GIORNATA DELLA RICERCA UCBM

CLINICAL AND TRANSLATIONAL RESEARCH IN ONCOLOGY

Prof. Daniele Santini, MD PhD

Medical Oncology
Translational Oncology Laboratory
Campus Bio-Medico of Rome

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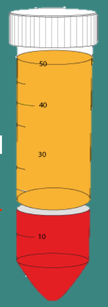
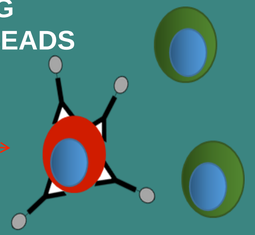
IN-VITRO MODELS OF BONE CELLS

• PRIMARY HUMAN OSTEOCLASTS

PBMCs PURIFICATION

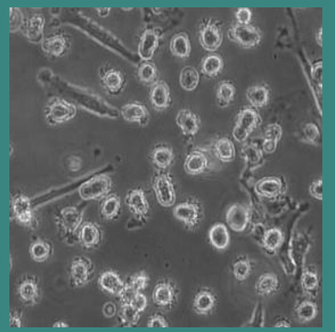


CD14 + CELLS LABELING WITH MICROBEADS

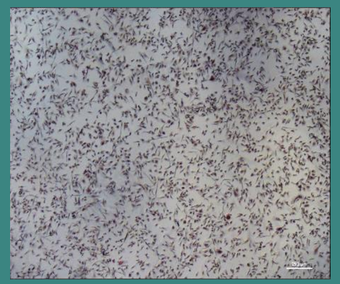


MAGNETIC ISOLATION

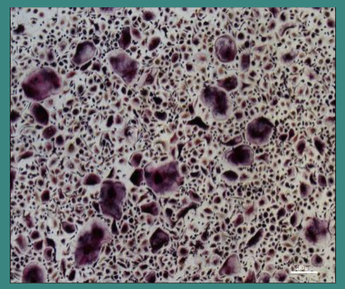
SEEDING



DIFFERENTIATION (TRAP ASSAY)



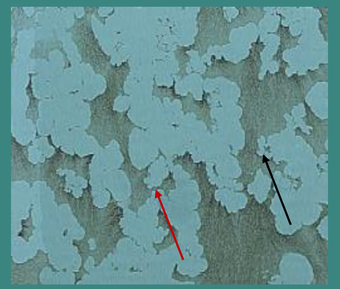
UNDIFFERENTIATED



DIFFERENTIATED

ACTIVITY (OSTEOASSAY)

UNDIFFERENTIATED



DIFFERENTIATED

BONE LAYER

RESORBED AREA

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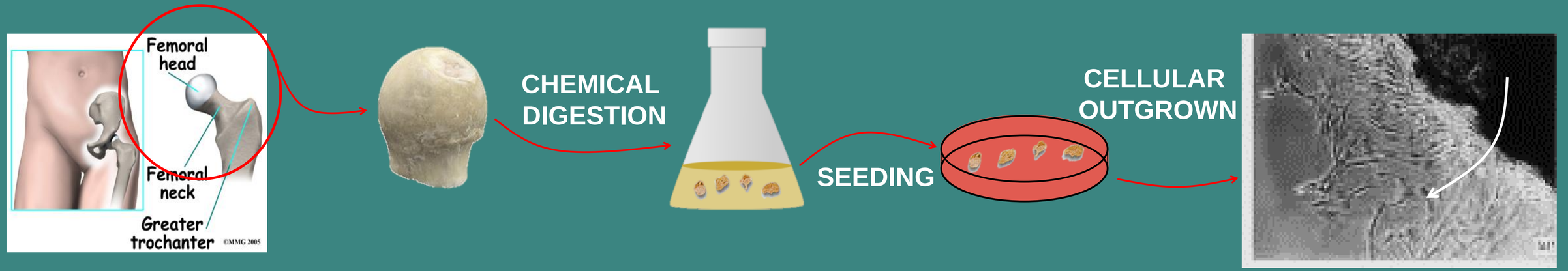
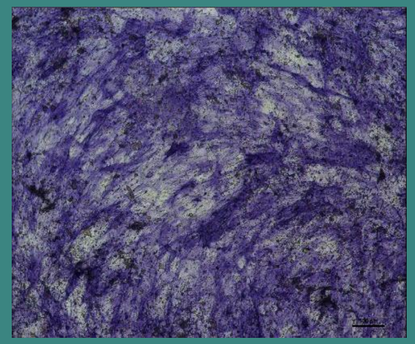
IN-VITRO MODELS OF BONE CELLS

- PRIMARY HUMAN OSTEOBLASTS



DIFFERENTIATION (ALP ASSAY)

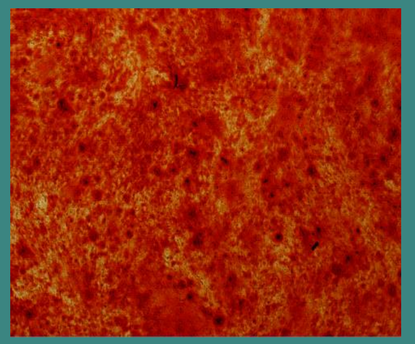
UNDIFFERENTIATED



DIFFERENTIATED

ACTIVITY (ALIZARIN RED ASSAY)

UNDIFFERENTIATED



DIFFERENTIATED

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IN-VITRO COCOLTURE SYSTEMS

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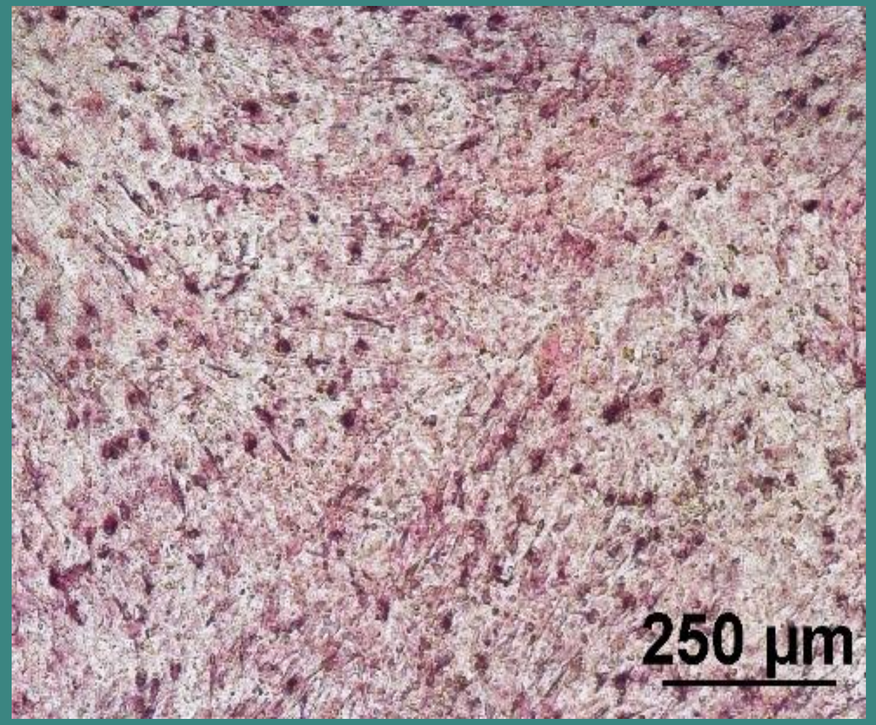
Direct cocultures:

- Osteoblasts/ Osteoclasts

Osteoclasts

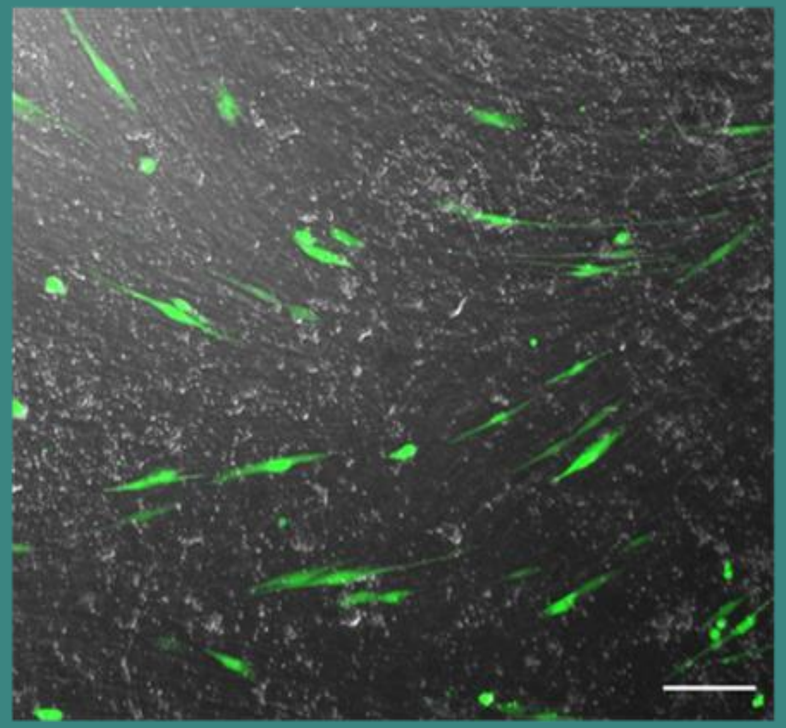
Osteoblasts



- Osteoblasts/ Cancer cells

Prostate cancer cell

Osteoblasts

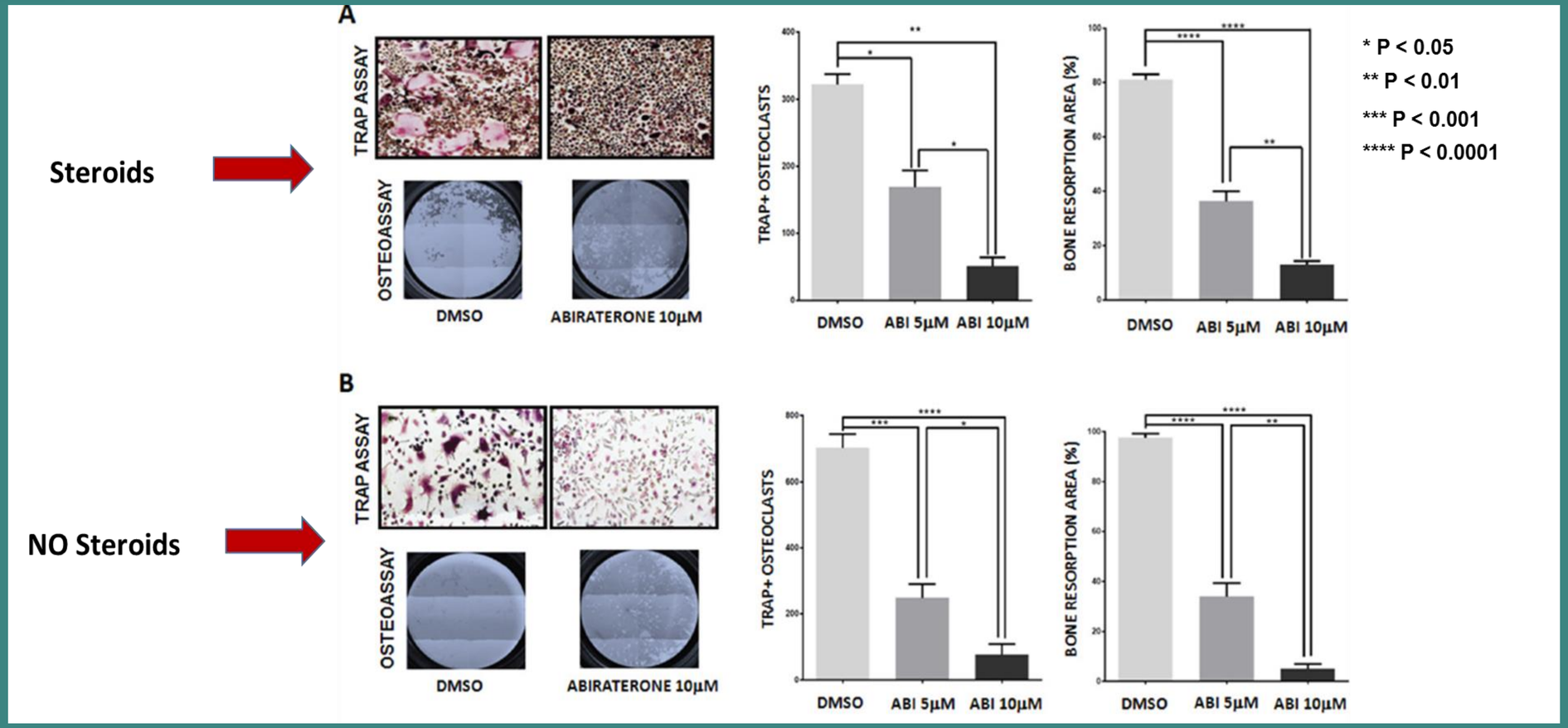


www.impactjournals.com/oncotarget/ Oncotarget, Advance Publications 2015

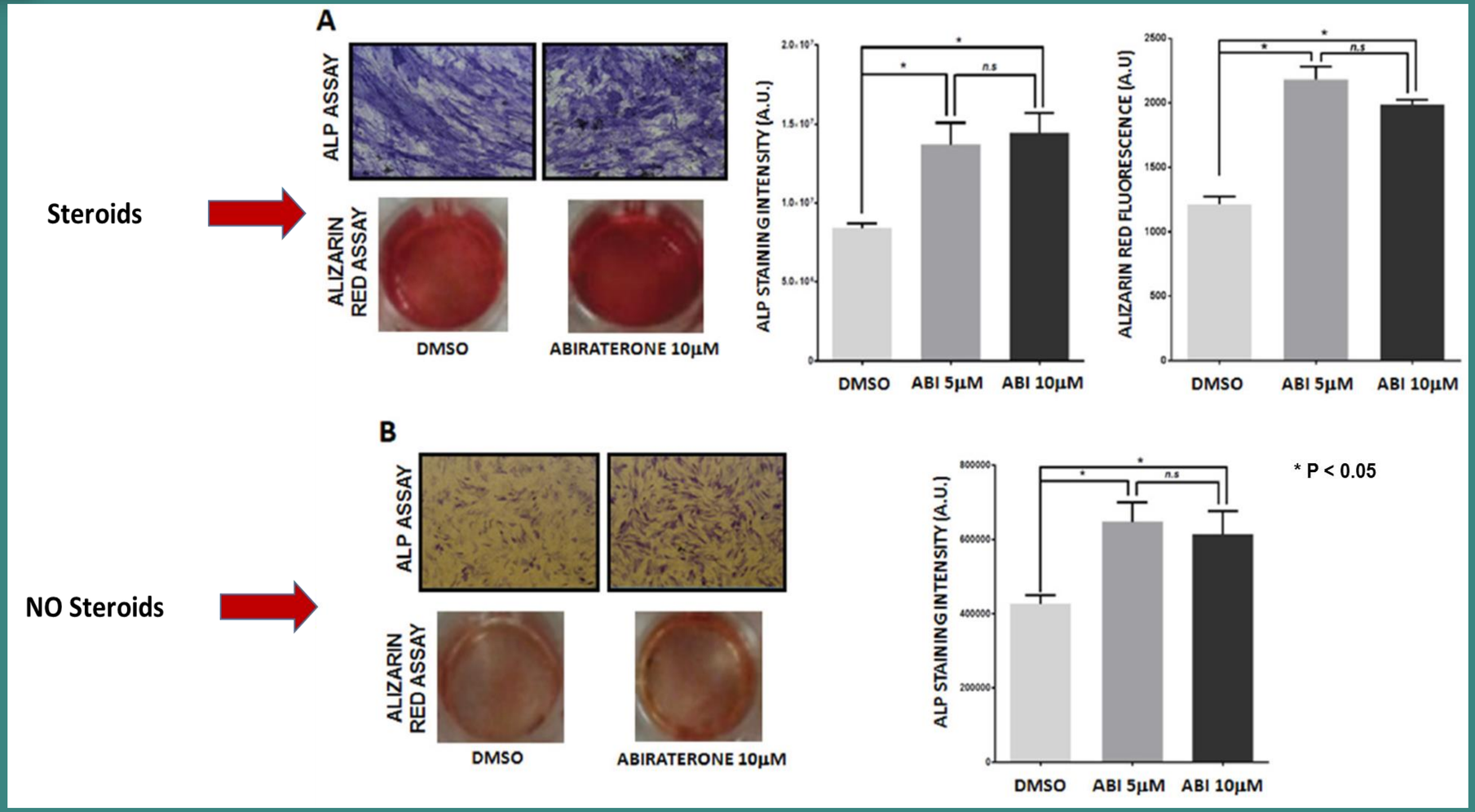
Biological and clinical effects of abiraterone on anti-resorptive and anabolic activity in bone microenvironment

Michele Iuliani[1,*], Francesco Pantano[1,*], Consuelo Buttigliero[2], Marco Fioramonti[1], Valentina Bertaglia[2], Bruno Vincenzi[1], Alice Zoccoli[1], Giulia Ribelli[1], Marcello Tucci[2], Francesca Vignani[2], Alfredo Berruti[3], Giorgio Vittorio Scagliotti[2], Giuseppe Tonini[1] and Daniele Santini[1]

- Blocks alpha-hydroxylase (CYP17)
- Indication: First line metastatic castration resistant prostate cancer



Abiraterone treatment inhibits osteoclast differentiation and activity both in presence and absence of steroids



Abiraterone treatment increases osteoblast differentiation and activity both in presence and absence of steroids

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www.impactjournals.com/oncotarget/ Oncotarget, 2017, Vol. 8, (No. 12), pp: 20113-20121

Research Paper

Cabozantinib targets bone microenvironment modulating human osteoclast and osteoblast functions

Marco Fioramonti[1,*], Daniele Santini[1,*], Michele Iuliani[1], Giulia Ribelli[1], Paolo Manca[1], Nicola Papapietro[2], Filippo Spiezia[2], Bruno Vincenzi[1], Vincenzo Denaro[2], Antonio Russo[3], Giuseppe Tonini[1], Francesco Pantano[1]

- Blocks MET and VEGFR2
- Indication: Second line metastatic renal cancer

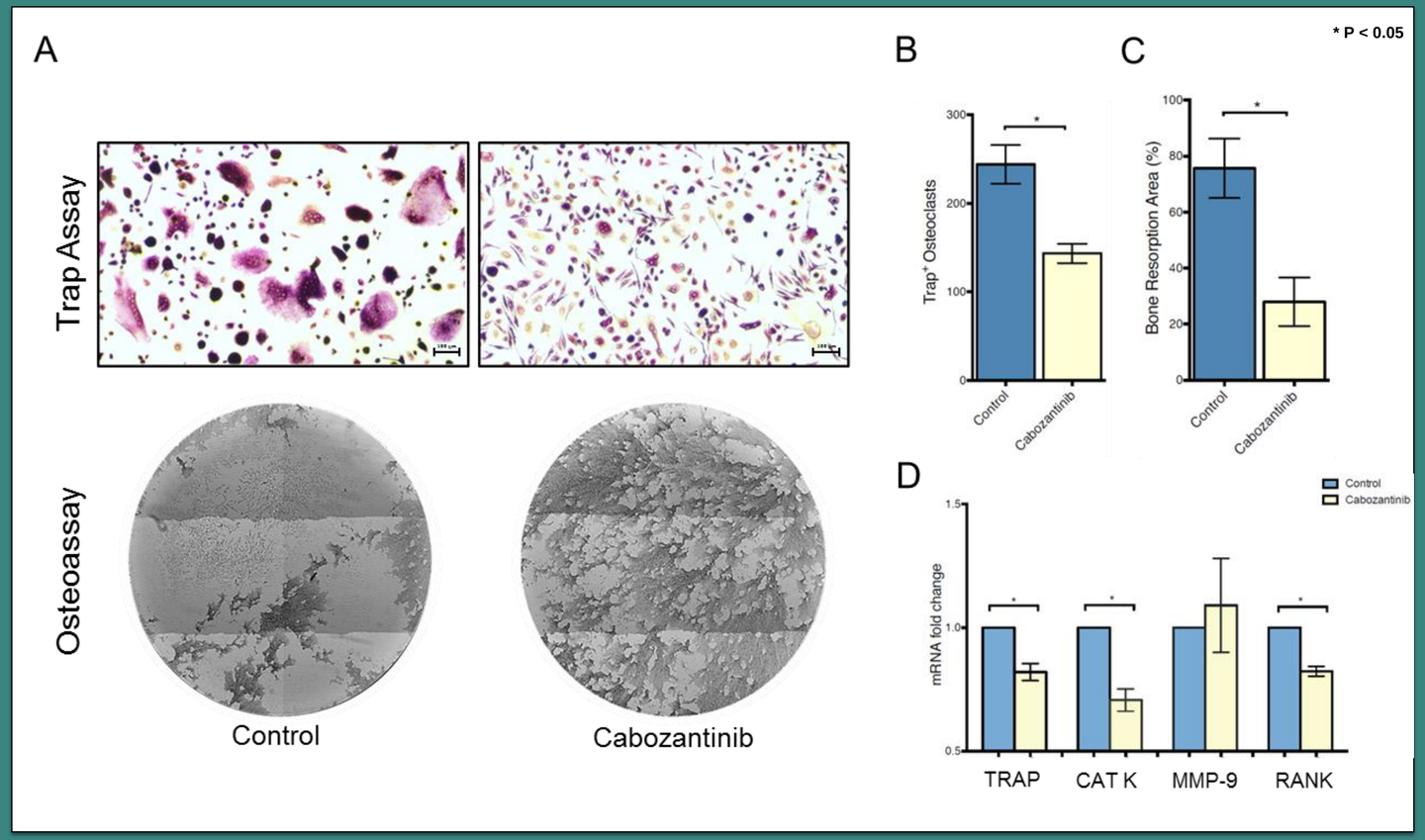
The NEW ENGLAND JOURNAL of MEDICINE

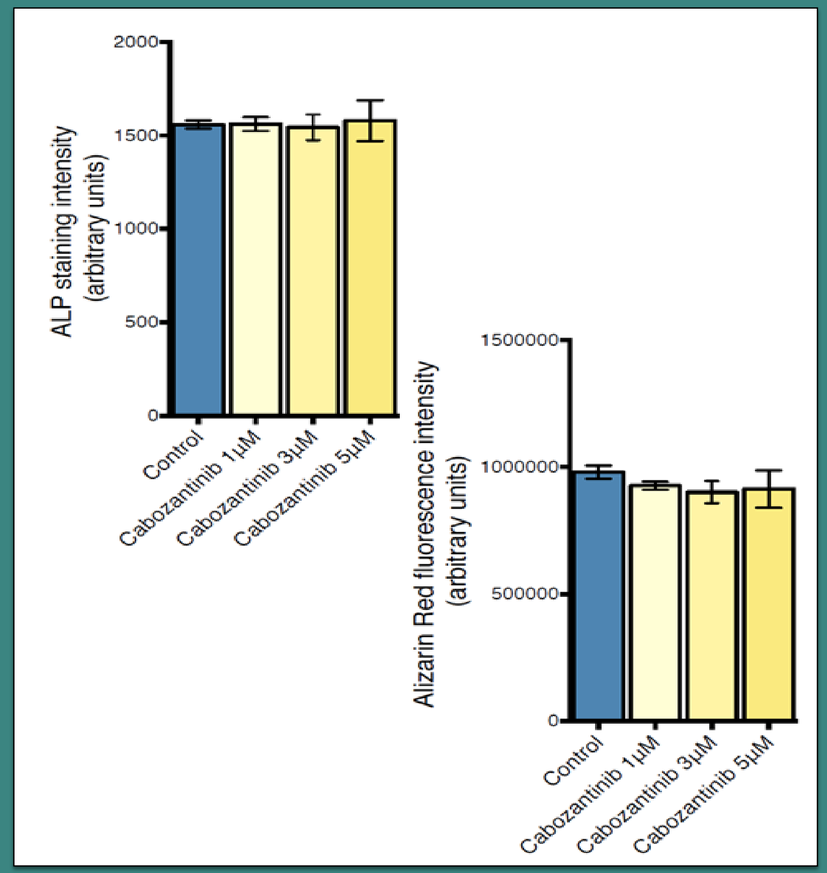
CORRESPONDENCE

Treatment of Advanced Renal-Cell Carcinoma

N Engl J Med 2016; 374:888-890 | March 3, 2016 | DOI: 10.1056/NEJMc1515613

Daniele Santini, M.D., Ph.D.
Giuseppe Tonini, M.D., Ph.D.
Campus Bio-Medico University of Rome, Rome, Italy
d.santini@unicampus.it





Cabozantinib inhibits osteoclast differentiation and activity

Cabozantinib does not affect osteoblast differentiation and activity

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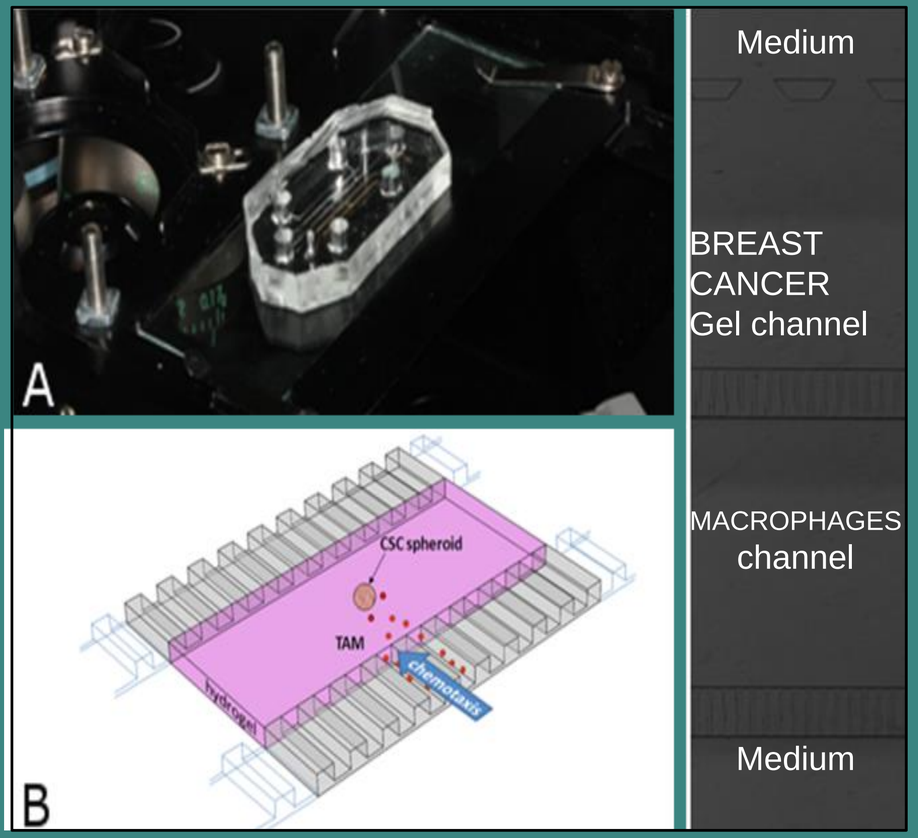
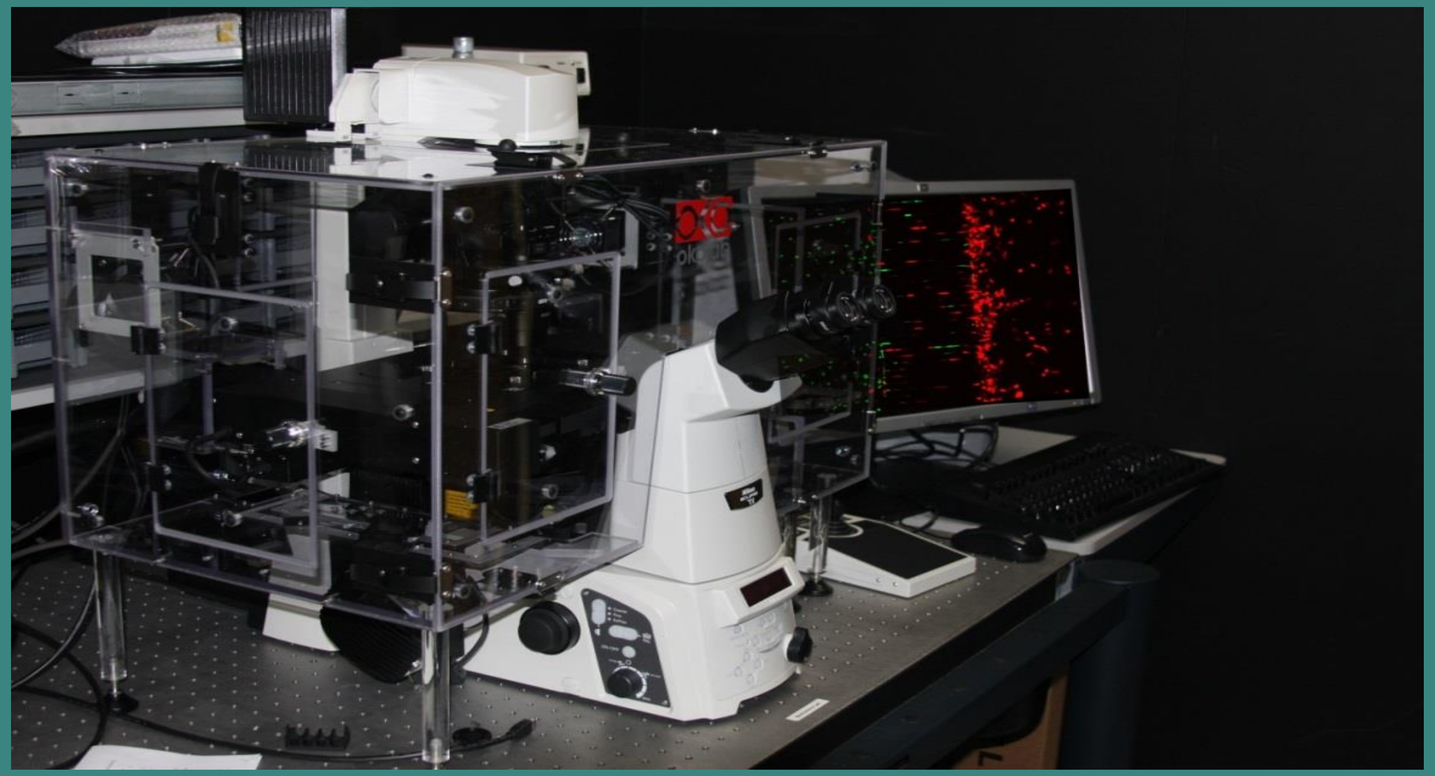
BREAST CANCER STEM CELLS AND TUMOR ASSOCIATED MACROPHAGES (TAM) CO-COLTURE USING *CELL-ON-CHIP MODELS*

(In collaboration with Prof Trombetta, Dr Rainer, TISSUE ENGINEERING LABORATORY UCBM)





Establishment of a cells-on-chip model re-creates the physiology of the tumor milieu to study the Cancer Stem Cells /TAM interplay within a time lapse microscopy system

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MACROPHAGES INTERACTION WITH CANCER STEM CELLS: CELL-ON-CHIP MODEL

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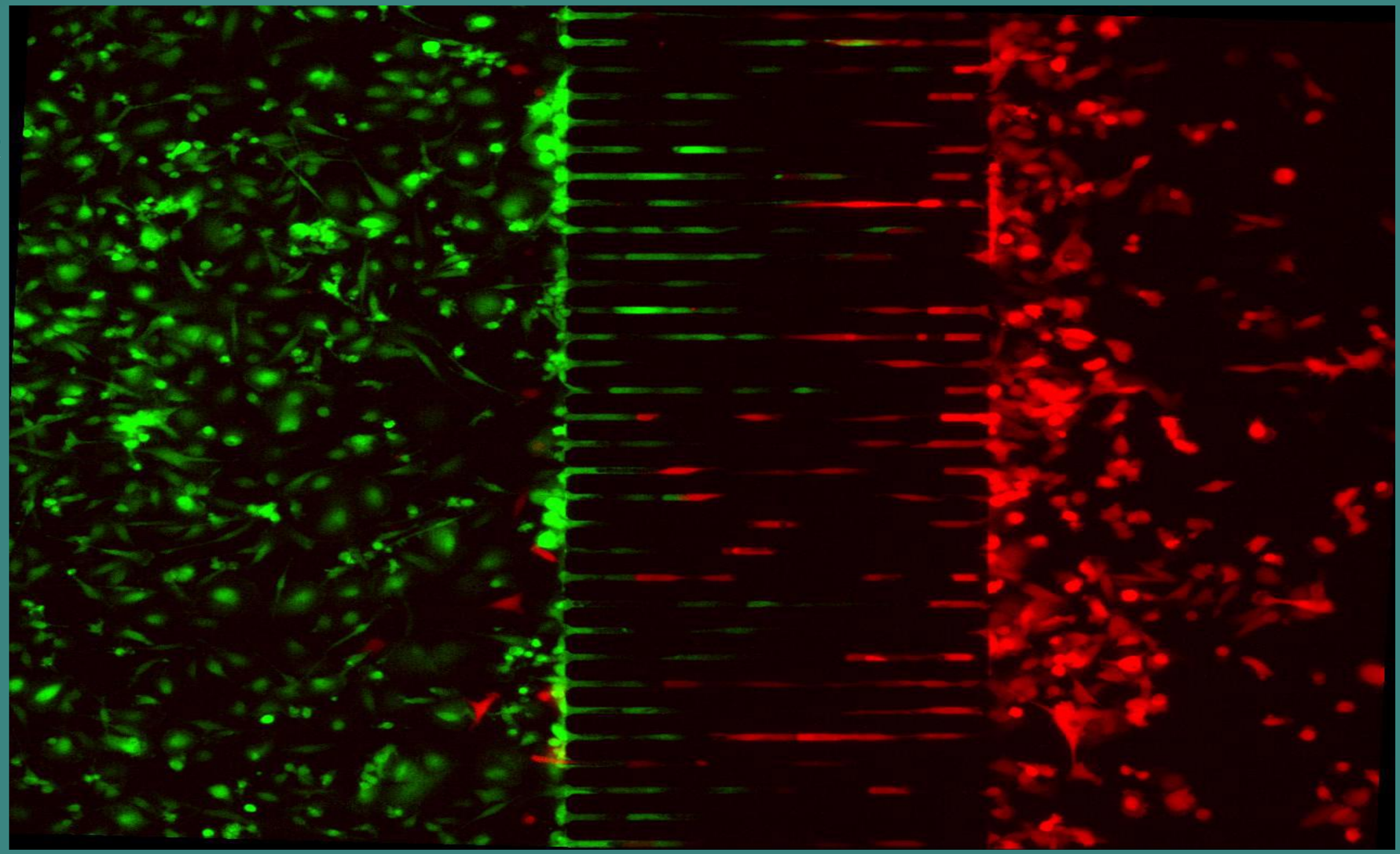
- MACROPHAGES
- BREAST CANCER CELL LINE



In collaboration with TISSUE ENGINEERING LABORATORY UCBM

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UNIVERSITÀ CAMPUS BIO-MEDICO DI ROMA

Annals of Oncology 23: 2072–2077, 2012
doi:10.1093/annonc/mdr572
Published online 4 January 2012

Natural history of bone metastasis in colorectal cancer: final results of a large Italian bone metastases study

D. Santini[1*], M. Tampellini[2], B. Vincenzi[1], T. Ibrahim[3], C. Ortega[4], V. Virzì[1], N. Silvestris[5], R. Berardi[6], C. Masini[7], N. Calipari[8], D. Ottaviani[9], V. Catalano[10], G. Badalamenti[11], R. Giannicola[12], F. Fabbri[3], O. Venditti[1], M. E. Fratto[1], C. Mazzara[1], T. P. Latiano[13], F. Bertolini[7], F. Petrelli[14], A. Ottone[2], C. Caroti[15], L. Salvatore[16], A. Falcone[16], P. Giordani[10], R. Addeo[17], M. Aglietta[4,18], S. Cascinu[6], S. Barni[14], E. Maiello[13] & G. Tonini[1]

OPEN ACCESS Freely available online 2013 PLOS ONE

Natural History of Malignant Bone Disease in Gastric Cancer: Final Results of a Multicenter Bone Metastasis Survey

Nicola Silvestris[1]*, Francesco Pantano[2], Toni Ibrahim[3], Teresa Gamucci[4], Fernando De Vita[5], Teresa Di Palma[6], Paolo Pedrazzoli[7], Sandro Barni[8], Antonio Bernardo[9], Antonio Febbraro[10], Maria Antonietta Satolli[11], Paola Bertocchi[12], Vincenzo Catalano[13], Elisa Giommoni[14], Alessandro Comandone[15], Evaristo Maiello[16], Ferdinando Riccardi[17], Raimondo Ferrara[18], Antonio Trogu[19], Rossana Berardi[20], Silvana Leo[21], Alessandro Bertolini[22], Francesco Angelini[23], Saverio Cinieri[24], Antonio Russo[25], Salvatore Pisconti[26], Anna Elisabetta Brunetti[1], Amalia Azzariti[27], Daniele Santini[2]

SCIENTIFIC REPORTS

OPEN

Natural History of Non-Small-Cell Lung Cancer with Bone Metastases

Received: 13 July 2015
Accepted: 18 November 2015
Published: 22 December 2015

Daniele Santini[1], Sandro Barni[2], Salvatore Intagliata[1], Alfredo Falcone[3], Francesco Ferraù[4], Domenico Galetta[5], Luca Moscetti[6], Nicla La Verde[7], Toni Ibrahim[8], Fausto Petrelli[2], Enrico Vasile[3], Laura Ginocchi[3], Davide Ottaviani[9], Flavia Longo[10], Cinzia Ortega[11], Antonio Russo[12], Giuseppe Badalamenti[12], Elena Collovà[13], Gaetano Lanzetta[14], Giovanni Mansueto[15], Vincenzo Adamo[16], Filippo De Marinis[17], Maria Antonietta Satolli[18], Flavia Cantile[19], Andrea Mancuso[20], Francesca Maria Tanca[21], Raffaele Addeo[22], Marco Russano[1], Michelle Sterpi[1], Francesco Pantano[1], Bruno Vincenzi[1] & Giuseppe Tonini[1]

OPEN ACCESS Freely available online 2014 PLOS ONE

Natural History of Malignant Bone Disease in Hepatocellular Carcinoma: Final Results of a Multicenter Bone Metastasis Survey

Daniele Santini[1], Francesco Pantano[1], Ferdinando Riccardi[2], Giovan Giuseppe Di Costanzo[3], Raffaele Addeo[4], Francesco Maria Guida[1], Mariella Spalato Ceruso[1], Sandro Barni[5], Paola Bertocchi[6], Sara Marinelli[7], Paolo Marchetti[8], Antonio Russo[9], Mario Scartozzi[10], Luca Faloppi[10], Matteo Santoni[10], Stefano Cascinu[10], Evaristo Maiello[11], Franco Silvestris[12], Marco Tucci[12], Toni Ibrahim[13], Gianluca Masi[14], Antonio Gnoni[15], Alessandro Comandone[16], Nicola Fazio[17], Alessandro Conti[18], Ilaria Imarisio[19], Salvatore Pisconti[20], Elisa Giommoni[21], Saverio Cinieri[22], Vincenzo Catalano[23], Vincenzo Ostilio Palmieri[24], Giovanni Infante[25], Michele Aieta[26], Antonio Trogu[27], Cosmo Damiano Gadaleta[28], Anna Elisabetta Brunetti[29], Vito Lorusso[29], Nicola Silvestris[29]*

OPEN ACCESS Freely available online 2013 PLOS ONE

Natural History of Malignant Bone Disease in Renal Cancer: Final Results of an Italian Bone Metastasis Survey

Daniele Santini[1], Giuseppe Procopio[2], Camillo Porta[3], Toni Ibrahim[4], Sandro Barni[5], Calogero Mazzara[1], Andrea Fontana[6], Alfredo Berruti[7], Rossana Berardi[8], Bruno Vincenzi[1], Cinzia Ortega[9], Davide Ottaviani[10], Giacomo Carteni[11], Gaetano Lanzetta[12], Vladimir Virzì[1], Matteo Santoni[13], Nicola Silvestris[14]*, Maria Antonietta Satolli[15], Elena Collovà[16], Antonio Russo[17], Giuseppe Badalamenti[17], Stefano Luzi Fedeli[18], Francesca Maria Tanca[19], Vincenzo Adamo[20], Evaristo Maiello[21], Roberto Sabbatini[22], Alessandra Felici[23], Saverio Cinieri[24], Giuseppe Tonini[1], Sergio Bracarda[25]

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Can we overlap the second step (WHO) in bone related moderate pain? Yes, we can

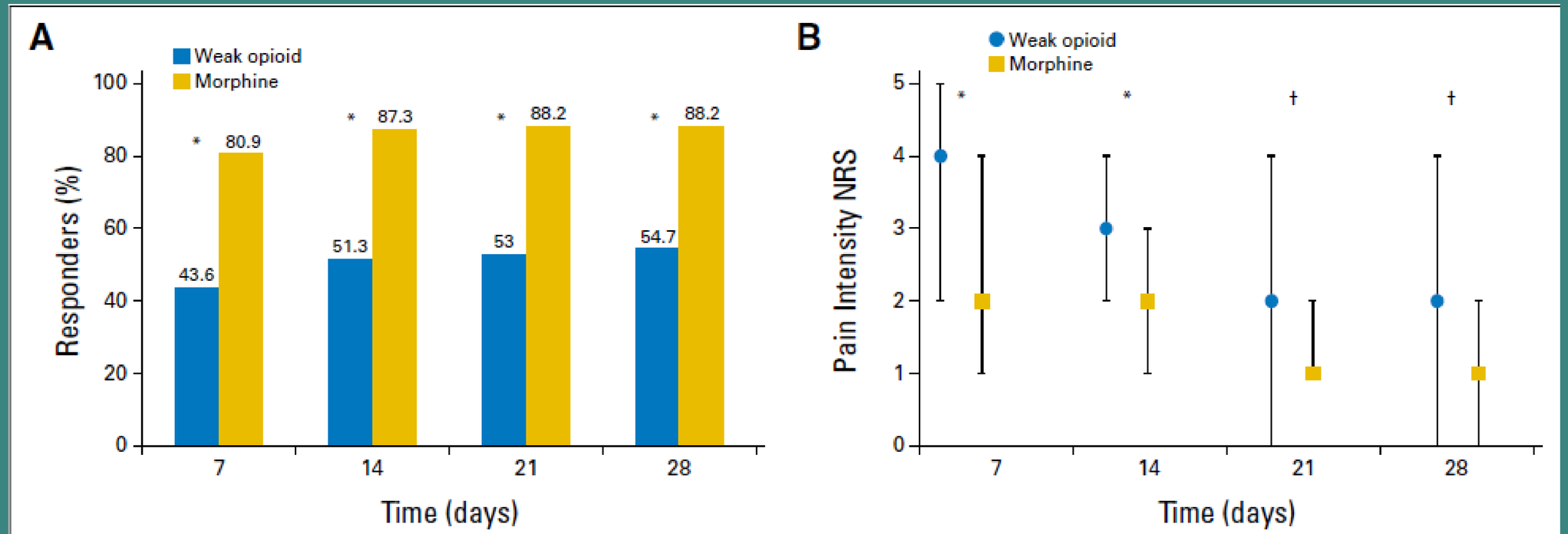
VOLUME 34 · NUMBER 5 · FEBRUARY 10, 2016

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

Randomized Trial of Low-Dose Morphine Versus Weak Opioids in Moderate Cancer Pain

Elena Bandieri, Marilena Romero, Carla Ida Ripamonti, Fabrizio Artioli, Daniela Sichetti, Caterina Fanizza, Daniele Santini, Luigi Cavanna, Barbara Melotti, Pier Franco Conte, Fausto Roila, Stefano Cascinu, Eduardo Bruera, Gianni Tognoni, and Mario Luppi

See accompanying editorial on page 399



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SOFT TISSUE SARCOMAS AND OSTEOSARCOMA: RESEARCH FIELDS

EORTC
The future of cancer therapy

Italian Sarcoma Group

RTR Rete Tumori Rari — Rete Nazionale Tumori Rari

New drug development

Evaluation of the effects of the new anticancer agents on preclinical models of osteosarcoma cell lines

CANDIOLO Fondazione del Piemonte per l'Oncologia

UNIVERSITÀ CAMPUS BIO-MEDICO DI ROMA

MARIO NEGRI ISTITUTO DI RICERCHE FARMACOLOGICHE

FONDAZIONE IRCCS ISTITUTO NAZIONALE DEI TUMORI

MAIN NATIONAL AND INTERNATIONAL RESEARCH COLLABORATIONS

Prof. Philippe Clézardin

- National Institute of Health and Medical Research (INSERM), Lyon France.

Prof. Robert E Coleman

- The University of Sheffield, Department of Oncology Sheffield, South Yorkshire, United Kingdom

Prof Aleix Prat

- Vall D'HEBRON, Istituto de Oncologia, Barcelona

Dr. Toni Ibrahim

- Osteoncology and Rare Tumors Center, IRCCS Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST), Meldola (FC)

Dr. Rita Zamarchi

- Department of Surgery, Oncology and Gastroenterology, University of Padova, IOV-IRCCS, Padova

Prof. Paolo Casali

- Fondazione IRCCS, Istituto Nazionale dei Tumori

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AWARDS:

UNIVERSITÀ CAMPUS BIO-MEDICO DI ROMA

TEMPLE UNIVERSITY®

From 2015- Adjunct Associate Professorat Department of Biology, Temple University's College of Science and Technology, Philadelphia (USA)

Fondazione Guido Berlucchi

ORGANIZZAZIONE NON LUCRATIVA DI UTILITA' SOCIALE - ONLUS

2013- *"Cell-on-chip models for the development of integrated therapies of immunotherapy with the aim to overcome the resistance to conventional treatments in non small cell lung cancer: the role of interaction between cancer stem cells and macrophage polarization"*
In collaboration with **Tissue Engineering Unit CBM**

REPVBBLICA ITALIANA

Ministero degli Affari Esteri

2013-2014 Coordinator project "Understanding the interplay between cancer stem cells and immune system: an innovative cells-on-chip approach"
*In collaboration with **Tissue Engineering Unit CBM***

MIUR PRIN

Coordinator: Prof. Trombetta
2012- "Cells-on-chip technologies for the study of endocannabinoid system in an in vivo model of cancer/immunity system interactions"
In collaboration with **Tissue Engineering Unit CBM**

GIORNATA DELLA RICERCA UCBM

Thanks to Prof Giuseppe Tonini ….and

To our Translational Oncology Laboratory
dream Team

Special thanks to:

Prof. Vincenzo Denaro and

Dr Alberto Di Martino-

Orthopaedics and Traumatology Unit (CBM)

Prof. Silvia Sterzi-

Physical Medicine and Reabilitation Unit (CBM)

Prof. Marcella Trombetta and

Dr. Alberto Rainer-

Tissue Engineering Laboratory (CBM)