

BIOGRAPHICAL SKETCH

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NAME: Niger, Monica

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

POSITION TITLE: Member of the Board of Directors

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)	END DATE MM/YYYY	FIELD OF STUDY
University of Milan, Milan	MD	10/2011	
University of Milan	Fellow	07/2017	Medical Oncology Fellowship
ASCO/AACR, Vial	Other training	08/2017	Methods in Clinical Cancer Research workshop - competitive workshop to design clinical trials

A. Personal Statement

I am a Medical Oncologist at the National Cancer Institute (INT) of Milan, where I also studied to become a Medical Oncologist. During my fellowship, I developed a strong interest in clinical and translational cancer research with the guidance of great mentors, including Dr. Filippo Pietrantonio (INT) and Dr. Patricia Lo Russo (Yale). Throughout my training and now as a gastrointestinal (GI) oncologist at INT, I have been actively involved as co-investigator and Principal Investigator in clinical research for gastrointestinal cancers in various international sponsored and academic studies. During my fellowship, I contributed to the development of various now published investigator-initiated clinical trials, including VALENTINO (NCT02476045), MAYA (NCT03832621) and ARMANI trial (NCT02934464), ideated and led by my mentors. Over the years, I have worked both on the clinical aspects and the translational analyses of these studies. At Yale, under the brilliant mentorship of Dr. R. Bindra and Dr. P. LoRusso, I saw first-hand the meaning of translating a research hypothesis “from bench to bedside”, when, after testing its rationale in the laboratory, I wrote the protocol for a phase II trial evaluating the efficacy of olaparib in IDH1/2-mutant solid tumors (NCT03878095). As a medical oncologist, At INT, I joined the GI Cancer Team with enthusiasm, maintaining involvement in all GI cancers while also building a dedicated research program in biliopancreatic cancers. As testified by multiple peer-reviewed publications, our group has a specific interest on clinical and translational research and we have a solid experience on molecular tumor profiling of biliopancreatic cancers, with various ongoing national and international collaborations. With a specific focus on pancreatic cancer, the focus of this proposal, I was the senior author on the first systemic review and meta-analysis designed to derive survival, response, and toxic effects data from phase 3 clinical trials on first-line treatment for advanced disease. Additionally, we evaluated the clinical relevance of MGMT alterations in pancreatic cancer and we collaborated with other groups to deepen the knowledge regarding BRCA mutant and MSI-H pancreatic cancers. In summary, I have the expertise, leadership, training, expertise, and motivation necessary to successfully carry out the proposed research project. Finally that I would like to add that I designed and I am national PI of two randomized no profit trials: - NCT06037980 phase II/III randomized clinical trial of CisPlatin pLUs Gemcitabine and Nabpaclitaxel (GAP) as pReoperative chemotherapy versus immediate resection in patients with resectable Biliary Tract Cancers (BTC) at high risk for recurrence: PURITY Study - NCT06897644 Gemcitabine plus nab-Paclitaxel as switch maintenance versus continuation of mFOLFIRINOX as first-line chemotherapy in patients with advanced pancreatic cancer: the PANThEON phase III Trial For the PANThEON trial, I received as PI a grant from the Rising Tide Foundation.

1. Nichetti F, Silvestri M, Agnelli L, Franza A, Pircher C, Rota S, Ambrosini P, Fotia G, Hülle J, Randon G, Lajer P, Perrone F, Tamborini E, Leoncini G, Coppa J, Busset MDD, Pusceddu S, Milione M, Morano F, Pietrantonio F, Pruneri G, Mazzaferro V, Lipka DB, Köhler BC, Hübschmann D, Fröhling S, de Braud F, Niger M. Molecular Characterization and Clinical Relevance of MGMT-Silenced Pancreatic Cancer. Cancer Med. 2024 Dec;13(23):e70393. PubMed Central PMCID: PMC11609587.

2. Nichetti F, Rota S, Ambrosini P, Pircher C, Gusmaroli E, Droz Dit Busset M, Pusceddu S, Sposito C, Coppa J, Morano F, Pietrantonio F, Di Bartolomeo M, Mariani L, Mazzaferro V, de Braud F, Nigam M. NALIRIFOX, FOLFIRINOX, and Gemcitabine With Nab-Paclitaxel as First-Line Chemotherapy for Metastatic Pancreatic Cancer: A Systematic Review and Meta-Analysis. JAMA Netw Open. 2024 Jan 2;7(1):e2350756. PubMed Central PMCID: PMC10774994.
3. Taïeb J, Sayah L, Heinrich K, Kunzmann V, Boileve A, Cirkel G, Lonardi S, Chibaudel B, Turpin A, Beller T, Hautefeuille V, Vivaldi C, Mazard T, Bauguion L, Nigam M, Prager GW, Coutzac C, Benedikt Westphalen C, Auclin E, Pilla L. Efficacy of immune checkpoint inhibitors in microsatellite unstable/mismatch repair-deficient advanced pancreatic adenocarcinoma: an AGEO European Cohort. Eur J Cancer. 2023 Jul;188:90-97. PubMed PMID: 37229836.
4. Orsi G, Cavaliere A, Tortora G, Lonardi S, Macchini M, Di Marco M, Giordano G, Vasile E, Scartozzi M, Bozzarelli S, Noventa S, Rodriquez MG, Militello AM, Rapposelli IG, Garajova I, De Lorenzo S, Merelli B, Bittoni A, Salvatore L, Procaccio L, Paratore C, Spallanzani A, Peretti U, Nigam M, Giommoni E, Bernardini I, Tamburini E, Bernardino K, Forti L, Valente MM, Cascinu S, Milella M, Reni M. Second-line therapy in pancreatic ductal adenocarcinoma (PDAC) patients with germline BRCA1-2 pathogenic variants (gBRCA1-2pv). Br J Cancer. 2023 Mar;128(5):877-885. PubMed Central PMCID: PMC9977912.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2024 -	Member of the Board of Directors, Gruppo Oncologico Nord-Ovest (G.O.N.O.) Foundation
2022 - 2024	Member of the working group to write the National Guidelines for the treatment of Pancreatic Cancer, Italian Medical Oncologists Association (AIOM)
2022 -	Member of the working group for Quality of Research, Fondazione IRCCS Istituto Nazionale dei Tumori , Milan
2021 -	Member of Molecular Tumor Board, Fondazione IRCCS Istituto Nazionale dei Tumori
2021 - 2024	Member of local Internal Review Board for interventional studies , Fondazione IRCCS Istituto Nazionale dei Tumori , Milano
2020 -	Medical Oncologist, Consultant, GI Cancer Unit. Group leader for biliopancreatic cancer research, Fondazione IRCCS Istituto Nazionale dei Tumori , Milan
2017 - 2020	Medical Oncologist, Fondazione IRCCS Istituto Nazionale dei Tumori , Milan
2017 - 2017	Research Associate, Yale Cancer Center, New Haven, CT
2012 - 2017	Medical Oncology Fellow, Fondazione IRCCS Istituto Nazionale dei Tumori , Milano
2009 - 2012	Medical Student, Fondazione IRCCS Istituto Nazionale dei Tumori

Honors

2018 - 2018	Young Investigator Award, Fondazione IRCCS Istituto Nazionale dei Tumori di Milano
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C. Contribution to Science

1. Over the years, I was involved in the design and in the development of various investigator-initiated clinical trials for patients affected by gastrointestinal cancers, including but not limited to those selected as citation and: - NCT05594290: Window-of-opportunity study of chemo-immunotherapy in patients with resectable MERkel Cell carcinoma prior to sUrgeRY: the MERCURY trial (MERCURY, ongoing) - NCT02476045: Panitumumab-based Maintenance in Patients With RAS Wild- type, Metastatic Colorectal Cancer (Valentino, published) - NCT02414009: Study to Compare CAPTEM vs FOLFIRI as Second Line Treatment in Advanced, Colorectal Cancer Patients (CAPTEM, published).
 - a. Raimondi A, Lonardi S, Murgioni S, Cardellino GG, Tamperi S, Strippoli A, Palermo F, De Manzoni G, Bencivenga M, Bittoni A, Chiodoni C, Lorenzini D, Todoerti K, Manca P, Sangaletti S, Prisciandaro M, Randon G, Nichetti F, Bergamo F, Brich S, Belfiore A, Bertolotti A, Stetco D, Guidi A, Torelli T, Vingiani A, Joshi RP, Khoshdeli M, Beaubier N, Stumpe MC, Nappo F, Leone AG, Pircher CC, Leoncini G, Sabella G, Airo' Farulla L, Alessi A, Morano F, Martinetti A, Nigam M, Fassan M, Di Maio M, Kaneva K, Milione M, Nimeiri H, Sposito C, Agnelli L, Mazzaferro V, Di Bartolomeo M, Pietrantonio F.

Tremelimumab and durvalumab as neoadjuvant or non-operative management strategy of patients with microsatellite instability-high resectable gastric or gastroesophageal junction adenocarcinoma: the INFINITY study by GONO. *Ann Oncol*. 2025 Mar;36(3):285-296. PubMed PMID: 39637944.

- b. Cecchini M, Pilat MJ, Uboha N, Azad NS, Cho M, Davis EJ, Ahnert JR, Tinoco G, Shapiro GI, Khagi S, Powers B, Spencer K, Groisberg R, Drappatz J, Chen L, Das B, Bao X, Li J, Narayan A, Vu D, Patel A, Niger M, Doroshow D, Durecki D, Boerner SA, Bindra R, Ivy P, Shyr D, Shyr Y, LoRusso PM. Olaparib in treatment-refractory isocitrate dehydrogenase 1 (IDH1)- and IDH2-mutant cholangiocarcinoma: Safety and antitumor activity from the phase 2 National Cancer Institute 10129 trial. *Cancer*. 2025 Feb 15;131(4):e35755. PubMed Central PMCID: PMC11949439.
 - c. Randon G, Lonardi S, Fassan M, Palermo F, Tamberi S, Giommoni E, Ceccon C, Di Donato S, Fornaro L, Brunetti O, De Vita F, Bittoni A, Chini C, Spallanzani A, Nappo F, Bethaz V, Strippoli A, Latiano T, Cardellino GG, Giuliani F, Morano F, Niger M, Raimondi A, Prisciandaro M, Pircher CC, Sciortino C, Marchesi S, Garattini SK, Airò G, Miceli R, Di Bartolomeo M, Pietrantonio F. Ramucirumab plus paclitaxel as switch maintenance versus continuation of first-line oxaliplatin-based chemotherapy in patients with advanced HER2-negative gastric or gastro-oesophageal junction cancer (ARMANI): a randomised, open-label, multicentre, phase 3 trial. *Lancet Oncol*. 2024 Dec;25(12):1539-1550. PubMed PMID: 39557058.
 - d. Morano F, Raimondi A, Pagani F, Lonardi S, Salvatore L, Cremolini C, Murgioni S, Randon G, Palermo F, Antonuzzo L, Pella N, Racca P, Prisciandaro M, Niger M, Corti F, Bergamo F, Zaniboni A, Ratti M, Palazzo M, Cagnazzo C, Calegari MA, Marmorino F, Capone I, Conca E, Busico A, Brich S, Tamborini E, Perrone F, Di Maio M, Milione M, Di Bartolomeo M, de Braud F, Pietrantonio F. Temozolomide Followed by Combination With Low-Dose Ipilimumab and Nivolumab in Patients With Microsatellite-Stable, O(6)-Methylguanine-DNA Methyltransferase-Silenced Metastatic Colorectal Cancer: The MAYA Trial. *J Clin Oncol*. 2022 May 10;40(14):1562-1573. PubMed Central PMCID: PMC9084437.
 2. In the past few years, I designed two academic randomized trials for resectable biliary tract cancers and advanced pancreatic cancer, respectively. The PURITY trial is a no-profit, multicentre, randomized adaptive phase II/III trial aimed at improving clinical practice by evaluating the efficacy of the combination of gemcitabine, cisplatin and nabpaclitaxel (GAP) as neoadjuvant treatment in patients with resectable BTC at high risk for recurrence. The PANTheON trial is a no-profit, multicentre, randomized phase III aimed at improving clinical practice by investigating whether switching first-line treatment to Gem-NabP after a mFOLFIRINOX-based 3 months induction may improve patients' OS and tolerability as compared with mFOLFIRINOX continuation. Additionally, as the lead oncologist in my institution for the treatment of Cholangiocarcinoma, I contributed to designing a single-institution trial investigating liver transplantation as a therapeutic approach for patients affected by intrahepatic Cholangiocarcinoma. All these studies are currently open to accrual.
 - a. Maspero M, Sposito C, Bongini MA, Cascella T, Flores M, Maccauro M, Chiesa C, Niger M, Pietrantonio F, Leoncini G, Bellia V, Bhoori S, Mazzaferro V. Liver Transplantation for Intrahepatic Cholangiocarcinoma After Chemotherapy and Radioembolization: An Intention-To-Treat Study. *Transpl Int*. 2024;37:13641. PubMed Central PMCID: PMC11560448.
 - b. Niger M, Nichetti F, Fornaro L, Pircher C, Morano F, Palermo F, Rimassa L, Pressiani T, Berardi R, Gardini AC, Sperti E, Salvatore L, Melisi D, Bergamo F, Siena S, Mosconi S, Longarini R, Arcangeli G, Corallo S, Delliponti L, Tamberi S, Fea E, Brandi G, Rapposelli IG, Salati M, Baili P, Miceli R, Ljevar S, Cavallo I, Sottotetti E, Martinetti A, Busset MDD, Sposito C, Di Bartolomeo M, Pietrantonio F, de Braud F, Mazzaferro V. A phase II/III randomized clinical trial of CisPlatin pLUs Gemcitabine and Nabpaclitaxel (GAP) as pReoperative chemotherapy versus immediate resection in patlents with resecTable BiliarY Tract Cancers (BTC) at high risk for recurrence: PURITY study. *BMC Cancer*. 2024 Apr 8;24(1):436. PubMed Central PMCID: PMC11003088.
 3. Throughout my training and now as a gastrointestinal (GI) oncologist at INT I have been actively involved in international collaborations investigating the impact of molecular alterations on GI cancers. At Yale, we performed a preclinical study that discovered that two oncometabolites, fumarate and succinate, potentially suppress HR and leads to exquisite PARP inhibitor sensitivity. I collaborated in a multicenter study aimed at evaluating the regulation of the tumour immune microenvironment through epigenetic alternate promoter use in gastrointestinal tumours; its results were published in GUT. More recently, I coordinated as first or senior author translational international studies on biliary tract and pancreatic cancer, including an

evaluation of the clinical relevance of MGMT methylation in biliary tract and pancreatic cancers and genomic and clinical detailed analysis of BRAF-mutated advanced biliary tract cancer

- a. Nichetti F, Silvestri M, Agnelli L, Franza A, Pircher C, Rota S, Ambrosini P, Fotia G, Hülle J, Randon G, Lajer P, Perrone F, Tamborini E, Leoncini G, Coppa J, Busset MDD, Pusceddu S, Milione M, Morano F, Pietrantonio F, Pruner G, Mazzaferro V, Lipka DB, Köhler BC, Hübschmann D, Fröhling S, de Braud F, Nigam M. Molecular Characterization and Clinical Relevance of MGMT-Silenced Pancreatic Cancer. *Cancer Med.* 2024 Dec;13(23):e70393. PubMed Central PMCID: PMC11609587.
 - b. Sulkowski PL, Sundaram RK, Oeck S, Corso CD, Liu Y, Noorbakhsh S, Nigam M, Boeke M, Ueno D, Kalathil AN, Bao X, Li J, Shuch B, Bindra RS, Glazer PM. Krebs-cycle-deficient hereditary cancer syndromes are defined by defects in homologous-recombination DNA repair. *Nat Genet.* 2018 Aug;50(8):1086-1092. PubMed Central PMCID: PMC6072579.
 - c. Sundar R, Huang KK, Kumar V, Ramnarayanan K, Demircioglu D, Her Z, Ong X, Bin Adam Isa ZF, Xing M, Tan AL, Tai DWM, Choo SP, Zhai W, Lim JQ, Das Thakur M, Molinero L, Cha E, Fasso M, Nigam M, Pietrantonio F, Lee J, Jeyasekharan AD, Qamra A, Patnala R, Fabritius A, De Simone M, Yeong J, Ng CCY, Rha SY, Narita Y, Muro K, Guo YA, Skanderup AJ, So JBY, Yong WP, Chen Q, Göke J, Tan P. Epigenetic promoter alterations in GI tumour immune-editing and resistance to immune checkpoint inhibition. *Gut.* 2022 Jul;71(7):1277-1288. PubMed Central PMCID: PMC9185816.
 - d. Tang TY, Nichetti F, Kaplan B, Lonardi S, Pietrantonio F, Salvatore L, Vivaldi C, Rimassa L, de Braud F, Rizzato MD, Pavlick D, Chu R, Danner De Armas A, Sharaf R, Sokol E, Rodon Ahnert J, Ross JS, Javle M, Nigam M. Comparative Genomic Analysis and Clinical Outcomes of BRAF-mutated Advanced Biliary Tract Cancers. *Clin Cancer Res.* 2023 Dec 1;29(23):4853-4862. PubMed PMID: 37773629.
4. As part of the research program on biliopancreatic cancers, I worked in various national and international real-world studies assessing the impact of novel treatment strategy on the outcomes of patients affected by biliopancreatic cancer, as shown by the selected publications below. Furthermore, I coordinated a real-world multicentric, international, retrospective, observational study evaluating the survival outcomes of a relatively large cohort of 46 patients affected by advanced IDH1 mutant cholangiocarcinoma and treated with the IDH1 inhibitor ivosidenib as second-line or later therapy.
- a. Nigam M, Rimini M, Castet F, Melzer A, Rizzato MD, Pressiani T, Lavacchi D, Aprile G, Angela T, Saladino T, Silvia N, Cito P, Pastorino A, Terán-Brage E, Sciortino C, Camera S, Pircher C, Persano M, Mazzaferro V, Foti S, Vega KS, Ettrich TJ, Antonuzzo L, Rimassa L, Lonardi S, Perkhof L, Macarulla T, Pietrantonio F, Casadei-Gardini I. Ivosidenib for IDH1-Mutant Intrahepatic Cholangiocarcinoma: Insights from a Multicenter Real-World Study. *Liver Int.* 2025 Sep;45(9):e70295. doi: 10.1111/liv.70295. PMID: 40856270
 - b. Milella M, Orsi G, di Marco M, Salvatore L, Procaccio L, Noventa S, Bozzarelli S, Garajova I, Vasile E, Giordano G, Macchini M, Cavaliere A, Gaule M, Bergamo F, Chiaravalli M, Palloni A, Carloni R, Bittoni A, Nigam M, Rapposelli IG, Rodriquenz MG, Scartozzi M, Mosconi S, Giommoni E, Bernardini I, Paratore C, Spallanzani A, Bencardino K, Forti L, Tamburini E, Lonardi S, Scarpa A, Cascinu S, Tortora G, Sperduti I, Reni M. Real-World Impact of Olaparib Exposure in Advanced Pancreatic Cancer Patients Harboring Germline BRCA1-2 Pathogenic Variants. *Cancer Med.* 2025 Feb;14(3):e70364. PubMed Central PMCID: PMC11761426.
 - c. Rimini M, Fornaro L, Rizzato MD, Antonuzzo L, Rossari F, Satake T, Vandeputte H, Vivaldi C, Pressiani T, Lucchetti J, Kim JW, Abidoye O, Rapposelli IG, Tamberi S, Finkelmeier F, Giordano G, Nichetti F, Chon HJ, Braconi C, Pirrone C, Castet F, Tamburini E, Yoo C, Parisi A, Diana A, Scartozzi M, Prager GW, Avallone A, Schirripa M, Kim IH, Perkhof L, Oneda E, Verrico M, Adeva J, Chan SL, Spinelli GP, Personeni N, Garajova I, Rodriquenz MG, Leo S, Salani F, De Rosa A, Lavacchi D, Foti S, Ikeda M, Dekervel J, Nigam M, Balsano R, Tonini G, Kang M, Bekaii-Saab T, Esposito L, Boccaccino A, Himmelsbach V, Landriscina M, Djaballah SA, Zanuso V, Masi G, Lonardi S, Rimassa L, Casadei-Gardini A. Durvalumab plus gemcitabine and cisplatin in advanced biliary tract cancer: A large real-life worldwide population. *Eur J Cancer.* 2024 Sep;208:114199. PubMed PMID: 39002348.
 - d. Taïeb J, Sayah L, Heinrich K, Kunzmann V, Boileve A, Cirkel G, Lonardi S, Chibaudel B, Turpin A, Beller T, Hautefeuille V, Vivaldi C, Mazard T, Bauguion L, Nigam M, Prager GW, Coutzac C, Benedikt Westphalen C, Auclin E, Pilla L. Efficacy of immune checkpoint inhibitors in microsatellite unstable/mismatch repair-deficient advanced pancreatic adenocarcinoma: an AGEO European Cohort. *Eur J Cancer.* 2023 Jul;188:90-97. PubMed PMID: 37229836.