



Innovazione in Oncologia
L'esperienza della Regione Toscana

Siena, 16 Giugno, 2017



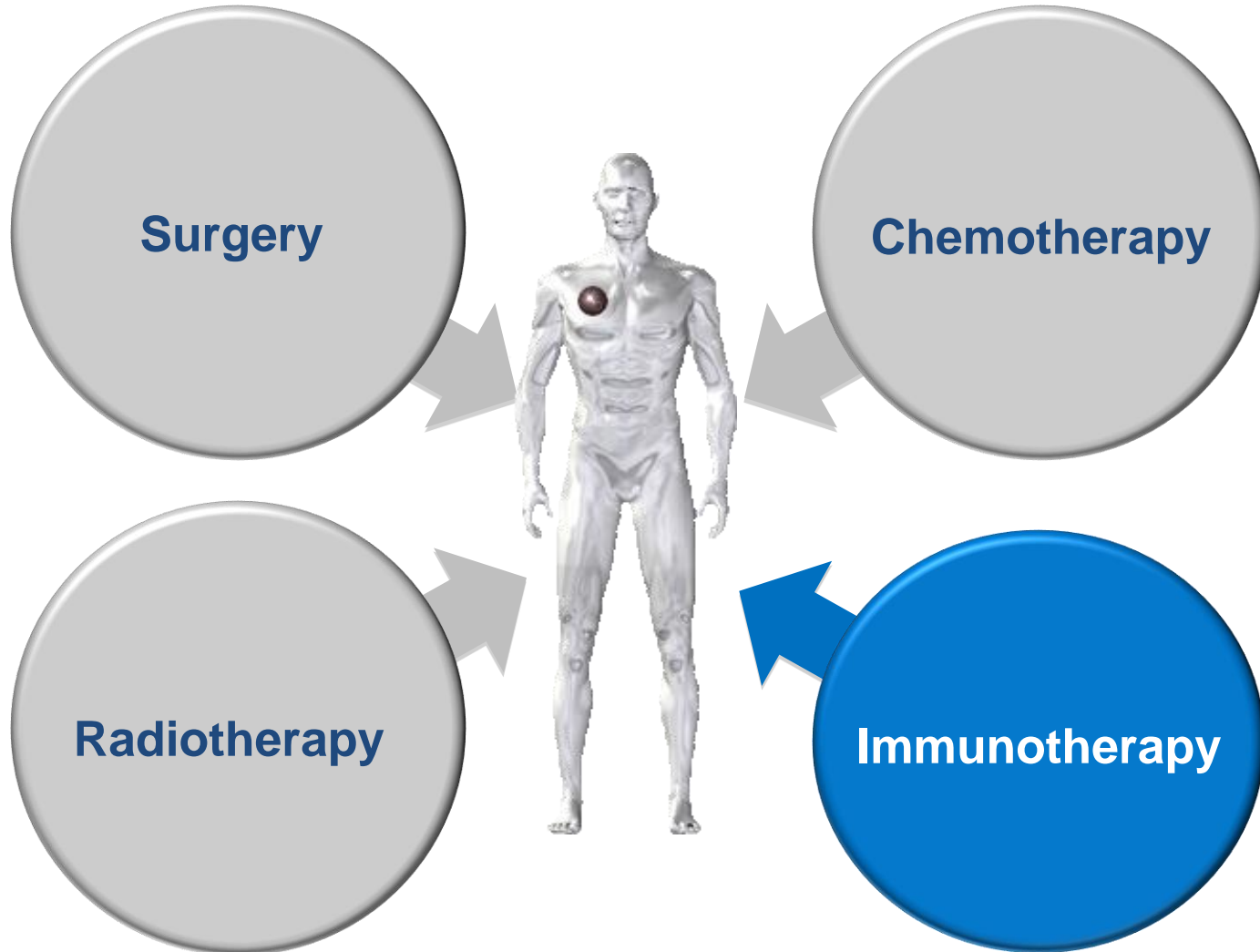
**Stato dell'arte sulle aree terapeutiche
Ricerca Clinica**

Michele Maio

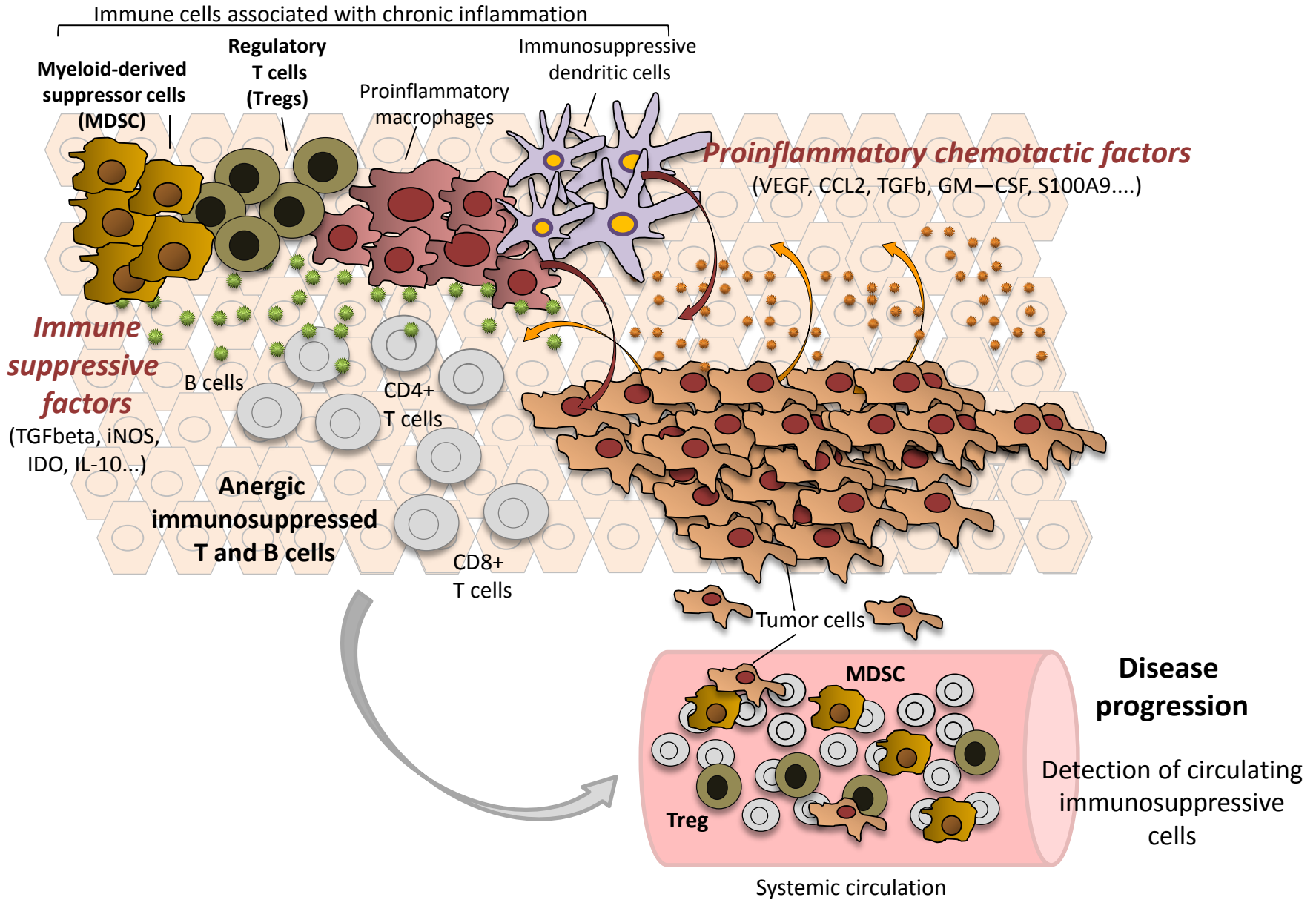
Medical Oncology and Immunotherapy
Center for Immuno-Oncology
SIENA, ITALY



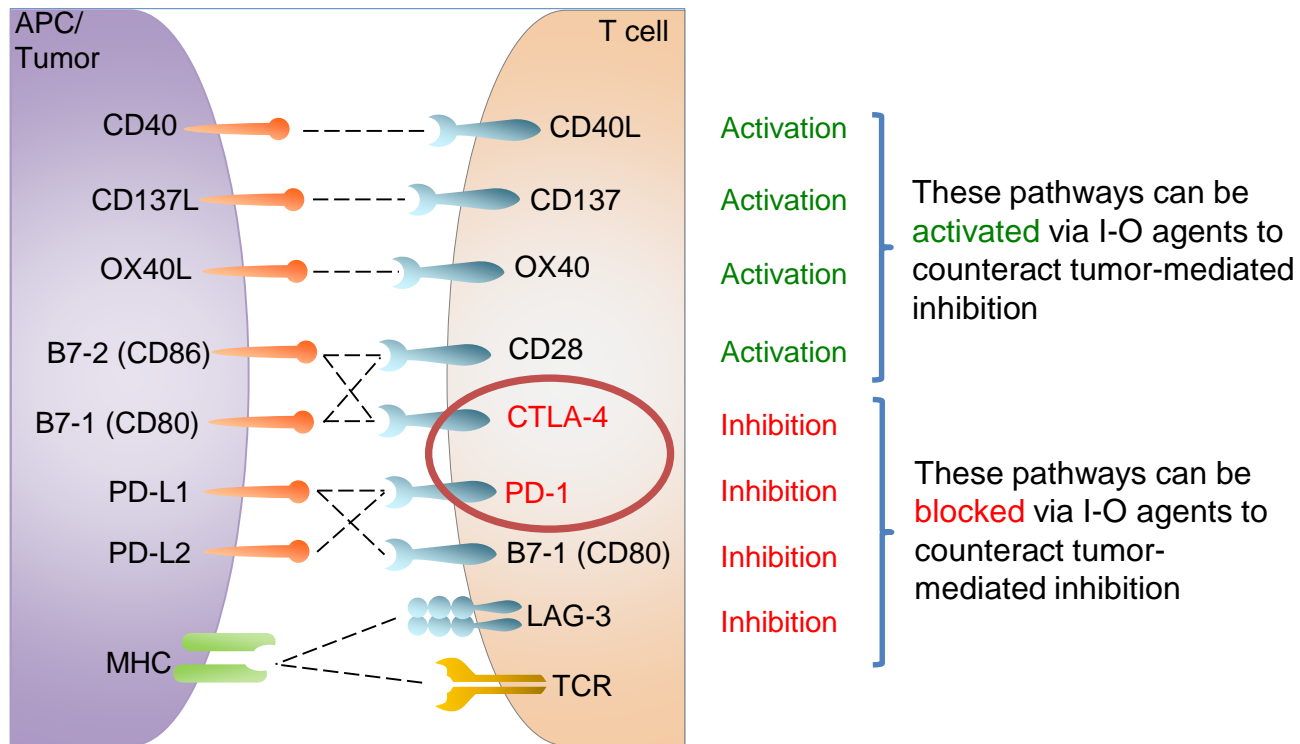
Evolving Therapeutic Options for Cancer Treatment



The immune system complexity



T-cell Checkpoint and Co-stimulatory Pathways



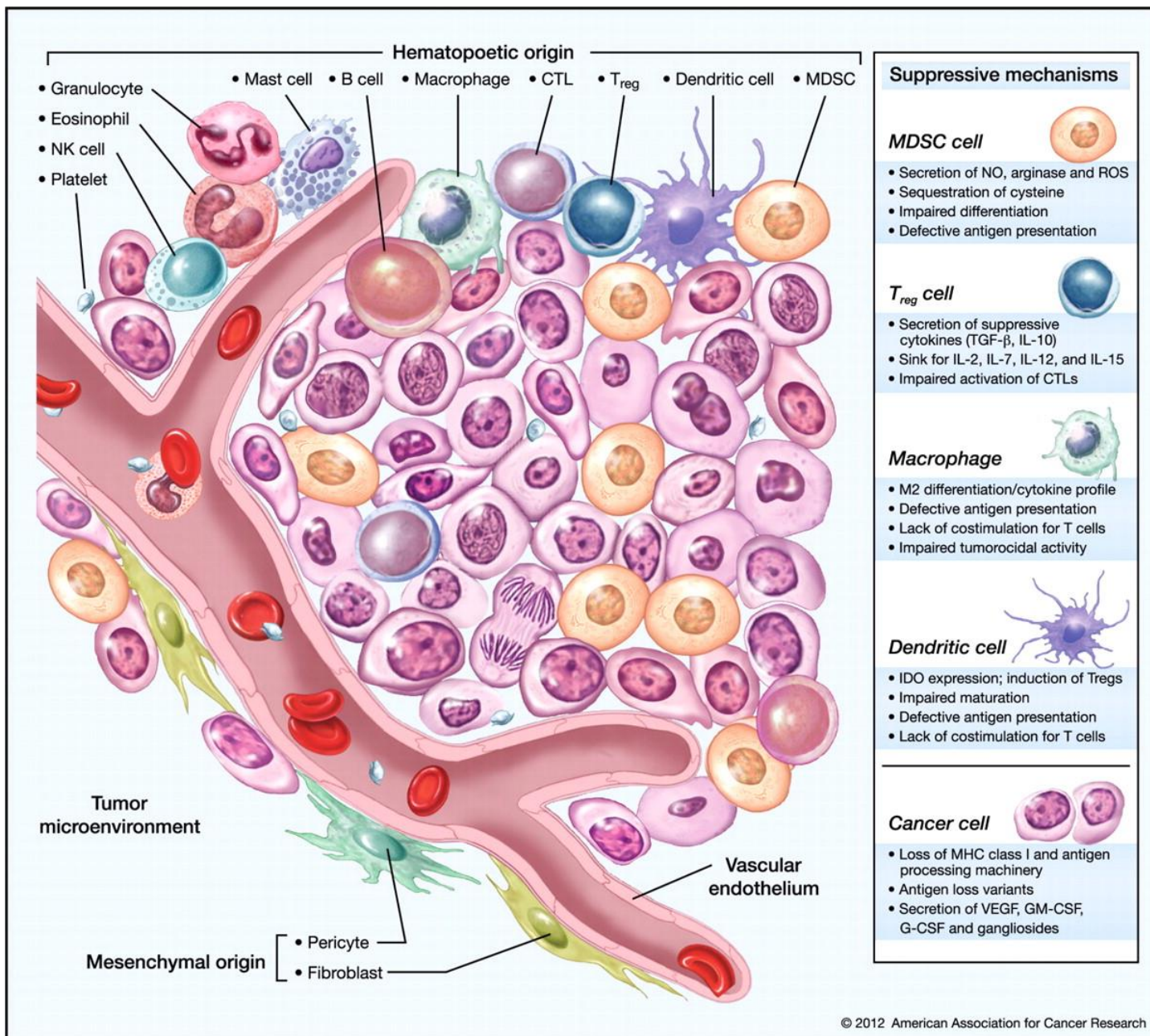
Adapted from Pardoll DM 2012.

APC=antigen-presenting cell; CTLA-4=cytotoxic T-lymphocyte antigen-4; LAG-3=lymphocyte activation gene-3; MHC=major histocompatibility complex;

PD-1=programmed death-1; PD-L1=PD ligand-1; PD-L2=PD ligand-2; TCR=T-cell receptor.

Pardoll DM. *Nat Rev Cancer*. 2012;12:252-264.

Tumor microenvironment

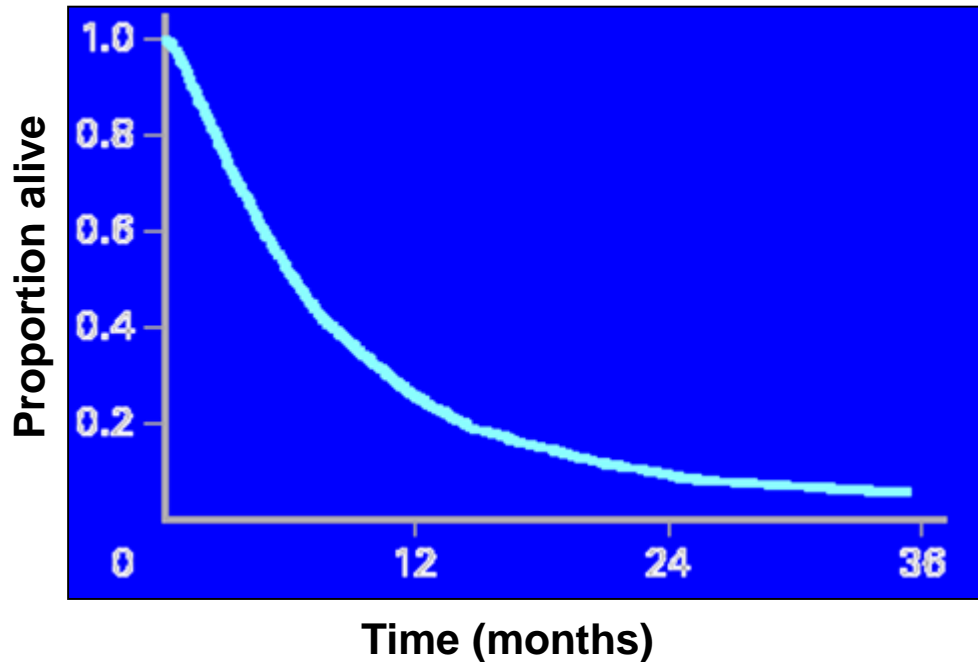


Melanoma as a tool for cancer research

- ✓ **Tissue samples readily accessible**
- ✓ **Adaptable to tissue culture**
- ✓ **Amenable to testing of novel therapies**



Overall Survival for Metastatic Melanoma



Adapted from Korn 2008

Survival data from 42 Phase II trials with over 2,100 stage IV patients¹:

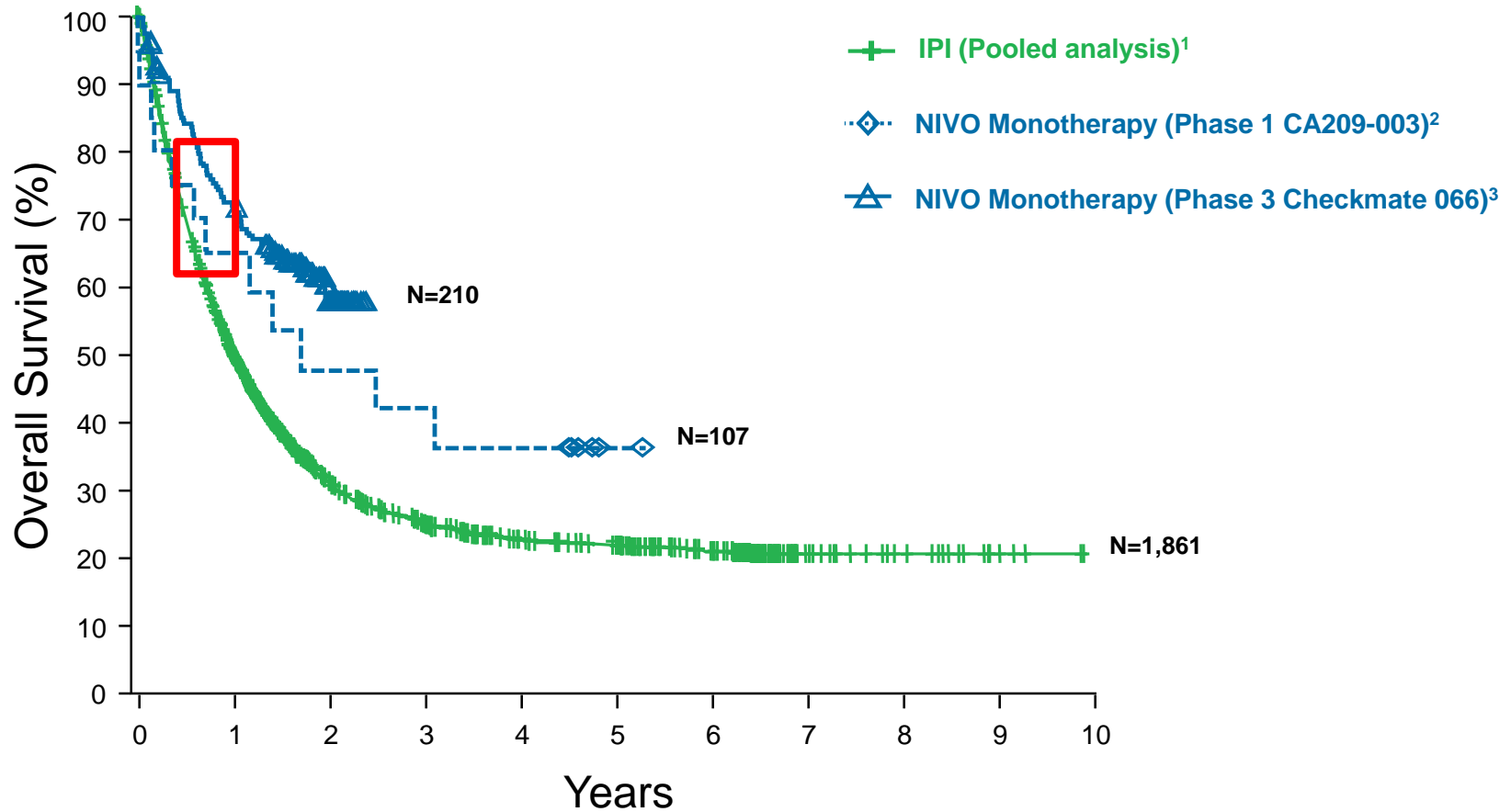
12 month OS: 25.5 %, median OS: 6.2 months (stage IV melanoma including patients with brain metastases)

Due to the lack of efficacious therapy, the preferred treatment for metastatic melanoma remains the inclusion in a clinical trial²

¹Korn EL et al. J Clin Oncol 2008;26(4):527-34.

²Dummer R, Hauschild A, Jost L. Cutaneous malignant melanoma: ESMO clinical recommendations for diagnosis, treatment and follow-up. Ann Oncol 2008;19 Suppl 2:ii86-8.

Immune Checkpoint Inhibitors Provide Durable Long-term Survival for Patients with Advanced Melanoma



1. Schadendorf et al. *J Clin Oncol* 2015;33:1889-1894; 2. Current analysis; 3. Poster presentation by Dr. Victoria Atkinson at SMR 2015 International Congress.

PRE



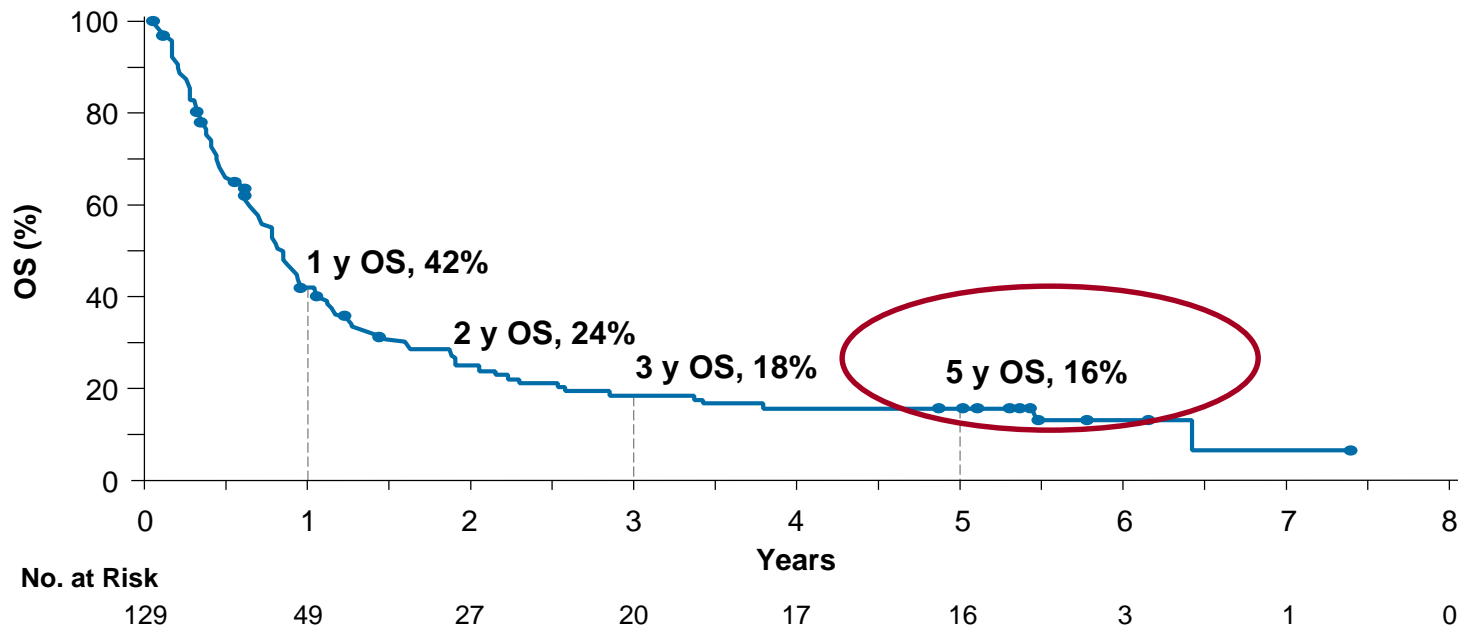
POST



5-Year Estimates of OS

BMS CA209-003: phase 1 dose finding study in NSCLC

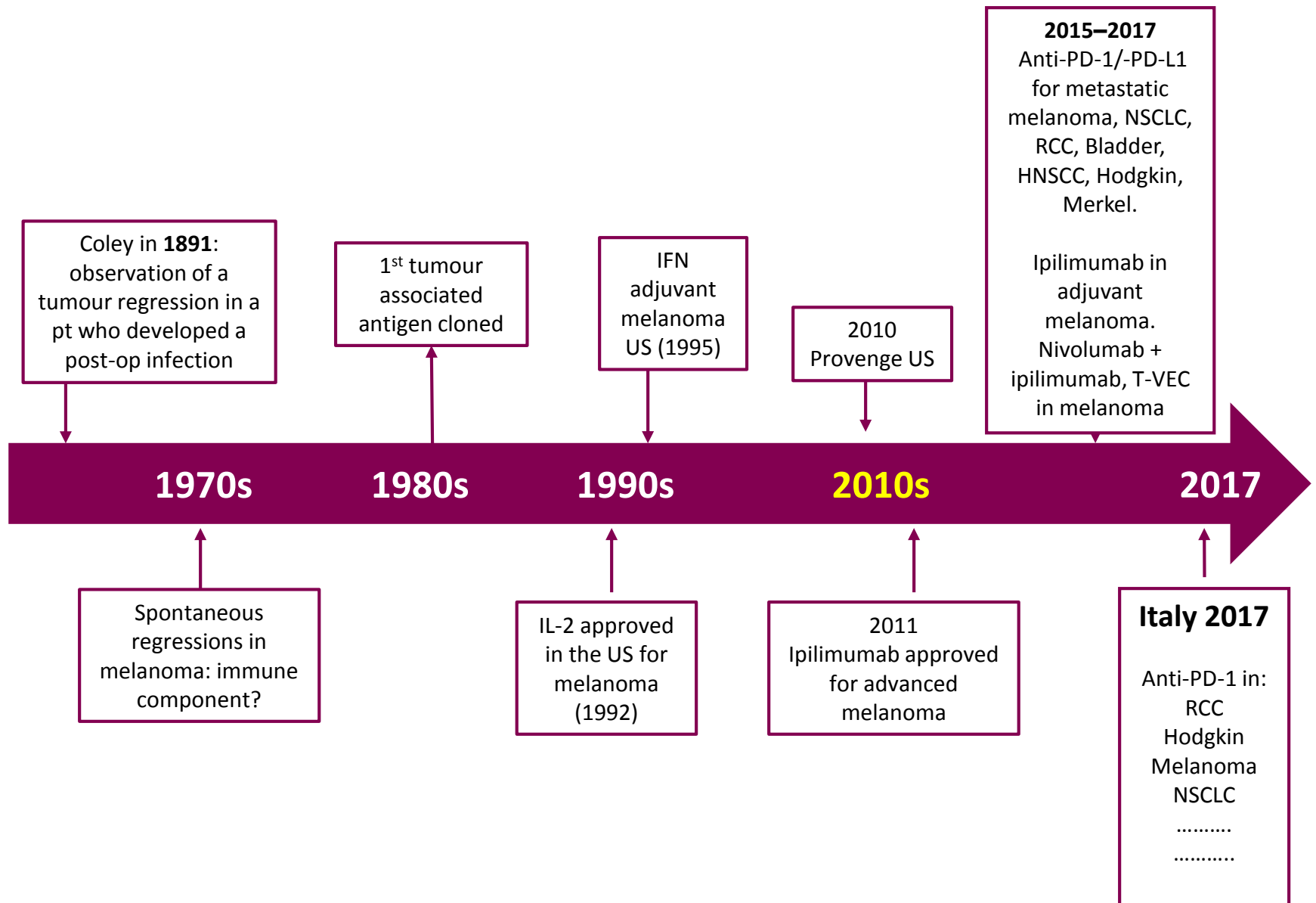
	Median OS (95% CI), mo
Overall (N = 129)	9.9 (7.8, 12.4)



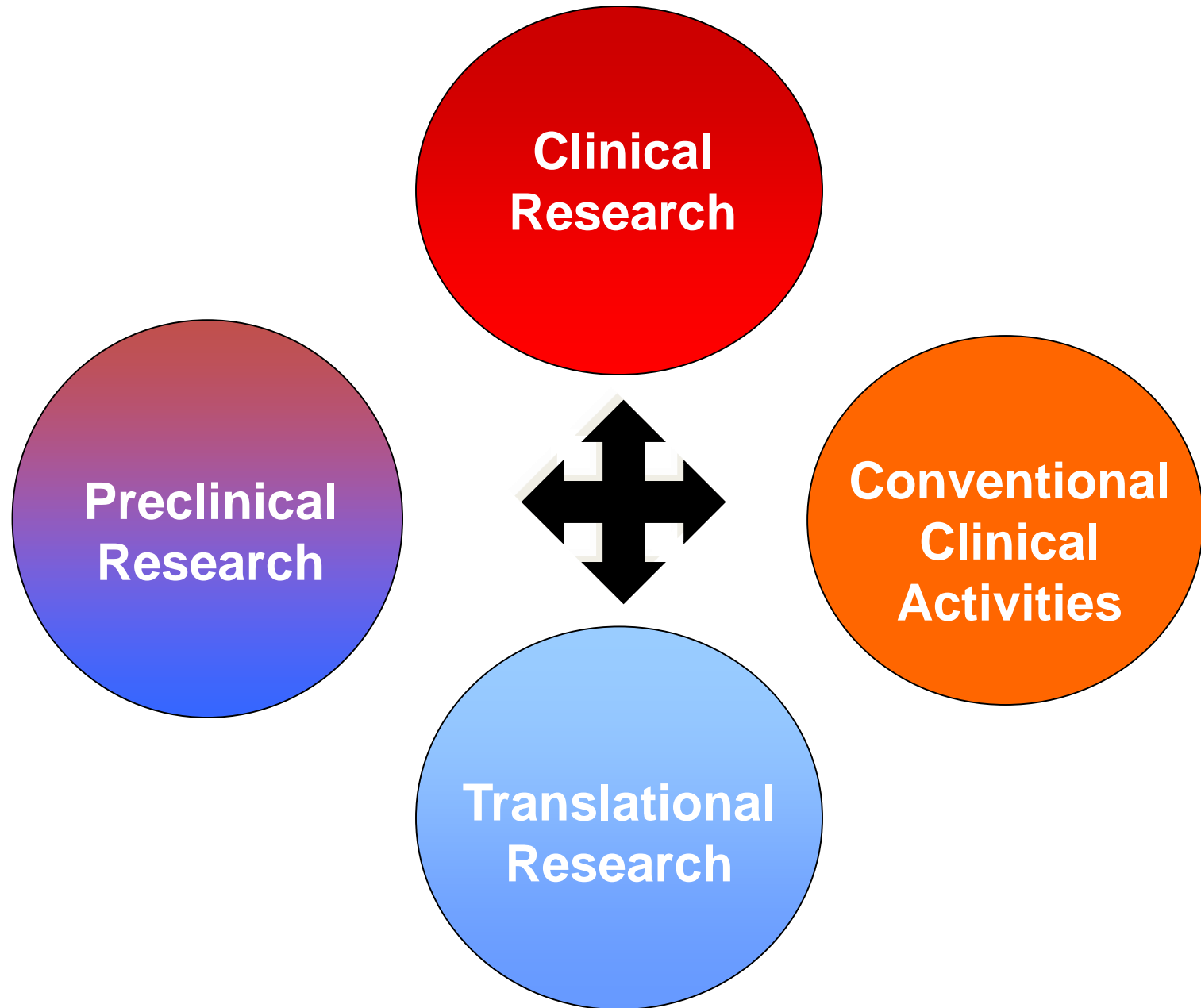
^aThere were 3 deaths between 3 and 5 years, all due to disease progression; 1 surviving patient was censored for OS prior to 5 years (OS: 58.2+ months)



A historical view of immunotherapy...

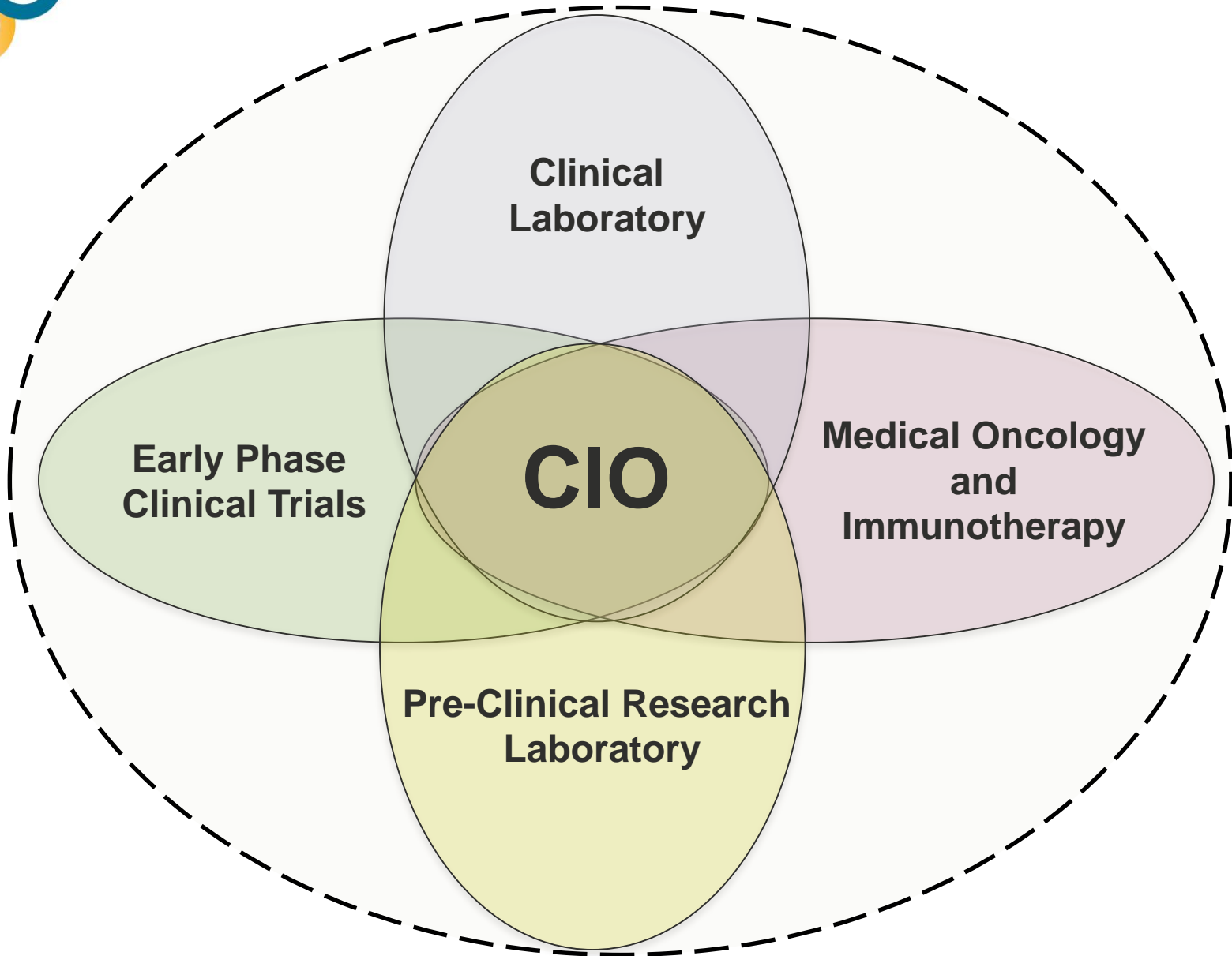






The Center for Immuno-Oncology

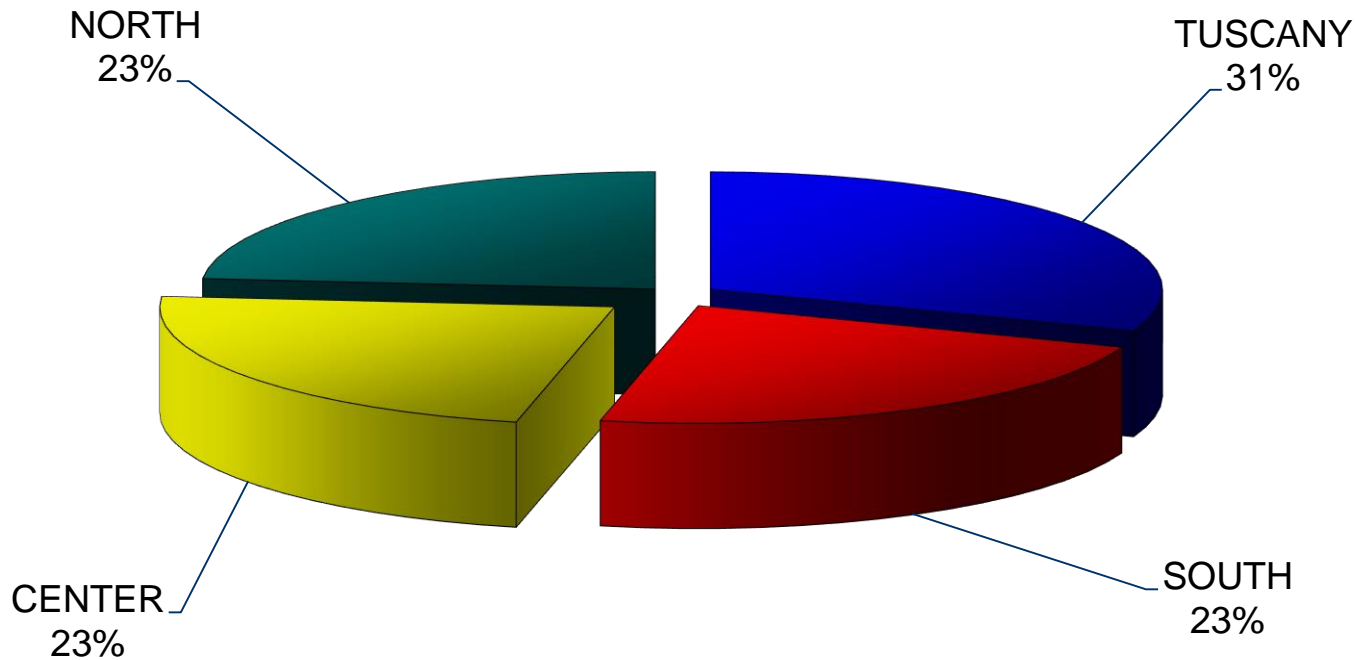
University Hospital of Siena - Italy



The Center for Immuno-Oncology

Nationwide patient referrals

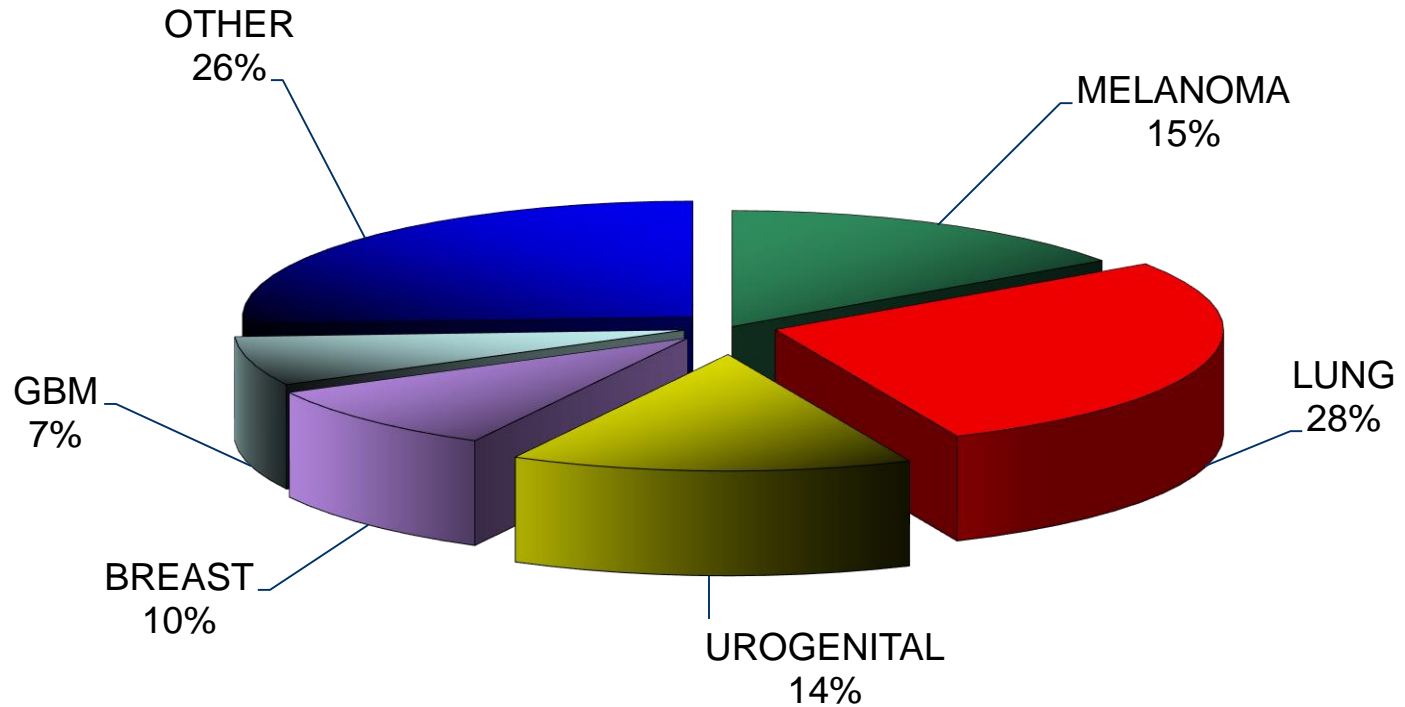
>2.200 new patients in 2016



The Center for Immuno-Oncology

Nationwide patient referrals

>2.200 new patients in 2016



Clinical trials (2006-2016)

Phase I = 11

Phase II = 35

Phase III = 46

EAP = 8

IIT = 6

IIT:

NIBIT-M1

NIBIT-M2

NIBIT-M4

MESOT-TREM-2008

MESOT-TREM-2012

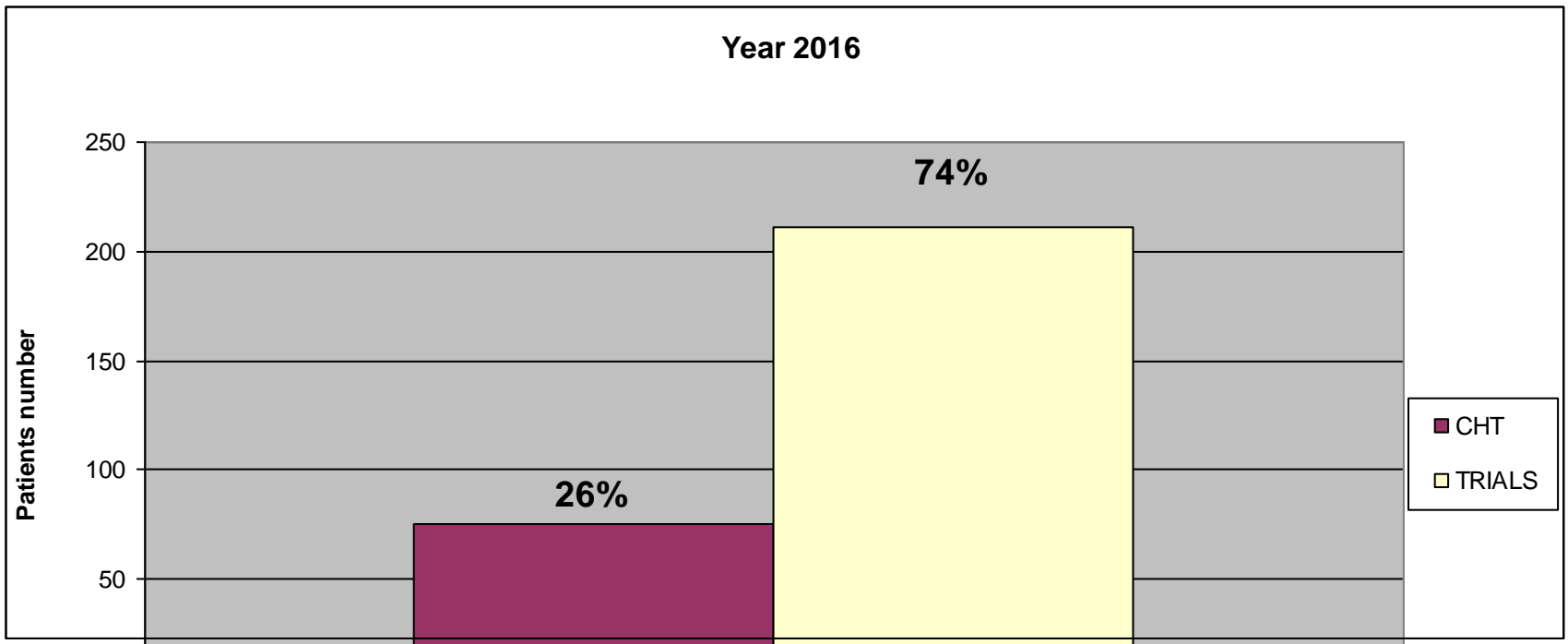
NIBIT-MESO-1

Therapeutic agents

- Vaccines
- Cytokines
- Checkpoint Inhibitors
- Armed antibodies
- Targeted therapies
- Epigenetic drugs
- Anti-angiogenetics
- Anti-apoptotics



Clinical Trials Enrollment rate 2016



.... <5% of adults with cancer each year will be enrolled in a clinical trial in US (NCI, 2012)

Granting Agencies

Associazione Italiana per la Ricerca sul Cancro
Fondazione Italiana per la Ricerca sul Cancro
Ministero della Sanità Italiano
Istituto Superiore della Sanità Italiano,
Consiglio Nazionale delle Ricerche
Ministero dell'Università e della Ricerca Scientifica
European Union
National Cancer Institute-Bethesda-MD-USA,
Industry
Contract Research Organizations

Pharma collaborations

Bristol-Myers Squibb
GlaxoSmithKline
Incyte
Merck Serono
Merck Sharp & Dohme
MedImmune
AstraZeneca
Roche
Astex
Novartis
Pfizer
Philogen
AB Science
Sigma-Tau

Scientific Publications : # 221

Total IF 1729,044,
H-index 55

Lancet, New England Journal of Medicine, Journal of Clinical Investigation, Human Gene Therapy, Blood, Breast Cancer Research and Treatment, Journal of Clinical Oncology, Seminars in Oncology, International Journal of Oncology, American Journal of Clinical Oncology, Clinical Cancer Research, Cancer Immunology Immunotherapy, Journal of Immunotherapy, Journal of Immunology, Cancer Research, Immunology Today, European Journal of Immunology, British Journal of Cancer, International Journal of Cancer, Cell Growth and Differentiation, Cytokine, Scandinavian Journal of Immunology, Tissue Antigens, Laboratory Investigation, Melanoma Research, Leukemia and Lymphoma, Women's Oncology Review, The Journal of Clinical Endocrinology and Metabolism, Current Drug Targets, Oncogen,

The “enlarged” CIO Composition

The Multidisciplinary Team

Dermatologist
Gastroenterologist
Radiologist
Pathologist
Neurologist
Neuroradiologist
Ophthalmologist
Endocrinologist
Cardiologist
Nephrologist

External Programs

NIBIT
NIBIT Foundation

NIBIT

Network Italiano per la Bioterapia dei Tumori





FONDAZIONE
NIBIT
ONLUS

Network Italiano per la Bioterapia dei Tumori

NIBIT Foundation

Established in 2012 by the NIBIT Board of Directors as a not-for-profit organization (www.fondazioneenibit.org), to focus within a legally distinct entity the comprehensive activities connected with the conception, planning, and implementation of clinical trials on cancer bio-immunotherapy.

Main objectives:

- ✓ **Design, develop and implement phase I-IV clinical trials.**
- ✓ **Coordinate and/or cooperate at multicenter clinical studies.**
- ✓ **Promote scientific and educational activities in cancer bio-immunotherapy.**
- ✓ **Support basic and/or translational research projects.**

The NIBIT Foundation Interactions and Infrastructures

The Center for Immuno-Oncology:

University Hospital, Siena, Italy

Research Laboratories:

At Toscana Life Science Park, Siena, Italy

Contract Research Organization:

Clinical Research Technology - Via San Leonardo, Salerno, Italy

Research Statistics:

Statistical Unit, National Cancer Institute, Rome, Italy

Bioinformatics:

Biocenter, Division for Bioinformatics Medical University, Innsbruck, Austria

Press Office:

Pro Format Comunicazione - Viale Aventino 45, Rome, Italy

Legal Offices:

Via Goffredo Mameli 3/1, Genoa, Italy

Scientific Network and Collaborations (selected)

Academia:

More than 50 scientific Institutions across Europe and I-O Center of Sienna, Italy

Scientific Societies:

Society for Immunotherapy of Cancer (SITC - USA), Cancer Immunotherapy (CIMT - Germany), European Academy of Tumor Immunology (EATI - France), National Cancer Institute (NIH, USA), European Society of Medical Oncology (ESMO - Europe), New York Academy of Science (NYAS - USA), Italian Association for Medical Oncology (AIOM - Italia), Italian Association for Cancer Research (AIRC - Italia)

Pharma:

Bristol-Myers Squibb, Astex Pharmaceuticals, Astra Zeneca, Merck Serono, Merck Sharp & Dohme, MedImmune, Roche, Incyte, Amgen

EMBARGOED UNTIL 6 A.M. EST, DEC. 1, 2016

December 1, 2016

**Parker Institute for Cancer Immunotherapy and Cancer Research
Institute Launch Collaboration on Cancer Neoantigens**

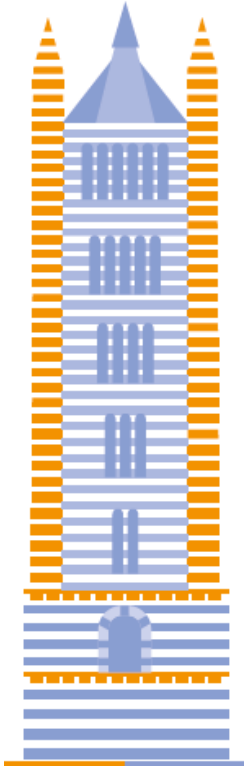
*Researchers at 30 organizations to test algorithms that predict tumor
markers from DNA in hunt for new personalized cancer treatments*

Participating Organizations

Currently, the research institutions taking part include the Broad Institute of MIT and Harvard, Caltech, the Dana-Farber Cancer Institute, the La Jolla Institute for Allergy and Immunology, the Ludwig Institute for Cancer Research, Roswell Park Cancer Institute, The Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai, the University of California, Santa Cruz, the University of Connecticut and Washington University School of Medicine. Internationally, scientists from the Fondazione Network Italiano per la Bioterapia dei Tumori, National Cancer Centre Singapore, the National Center for Tumor Diseases at Heidelberg University Hospital and the Netherlands Cancer Institute have also stepped forward to join the project.

Educational activities (selected)

- ✓ **1st Level I-O Masterclasses for Medical Oncologists**
(8 CME editions in 2014 - 2016)
- ✓ **I-O Masteclasses in Thoracic Oncology**
(3 CME editions in 2016)
- ✓ **2nd Level I-O Masterclasses for Medical Oncologists**
(1st CME edition in 2016)
- ✓ **ESMO Preceptorship on Immuno-Oncology**
(CME edition - July 2016)
- ✓ **European I-O Masterclasses for PIs of Pharma trials**
(1st edition in December 2016)
- ✓ **I-O Masterclasses for Pharma employees**
(1st edition in January 2017)
- ✓ **I-O Masterclasses for Radiologists**
(1st edition in March 2017)



The Duomo Tower - Siena

A large circular graphic on the left side of the page features a close-up of a person's eye and a slight smile. The eye is light blue and looking upwards and to the right. The smile is subtle, showing the top teeth. The background of the circle is a teal color.

Il primo **portale italiano** di
Immunoterapia applicata
al trattamento dei tumori

si arricchisce oggi di una veste
grafica totalmente rinnovata,
nuovi contenuti
e **nuove funzioni**

ImmunOncologia.org

Un indispensabile strumento
di approfondimento
e di aggiornamento dedicato
alla **comunità scientifica**

Una fonte
d'informazione chiara,
semplice ed esaustiva
aperta al **pubblico**

Molto più di un sito web

In collaborazione con



MICHELE
MAIO
Agnese Codignola
**IL CORPO
ANTI
CANCRO**

Come con l'**IMMUNOTERAPIA**
si può vincere la lotta contro i tumori

PIEMME

Francesco



Melanoma
Lung cancer

CTLA-4
PD1-PDL1
CTLA-4/PD1

Other tumors

Breast

Gastro-intestinal

Mesothelioma

Urothelial

Glioblastoma

Ovarian

Renal

Head-Neck

Combos/Sequences

Novel targets

LAG-3

4-1BB

CD40

TIM-3

OX-40

ICOS

IDO

KIR

GITR



Medical Oncology and Immunotherapy

Center for Immuno-Oncology

University Hospital of Siena - Italy



- Maresa Altomonte
- Erika Bertocci
- Luana Calabrò
- Ornella Cutaia
- Riccardo Danielli
- Anna Maria Di Giacomo
- Carolina Fazio
- Ester Fonsatti
- Carla Chiarucci
- Gianluca Giacobini
- Andrea Lazzeri



- Francesca Colizzi
- Sandra Coral
- Alessia Covre
- Elisabetta Fratta
- Hugues Nicolay
- Luca Sigalotti
- Maria Lofiego
- Patrizia Tunicì
- Antonello Lamboglia
- Monica Valente
- Armida D'Incecco

