

BOZZA  
AD ESCLUSIVO  
USO INTERNO

2016 MOTORE  
SANITÀ  
OSPEDALE e  
TERRITORIO

**INNOVAZIONE  
E APPROPRIATEZZA  
IN ONCOEMATOLOGIA**  
BEST PRACTICES A  
CONFRONTO PER UN USO  
APPROPRIATO DELLE  
RISORSE

**23 NOVEMBRE 2016 PADOVA**  
AULA MAGNA PALAZZINA DEI SERVIZI  
AZIENDA OSPEDALIERA  
VIA GIUSTINIANI, 2

# **Rete Oncologica Veneta e Ruolo dello IOV nella Ricerca Oncologica**

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Dipartimento di Oncologia Clinica e  
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Padova



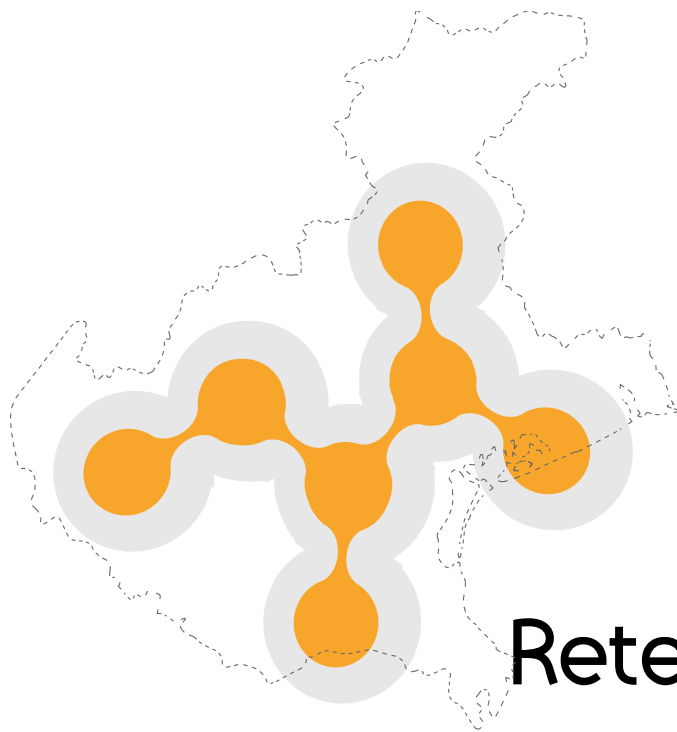
Regione del Veneto

# The Networks

**Networks are the best solution to:**

- **clinical**
- **research**
- **organizational and**
- **sustainability**

**to ensure the best cancer care to all citizens.**



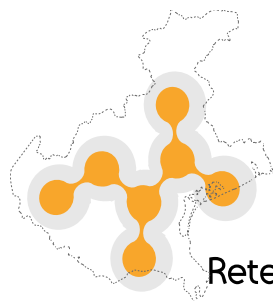
# Rete Oncologica Veneta

Ricerca, innovazione, assistenza

**Coordinatore: P.F. Conte**  
***Hub: Istituto Oncologico Veneto, IRCCS***

# ROV: ambiti d'intervento

(DGR 2067/2013)



Rete Oncologica Veneta

Ricerca, innovazione, assistenza

**Gruppi Multidisciplinari  
attivati nel 2014**

**Percorsi Diagnostico  
Terapeutici Assistenziali**

**Diagnostica molecolare  
e Biobanche**

**Sito WEB**

**Gruppi di lavoro attivati  
nel 2015**

**Raccomandazioni  
Farmaci Innovativi**

**Ricerca Clinica**

**Formazione**

**Gruppi Multidisciplinari  
Attivati nel 2016**

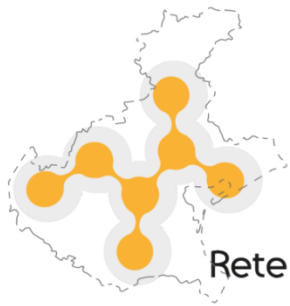
**Informatizzazione**

**Indicatori, volumi di  
attività per PDTA**

**Schemi di trattamento**

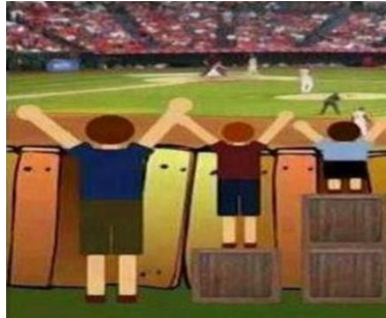
**Punti di accoglienza  
ROV**

# PDTA ROV



Rete Oncologica Veneta

Ricerca, innovazione, assistenza

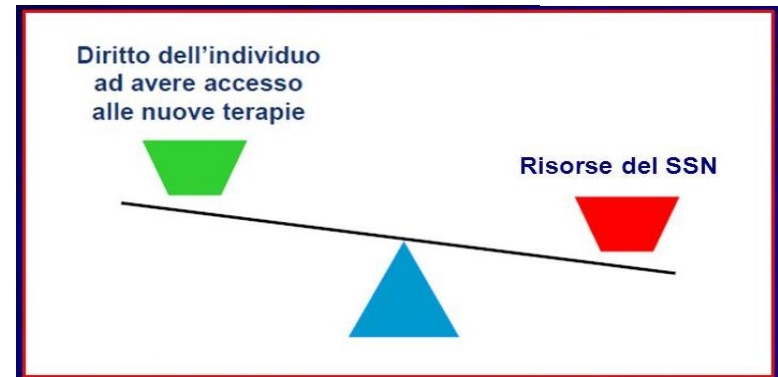
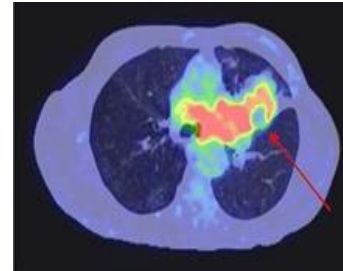


➤ **EQUITA'**

➤ **APPROPRIATEZZA**

➤ **SOSTENIBILITA'**

➤ **CONDIVISIONE**



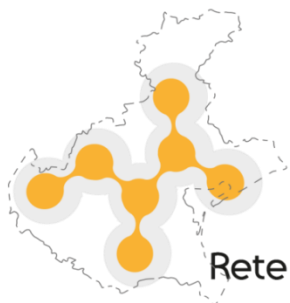
RESPONSABILI SCIENTIFICI  
Walter Artibani, Umberto Basso

RESPONSABILI SCIENTIFICI  
Giovanni de Manzoni, Fabio Farnesi, Donato Nitti

RESPONSABILI SCIENTIFICI  
Umberto Cillo, Alfredo Gagliardi, Nicolò Bassi, Vittorina Zagonel

# What makes the difference for survival and quality of life in cancer patients?

- **Professional skills (high volume)**
- **Technology & facilities (hospital)**
- **Multidisciplinary treatment planning**
- **New drugs & Clinical trials**
- **Supportive, Simultaneous & Palliative care**
- **Rehabilitation**



Rete Oncologica Veneta

Ricerca, innovazione, assistenza



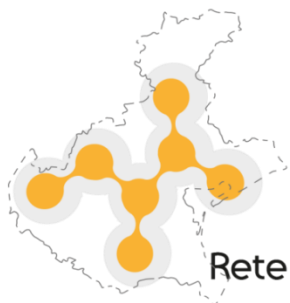
# PDTA ROV: punti di forza

- **Multidisciplinarietà** come cardine del percorso di diagnosi, cura e assistenza, condiviso
- Inserimento delle **Raccomandazioni ROV per l'utilizzo di farmaci oncologici sottoposti a monitoraggio**
- **Precoce integrazione delle cure palliative** (modello cure simultanee)
- Inserimento di **indicatori di processo e di esito**
- **Strumento di governo clinico, organizzativo e gestionale per valutare la performance non solo dei singoli operatori ma delle strutture sanitarie.**

<b>Gruppo</b>	<b>Diagnosi e stadiazione</b>	<b>Trattamento</b>	<b>Follow-up</b>	<b>Indicatori di performance</b>	<b>Avanzamento</b>
<b>Colon-retto</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>Decreto 2015</b>
<b>Sarcomi e GIST</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>Decreto 2015</b>
<b>Melanoma</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>Decreto 2015</b>
<b>Mammella</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>Decreto 2016</b>
<b>Rene</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>Decreto 2016</b>
<b>Prostata</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>In attesa di decreto</b>
<b>Polmone</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>In attesa di decreto</b>
<b>Testa e Collo</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>In attesa di decreto</b>
<b>Esofago</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>In attesa di decreto</b>
<b>Epatobiliare</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>in attesa di decreto</b>
<b>Stomaco</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>In attesa di decreto</b>
<b>Ovaio</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>In attesa di decreto</b>
<b>Ereditari <i>Mammella e Ovaio</i></b>	<b>70%</b>	<b>70%</b>	<b>70%</b>	<b>In corso</b>	
<b>Neuroendocrini</b>	<b>100%</b>	<b>100%</b>	<b>100%</b>	<b>In corso</b>	
<b>Metastasi ossee</b>	<b>100%</b>	<b>70%</b>	<b>70%</b>	<b>In corso</b>	

**12 PDTA operativi per fine 2016 entro 2017 previsto completamento di tutti i PDTA**





Rete Oncologica Veneta

Ricerca, innovazione, assistenza

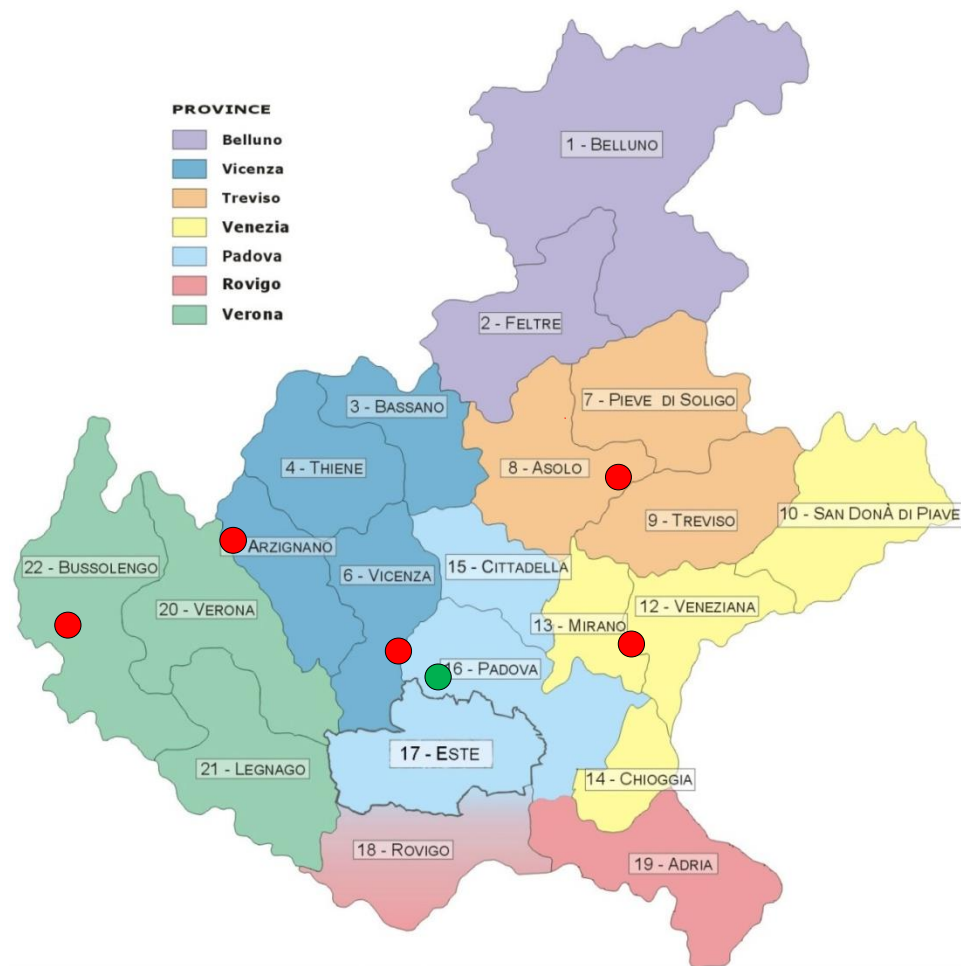


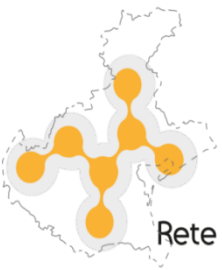
# GOVERNANCE DEL PDTA

**Il Dipartimento Oncologico  
del Polo ed i suoi gruppi  
multidisciplinari**



**Contestualizzare il PDTA  
elaborato dal gruppo di  
esperti della ROV,  
per renderlo operativo  
in sede.**





Rete Oncologica Veneta  
Ricerca, innovazione, assistenza

# Gruppo farmaci innovativi

Valutate 21 molecole e formulate 48 raccomandazioni

- ***Pertuzumab mammella***
- ***Everolimus mammella***
- ***Bevacizumab ovaio***
- ***Trastuzumab-Emtansine mamm.***
- ***Aflibercept colon e retto***
- ***Bevacizumab colon e retto***
- ***Cabazitaxel prostata***
- ***Enzatumamide prostata***
- ***Abiraterone prostata***
- ***Regorafenib colon e retto***
- ***Regorafenib GIST***
- ***Crizotinib polmone***
- ***Permetrexed polmone***
- ***Afatinib polmone***
- ***Radio 223-Dicloruro prostata***
- ***Paclitaxel-Albumina pancreas***
- ***Vismodegib basocellulare***
- ***Sunitinib pNET***
- ***Ramucirumab gastrico***
- ***Olaparib ovaio***
- ***Nivolumab NSCLC***

Vedi Decreti Regionali o sito ROV

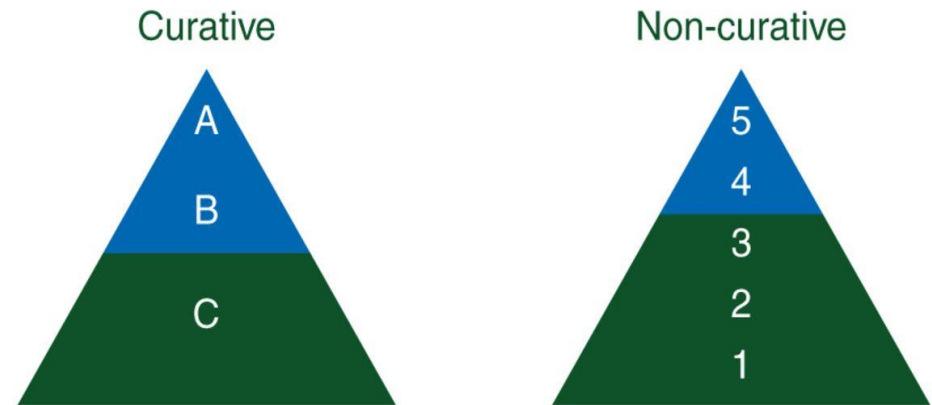
## A standardised, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies: the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS)

N. I. Cherny<sup>1\*</sup>, R. Sullivan<sup>2</sup>, U. Dafni<sup>3</sup>, J. M. Kerst<sup>4</sup>, A. Sobrero<sup>5</sup>, C. Zielinski<sup>6</sup>, E. G. E. de Vries<sup>7</sup> & M. J. Piccart<sup>8,9</sup>

**Table 1.** Potential benefits of a new treatment

Living longer
Improved OS
Improved surrogate of OS
DFS (when OS data are immature in adjuvant setting)
Improved PFS
Living better
Improved quality of life
Improved surrogate of quality of life
Improved PFS
Reduced toxicity

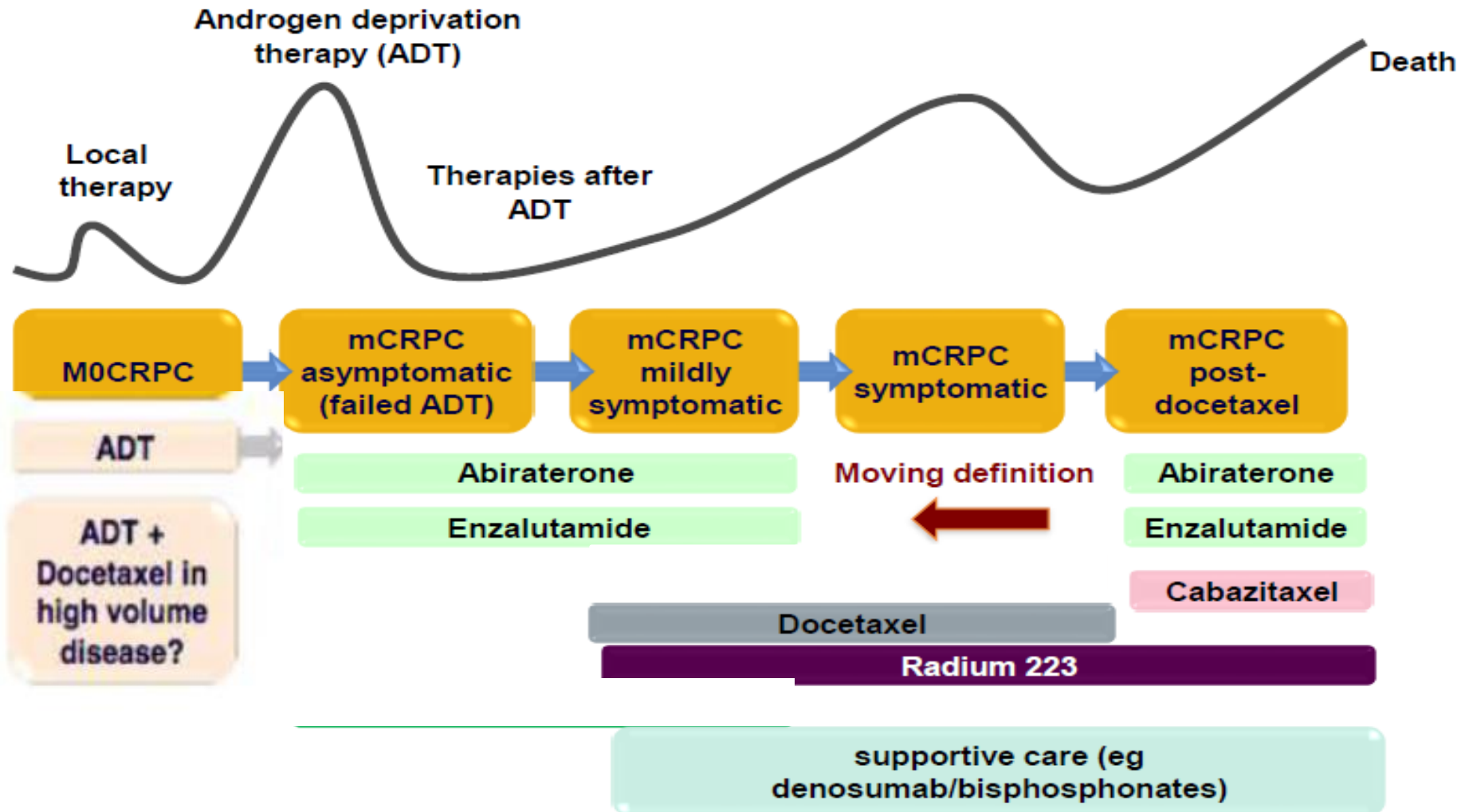
### ESMO MCBS evaluation



Curative-Evaluation form 1: for new approaches to adjuvant therapy or new potentially curative therapies

Non-curative-Evaluation forms 2a, b or c: for therapies that are not likely to be curative

# Dalla valutazione di un farmaco alla strategia terapeutica: l'esempio del ca prostata



# ROV e RICERCA

- **Comunicazione diretta tramite mail e sito ROV delle nuove sperimentazioni disponibili**
- **Disponibilità di valutare il paziente per eventuale inserimento in trial**
- **Raccolta del materiale istologico per indagini molecolari**
- **Apertura ai centri di sperimentazioni indipendenti proposte dallo IOV.**

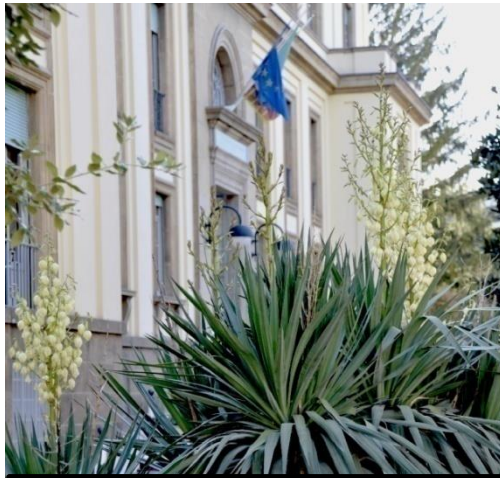


REGIONE DEL VENETO



**ESMO**

Designated Centers  
of Integrated  
Oncology and  
Palliative Care



**Edificio Busonera**



**Palazzina  
Immunologia**

# IOV, IRCCS PADOVA



**Uffici amministrativi  
Palazzo S. Stefano  
- sede provvisoria-**



**Laboratori c/o  
Torre della ricerca**



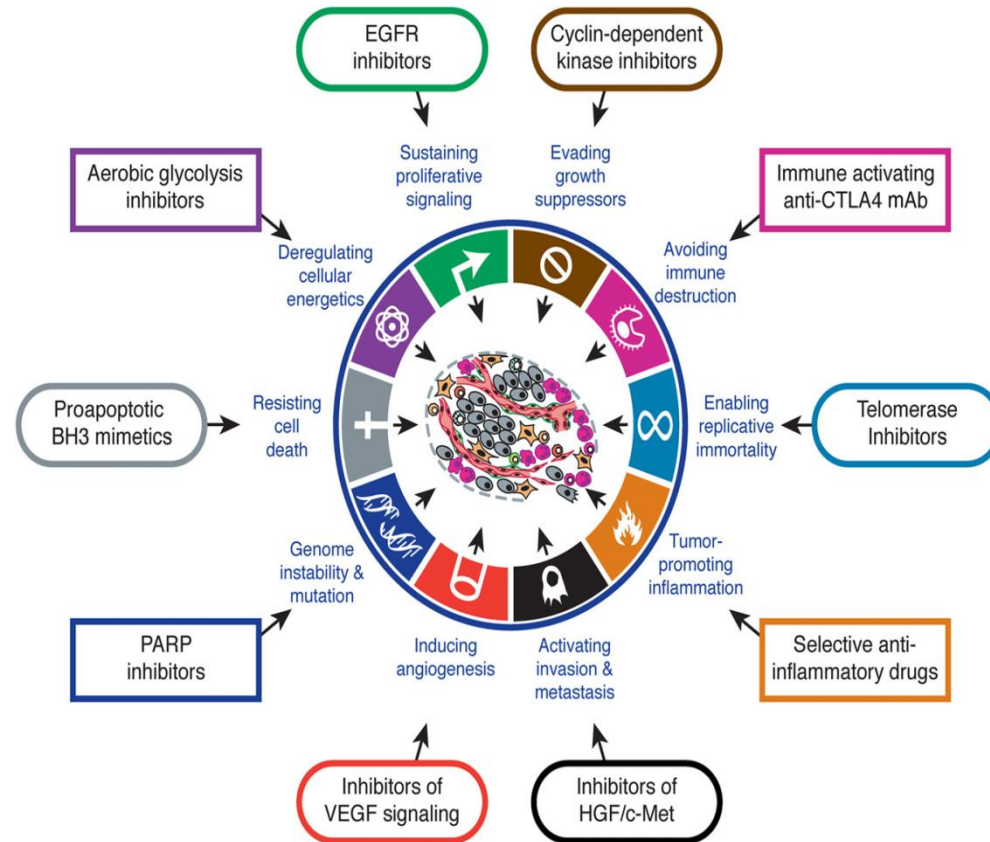
**Edificio  
Radioterapia**

# IOV: Quale ricerca?

➤ **Ricerca di base**

➤ **Ricerca traslazionale**

➤ **Ricerca clinica**



# With respect to research the network is crucial to face

- **Biological complexity:** all cases of cancer becomes “rare” considering the mutations that expresses
- **Scientific complexity** It's 'impossible by a single scientist, to know in real time all informations published every day
- **Organizational complexity:** you need to share the knowledge to achieve results within a reasonable time



# Nuovo test standard di screening per l'infezione da HPV

## Efficacy of human papillomavirus testing for the detection of invasive cervical cancers and cervical intraepithelial neoplasia: a randomised controlled trial



*Guglielmo Ronco, Paolo Giorgi-Rossi, Francesca Carozzi, Massimo Confortini, Paolo Dalla Palma, Annarosa Del Mistro, Bruno Ghiringhello, Salvatore Girlando, Anna Gillio-Tos, Laura De Marco, Carlo Naldoni, Paola Pierotti, Raffaella Rizzolo, Patrizia Schincaglia, Manuel Zorzi, Marco Zappa, Nereo Segnan, Jack Cuzick, and the New Technologies for Cervical Cancer screening (NTCC) Working Group\**

### Summary

**Background** Human papillomavirus (HPV) testing is known to be more sensitive, but less specific than cytology for *Lancet Oncol 2010; 11: 249-57*

**Interpretation** HPV-based screening is more effective than cytology in preventing invasive cervical cancer, by detecting persistent high-grade lesions earlier and providing a longer low-risk period. However, in younger women, HPV screening leads to over-diagnosis of regressive CIN2.

# Correlazione tra efficacia della terapia antivirale e l'inibizione di hTERT

Clinical  
Cancer  
Research

*Cancer Therapy: Preclinical*

## hTERT Inhibition Triggers Epstein–Barr Virus Lytic Cycle and Apoptosis in Immortalized and Transformed B Cells: A Basis for New Therapies

Silvia Giunco<sup>1</sup>, Riccardo Dolcetti<sup>3</sup>, Sonia Keppel<sup>2</sup>, Andrea Celeghin<sup>1</sup>, Stefano Indraccolo<sup>2</sup>, Jessica Dal Col<sup>3</sup>, Katy Mastorci<sup>3</sup>, and Anita De Rossi<sup>1,2</sup>

**Conclusions:** These results suggest that combination of antiviral drugs with strategies able to inhibit hTERT expression may result in therapeutically relevant effects in patients with EBV-related malignancies.

*Clin. Cancer Res; 19(8); 2036–47. ©2013 AACR.*

# Yeast model for evaluating the pathogenic significance of *SDHB*, *SDHC* and *SDHD* mutations in PHEO–PGL syndrome

Elena Panizza<sup>1</sup>, Tonino Ercolino<sup>2</sup>, Luigi Mori<sup>3</sup>, Elena Rapizzi<sup>6</sup>, Maurizio Castellano<sup>3</sup>, Giuseppe Opocher<sup>4</sup>, Ileana Ferrero<sup>1</sup>, Hartmut P.H. Neumann<sup>5</sup>, Massimo Mannelli<sup>6,7</sup> and Paola Goffrini<sup>1,\*</sup>

The aim of this study was to evaluate whether and to which extent the yeast model may be useful for establishing the pathological significance of missense SDH mutations in humans. The results of our study demonstrate that the yeast is a good functional model to validate the pathogenic significance of *SDHB* missense mutations while, for missense mutations in *SDHC* and *SDHD* genes, the model can be informative only when the variation involves a conserved residue in a conserved domain.

## Cancer stem cells from epithelial ovarian cancer patients privilege oxidative phosphorylation, and resist glucose deprivation

**Anna Pastò<sup>1,\*</sup>, Chiara Bellio<sup>1,\*</sup>, Giorgia Pilotto<sup>1,\*</sup>, Vincenzo Ciminale<sup>1,2</sup>, Micol Silic-Benussi<sup>2</sup>, Giulia Guzzo<sup>3</sup>, Andrea Rasola<sup>3</sup>, Chiara Frasson<sup>4</sup>, Giorgia Nardo<sup>2</sup>, Elisabetta Zulato<sup>2</sup>, Maria Ornella Nicoletto<sup>2</sup>, Mariangela Manicone<sup>2</sup>, Stefano Indraccolo<sup>2,\*</sup> and Alberto Amadori<sup>1,2,\*</sup>**

<sup>1</sup> Department of Surgery, Oncology, and Gastroenterology, Oncology Section, University of Padova, Padova, Italy

<sup>2</sup> Istituto Oncologico Veneto-IRCCS (IOV), Padova, Italy

<sup>3</sup> Department of Biomedical Sciences, University of Padova, Padova, Italy

<sup>4</sup> Department of Woman and Child Health, Laboratory of Hemato-Oncology, University of Padova, Padova, Italy

\* These Authors contributed equally to this work

**Correspondence to:** Alberto Amadori, **email:** [albido@unipd.it](mailto:albido@unipd.it)

**Keywords:** Ovarian cancer, Cancer Stem Cells, metabolism, glucose, Warburg effect

**Received:** February 27, 2014

**Accepted:** May 24, 2014

**Published:** May 26, 2014

**These observations may explain the CSC resistance to anti-angiogenic therapies, and indicate this peculiar metabolic profile as a possible target of novel treatment strategies.**

# Test diagnostico per presenza di cellule tumorali circolanti nel tumore alla mammella



## Clinical validity of circulating tumour cells in patients with metastatic breast cancer: a pooled analysis of individual patient data

*François-Clément Bidard, Dieter J Peeters, Tanja Fehm, Franco Nolé, Rafael Gisbert-Criado, Dimitrios Mavroudis, Salvatore Grisanti, Daniele Generali, Jose A Garcia-Saenz, Justin Stebbing, Carlos Caldas, Paola Gazzaniga, Luis Manso, Rita Zamarchi, Angela Fernandez de Lascoiti, Leticia De Mattos-Arruda, Michail Ignatiadis, Ronald Lebofsky, Steven J van Laere, Franziska Meier-Stiegen, Maria-Teresa Sandri, Jose Vidal-Martinez, Eleni Politaki, Francesca Consoli, Alberto Bottini, Eduardo Diaz-Rubio, Jonathan Krell, Sarah-Jane Dawson, Cristina Raimondi, Annemie Rutten, Wolfgang Janni, Elisabetta Munzone, Vicente Carañana, Sofia Agelaki, Camillo Almici, Luc Dirix, Erich-Franz Solomayer, Laura Zorzino, Helene Johannes, Jorge S Reis-Filho, Klaus Pantel\*, Jean-Yves Pierga\*, Stefan Michiels\**

### Summary

**Background** We aimed to assess the clinical validity of circulating tumour cell (CTC) quantification for prognostication of patients with metastatic breast cancer by undertaking a pooled analysis of individual patient data.

*Lancet Oncol* 2014; 15: 406-14

Published Online

11 May 2014



# HHS Public Access

Author manuscript

*JAMA*. Author manuscript; available in PMC 2015 August 15.

Mutazione *BRCA1-2*  
e rischio di cancro

Published in final edited form as:

*JAMA*. 2015 April 7; 313(13): 1347–1361. doi:10.1001/jama.2014.5985.

## Association of Type and Location of *BRCA1* and *BRCA2* Mutations With Risk of Breast and Ovarian Cancer

Timothy R. Rebbeck, PhD, Nandita Mitra, PhD, Fei Wan, MS, Olga M. Sinilnikova, PhD<sup>†</sup>, Sue Healey, Lesley McGuffog, Sylvie Mazoyer, PhD, Georgia Chenevix-Trench, PhD, Douglas F. Easton, PhD, Antonis C. Antoniou, PhD, Katherine L. Nathanson, MD, and the CIMBA Consortium Marco Montagna

**CONCLUSIONS AND RELEVANCE**—Breast and ovarian cancer risks varied by type and location of *BRCA1/2* mutations. With appropriate validation, these data may have implications for risk assessment and cancer prevention decision making for carriers of *BRCA1* and *BRCA2* mutations.

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# Fenotipo glicolitico conferisce resistenza alla terapia antiangiogenica

Therapeutics, Targets, and Chemical Biology

Cancer  
Research

## VEGF-Targeted Therapy Stably Modulates the Glycolytic Phenotype of Tumor Cells

Cancer Res; 75(1) January 1, 2015

Matteo Curtarello<sup>1</sup>, Elisabetta Zulato<sup>1</sup>, Giorgia Nardo<sup>1</sup>, Silvia Valtorta<sup>2,3</sup>, Giulia Guzzo<sup>4</sup>, Elisabetta Rossi<sup>5</sup>, Giovanni Esposito<sup>1</sup>, Aichi Msaki<sup>1</sup>, Anna Pastò<sup>1</sup>, Andrea Rasola<sup>4</sup>, Luca Persano<sup>6</sup>, Francesco Ciccarese<sup>1</sup>, Roberta Bertorelle<sup>1</sup>, Sergio Todde<sup>2</sup>, Mario Plebani<sup>7</sup>, Henrike Schroer<sup>8</sup>, Stefan Walenta<sup>8</sup>, Wolfgang Mueller-Klieser<sup>8</sup>, Alberto Amadori<sup>1,5</sup>, Rosa Maria Moresco<sup>2,3</sup>, and Stefano Indraccolo<sup>1</sup>

Our results support the hypothesis that the highly glycolytic phenotype of tumor cells studied in xenograft models, either primary or secondary, is a cell-autonomous trait conferring resistance to VEGF blockade. The finding that metabolic traits of tumors can be selected by antiangiogenic therapy suggests insights into the evolutionary dynamics of tumor metabolism. *Cancer Res*; 75(1); 120–133. ©2014 AACR.



ORIGINAL RESEARCH

OPEN ACCESS

## Retargeting cytokine-induced killer cell activity by CD16 engagement with clinical-grade antibodies

Elisa Cappuzzello<sup>a</sup>, Anna Tosi<sup>a</sup>, Paola Zanovello<sup>a,b</sup>, Roberta Sommaggio<sup>a,\*</sup>, and Antonio Rosato<sup>a,b,\*</sup>

<sup>a</sup>Department of Surgery, Oncology and Gastroenterology, Oncology and Immunology Section, University of Padova, Padua, Italy; <sup>b</sup>Department of Clinical and Experimental Oncology, Veneto Institute of Oncology IOV-IRCCS, Padua, Italy

Overall, these data provide a new therapeutic strategy for the treatment of Her2 and EGFR expressing tumors by adoptive cell therapy, which could find wide implementation and application, and could also be expanded to the use of additional therapeutic antibodies.



# Gruppi Cooperativi Nazionali ed Internazionali

- **GONO**
- **GISCAD**
- **FIL**
- **AINO**
- **EORTC**
- .....

**Ricerca  
traslazionale-clinica  
INDIPENDENTE**

# Nuovo standard di trattamento pazienti mCRC

The NEW ENGLAND JOURNAL of MEDICINE

**GONO**  
**trial**

ORIGINAL ARTICLE

## Initial Therapy with FOLFOXIRI and Bevacizumab for Metastatic Colorectal Cancer

Fotios Loupakis, M.D., Ph.D., Chiara Cremolini, M.D., Gianluca Masi, M.D., Sara Lonardi, M.D., Vittorina Zagonel, M.D., Lisa Salvatore, M.D., Enrico Cortesi, M.D., Gianluca Tomasello, M.D., Monica Ronzoni, M.D., Rosella Spadi, M.D., Alberto Zaniboni, M.D., Giuseppe Tonini, M.D., Angela Buonadonna, M.D., Domenico Amoroso, M.D., Silvana Chiara, M.D., Chiara Carlomagno, M.D., Ph.D., Corrado Boni, M.D., Giacomo Allegrini, M.D., Luca Boni, M.D., and Alfredo Falcone, M.D.



**FOLFOXIRI plus bevacizumab versus FOLFIRI plus bevacizumab as first-line treatment of patients with metastatic colorectal cancer: updated overall survival and molecular subgroup analyses of the open-label, phase 3 TRIBE study**

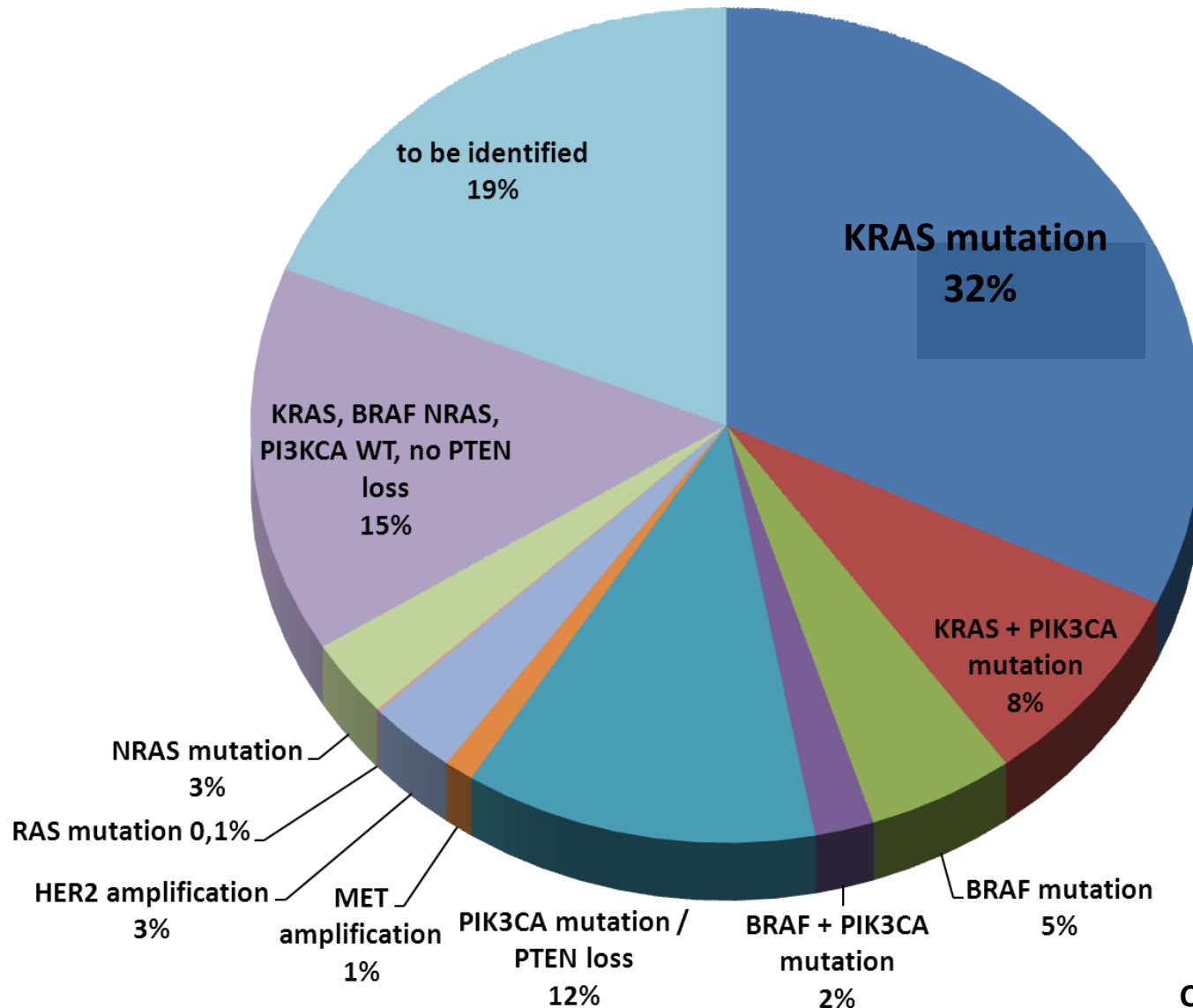
Chiara Cremolini\*, Fotios Loupakis\*, Carlotta Antoniotti, Cristiana Lupi, Elisa Sensi, Sara Lonardi, Silvia Mezi, Gianluca Tomasello, Monica Ronzoni, Alberto Zaniboni, Giuseppe Tonini, Chiara Carlomagno, Giacomo Allegrini, Silvana Chiara, Mauro D'Amico, Cristina Granetto, Marina Cazzaniga, Luca Boni, Gabriella Fontanini, Alfredo Falcone

### Summary

**Background** In the TRIBE study, FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan) plus bevacizumab

# Precision medicine stands on exceptions.....

## mCRC



# HERACLES First trial in HER2+ mCRC

Validazione del test molecolare HER2 in oltre 800 pazienti con carcinoma del colon e retto metastatici

MODERN PATHOLOGY (2015) 28, 1481–1491

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1481

## Assessment of a HER2 scoring system for colorectal cancer: results from a validation study

Emanuele Valtorta<sup>1,19</sup>, Cosimo Martino<sup>2,19</sup>, Andrea Sartore-Bianchi<sup>1</sup>,  
Frédérique Penault-Llorca<sup>3</sup>, Giuseppe Viale<sup>4</sup>, Mauro Risio<sup>2</sup>, Massimo Rugge<sup>5</sup>,  
Walter Grigioni<sup>6</sup>, Katia Bencardino<sup>1</sup>, Sara Lonardi<sup>7</sup>, Vittorina Zagonel<sup>7</sup>, Francesco Leone<sup>2</sup>,  
Johannes Noe<sup>8</sup>, Fortunato Ciardiello<sup>9</sup>, Carmine Pinto<sup>6</sup>, Roberto Labianca<sup>10</sup>,  
Stefania Mosconi<sup>10</sup>, Claudio Graiff<sup>11</sup>, Giuseppe Aprile<sup>12</sup>, Barbara Frau<sup>13</sup>, Carlo Garufi<sup>14</sup>,  
Fotios Loupakis<sup>15</sup>, Patrizia Racca<sup>16</sup>, Giuseppe Tonini<sup>17</sup>, Calogero Lauricella<sup>1</sup>,  
Silvio Veronese<sup>1</sup>, Mauro Truini<sup>1</sup>, Salvatore Siena<sup>1,18,20</sup>, Silvia Marsoni<sup>2,20</sup> and  
Marcello Gambacorta<sup>1,20</sup>

# What it means to be Network



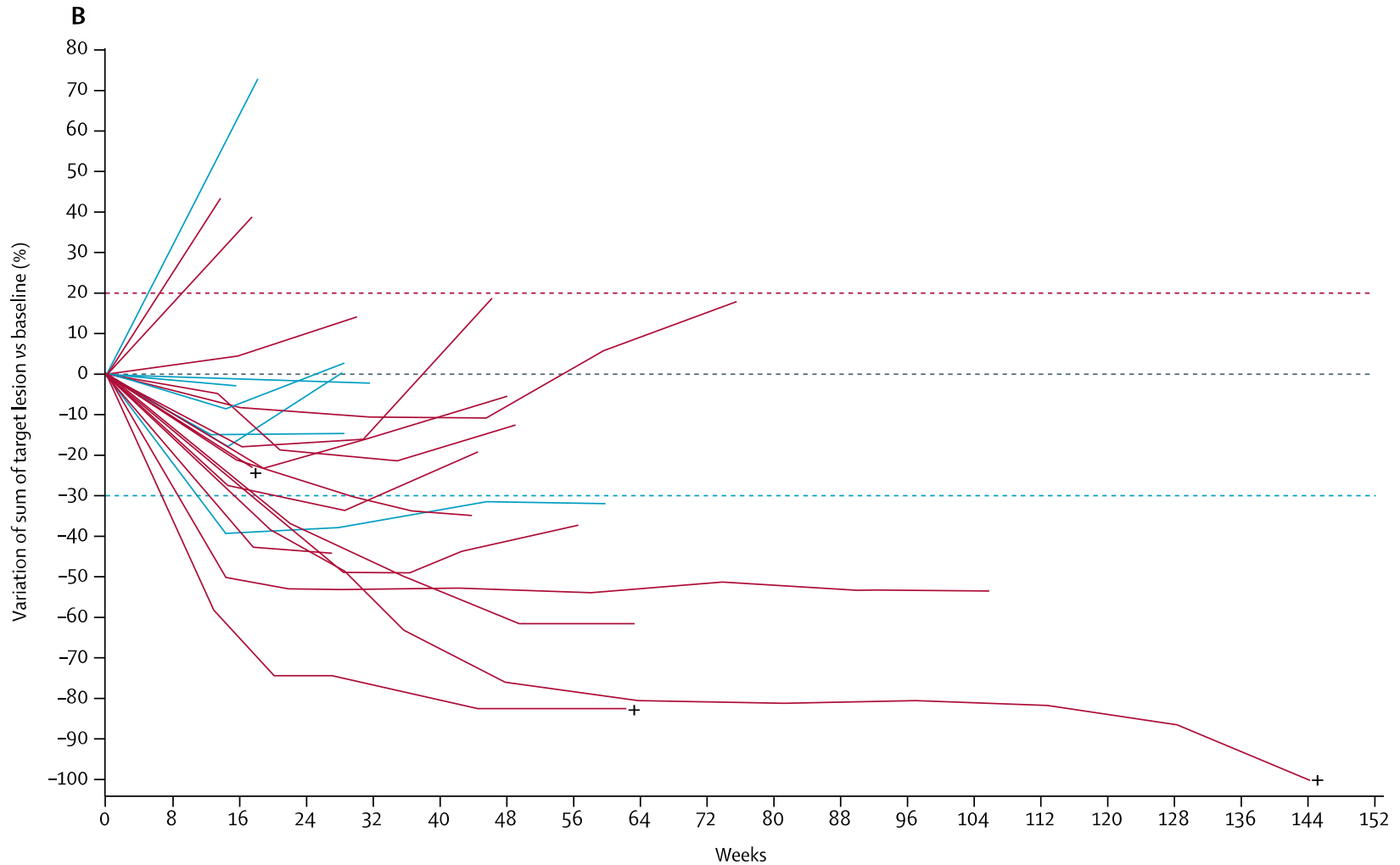
Dual-targeted therapy with trastuzumab and lapatinib in treatment-refractory, *KRAS* codon 12/13 wild-type, HER2-positive metastatic colorectal cancer (HERACLES): a proof-of-concept, multicentre, open-label, phase 2 trial

*Andrea Sartore-Bianchi, Livio Trusolino\*, Cosimo Martino, Katia Bencardino, Sara Lonardi, Francesca Bergamo, Vittorina Zagonel, Francesco Leone, Ilaria Depetris, Erika Martinelli, Teresa Troiani, Fortunato Ciardiello, Patrizia Racca, Andrea Bertotti, Giulia Siravegna, Valter Torri, Alessio Amatu, Silvia Ghezzi, Giovanna Marrapese, Laura Palmeri, Emanuele Valtorta, Andrea Cassingena, Calogero Lauricella, Angelo Vanzulli, Daniele Regge, Silvio Veronese, Paolo M Comoglio, Alberto Bardelli, Silvia Marsoni\*, Salvatore Siena\**

## Highlights

- **70% Disease control rate**
- **30% Objective Response rate (2 CRs )**
- **Long lasting responses in EGFRs resistant patients**

# HERACLES TRIAL: deepness and duration of response



# Current FUNNEL Trials



## HERACLES A

Lapatinib+ trastuzuman in naïve pts (terminated)

## HERACLES RESCUE

TDM1 in antiHER2 resistant pts

## HERACLES B

TDMI + pertuzumab in naïve pts

## CHRONOS

Rechallenge with panitutumab in secondary KRAS resistance

## STARTRK2

Entrectenib Phase 2 (Pharma basket trial including CRC)

## ARETHUSA

MMR-status guided Immunotherapy

Courtesy Marsoni S, Candiolo IRCCS



**ESMO**

Designated Centers  
of Integrated  
Oncology and  
Palliative Care



# REGOMA trial

*Regorafenib in relapsed Glioblastoma*

*Randomized, controlled open-label phase II clinical trial*

## Regoma Trial TEAM

Study Coordinator: *Dr. V. Zagonel*

Clinical Trials and Biostatistics: *Dr. G.L. De Salvo*

Transatlantical Research: *Dr. Stefano Indraccolo, Dr. G. Cabrini, Dr. MP Gardiman*

Medical Monitor: *Dr. G. Lombardi; (+39)-0498215888; giuseppe.lombardi@ioveneto.it*

Drug management and pharmacovigilance: *Dr. D. Maran; (+39)-0498215729; daniele.maran@ioveneto.it*

Data Manager: *Dr. M. Farina; (+39)-0498215908; miriam.farina@ioveneto.it*

eCRF Coordinator: *Dr. M. Braggion; (+39)-0498215524; marco.braggion@ioveneto.it*

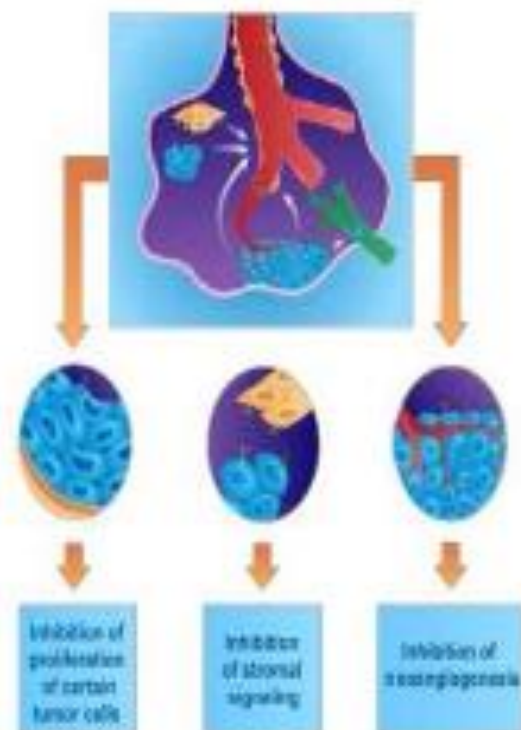




# Mode of Action of Regorafenib



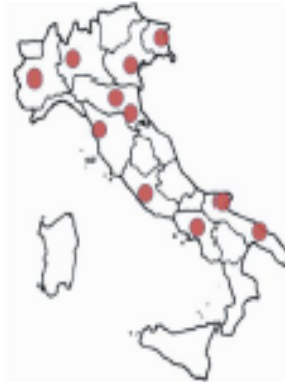
- Regorafenib inhibits multiple cell-signaling kinases:
  - Angiogenic
    - VEGFR1-3, TIE2
  - Stromal
    - PDGFR- $\beta$ , FGFR
  - Oncogenic
    - KIT, PDGFR, RET
- $T_{1/2}$  in man: approx. 26-28 hrs
  - Two major metabolites (M2, M5) are pharmacologically active



# REGOMA trial

## ACTIVE SITES: 11 Italian sites

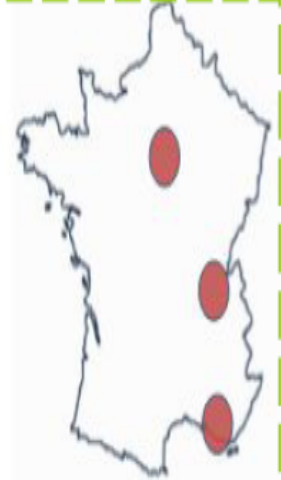
- IOV Istituto Oncologico Veneto IRCCS (PD) (PI: Dr. Zagone/Lombardi)
- Istituto Neurologico C. Besta (MI) (PI: Dr. Eoli)
- Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (I.R.S.T.) ( Meldola - FC) (PI: Dr. Feedi)
- A.O.U. S. Maria della Misericordia di Udine (UD) (PI: Dr. Rizzato)
- IRRCS "De Bellis" (Castellana Grotte - BA) (PI: Dr. Loli)
- A.O.U. Città della Salute e della Scienza di Torino (TO) (Dr. Rudà)
- Ospedale Casa Sollievo della Sofferenza IRCCS (San Giovanni Rotondo – FG) (PI: Dr. Maiello)
- Azienda Ospedaliera "Rummo"(BN) (PI: Dr. Daniele)
- Ospedale Santa Chiara (PI) (PI: Dr. Pasqualetti)
- Istituto Nazionale Tumori Regina Elena (RO) (PI: Dr. Pace)
- Ospedale Bellaria (BO) (PI: Dr. Brandes)



REGOMA Newsletter n. 4 September 2016

## FRENCH SITES:

- Hospices Civils de Lyon, Lyon Cedex
- Hopitaux Universitaires Pitié Salpêtrière Charles Foix, Paris
- Hôpital de la Timone, Marseille

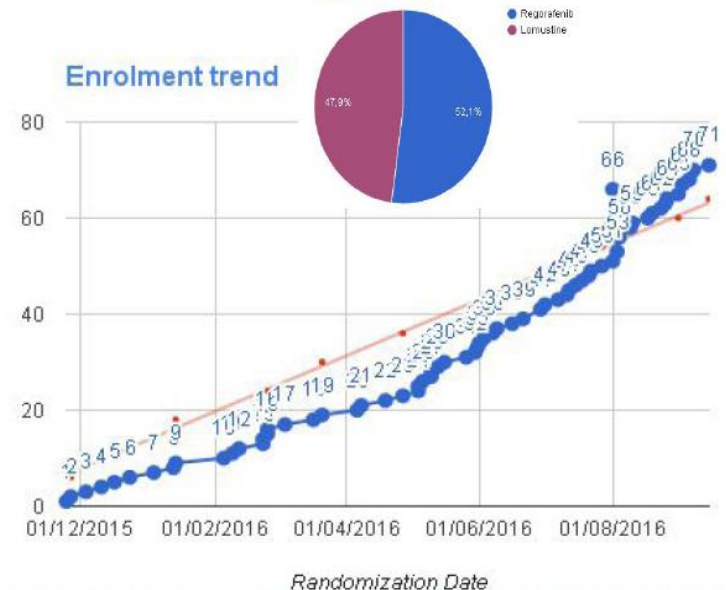


## ENROLLMENT UPDATE:

71 patients were randomized. The final target is 112 subjects.  
Date of first randomized patient: 25th November 2015 at IOV.

Enrolling sites	N. of Randomized Subjects
IOV (PD)	23
Besta (MI)	16
Città della Salute e della Scienza (TO)	9
Bellaria (BO)	7
IRST (FC)	6
Regina Elena (RM)	3
Castellana Grotte (BA)	2
Rummo (BN)	2
Santa Maria della Misericordia (UD)	2
Santa Chiara (PI)	2

N. Randomized Subjects Real (blue) vs Expected (red)





# Panda Study

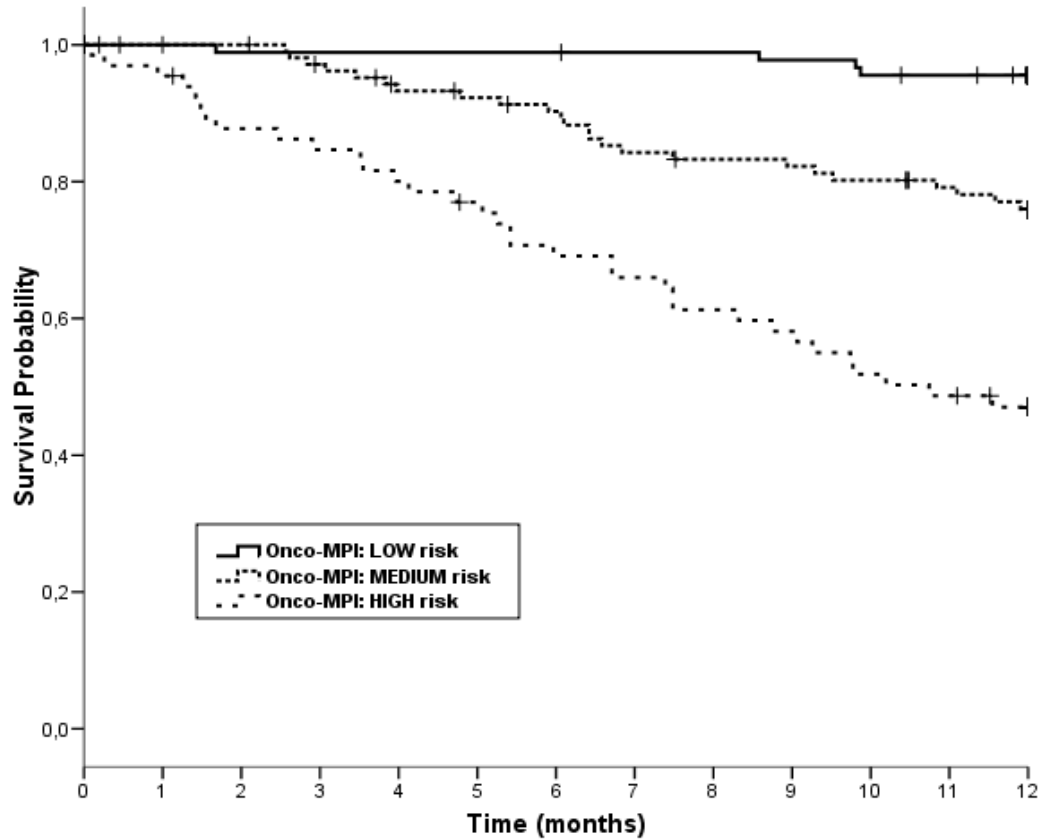
**Randomized phase 2 study of first-line  
FOLFOX plus panitumumab versus 5FU plus pan  
in elderly RAS/BRAF wild-type mCRC**



**Co-PI Sara LONARDI Fotios LOUPAKIS**

# Onco-MPI & mCRC

N = 475



p < 0,001

Keywords: *BRAF*; *RAS*; metastatic colorectal cancer; liver; prognostic

Identificazione di mutazioni prognostiche

# ***BRAF* and *RAS* mutations as prognostic factors in metastatic colorectal cancer patients undergoing liver resection**

M Schirripa<sup>1,9</sup>, F Bergamo<sup>2,9</sup>, C Cremolini<sup>1</sup>, M Casagrande<sup>3</sup>, S Lonardi<sup>2</sup>, G Aprile<sup>3</sup>, D Yang<sup>4</sup>, F Marmorino<sup>1</sup>, G Pasquini<sup>1</sup>, E Sensi<sup>5</sup>, C Lupi<sup>5</sup>, G De Maglio<sup>6</sup>, N Borrelli<sup>5</sup>, S Pizzolitto<sup>6</sup>, G Fasola<sup>3</sup>, R Bertorelle<sup>7</sup>, M Ruge<sup>8</sup>, G Fontanini<sup>5</sup>, V Zagonel<sup>2</sup>, F Loupakis<sup>\*,1,10</sup> and A Falcone<sup>1,10</sup>

**Ramucirumab versus placebo in combination with second-line FOLFIRI in patients with metastatic colorectal carcinoma that progressed during or after first-line therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine (RAISE): a randomised, double-blind, multicentre, phase 3 study**



Nuovo standard terapeutico

Josep Tabernero, Takayuki Yoshino, Allen Lee Cohn, Radka Obermannova, Gyorgy Bodoky, Rocio Garcia-Carbonero, Tudor-Eliade Ciuleanu, David C Portnoy, Eric Van Cutsem, Axel Grothey, Jana Prausová, Pilar Garcia-Alfonso, Kentaro Yamazaki, Philip R Clingan, Sara Lonardi, Tae Won Kim, Lorinda Simms, Shao-Chun Chang, Federico Nasroulah, and the RAISE Study Investigators

## Summary

**Background** Angiogenesis is an important therapeutic target in colorectal carcinoma. Ramucirumab is a human IgG-1 *Lancet Oncol* 2015; 16: 499–508

# Ricerca sponsorizzata

## Nivolumab ± Ipilimumab in Treatment of Patients With Metastatic Colorectal Cancer With and Without High Microsatellite Instability: CheckMate 142 Interim Results

Michael Overman,<sup>1</sup> Scott Kopetz,<sup>1</sup> Ray McDermott,<sup>2</sup> Joseph Leach,<sup>3</sup> Sara Lonardi,<sup>4</sup> Heinz-Josef Lenz,<sup>5</sup> Michael Morse,<sup>6</sup> Jayesh Desai,<sup>7</sup> Andrew Hill,<sup>8</sup> Michael Axelson,<sup>9</sup> Rebecca A. Moss,<sup>9</sup> Chen-Sheng Lin,<sup>9</sup> Monica Goldberg,<sup>9</sup> Thierry Andre<sup>10</sup>

<sup>1</sup>MD Anderson Cancer Center, Houston, TX, USA; <sup>2</sup>St Vincent's University Hospital, Dublin, Ireland; <sup>3</sup>Allina Health System, Minneapolis, MN, USA; <sup>4</sup>Istituto Oncologico Veneto IOV-IRCSS, Padova, Italy; <sup>5</sup>USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA; <sup>6</sup>Duke University Office of Research Administration, Durham, NC, USA; <sup>7</sup>Royal Melbourne Hospital, Victoria, Australia; <sup>8</sup>Tasman Oncology Research Pty Ltd, Southport, Queensland, Australia; <sup>9</sup>Bristol-Myers Squibb, Princeton, NJ, USA; <sup>10</sup>Hopital Saint Antoine, Paris, France

PRESENTED AT: **ASCO ANNUAL MEETING '16**

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Rete Oncologica Veneta

Ricerca, innovazione, assistenza



# What it means networking

Disponibilità di nuovi trattamenti

**studio Check-mate 209-142 con Nivo+IPI**

Pazienti con carcinoma del colon metastatico MSI-H

**35 pazienti arruolati c/o l'Oncologia Medica 1, IOV**

## Sintesi dei risultati

<b>Overall Response Rate %</b>	<b>33.3%</b>
<b>PFS rate at 6 months % (CI)</b>	<b>66.6 (45.5, 81.1)</b>
<b>OS rate (6 months) % (CI)</b>	<b>85.1 (65.0, 94.2)</b>

# Nuova terapia adiuvante aumenta la sopravvivenza

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Prolonged Survival in Stage III Melanoma with Ipilimumab Adjuvant Therapy

A.M.M. Eggermont, V. Chiarion-Sileni, J.-J. Grob, R. Dummer, J.D. Wolchok,  
H. Schmidt, O. Hamid, C. Robert, P.A. Ascierto, J.M. Richards, C. Lebbé,  
V. Ferraresi, M. Smylie, J.S. Weber, M. Maio, L. Bastholt, L. Mortier, L. Thomas,  
S. Tahir, A. Hauschild, J.C. Hassel, F.S. Hodi, C. Taitt, V. de Pril, G. de Schaetzen,  
S. Suciú, and A. Testori

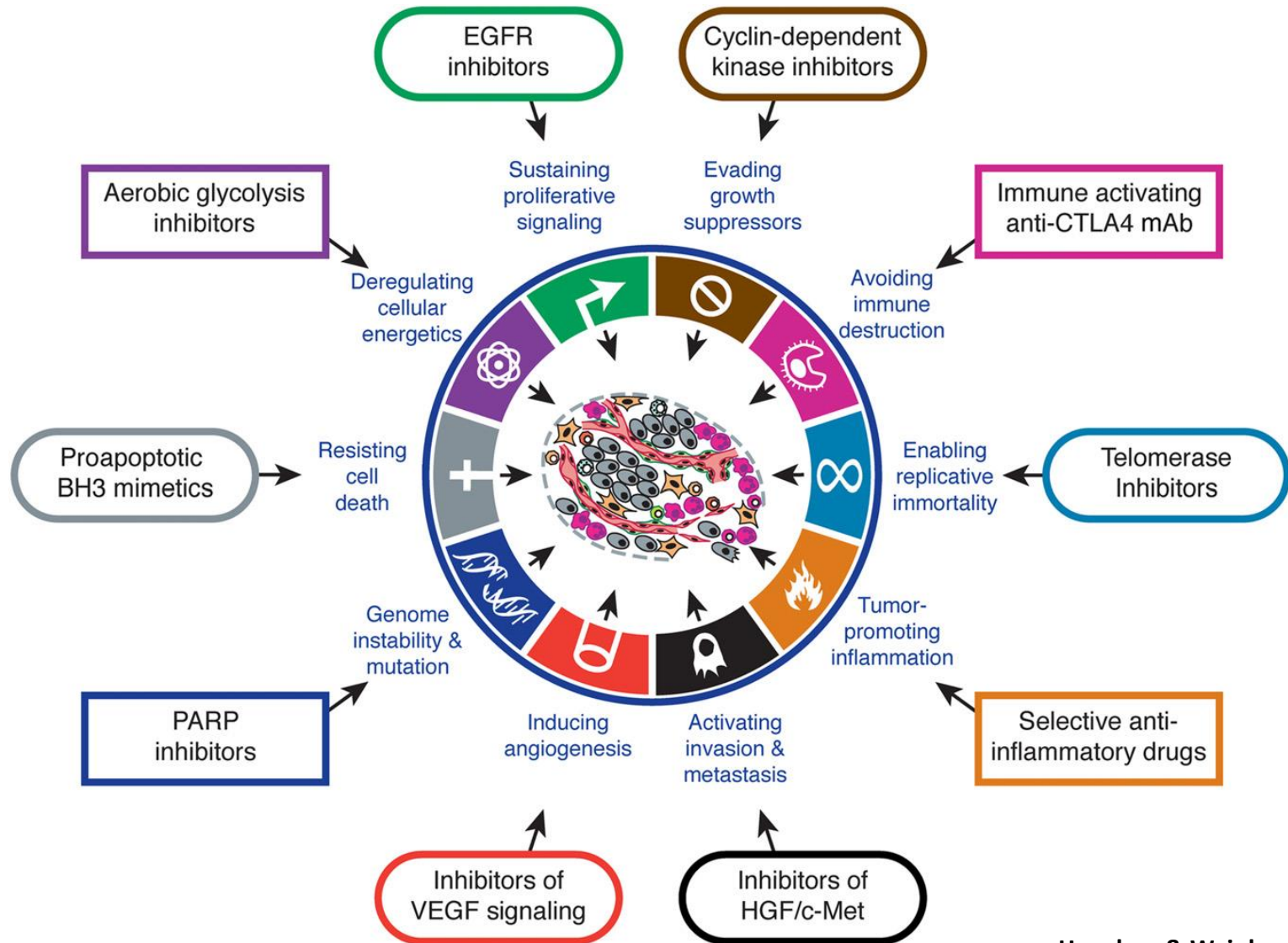
**N Engl J Med 2016;375:1845-55.**

**DOI: 10.1056/NEJMoa1611299**

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# Molecular landscape of cancer





ELSEVIER

journal homepage: [www.ejccancer.com](http://www.ejccancer.com)



# Nuovi modelli di presa in carico dei pazienti

Original Research

Systematic versus on-demand early palliative care: results from a multicentre, randomised clinical trial



Marco Maltoni <sup>a</sup>, Emanuela Scarpi <sup>b,\*</sup>, Monia Dall'Agata <sup>b</sup>, Vittorina Zagonel <sup>c</sup>, Raffaella Bertè <sup>d</sup>, Daris Ferrari <sup>e</sup>, Chiara Maria Brogna <sup>f</sup>, Roberto Bortolussi <sup>g</sup>, Leonardo Trentin <sup>h</sup>, Martina Valgiusti <sup>i</sup>, Sara Pini <sup>i</sup>, Alberto Farolfi <sup>i</sup>, Andrea Casadei Gardini <sup>i</sup>, Oriana Nanni <sup>b</sup>, Dino Amadori <sup>i</sup> on behalf of Early Palliative Care Italian Study Group (EPCISG)

Adesione a linee guida

*Annals of Oncology* 24: 1685–1691, 2013

doi:10.1093/annonc/mdt031

Published online 27 February 2013

## Adherence to treatment guidelines for primary sarcomas affects patient survival: a side study of the European CONnective Tissue CAncer NETwork (CONTICANET)

C. R. Rossi<sup>1,2\*</sup>, A. Vecchiato<sup>1</sup>, G. Mastrangelo<sup>3</sup>, M. C. Montesco<sup>4</sup>, F. Russano<sup>2</sup>, S. Mocellin<sup>2</sup>, S. Pasquali<sup>2</sup>, G. Scarzello<sup>5</sup>, U. Basso<sup>6</sup>, A. Frasson<sup>2</sup>, P. Pilati<sup>2</sup>, D. Nitti<sup>2</sup>, A. Lurkin<sup>7</sup> & I. Ray-Coquard<sup>7</sup>

<sup>1</sup>Melanoma and Sarcomas Unit, Veneto Institute of Oncology-IRCCS, Padova; Departments of <sup>2</sup>Surgery, Oncology and Gastroenterology; <sup>3</sup>Molecular Medicine, University of Padova, Padova; <sup>4</sup>Pathology Unit; <sup>5</sup>Radiotherapy Unit and; <sup>6</sup>Medical Oncology, Veneto Institute of Oncology-IRCCS, Padova, Italy; <sup>7</sup>Department of Medical Oncology, Leon Berard Cancer Center, University of Lyon, Lyon, France

**IOV**



**ULSS 16**



- **Anatomia Patologica**
- **Chirurgie**
- **Servizi**

etc

**AOU**



**Dipartimento  
Oncologico  
Interaziendale**

# GRUPPI MULTIDISCIPLINARI DI PATOLOGIA

## che cosa condividiamo?



- **Clinical activity** 40%
- **Research** 20%
- **Guidelines / PDTA** 10%
- **Clinical trials** 20%
- **Training** 10%

# MDT: mandatory requirements

- **Critical mass**
- **Documentation/audit**
- **Core team/associated services**
- **Patients' rights & empowerment**
- **Organization (nurse navigator)**
- **Policy Support**



# Le reti nazionali

workshop



## Presentazione della Rete Nazionale sui Percorsi Oncologici



**Aula Pocchiari, ISS**

Roma, 14 novembre 2016, ore 9.30

**Identificare le best practice clinico organizzative del PDTA per il paziente affetto da carcinoma del colon e del retto**

- **Arcispedale Reggio Emilia, IRCCS**
- **ASST Papa Giovanni XXIII, Bergamo**
- **Fondazione Poliambulanza, Brescia**
- **Istituto Humanitas, IRCCS Rozzano**
- **Istituto Oncologico Veneto, Padova**
- **Ospedale Niguarda, Milano**
- **Policlinico Gemelli Roma**

# Sopravvivenza di pazienti Oncologia medica 1, IOV 2010-2013

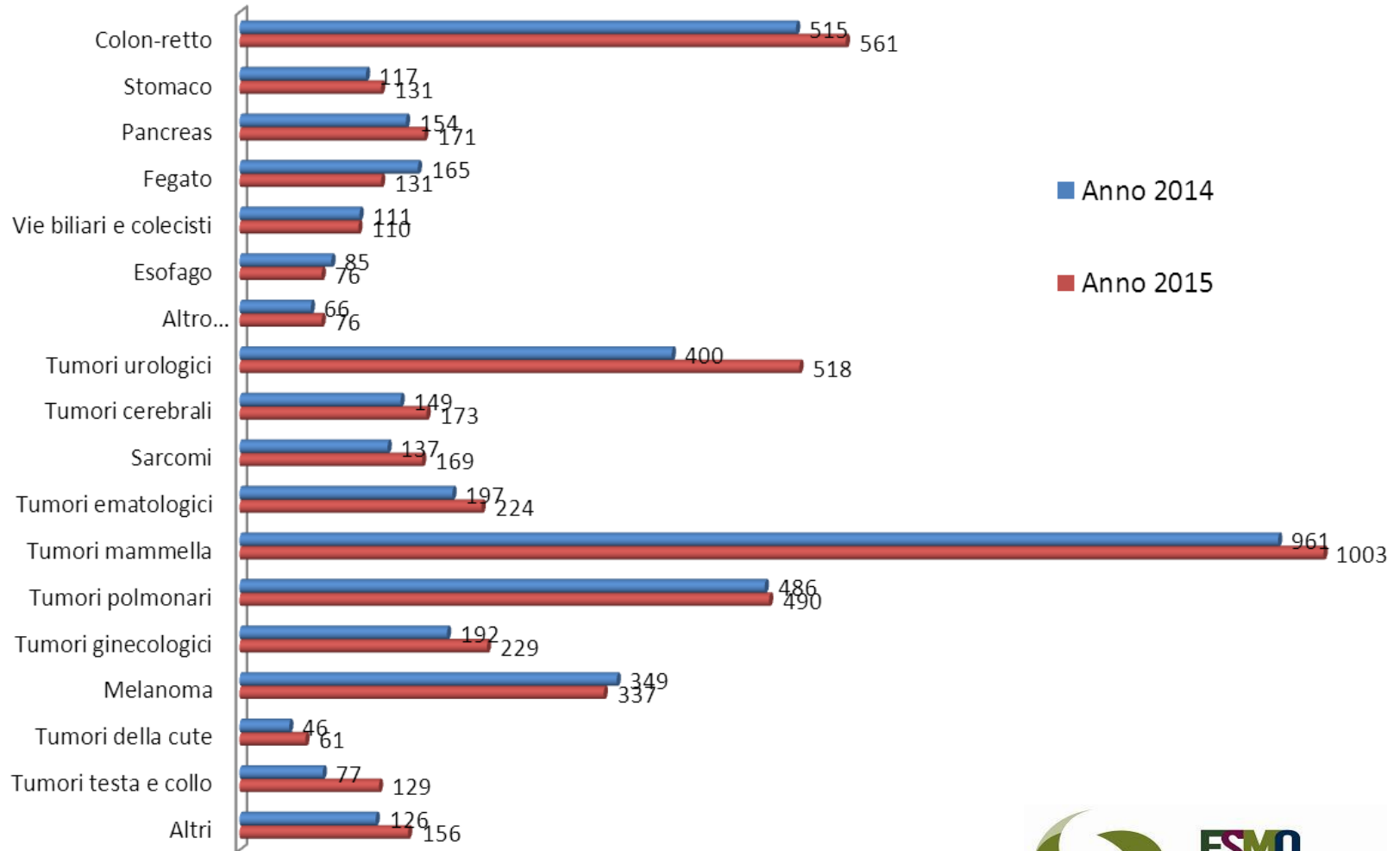


TIPO TUMORE	N. Paz in carico IOV/ N. Paz. Visitati (%)	Paz. non Trattati %	% Paz. inseriti in trials clinici	Media na N. linee terapie	mOS Paz. non trattati (mesi)	<b>mOS Paz. IOV/ studio di riferimento (mesi)</b>	Mediana ultima chemio-decesso (giorni)
COLON-RETTO	461/584 (79)	9.8	38	2	3.67	<b>24,13 vs 25-30</b>	83
STOMACO	97/127 (76)	16	8	1	2.2	<b>10,2 vs 10-13</b>	49
PANCREAS	141/143 (99)	11	0	1	1.28	<b>8,6 vs 8,6-11</b>	68
VIE BILIARI	198/315 (63)	34	0	1	1,43	<b>13,4 vs 11,7</b>	65
FEGATO	233/335 (69)	5	11	1	4.6	<b>9.77 vs 10.7</b>	NV



REGIONE DEL VENETO

# PRIME VISITE ONCOLOGIA MEDICA



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Designated Centers  
of Integrated  
Oncology and  
Palliative Care





REGIONE DEL VENETO

# IL CONTESTO NAZIONALE



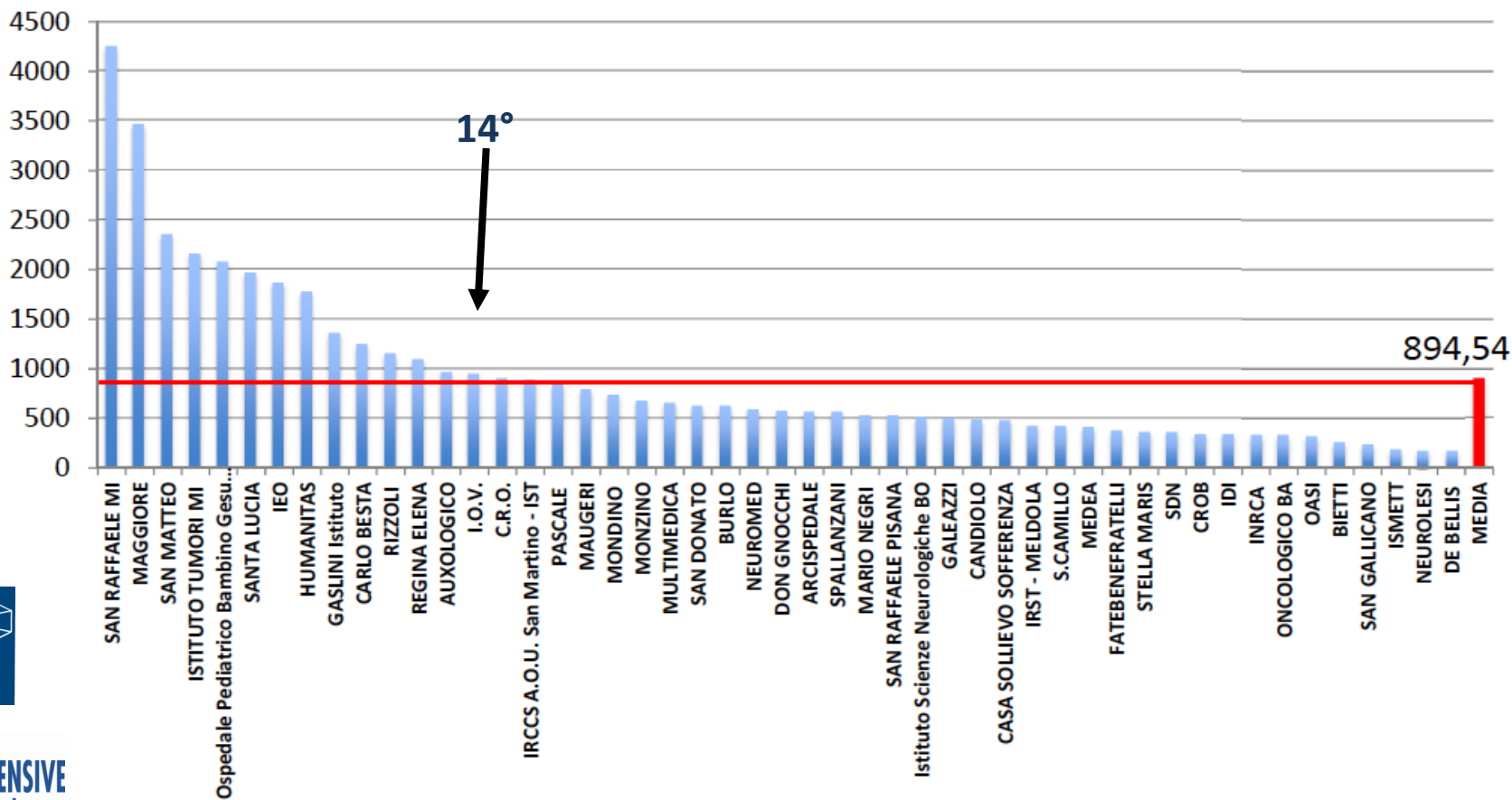
Ministero della Salute

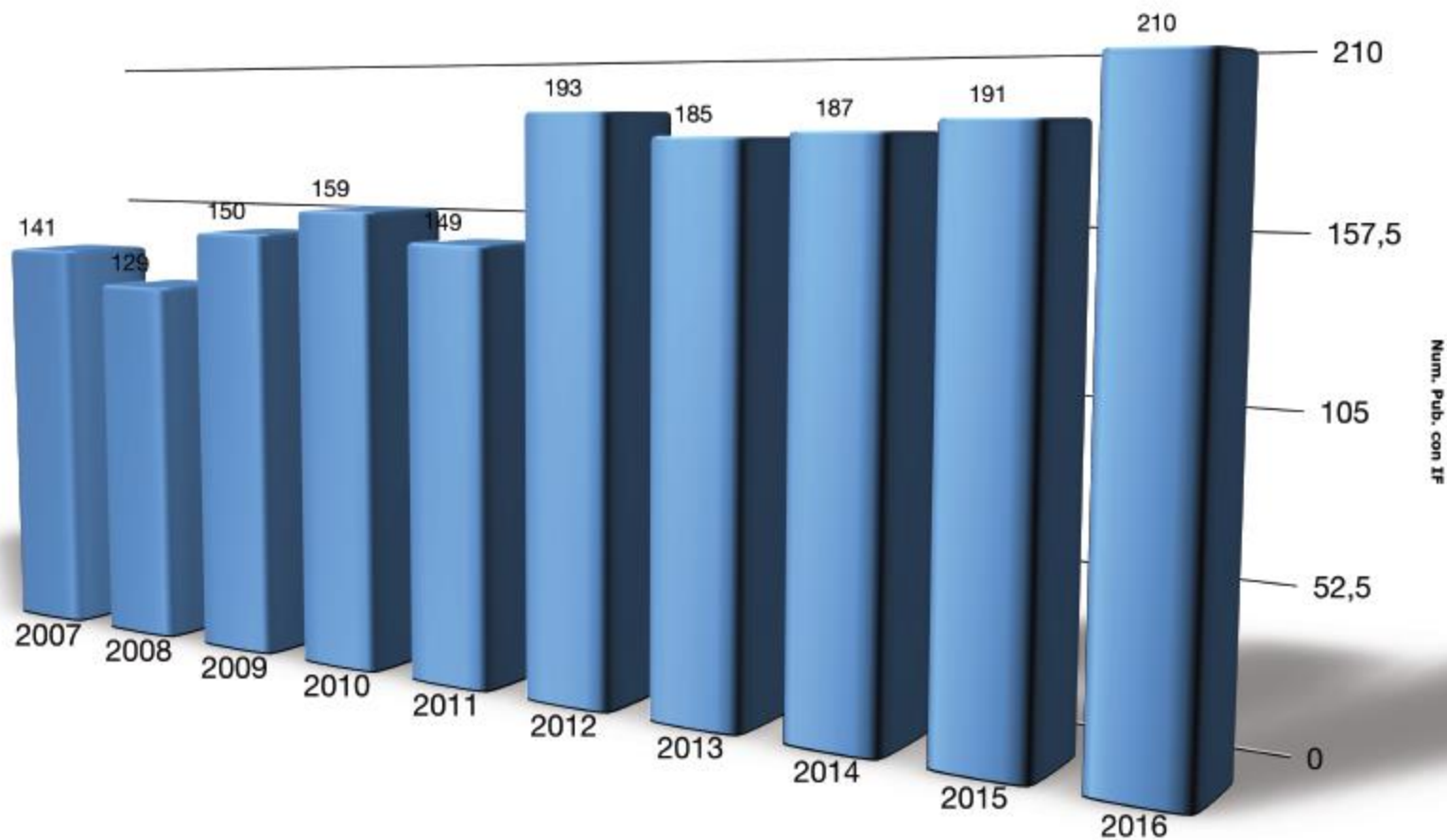
RICERCA CORRENTE IRRCs Attività 2014

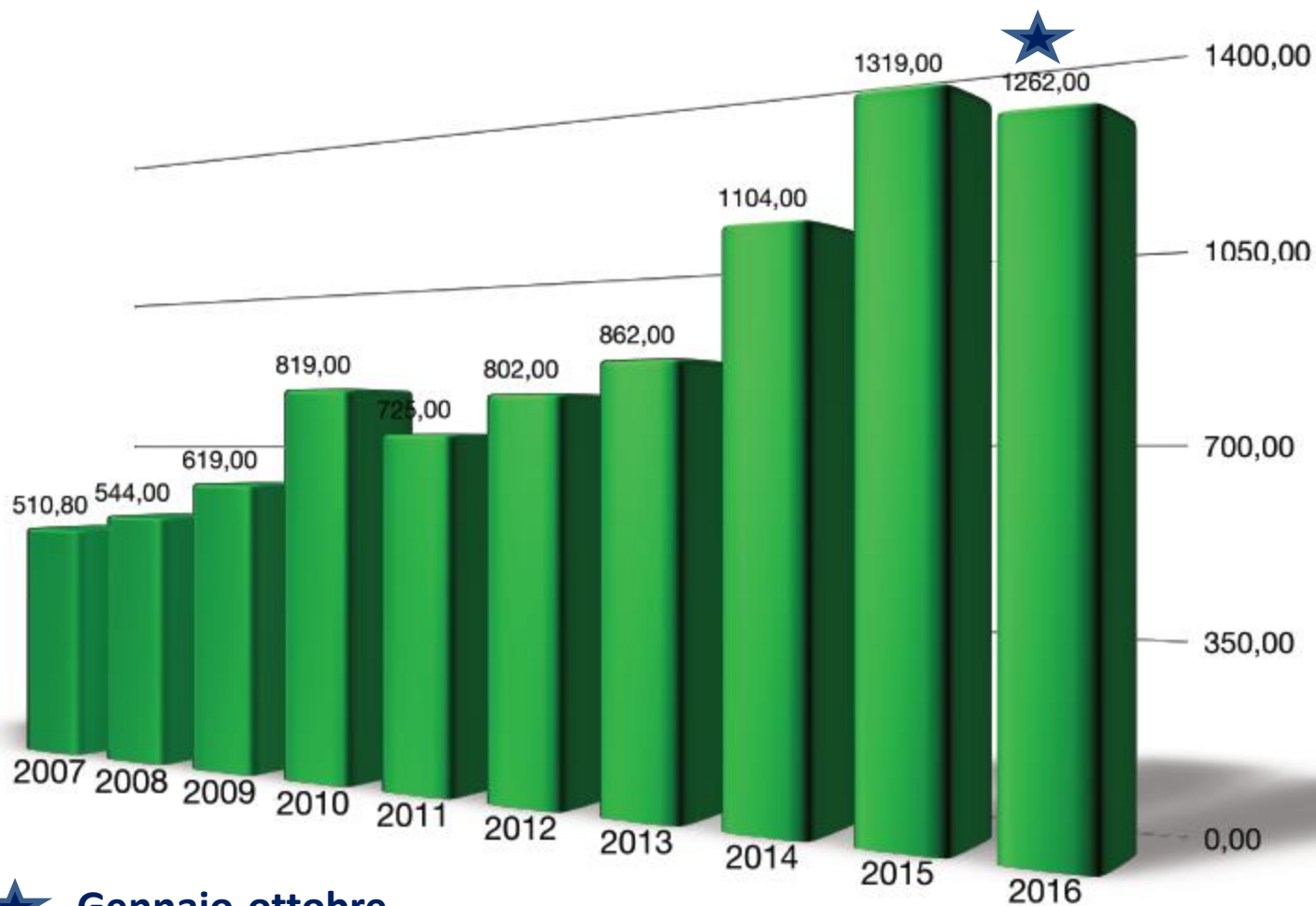


Direzione Generale della Ricerca e dell'Innovazione in Sanità

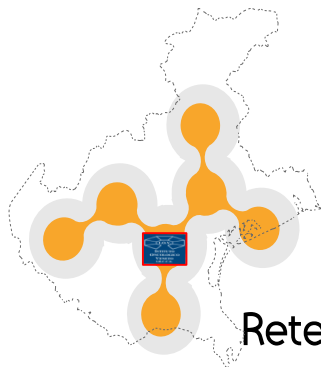
## IFN Validato







★ **Gennaio-ottobre**



Rete Oncologica Veneta

Ricerca, innovazione, assistenza



- *P.D.T.A.*
- *Raccomandazioni farmaci innovativi*
- *Sperimentazioni cliniche*
- *Diagnostica molecolare e biobanche*
- *Informatizzazione*



- *AGENAS:PNE*
  - *ISS*
  - *AIFA*
  - *Min. della Salute*
- RETI**

- *Organisation of European Cancer Institutes-OECI*
- *Cancer Control Joint Action - CanCon*
- *Accreditamento Strutture per cittadini CE*



# NON AVER PAURA DI SOGNARE

- **Passione**
- **Umiltà**
- **Ascolto**
- **Rispetto**
- **Determinazione**
- **Sfida**
- **Condivisione**



**Alberto Mantovani**  
*Decalogo per aspiranti scienziati*