



RESEARCH TOPIC CLI19

Advanced diagnostic characterization through comprehensive molecular profiling to tailor appropriate treatments such as antibody-drug conjugates (ADCs), bispecific antibodies and new targeted therapies in metastatic breast cancer

Clinical Unit name

Medical Oncology Unit
IRCCS – Humanitas Research Hospital

Supervisor

Armando Santoro
armando.santoro@humanitas.it

Abstract

Breast cancer is one of the leading causes of death in women¹. Advances in diagnostics have enabled tumour comprehensive molecular profiling to detect alterations at the multi-omics level (genomic, transcriptomic, proteomic and epigenomic) associated with metastatic breast cancer (MBC)^{2,3}. In parallel with these increasing molecular insights^{4,5,6}, the treatment landscape for MBC is undergoing a profound renewal with the introduction of innovative drugs such as antibody-drug conjugates, bispecific antibodies and new target therapies^{7,8}. These advances have greatly improved survival, but also pose an increasing challenge to oncologists who lack robust predictive biomarkers of response or resistance to support optimal treatment decision-making process. This project aims to explore the feasibility and effectiveness of a comprehensive molecular profiling in MBC to tailor appropriate treatments and to identify potential multi-omics biomarkers able to predict response to next-generation therapies.

Scientific references

1. DeSantis CE, Ma J, Gaudet MM, et al. Breast cancer statistics, 2019. *CA Cancer J Clin.* 2019;69(6):438-451. doi:10.3322/caac.21583
2. Koboldt DC, Fulton RS, McLellan MD, et al. Comprehensive molecular portraits of human breast tumours. *Nature.* 2012;490(7418):61-70. doi:10.1038/nature11412
3. Nik-Zainal S, Davies H, Staaf J, et al. Landscape of somatic mutations in 560 breast cancer whole-genome sequences. *Nature.* 2016; 534(7605):47-54. doi: 10.1038/ nature
4. Kawaji H, Kubo M, Yamashita N, et al. Comprehensive molecular profiling broadens treatment options for breast cancer patients. *Cancer Med.* 2021; 10(2):529-539. doi:10.1002/cam4.3619



5. Zardavas D, Piccart-Gebhart M. Clinical Trials of Precision Medicine through Molecular Profiling: Focus on Breast Cancer. *Am Soc Clin Oncol Educ B*. 2015; (35):e183-e190. doi: 10.14694/edbook_am.2015.35.e183
6. Zambelli A, Sgarra R, Sanctis R De, Agostinetto E, Santoro A, Manfioletti G. Heterogeneity of triple-negative breast cancer: understanding the Daedalian labyrinth and how it could reveal new drug targets. *Expert Opin Ther Targets*. 2022;26(6):557-573. doi:10.1080/14728222.2022.2084380
7. Torres ETR, Emens LA. Emerging combination immunotherapy strategies for breast cancer: dual immune checkpoint modulation, antibody–drug conjugates and bispecific antibodies. *Breast Cancer Res Treat*. 2022;191(2):291-302. doi:10.1007/s10549-021-06423-0
8. Subhan MA, Torchilin VP. Advances in Targeted Therapy of Breast Cancer with Antibody-Drug Conjugate. *Pharmaceutics*. 2023;15(4):1-21. doi: 10.3390/pharmaceutics15041242

Type of contract

PhD scholarship of € 22.400 gross per year awarded by Humanitas University. This sum is exempt from IRPEF income tax according to the provisions of art. 4 of Law no. 476 of 13th August 1984, and is subject to social security contributions according to the provisions of art. 2, section 26 and subsequent sections, of Law no. 335 of 8th August 1995 and subsequent modifications.

Borsa di dottorato pari a € 22.400 annui lordi erogata da Humanitas University. Importo non soggetto a tassazione IRPEF a norma dell'art. 4 della L. 13 agosto 1984 n. 476 e soggetto, in materia previdenziale, alle norme di cui all'art. 2, commi 26 e segg., della L. 8 agosto 1995, n. 335 e successive modificazioni.