

BIOGRAPHICAL SKETCH

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NAME: Michele Reni

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Medical Doctor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Università degli studi di Milano, Milan	Medicine and Surgery	15/07/1988	General Medicine
Università degli studi di Milano, Milan	Radiation Oncology Specialist	10/07/1992	Radiation Oncology
Università degli studi di Milano, Milan	Clinical Oncology Specialist	12/11/1996	Clinical Oncology

A. Personal Statement

I am the Chief of Medical Oncology Unit at San Raffaele Hospital in Milan and Associate Professor at Vita-Salute San Raffaele University. Moreover, I am member of multiple national and European committees and coordinator of the team of pancreatic oncologists. During the year as an oncologist and radiotherapist I focused my attention and my work on aggressive tumors such as pancreatic ductal adenocarcinoma (PDAC), for whom my team are spending a big effort to overcome the general resistance to antitumor response. One of the primary areas of my research involves the phenotypic and genomic characterization of pancreatic cancer and its correlation with clinical outcomes. Specifically, my research aims not only to identify prognostic and predictive factors that can improve patients' stratification, but also to investigate novel therapeutic strategies to improve tumor regression and patient quality of life. To do this, my effort relies mainly in the design and management of randomized clinical trials, in which we can obtain both clinical and molecular data. The final goal will be definitely the better management of PDAC patients in the optic of precision medicine. International and external collaboration has been a key component of my research efforts. The discovery of new therapeutic options and the identification of reliable prognostic and predictive factors to improve patient stratification will pave the way to a revolutionary management of this dismal cancer. Although immunotherapies generally failed in PDAC context, research has unveiled that immune compartment inside this immunologically "cold" tumor can be indeed modulated and important to stratify patients. However, the immune microenvironment and the complex link between cancer and immune response is a field largely unexplored in PDAC but novel data demonstrate that it could open new interesting field to explore. Therefore, my team is currently assessing the effects of new combinatorial strategies of historical drugs on tumor microenvironment, to the final hope to translate our findings into clinical applications and ever better patient tailored therapies.

B. Positions, Scientific Appointments, and Honors

POSITIONS:

POSITIONS		
Date	Position	Institution
from 2004/ongoing	Coauthor of national guidelines for pancreatic and central nervous system tumor	AIOM
01-feb-2012/ongoing	Strategic Program Pancreas Center Director	Pancreas Center, San Raffaele Hospital
from 2021	Cancer Center Board member	San Raffaele Hospital
01-feb-2022/ongoing	Associate Professor	Università Vita Salute San Raffaele
23-dec-2022/ongoing	Chief of Medical Oncology	San Raffaele Hospital
from March 2024	Member of 'Pancreas Unit' network creation	DM 22/02/2024

SCIENTIFIC APPOINTMENTS:

Relevant Grant awarded:

- 2008-2011 Unrestricted grant Fondazione CARIPLO. PACT-12 - trial Maintenance therapy with sunitinib or observation in metastatic pancreatic cancer (NCT00967603)
- 2009-2012 Unrestricted grant Novartis. GICNO 08-002 Hydroxyurea with or without imatinib in the treatment of recurrent or progressive meningiomas: a randomized phase II trial by Gruppo Italiano Cooperativo di Neuro-Oncologia (GICNO)
- 2011-2014 AIRC 5 per mille. Innovative tools for early diagnosis and risk assessment of pancreatic cancer Associazione Italiana per la Ricerca sul Cancro Coordinator: Aldo Scarpa. Internal Collaborator
- 2011-2014 AIRC IG 11783. A randomized phase II trial of chemotherapy $\pm$ metformin in metastatic pancreatic carcinoma. Associazione Italiana per la Ricerca sul Cancro. PI Lorenzo Piemonti. CoPrincipal Investigator
- 2011-2014 IG AIRC. Reciprocal influence of the pancreatic microenvironment and CD4+ Th2 immunity in tumor progression. PI Maria Pia Protti. Internal collaborator.
- 2016 AIRC IG-2016. Targeting the chromogranin A-angiogenic switch in non-neuroendocrine tumors IG-2016, PI Prof. Angelo Corti, Collaboratore Interno
- 2018 Unrestricted grant Celgene. Primary chemotherapy-induced microenvironment modifications in non-metastatic pancreatic ductal adenocarcinoma evaluated by data integration of tumor genomic and immune profiles.
- 2019 AIRC 5 per mille id 22737: Advanced immune gene and cell therapies for liver metastases. PI Chiara Bonini. Group Leader.
- 2021 Grant Daichii-Sanchio/Astra-Zeneca: Efficacy of DS-8201 alone or with selected combination in pre-clinical models and in patients affected by resistant pancreatic cancer or other orphan cancers. Principal Investigator
- 2021 AISP-MERUS Full molecular analysis by RNA/DNA next generation sequencing to detect genetic alterations (including NRG1 fusions) in PDAC < 60y. Principal Investigator
- 2021 PACT-21 trial - Short-course Versus Long-course Pre-operative Chemotherapy With mFOLFIRINOX or PAXG (CASSANDRA TRIAL; (NCT04793932) founded by: ONLUS MyEverest, ONLUS PerLaVita, CODICE VIOLA, FONDAZIONE NATALUCCI, OLTRE LA RICERCA.

Steering committee member:

- NCT00844649 A Randomized Phase III Study of Weekly ABI-007 Plus Gemcitabine Versus Gemcitabine Alone in Patients With Metastatic Adenocarcinoma of the Pancreas
- D081FC00001 POLO - A Phase III, Randomised, Double Blind, Placebo Controlled, Multicentre Study of Maintenance Olaparib Monotherapy in Patients with gBRCA Mutated Metastatic Pancreatic Cancer whose Disease Has Not Progressed on First Line Platinum Based Chemotherapy
- ABI-007-PANC-003 A Phase 3, Multicenter, Open-label, Randomized Study of nab-Paclitaxel Plus Gemcitabine versus Gemcitabine Alone as Adjuvant Therapy in Subjects with Surgically Resected Pancreatic Adenocarcinoma
- CanStem111P A phase III study of BBI-608 plus nab-Paclitaxel with gemcitabine in adult patients with metastatic pancreatic adenocarcinoma

Moreover, I am the principal investigator of more than 50 clinical trial both sponsored by pharmaceuticals or investigators initiative.

Finally, I Co-supervise theses for the degree course in Medicine and Surgery at the Vita e Salute University of Milan and at the University of Pavia, for the degree course in Psychology at the Vita e Salute University of Milan and for the School of Specialization in Internal Medicine at the Vita e Salute University of Milan.

C. Contributions to Science

Author or coauthor of 18 book chapters and more than 280 peer-reviewed publications.

REPRESENTATIVE BOOK CHAPTERS:

- 1) Brandes A, Reni M, Carapella C, Labianca R, Zorat P. Linee guida AIOM per le neoplasie cerebrali. Intermedia Editore Healthcare Communication Network. San Zeno Naviglio, Brescia. Settembre 2004
- 2) Brandes AA, Gatta G, Reni M, Vecht C. Glioblastoma multiforme. www.startoncology.net
- 3) Reni M, Peretti U, Burgio V, Cascinu S. Capitolo 47 - Tumori maligni dell'apparato digerente, del fegato, delle vie biliari e del pancreas. In *MEDICINA INTERNA SISTEMATICA* Settima Edizione luglio 2020 Claudio Rugarli – Elsevier

RELEVANT PUBLICATIONS:

- 1) Macchini M, Reni M* et al. Chemotherapy in elderly patients with pancreatic cancer: Efficacy, feasibility and future perspectives. *Cancer Treat Rev.* 2019 Jan;72:1-6.
- 2) Hammel P, Reni M, et Al. Health-related quality of life in patients with a germline BRCA mutation and metastatic pancreatic cancer receiving maintenance olaparib. *Ann Oncol.* 2019 Sep 28.
- 3) Morganti AG, Reni M, et Al. Adjuvant chemoradiation in pancreatic cancer: impact of radiotherapy dose on survival. *BMC Cancer.* 2019 Jun 11;19(1):569
- 4) Seufferlein T, Reni M, et Al. Optimizing the management of locally advanced pancreatic cancer with a focus on induction chemotherapy: Expert opinion based on a review of current evidence. *Cancer Treat Rev.* 2019 Jul;77:1-10.
- 5) Golan T, Reni M, et Al. Maintenance Olaparib for Germline BRCA-Mutated Metastatic Pancreatic Cancer. *N Engl J Med.* 2019 Jul 25;381(4):317-327. doi: 10.1056/NEJMoa1903387. Epub 2019 Jun 2.
- 6) Pecorelli N, Reni M, et Al. Postoperative Outcomes and Functional Recovery After Preoperative Combination Chemotherapy for Pancreatic Cancer: A Propensity Score-Matched Study. *Front Oncol.* 2019 Nov 26;9:1299. doi: 10.3389/fonc.2019.01299. eCollection 2019. *Front Oncol.* 2019. PMID: 31850203 Free PMC article.
- 7) Consolandi M, Reni M, et al. COMMUNI.CARE (COMMUNICation and Patient Engagement at Diagnosis of PAncreatic CAncer): Study Protocol. *Front Med (Lausanne).* 2020 Apr 30;7:134. doi: 10.3389/fmed.2020.00134. eCollection 2020. *Front Med (Lausanne).* 2020. PMID: 32426356 Free PMC article.
- 8) Reni M, et al. Time to CA19-9 nadir: a clue for defining optimal treatment duration in patients with resectable pancreatic ductal adenocarcinoma. *Cancer Chemother Pharmacol.* 2020 Apr;85(4):641-650. doi: 10.1007/s00280-020-04047-7. Epub 2020 Mar 10. *Cancer Chemother Pharmacol.* 2020. PMID: 32157412
- 9) Caccialanza R, Reni M, et al. Early intravenous administration of nutritional support (IVANS) in metastatic gastric cancer patients at nutritional risk, undergoing first-line chemotherapy: study protocol of a pragmatic, randomized, multicenter, clinical trial. *Ther Adv Med Oncol.* 2020 Feb 22;12:1758835919890281. doi: 10.1177/1758835919890281. eCollection 2020. *Ther Adv Med Oncol.* 2020. PMID: 32127922 Free PMC article.
- 10) Golan T, Reni M, et al. Geographic and Ethnic Heterogeneity of Germline BRCA1 or BRCA2 Mutation Prevalence Among Patients With Metastatic Pancreatic Cancer Screened for Entry Into the POLO Trial. *J Clin Oncol.* 2020 May 1;38(13):1442-1454. doi: 10.1200/JCO.19.01890. Epub 2020 Feb 19. *J Clin Oncol.* 2020. PMID: 32073954
- 218) Goldstein D, Von Hoff DD, Chiorean EG, Reni M, Tabernero J, Ramanathan RK, Botteman M, Aly A, Margunato-Debay S, Lu B, Louis CU, McGovern D, Lee CK. Nomogram for Estimating Overall Survival in Patients With Metastatic Pancreatic Cancer. *Pancreas.* 2020 Jul;49(6):744-750. doi: 10.1097/MPA.0000000000001563. PMID: 32541630 Free PMC article.
- 11) Balzano G, Reni M, et al. A four-step method to centralize pancreatic surgery, accounting for volume, performance and access to care. *HPB (Oxford).* 2020 Nov 27:S1365-182X(20)31232-6. doi: 10.1016/j.hpb.2020.11.006. Online ahead of print. PMID: 33257170

- 12) Reni M*, et al. Circulating Chromogranin A Is Cleaved Into Vasoregulatory Fragments in Patients With Pancreatic Ductal Adenocarcinoma. *Front Oncol.* 2020 Dec 23;10:613582. doi: 10.3389/fonc.2020.613582. eCollection 2020.PMID: 33425767 Free PMC article.
- 12) Macchini M, Reni M*. Exploring chemotherapy holiday and drugs re-challenge in advanced pancreatic cancer patients. *Cancer Chemother Pharmacol.* 2021 Jan;87(1):95-101. doi: 10.1007/s00280-020-04190-1. Epub 2020 Nov 6.PMID: 33159215
- 13) Reni M*. APX005M, a CD40 monoclonal antibody, for patients with pancreatic adenocarcinoma. *Lancet Oncol.* 2021 Jan;22(1):10-11. doi: 10.1016/S1470-2045(20)30724-5.PMID: 33387488 No abstract available.
- 14) Tempero M, Reni M, et al. Ibrutinib in Combination with Nab-Paclitaxel and Gemcitabine for First-Line Treatment of Patients with Metastatic Pancreatic Adenocarcinoma: Phase 3 RESOLVE Study. *Ann Oncol.* 2021 Feb 1:S0923-7534(21)00098-3. doi: 10.1016/j.annonc.2021.01.070. Online ahead of print.PMID: 33539945 Free article.
- 14) Orsi G, Reni M*. Chemotherapy toxicity and activity in patients with pancreatic ductal adenocarcinoma and germlineBRCA1-2 pathogenic variants (gBRCA1-2pv). A multicentre survey. *ESMO Open* 2021 Oct;6(5):100238. doi: 10.1016/j.esmoop.2021.100238. Epub 2021 Aug 13.PMID: 34392104
- 15) Milella M, Reni M*. Evolving pancreatic cancer treatment: From diagnosis to healthcare management. *Crit Rev Oncol Hematol.* 2021 Dec 16;169:103571. doi: 10.1016
- 16) Trestini I, Reni M, et al. Pancreatic Enzyme Replacement Therapy in Patients Undergoing First-Line Gemcitabine Plus nab-paclitaxel for Advanced Pancreatic Adenocarcinoma. *Front Oncol.* 2021 Sep 9;11:688889. doi: 10.3389
- 17) Pecorelli N, Reni M, et al. Prognosis of Upfront Surgery for Pancreatic Cancer: A Systematic Review and Meta-Analysis of Prospective Studies. *Front Oncol.* 2022 Jan 10;11:812102. doi: 10.3389/fonc.2021.812102. eCollection 2021.PMID: 35083158 Free PMC article.
- 18) Milella M, Reni M*. Evolving pancreatic cancer treatment: From diagnosis to healthcare management. *Crit Rev Oncol Hematol.* 2022 Jan;169:103571. doi: 10.1016/j.critrevonc.2021.103571. Epub 2021 Dec 16.PMID: 34923121
- 19) Ferrara B, Reni M, et al. Comprehensive Characterization of Stemness in Cell Lines and Primary Cells of Pancreatic Ductal Adenocarcinoma. *Int. J. Mol. Sci.* 2022, 23, 10663. <https://doi.org/10.3390/ijms231810663>
- 20) Kindler HL, Reni M, et al. Overall Survival Results From the POLO Trial: A Phase III Study of Active Maintenance Olaparib Versus Placebo for Germline BRCA-Mutated Metastatic Pancreatic Cancer *J Clin Oncol.* 2022 Jul 14;JCO2101604. doi: 10.1200/JCO.21.01604
- 21) Reni M, Orsi G. Pancreatic cancer: still a cold case? *Lancet Oncol.* 2022 Aug;23(8):964-965. doi: 10.1016/S1470-2045(22)00394-1. Epub 2022 Jul 7.
- 21) Redegalli M, Reni M, et al. Routine Molecular Profiling in Both Resectable and Unresectable Pancreatic Adenocarcinoma: Relevance of Cytological Samples. *Clin Gastroenterol Hepatol.* 2022 Oct 22:S1542-3565(22)01003-5. doi: 10.1016/j.cgh.2022.10.014. Online ahead of print.PMID: 36280101
- 22) Bekaii-Saab T, Reni M, et al. Napabucasin plus nab-paclitaxel with gemcitabine versus nab-paclitaxel with gemcitabine in previously untreated metastatic pancreatic adenocarcinoma: an adaptive multicentre, randomised, open-label, phase 3, superiority trial. *Clinical Medicine.* 2023 Mar 16;58:101897. doi: 10.1016/j.eclinm.2023.101897. eCollection 2023 Apr.PMID: 36969338 Free PMC article.
- 23) Petrelli F, Reni M. The Role of Neoadjuvant FOLFIRINOX in Borderline Resectable Pancreatic Cancer: A Network Meta-Analysis. *J Gastrointest Cancer.* 2023 Mar 7. doi: 10.1007/s12029-023-00923-6. Online ahead of print.PMID: 36881248 No abstract available.
- 24) Reni M, et al. Overall Survival With Adjuvant mFOLFIRINOX for Pancreatic Cancer. *JAMA Oncol.* 2023 Mar 1;9(3):435-436. Doi 10.1001/jamaoncol.2022.7358. PMID: 36701148
- 25) De Monte L, Reni M, et al. Pro-tumor Tfh2 cells induce detrimental IgG4 production and PGE2-dependent IgE inhibition in pancreatic cancer. *EBioMedicine.* 2023 Nov;97:104819. doi: 10.1016/j.ebiom.2023.104819. Epub 2023 Sep 28.PMID: 37776595 Free PMC article

- 26) Militello AM, Reni M. Clinical outcomes and response to chemotherapy in a cohort of pancreatic cancer patients with germline variants of unknown significance (VUS) in BRCA1 and BRCA2 genes. *Cancer Chemother Pharmacol*. 2023 Dec;92(6):501-510. doi: 10.1007/s00280-023-04585-w. Epub 2023 Sep 19. PMID: 37725113
- 27) Taieb J, Reni M, et al. Treatment sequences and prognostic/predictive factors in metastatic pancreatic ductal adenocarcinoma: univariate and multivariate analyses of a real-world study in Europe. *BMC Cancer*. 2023 Sep 18;23(1):877. doi: 10.1186/s12885-023-11377-1. PMID: 37723453 Free PMC article.
- 28) Reni M, et al. Cyclophosphamide maintenance to extend combination chemotherapy-free interval in metastatic pancreatic ductal adenocarcinoma. *Dig Liver Dis*. 2023 Aug 14:S1590-8658(23)00784-3. doi: 10.1016/j.dld.2023.07.033. Online ahead of print. PMID: 37586911
- 29) Balzano G, Reni M, et al. Translating knowledge into policy: Organizational model and minimum requirements for the implementation of a regional pancreas unit network. *Dig Liver Dis*. 2024 Jun 7:S1590-8658(24)00776-X. doi: 10.1016/j.dld.2024.05.022. Online ahead of print. PMID: 38851973
- 30) Reni M, et al. Cyclophosphamide maintenance to extend combination chemotherapy-free interval in metastatic pancreatic ductal adenocarcinoma. *Dig Liver Dis*. 2024 Mar;56(3):509-513. doi: 10.1016/j.dld.2023.07.033. Epub 2023 Aug 14. PMID: 37586911
- 31) Budillon A, Reni M, et al. Randomized phase 2 study of valproic acid combined with simvastatin and gemcitabine/nab-paclitaxel-based regimens in untreated metastatic pancreatic adenocarcinoma patients: the VESPA trial study protocol. *BMC Cancer*. 2024 Sep 19;24(1):1167. doi: 10.1186/s12885-024-12936-w. PMID: 39300376
- 32) Reni M, et al. Survival analysis of the metastatic cohort of Italian Association of Medical Oncology (AIOM) GARIBALDI survey. *Pancreatology*. 2024 Nov;24(7):1160-1166. doi: 10.1016/j.pan.2024.10.002. Epub 2024 Oct 3. PMID: 39389862

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30 December 2024

