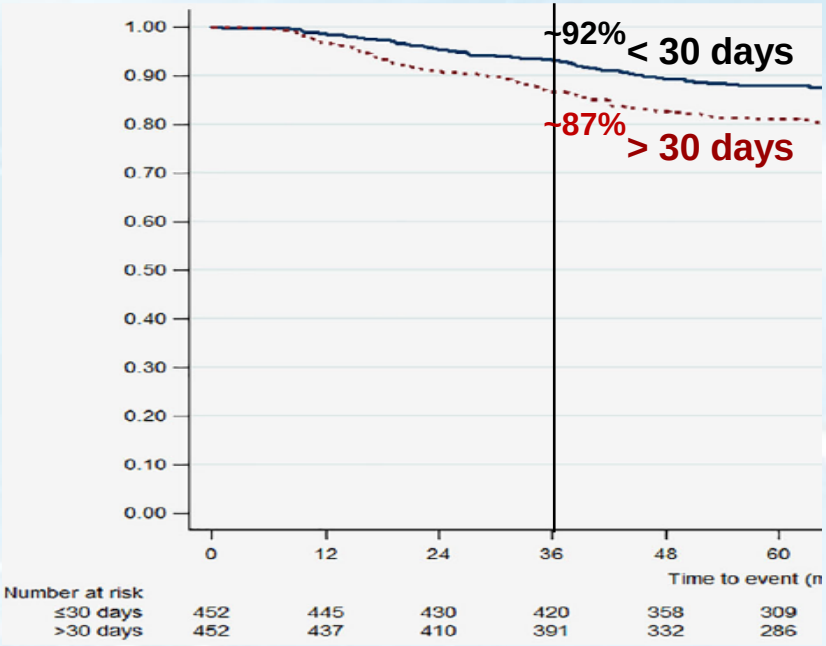
eTNBC: adjuvant treatments and outcome

Not to compare!
but to underline that not only drugs may impact on outcomes!

3 yrs OS: pembro vs placebo



3 yrs OS: time to chemo



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Patients' Journey in Oncology – Time to Treatment

Patients (%) who start adjuvant therapy within 8 weeks from definitive surgery

VENETO	LIGURIA	TOSCANA	PIEMONTE	UMBRIA	Benchmark
73.7 %	66.7 %	NA	71.8 %	69.9 %	≥ *80%*

No data available on chemotherapy and breast cancer subtypes

Guarneri V et al, JOP 2019

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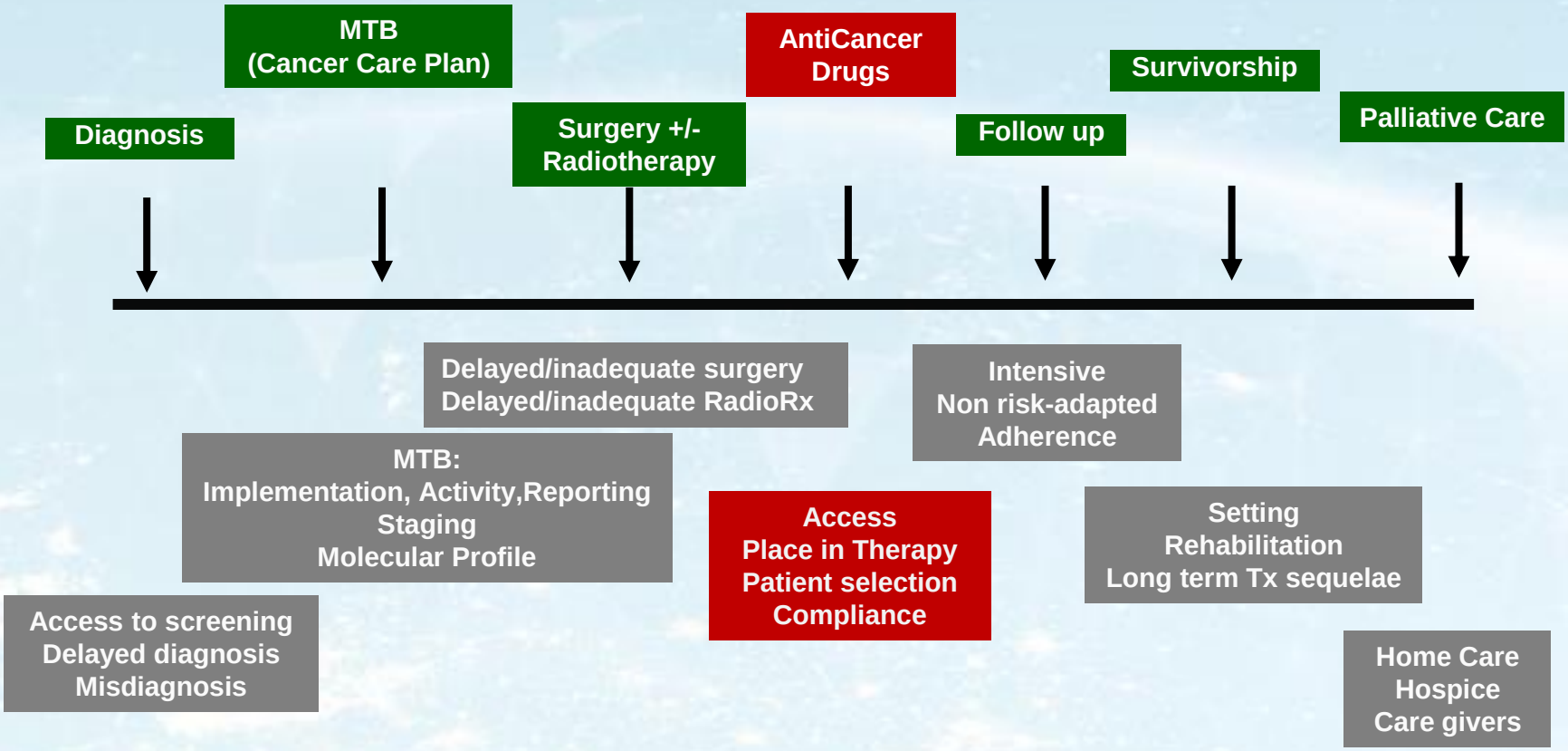
Patients' Journey in Oncology



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Thoracic Cancer
Open Access
Thoracic Cancer ISSN 1759-7706

ORIGINAL ARTICLE

Estimated direct costs of non-small cell lung cancer by stage at diagnosis and disease management phase: A whole-disease model

Alessandra Buja[1], Michele Rivera[1], Anna De Polo[1], Eugenio di Brino[6], Marco Marchetti[6], Manuela Scioni[2], Giulia Pasello[4], Alberto Bortolami[7], Vincenzo Rebba[3], Marco Schiavon[1], Fiorella Calabrese[1], Giovanni Mandoliti[5], Vincenzo Baldo[1] & PierFranco Conte[4,8]

Table 3 Estimates of average (and confidence interval) per-patient costs of care for NSCLC by disease stage (€) during the first year after diagnosis

	Average total costs	Cost ratio vs. stage I
Stage I	16 291 (95% CI: 15 284–17 505)	1
Stage II	19 530 (95% CI: 18 263–21 091)	1.19
Stage III	21 938 (95% CI: 20 271–25 252)	1.34
Stage IV	22 175 (95% CI: 22 127–22 190)	1.36
Pancoast	28 711 (95% CI: 27 711–29 890)	1.79
TOTAL	21 328 (95% CI: -20 897–22 322)	

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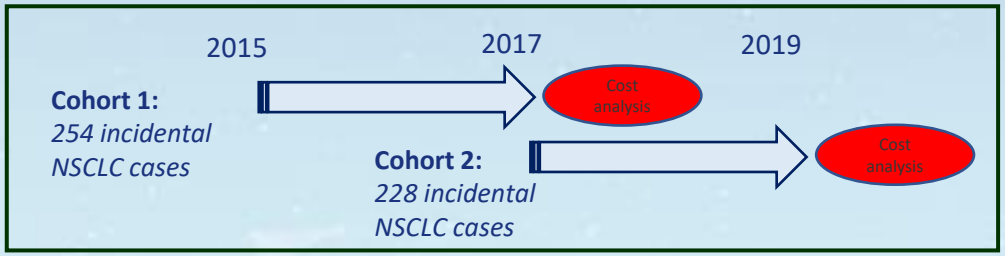
VALUE IN CANCER CARE ReCAP

Non–Small-Cell Lung Cancer: Real-World Cost Consequence Analysis

Alessandra Buja, MD, PhD[1]; Giulia Pasello, MD[2]; Giuseppe De Luca, MD[1]; Alberto Bortolami, PharmD[3]; Manuel Zorzi, MD[4]; Federico Rea, MD[1]; Carlo Pinato, MStat[3]; Antonella Dal Cin, BS[4]; Anna De Polo, MD[1]; Marco Schiavon, MD[1]; Andrea Zuin, MD[1]; Marco Marchetti, MD[4]; Giovanna Scroccaro, PharmD[5]; Vincenzo Baldo, MD[1]; Massimo Rugge, MD[4]; Valentina Guarneri, MD, PhD[2,6]; and PierFranco Conte, MD[2,6]; on behalf of Rete Oncologica Veneta



Regression models dependent variable	Coefficient 2017 (ref 2015)	95% CI	p-value
Hospitalization costs	343.9	383.7 ; 0.9	0.37
Outpatient visits costs	192.0	314.1 ; 0.6	0.541
Emergency room costs	39.8	27.6 ; 1.4	0.149
Hospice costs	-911.3	397.0 ; -2.3	0.022
Hospital delivered drugs costs	2976	1116.0 ; 2.7	0.008
Medical devices costs	522.6	371.9 ; 1.4	0.160
Other Drugs costs	-55.1	44.84; -1.2	0.219
Total costs	3006	1148.0 ; 2.6	0.009

- Total costs adjusted for age, stage at diagnosis, sex, cohort, at 2 yrs after cancer diagnosis
- significant **increase in the average costs** of patients in the 2017 cohort
- significant **decrease** in the average cost of **hospice care**
- significant **increase** in the average cost of **drugs**

The proportion of patients treated with targeted agents or ICPi increased by 523% for stage III and by 250% for stage IV disease.

Buja A et al, JOP 2021

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Non-Small Cell Lung Cancer: Real-world cost consequence analysis

Mean per-patient total cost and overall survival two years after diagnosis

2015					2017						
Disease stage at diagnosis	N°	Survival at two years (N° deaths)	Mean total cost at two years	Average cost ratio compared to Stage I	N°	Survival at two years (N° deaths)	Mean total cost at two years	Average cost ratio compared to Stage I	Difference in mean cost (2017-2015)	Difference in survival (2017-2015)	Log-rank test P-value
I	24 (9,45 %)	100% (0)	23.642,61 €	1	17 (7,46 %)	100% (0)	28.799,27 €	1,00	+5.156,66 €	0,00%	-
II	13 (5,12 %)	84,62% (2)	27.783,24 €	1,26	12 (5,26 %)	83,33% (2)	34.244,51 €	1,19	+6.461,27 €	-1,29%	0,999
III	43 (16,93 %)	37,21% (27)	41.187,41 €	1,71	41 (17,98 %)	46,34% (22)	48.229,86 €	1,67	+7.042,45 €	+9,13%	0,653
IV	118 (46,46 %)	5,93% (111)	39.389,07 €	1,68	133 (58,33 %)	14,29% (114)	49.621,96 €	1,72	+10.232,89 €	+8,36%	0,276
ND	56 (22,05 %)	14,29% (48)	25.696,11 €	1,01	25 (10,96 %)	20% (20)	31.748,13 €	1,10	+6.052,02 €	+5,71%	0,835
TOTALE	254 (100 %)	25,98% (188)	30.116,76 €	1,32	228 (100 %)	30,7% (158)	40.098,95 €	1,39	+9.982,19 €	+4,72%	0,594

Buja A et al, JOP 2021

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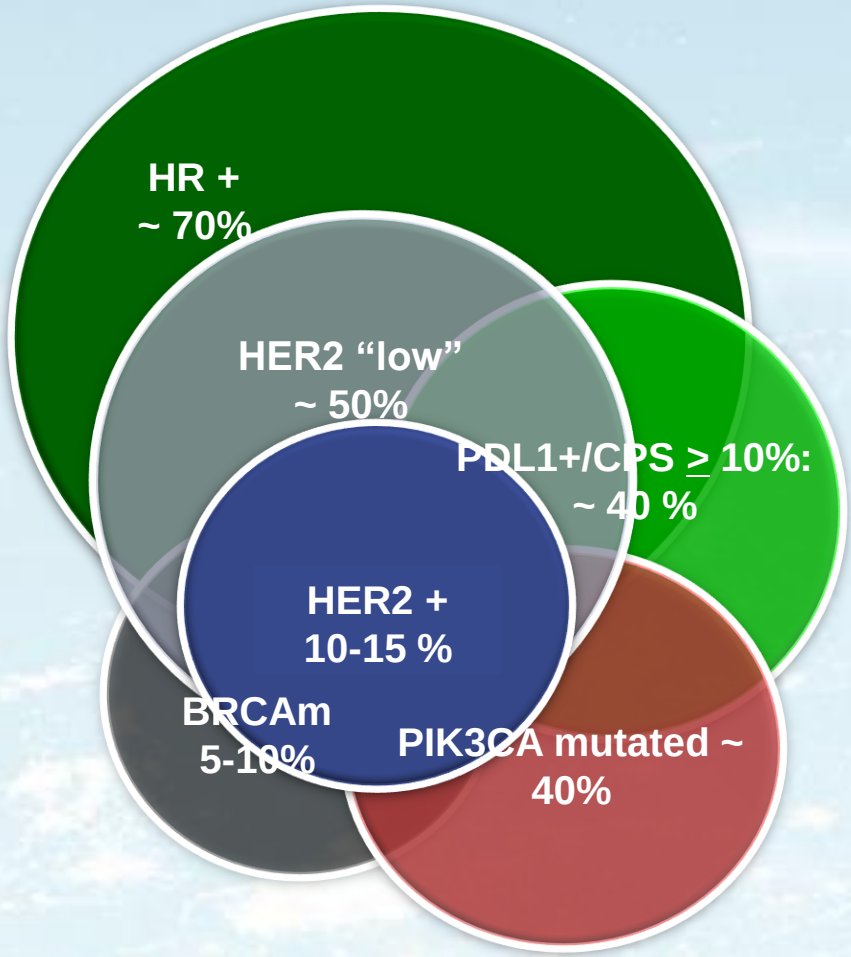
Patients' Journey in Oncology – Breast Cancer Molecular Profile



Qs to be addressed

- Who to test
- When to test
- Where to test
- Why to test

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Precision Cancer Medicine - Change of Paradigm ?

New Paradigm	
PRESENT	**FUTURE**
Histology	Biomarker
Population – Biomarker	Drug
Drug	Indications
Indications	Regardless cancer site
PARADIGM CHANGE: WHEN A BIOMARKER DEFINES THE INDICATIONS	

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Agnostic FDA & EMA drug approval based on basket trials

- **Pembrolizumab for MSI-H or mismatch-repair deficient tumors**

prevalence of MSI-H:

15% in CRC, 1.9% in Pancreatic Cancer

nb of tumors evaluated:

90 CRC
5 each endometrium and gastric
3 each biliary tract, pancreatic, small intestine, breast
1 each prostate, esophageal, small cell lung, retroperitoneal adenoca

- **Larotrectinib & Entrectinib for TRK-fusion positive cancers**

prevalence of TRK-fusion mutations:

90% in infantile fibrosarcoma, < 1% in CRC and lung cancer

nb of tumors evaluated (larotrectinib + entrectinib):

24 STS
19 Salivary Gland tumors
14 Lung cancers
10 Thyroid cancers
8 CRC
7 each BC, infantile fibrosarcoma
4 each Pancreas, Melanoma
3 each Neuroendocrine, GIST, Cholangiocarcinoma
1 each endometrtial, ovary, appendix

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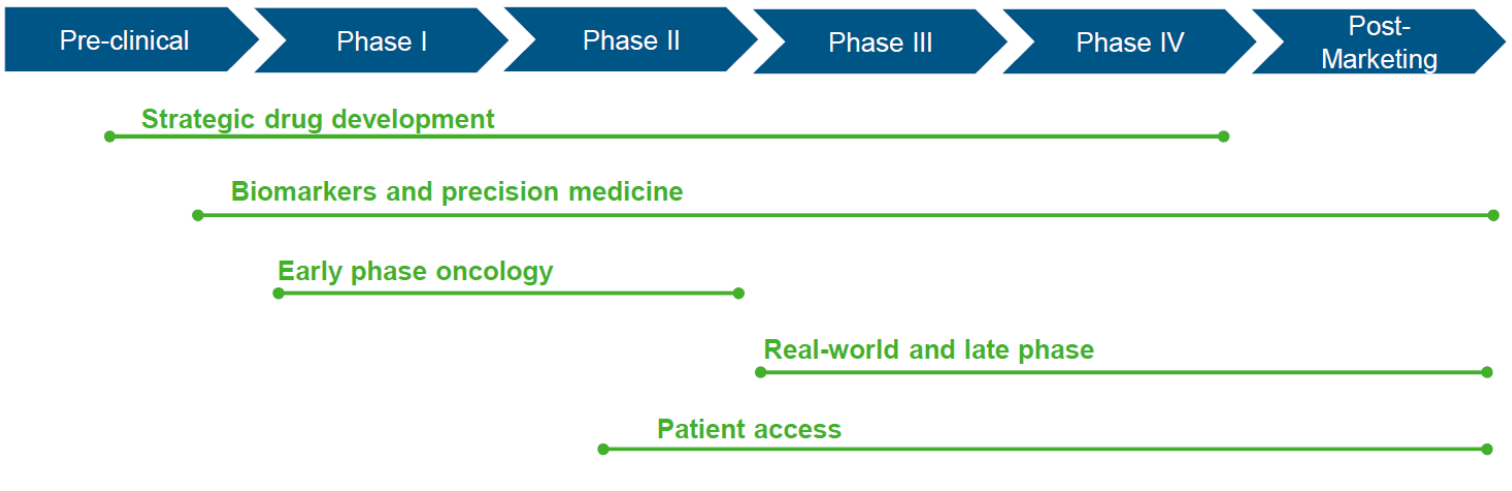
Innovative drugs and clinical research revolution

Genomic-driven trials are focused on rare tumors or subgroups with highly unmet needs and can lead to a rapid agnostic approval.

However:

- data aquisition and interpretation can be an issue
- analitycal and biological relaibility can be an issue
- centralised labs and companion diagnostics are key
- multidisciplinarity and multiprofessionality are mandatory
- external validity is necessary.



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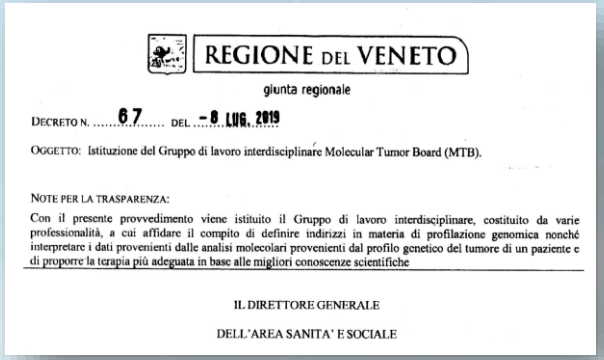
Criteri selezione pazienti
Test da eseguire
Registro per il monitoraggio
Individuazione laboratori
PDTA dedicato
Definizione delle tariffe
Analisi e valutazione casi sottoposti



REGIONE DEL VENETO

giunta regionale

DECRETO N. 67 DEL - 8 LUG. 2019

OGGETTO: Istituzione del Gruppo di lavoro interdisciplinare Molecular Tumor Board (MTB).

NOTE PER LA TRASPARENZA:

Con il presente provvedimento viene istituito il Gruppo di lavoro interdisciplinare, costituito da varie professionalità, a cui affidare il compito di definire indirizzi in materia di profilazione genomica nonché interpretare i dati provenienti dalle analisi molecolari provenienti dal profilo genetico del tumore di un paziente e di proporre la terapia più adeguata in base alle migliori conoscenze scientifiche

IL DIRETTORE GENERALE

DELL'AREA SANITA' E SOCIALE

REGIONE DEL VENETO

ALLEGATO A **Proposta n. 1346 / 2021**

c) Unico Molecular Tumor Board (MTB) multidisciplinare

Il coordinamento del MTB è affidato al Coordinatore della Rete Oncologica del Veneto

Inoltre il MTB deve essere dotato di una segreteria scientifica composta da un clinico, un patologo ed un case manager dedicato con specifiche competenze in oncologia.

Le figure professionali "fisse "che devono essere rappresentate nel MTB regionale sono:

- ✓ oncologo
- ✓ anatomopatologo
- ✓ bioinformatico
- ✓ biostatistico
- ✓ genetista
- ✓ farmacista ospedaliero
- ✓ patologo molecolare
- ✓ farmacologo
- ✓ ematologo
- ✓ bioeticista

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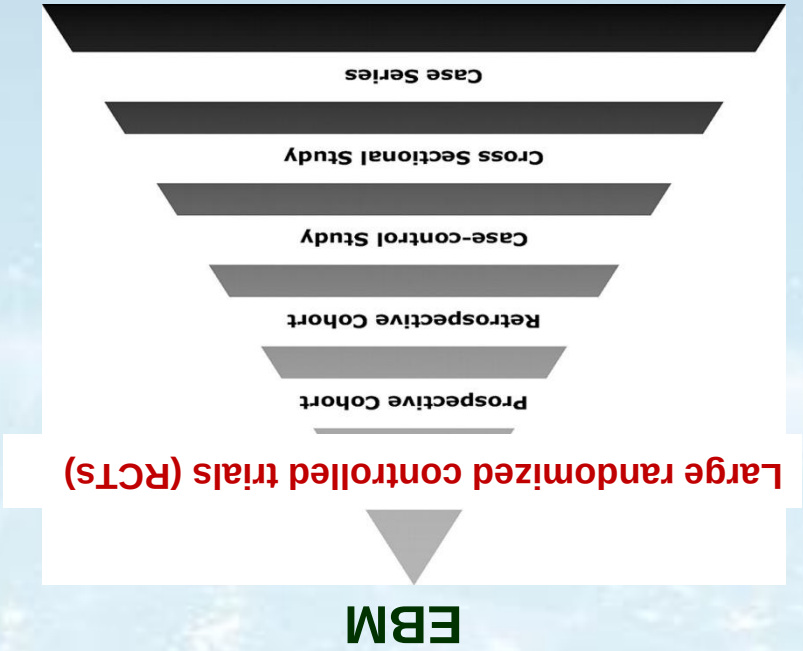
Evidence-based Medicine vs Real World Evidence



We believe that these findings raise the idea that ***overall survival in registration trials should be considered a surrogate for overall survival in the real world****, along with other surrogates, such as response rate and progression-free survival.*

Mailankody S & Prasad V, JAMA Oncology 2017; 3(7): 889-890

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LA RETE A PROTEZIONE DEL PAZIENTE ONCOLOGICO