Carmen Criscitiello, MD, PhD

Personal Details

Date and Place of Birth: November 22, 1980; Avellino, Italy
Work Address: Early Drug Development for Innovative Therapies Division
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Education and PHD/Masters/Courses

October 2005:
M.D. Degree, Medical School , University of Naples "Federico II", Italy
January 2010: Residency in Oncology, University of Naples "Federico II", Italy
January 2013: PhD in Medical Oncology and Surgery and Clinical Immunology, Division of Medical Oncology, Seconda Università degli Studi di Napoli (SUN), Italy

Experience

2003-2005: Internship, Division of Medical Oncology, Medical School, University of Naples "Federico II", Italy
April 2009- September 2011: TransBIG Fellowship, Translational Research Unit, Institut Jules Bordet - Brussels, Belgium
October 2011-December 2013: Clinical Fellowship, European Institute of Oncology, Milano- Italy
January 2014-present: Assistant, Early Drug Development for Innovative Therapies, European Institute of Oncology, Milano- Italy

Scientific Society memberships

2008-present: ESMO (European Society Medical Oncology)
2011-present: AACR (American Association Cancer Research)
2013-present: ASCO (American Society Clinical Oncology)
2013-present: AIOM (Associazione Italiana di Oncologia Medica)

RESEARCH INTERESTS

Experience in translational research:

During my fellowship in the Translational Research Unit of Institut Jules Bordet in Brussels, I have been involved in the detection of Circulating Tumor Cells in breast cancer patients using reverse transcriptase polymerase chain reaction (RT-PCR, molecular detection) and the CellSearch technology. I used to extract RNA and synthesize cDNA from the MCF-7 breast cancer cell line. Serial dilutions from this cDNA are used as a positive control in PCR experiments for the amplification of Cytokeratin19mRNA. I have been trained to isolate mononuclear cells from the peripheral blood of women with breast cancer using the Ficoll gradient centrifugation procedure. I have also been trained to detect Circulating Tumor Cells in the blood of women with breast cancer using the CellSearch technology. I am actively involved in CellSearch image analysis.
Furthermore, I have been deeply involved in the interpretation of gene expression profiling data.
Main projects I followed:

- Large-Scale Epigenetic, Gene Expression and Copy Number characterization of Luminal A Breast Cancers as a way to interpret their heterogeneous clinical behavior. To date, it is not known whether the worse outcome reported by Luminal A breast cancers with massive nodal involvement is due to their extensive tumor burden and late diagnosis or whether specific and still unknown genetic and epigenetic alterations accumulated during breast cancer progression. It is possible that luminal A tumors, having an indolent evolution, are usually diagnosed at a late stage and have time to accumulate more epigenetic aberrations during their progression. However, further data are warranted in order to confirm or refuse our hypothesis. The aim of this project is to determine whether advanced stage luminal A tumors have distinct epigenetic and genetic aberrations that could explain their aggressive clinical behavior. To achieve this goal, we molecularly characterized early and advanced stage Luminal A breast cancers by interrogating in an unbiased manner epigenetic and gene expression changes.
- Retrospective Evaluation of PI3 Kinase Pathway Alterations in Estrogen-receptor Positive HER2-negative Samples of Metastatic Breast Cancer Patients. Since genomic aberrations can predict responsiveness to targeted

therapies, and since multiple PI3K pathway members are frequently aberrant in human breast tumors through mutation and other anomalies, it is legitimate to think that targeting this pathway will provide an effective therapeutic approach in breast cancer. The identification of these genomic aberrations may facilitate the selection of patients who will benefit from PI3K pathway-targeted therapies. Since PTEN protein loss and PIK3CA mutations have markedly different functional effects on activation of signaling through the PI3K pathway in human breast cancers, it is possible that PI3K pathway activation by PTEN loss versus PIK3CA mutation could lead to different outcomes and could determine sensitivity to different targeted drugs. Although several papers have been published on this topic, their results are very discordant and there is still a large uncertainty about the frequency of PIK3CA mutations and PTEN loss in metastatic breast cancer and about their possible association with patients' prognosis in this setting. Currently, there are several unclear issues on the topic: whether these tumors may respond better to hormonal therapy; whether these mutations may be more important for initiation rather than progression of the disease; whether there is concordance between aberrations in the primary tumor and in the metastatic lesion(s). The primary objective of this study is to evaluate the frequency of PIK3CA mutations and PTEN loss in metastatic patients with ER+/HER2- breast cancer. The secondary objectives of this study are to compare the frequency of PIK3CA mutations and PTEN loss across different first- and second-line therapy; to compare the frequency of PIK3CA mutations and PTEN loss between the matched primary and the metastatic lesions; to identify prognostic implications of PIK3CA mutations and PTEN loss in ER+/ HER2- metastatic breast cancer.

- Heritable genetic variation may modulate breast tumorigenesis, it is associated with breast cancer survival and with response to therapy. Our specific aims were the identification of SNPs with different clinico-pathological and molecular characteristics, the identification of SNPs with the presence of minimal residual disease (tumor dissemination) and the identification of SNPs associated with the development of macro-metastases (colonization).

PERSONAL SKILLS AND COMPETENCES:

Mother Tongue: Italian
Other Languages: English and French

COURSES:

- Pre-IMPAKT Training Course. Brussels, Belgium 6-7 May 2009.
- The Vito Distante Project in Breast Cancer Clinical Research. Tuscany, Italy 30 August- 2 September 2009
- Pre-IMPAKT Training Course. Brussels, Belgium 5-6 May 2010.
- EORTC Course "Methodology of cancer clinical trials: the next generation". Brussels, Belgium 7-10 September 2010.
- Pre-IMPAKT Training Course. Brussels, Belgium 4-5 May 2011.
- ECCO-AACR-EORTC-ESMO Workshop "Methods in clinical cancer research". Flims, Switzerland — 18 - 24 June 2011

PRESENTATIONS:

- April 2010 Invited talk: "Biologics in adjuvant setting: where are we?" in: Winter Academy of Oncology: Early breast cancer, Pontresina, Switzerland.
- 19-02-2011 Abstract accepted for oral presentation during BSMO (Belgian Society of Medical Oncology), Brussels, Belgium "More advanced stage Luminal A early breast cancers show distinct gene expression patterns associated with worse clinical outcome.
- "The discrepancy between high pathological complete response (pCR) rate and low breast conserving surgery (BCS) following neoadjuvant therapy: analysis from the NeoALTTO trial (BIG 1-06)": abstract accepted for Proffered Paper (Oral) presentation during the ESMO 2012 Congress, 28 September - 2 October, Vienna, Austria.
- June 2013 Invited talk: "Chemotherapy benefit in Luminal breast cancer". Breast Cancer Progress and Controversies. Naples, Italy.
- January 2014 Invited talk: "METASTASES: faut-il les biopsier?". Biennale Monégasque de Cancérologie, Cours Francophone d'Oncologie. Monaco,

FELLOWSHIPS AND GRANTS:

October 2010-September 2011 TransBIG Fellowship – Institut Jules Bordet, Brussels, Belgium
Les Amis de l'Institut Bordet grant
October 2011- December 2013 Fellowship, European Institute of Oncology, Milano- Italy

LIST OF PUBLICATIONS

1. Prognostic value of tumor-infiltrating lymphocytes on residual disease after primary chemotherapy for triple-negative breast cancer: a retrospective multicenter study. Dieci MV, Criscitiello C, Goubar A, Viale G, Conte P, Guarneri V, Ficarra G, Mathieu MC, Delaloge S, Curigliano G, Andre F. Ann Oncol. 2014 Jan 8.
2. High Ki-67 score is indicative of a greater benefit from adjuvant chemotherapy when added to endocrine therapy in Luminal B HER2 negative and node-positive breast cancer. Criscitiello C, Disalvatore D, De Laurentiis M, Gelao L, Fumagalli L, Locatelli M, Bagnardi V, Rotmensz N, Esposito A, Minchella I, De Placido S, Santangelo M, Viale G, Goldhirsch A, Curigliano G. Breast. 2014 Feb;23(1):69-75.
3. Monitoring tumor-derived cell-free DNA in patients with solid tumors: Clinical perspectives and research opportunities. Esposito A, Bardelli A, Criscitiello C, Colombo N, Gelao L, Fumagalli L, Minchella I, Locatelli M, Goldhirsch A, Curigliano G. Cancer Treat Rev. 2013 Oct 23. pii: S0305-7372(13)00207-7
4. No Link between Breast Cancer and Meningioma: Results from a Large Monoinstitutional Retrospective Analysis. Criscitiello C, Disalvatore D, Santangelo M, Rotmensz N, Bazolli B, Maisonneuve P, Goldhirsch A, Curigliano G. Cancer Epidemiol Biomarkers Prev. 2013 Dec 19
5. Immunotherapeutics for breast cancer. Criscitiello C, Curigliano G. Curr Opin Oncol. 2013 Nov;25(6):602-8.
6. Developing an effective breast cancer vaccine: challenges to achieving sterile immunity versus resetting equilibrium. Curigliano G, Criscitiello C, Esposito A, Fumagalli L, Gelao L, Locatelli M, Minchella I, Goldhirsch A. Breast. 2013 Aug;22 Suppl 2:S96-9.
7. Tumor-associated antigens in breast cancer. Criscitiello C. Breast Care (Basel). 2012 Aug;7(4):262-6
8. Molecular Pathways: Human leukocyte antigen G (HLA-G). Curigliano G, Criscitiello C, Gelao L, Goldhirsch A. Clin Cancer Res. 2013 Jul 29.
9. Tumour dormancy and clinical implications in breast cancer. Gelao L, Criscitiello C, Fumagalli L, Locatelli M, Manunta S, Esposito A, Minchella I, Goldhirsch A, Curigliano G. Ecancermedicalscience. 2013 May 21;7:320.
10. Locoregional recurrence in patients with HER2 positive breast cancer. Brollo J, Kneubil MC, Botteri E, Rotmensz N, Duso BA, Fumagalli L, Locatelli MA, Criscitiello C, Lohsiriwat V, Goldhirsch A, Leonardi MC, Orecchia R, Curigliano G. Breast. 2013 Oct;22(5):856-62
11. Highlights from the 13th St Gallen International Breast Cancer Conference 2013. Access to innovation for patients with breast cancer: how to speed it up? Curigliano G, Criscitiello C, Andrè F, Colleoni M, Di Leo A. Ecancermedicalscience. 2013 Mar 26;7:299.
12. Factors associated with surgical management following neoadjuvant therapy in patients with primary HER2-positive breast cancer: results from the NeoALTTO phase III trial. Criscitiello C, Azim HA Jr, Agbor-tarh D, de Azambuja E, Piccart M, Baselga J, Eidtmann H, Di Cosimo S, Bradbury I, Rubio IT. Ann Oncol. 2013 Aug;24(8):1980-5.
13. HER2 signaling pathway and trastuzumab cardiotoxicity. Criscitiello C, Curigliano G. Future Oncol. 2013 Feb;9(2):179-81. doi: 10.2217/fon.12.193.
14. Cardiovascular toxicity induced by chemotherapy, targeted agents and radiotherapy: ESMO Clinical Practice Guidelines. Curigliano G, Cardinale D, Suter T, Plataniotis G, de Azambuja E, Sandri MT, Criscitiello C, Goldhirsch A, Cipolla C, Roila F; ESMO Guidelines Working Group. Ann Oncol. 2012 Oct;23 Suppl 7:vii155-66.
15. Understanding the biology of triple-negative breast cancer. Criscitiello C, Azim HA Jr, Schouten PC, Linn SC, Sotiriou C. Ann Oncol. 2012 Aug;23 Suppl 6:vi13-8.
16. Targeted therapies in breast cancer: are heart and vessels also being targeted? Criscitiello C, Metzger-Filho O, Saini KS, de Castro Jr G, Diaz M, La Gerche A, de Azambuja E, Piccart-Gebhart MJ. Breast Cancer Res. 2012 Jun 19;14(3):209. [Epub ahead of print]
17. Adjuvant trastuzumab in elderly with HER-2 positive breast cancer: A systematic review of randomized controlled trials. Brollo J, Curigliano G, Disalvatore D, Marrone BF, Criscitiello C, Bagnardi V, Kneubil MC, Fumagalli L, Locatelli M, Manunta S, Goldhirsch A. Cancer Treat Rev. 2012 Apr 26.
18. Gene Modules and Response to Neoadjuvant Chemotherapy in Breast Cancer Subtypes: A Pooled Analysis. Ignatiadis M, Singhal SK, Desmedt C, Haibe-Kains B, Criscitiello C, Andre F, Loi S, Piccart M, Michiels S, Sotiriou C. J Clin Oncol. 2012 Apr 16.
19. Elucidating prognosis and biology of breast cancer arising in young women using gene expression profiling. Azim HA Jr, Michiels S, Bedard PL, Singhal SK, Criscitiello C, Ignatiadis M, Haibe-Kains B, Piccart MJ, Sotiriou C, Loi S. Clin Cancer Res. 2012 Mar 1;18(5):1341-51. Epub 2012 Jan 18.
20. Targeting the subtypes of breast cancer: rethinking investigational drugs. Curigliano G, Locatelli M, Fumagalli L, Brollo J, Munzone E, Nolé F, Criscitiello C, Goldhirsch A. Expert Opin Investig Drugs. 2012 Feb;21(2):191-204. Epub 2012 Jan 10. Review.
21. Tamoxifen in early-stage estrogen receptor-positive breast cancer: overview of clinical use and molecular biomarkers for patient selection. Criscitiello C, Fumagalli D, Saini KS, Loi S. Onco Targets Ther. 2010 Dec 17;4:1-11.

22. HER2-positive circulating tumor cells in breast cancer. Ignatiadis M, Rothé F, Chaboteaux C, Durbecq V, Rouas G, Criscitiello C, Metallo J, Kheddoumi N, Singhal SK, Michiels S, Veys I, Rossari J, Larsimont D, Carly B, Pestrin M, Bessi S, Buxant F, Liebens F, Piccart M, Sotiriou C. PLoS One. 2011 Jan 10;6(1):e15624.
23. Circulating tumor cells and emerging blood biomarkers in breast cancer. Criscitiello C, Sotiriou C, Ignatiadis M. Curr Opin Oncol. 2010 Nov;22(6):552-8. Review.
24. Exemestane in the treatment of breast carcinoma: recent findings. De Laurentiis M, Criscitiello C, Montanino A, Falato C, Plaitano M. Tumori. 2008 Jan-Feb;94(1):suppl 10-21. Italian. No abstract available.
25. Taxane-based combinations as adjuvant chemotherapy of early breast cancer: a meta-analysis of randomized trials. De Laurentiis M, Cancello G, D'Agostino D, Giuliano M, Giordano A, Montagna E, Lauria R, Forestieri V, Esposito A, Silvestro L, Pennacchio R, Criscitiello C, Montanino A, Limite G, Bianco AR, De Placido S. J Clin Oncol. 2008 Jan 1;26(1):44-53.

Milano, 17/01/2014 Carmen Criscitiello