

“PREcision Medicine Approach: bringing biomarker research to clinic (PREMIA)”



Elenco studi clinici condotti e conclusi

1. NutrIPF; <https://clinicaltrials.gov/ct2/show/study/NCT03770845> Data inizio arruolamento 10/12/2018.
2. Studio osservazionale su fasi accelerate di IPF e patologie fibrosanti non-IPF (PF-ILDs); Delibera n. 1538, seduta 14.11.19.
3. Aspetti radiologici dell'IPF; Approvato da CE con emendamento del 07.07.20 a delibera n. 1538, seduta 14.11.19.
4. Studio SequelaeCoV; ClinicalTrials.gov Identifier: NCT04435327 Delibera n. 915, seduta 09.07.20.
5. Fibrosi e disfunzione endoteliale in risposta alle terapie dello scompenso cardiaco avanzato; Parere CE numero 301-062017.
6. Valutazione delle relazioni tra sindrome metabolica e biomarcatori di funzione e struttura arteriosa; Parere CE numero 2008-638.
7. Valutazioni delle relazioni tra acido urico e biomarcatori di funzione e struttura arteriosa; Parere CE numero 2008-638.
8. Valutazione delle relazioni tra acido urico ed interessamento coronarico; Parere CE numero 131-032019.
9. Valutazioni delle relazioni tra ankle brachial index ed outcome geriatrici in pazienti ospedalizzati; Parere CE numero 146-042018.
10. Valutazioni delle relazioni tra acido urico ed outcome in pazienti con acuzie cardiologica; Parere CE numero 12-022018.
11. COVID-19 Niguarda Research Working Group Parere CE numero 249-13052020 Concluso

Studi clinici in corso

12. CardiolPF; Link web: <https://clinicaltrials.gov/ct2/show/study/NCT04177251> Data inizio arruolamento 21/12/2019.
13. Studio osservazionale su PF-ILDs fibrosanti in 2 centri di riferimento; Delibera n. 1538, seduta 14.11.19.
14. Studio della concentrazione di ossido nitrico e delle citochine infiammatorie nell'esalato espiratorio come marcatore di danno polmonare acuto e evoluzione fibrotica in pazienti con ARDS (FeNO-ARDS); Approvaz. CE ASST Monza n 2809.

15. Caratterizzazione delle mutazioni somatiche e germline responsabili di Patologie Mieloproliferative di tipo triple-negative; Approvazione CE N° 0040864/19 Data di inizio: gennaio 2019
16. Studio molecolare nella colangite sclerosante primitiva Protocollo 321; (CE UNIMIB) Data inizio arruolamento 15/5/2017
17. PBC registry Protocollo PBC322; (Parere n. 2969 CE ASST Monza del 16/07/2019) Data inizio arruolamento 15/7/2019
18. ERN-RARE-LIVER Prospective Research Registry R-LIVER; Approvazione CE ASST Monza n 3347
19. FICUS: Studio prospettico, multicentrico sul ruolo della elastografia nella CSP in Europa
20. Biomarker-driven single-cell lung pathology prediction of disease progression in idiopathic pulmonary fibrosis

Studi clinici in fase di attivazione

21. Long-term cardiopulmonary sequelae after COVID-19 Valutare le sequele polmonari e del circolo polmonare tra i 2 e 3 anni dall'infezione da COVID-19; In corso sottomissione a CE
22. Studio prospettico multicentrico, italo-canadese atto a descrivere le caratteristiche cliniche, funzionali e prognostiche dei pz affetti da PF-ILDs; Non ancora sottomesso a CE
23. Studio multicentrico, prospettico volto a caratterizzare clinicamente ed in termini prognostici i pazienti affetti da interstitial pneumonia with autoimmune features (IPAF), Follow up pazienti post ARDS (anche da COVID)
24. Studio della fibrosi polmonare con tecniche non-distruttive (Micro CT),
25. Inibitori di NOX studio della sicurezza ed efficacia degli inibitori di NOX nella CSP;
26. VANC-IT studio della sicurezza ed efficacia della vancomicina orale nella CSP; (EudraCT number 2022-000875-37)
27. Identificazione di una signature radiomica nella CSP;
28. Sicurezza ed efficacia degli inibitori di IBAT (ileal bile acid transporter) nella CSP;
29. PNEUMO-HFpEF valutazione della presenza di fibrosi polmonare in pazienti con scompenso cardiaco a funzione ventricolare preservata (patologia nota per l'importante componente fibrotica del miocardio);
30. PCSK9-FMD Valutazione di biomarcatori di funzione vascolare (Flow Mediated Dilation, Pulse Wave Velocity, distensibilità carotidea) in un gruppo di pazienti che inizia anticorpi anti-PCSK9 per il controllo della dislipidemia;
31. Valutazione della cinetica dell'acido urico e della metabolomica durante sindrome coronarica acuta;

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Elenco dei lavori scientifici pubblicati con acknowledgment a PREMIA:

1. Stravalaci, M., Pagani, I., Paraboschi, E.M., et al. Recognition and inhibition of SARS-CoV-2 by humoral innate immunity pattern recognition molecules (2022) *Nature Immunology*, 23 (2), pp. 275-286.
2. Luppi, F., Sebastiani, M., Salvarani, C., et al. Acute exacerbation of interstitial lung disease associated with rheumatic disease (2022) *Nature Reviews Rheumatology*, 18 (2), pp. 85-96.
3. Weber, T., Protogerou, A.D., Agharazii, M., et al. Twenty-four-hour central (aortic) systolic blood pressure: Reference values and dipping patterns in untreated individuals (2022) *Hypertension*, 79 (1), pp. 251-260.
4. Rezoagli, E., Mariani, I., Rona, R., et al. Difference between prolonged versus standard duration of prone position in COVID-19 patients: a retrospective study (2021) *Minerva Anestesiologica*, 87 (12), pp. 1383-1385.
5. Maloberti, A., Ughi, N., Bernasconi, D.P., et al. Niguarda Covid-19 Working Group Heart rate in patients with sars-cov-2 infection: Prevalence of high values at discharge and relationship with disease severity (2021) *Journal of Clinical Medicine*, 10 (23), art. no. 5590
6. Graziano, F., Valsecchi, M.G., Rebora, P. Sampling strategies to evaluate the prognostic value of a new biomarker on a time-to-event end-point (2021) *BMC Medical Research Methodology*, 21 (1), art. no. 93
7. Luppi, F., Kalluri, M., Faverio, P., et al. Idiopathic pulmonary fibrosis beyond the lung: understanding disease mechanisms to improve diagnosis and management (2021) *Respiratory Research*, 22 (1), art. no. 109
8. Madotto, F., McNicholas, B., Rezoagli, et al. on behalf of the LUNG SAFE Investigators and the ESICM Trials Group Death in hospital following ICU discharge: insights from the LUNG SAFE study (2021) *Critical Care*, 25 (1), art. no. 144
9. Maloberti, A., Fribbi, F., Motto, E., et al. Ankle-Brachial Index Is a Predictor of In-Hospital Functional Status but Not of Complications in Hospitalized Elderly Patients (2021) *Gerontology*, 67 (6), pp. 674-680
10. Poletti, V., Vancheri, C., Albera, C., et al. the FIBRONET study group Clinical course of IPF in Italian patients during 12 months of observation: results from the FIBRONET observational study (2021) *Respiratory Research*, 22 (1), art. no. 66

11. Coppadoro, A., Benini, A., Fruscio, R., et al. Helmet CPAP to treat hypoxic pneumonia outside the ICU: an observational study during the COVID-19 outbreak (2021) *Critical Care*, 25 (1), art. no. 80
12. Sebastiani, M., Faverio, P., Manfredi, A., et al. Interstitial pneumonia with autoimmune features: Why rheumatologist–pulmonologist collaboration is essential (2021) *Biomedicines*, 9 (1), art. no. 17, pp. 1-15
13. Cappadona, C., Paraboschi, E.M., Ziliotto, N., et al. MEDTEC students against coronavirus: Investigating the role of hemostatic genes in the predisposition to COVID-19 severity (2021) *Journal of Personalized Medicine*, 11 (11), art. no. 1166
14. Bianchi, S., Maloberti, A., Peretti, A., et al. Determinants of Functional Improvement After Cardiac Rehabilitation in Acute Coronary Syndrome (2021) *High Blood Pressure and Cardiovascular Prevention*, 28 (6), pp. 579-587
15. Faverio, P., Luppi, F., Rebora, P., et al. Six-Month Pulmonary Impairment after Severe COVID-19: A Prospective, Multicentre Follow-Up Study (2021) *Respiration*, 100 (11), pp. 1078-1087.
16. Maloberti, A., Biolcati, M., Ruzzenenti, G., et al. The role of uric acid in acute and chronic coronary syndromes (2021) *Journal of Clinical Medicine*, 10 (20), art. no. 4750
17. Faverio, P., Stainer, A., Conti, S., et al. Differences between acute exacerbations of idiopathic pulmonary fibrosis and other interstitial lung diseases (2021) *Diagnostics*, 11 (9), art. no. 1623
18. Cordell, H.J., Fryett, J.J., Ueno, K., et al. PBC Consortia, Canadian PBC Consortium, Chinese PBC Consortium, Italian PBC Study Group, Japan-PBC-GWAS Consortium, US PBC Consortium, UK-PBC Consortium An international genome-wide meta-analysis of primary biliary cholangitis: Novel risk loci and candidate drugs (2021) *Journal of Hepatology*, 75 (3), pp. 572-581.
19. Ruzzenenti, G., Maloberti, A., Giani, V., et al. the Covid-19 Niguarda Working Group Covid and Cardiovascular Diseases: Direct and Indirect Damages and Future Perspective (2021) *High Blood Pressure and Cardiovascular Prevention*, 28 (5), pp. 439-445.
20. Gerussi, A., Restelli, U., Croce, D., et al. Cost of illness of Primary Biliary Cholangitis - a population-based study (2021) *Digestive and Liver Disease*, 53 (9), pp. 1167-1170.
21. Gerussi, A., Bernasconi, D.P., O'Donnell, S.E., et al. Italian PBC Study Group and the GLOBAL PBC Study Group Measurement of Gamma Glutamyl Transferase to Determine Risk of Liver Transplantation or Death in Patients With Primary Biliary Cholangitis (2021) *Clinical Gastroenterology and Hepatology*, 19 (8), pp. 1688-1697.e14.
22. Stainer, A., Faverio, P., Busnelli, S., et al. Molecular biomarkers in idiopathic pulmonary fibrosis: State of the art and future directions (2021) *International Journal of Molecular Sciences*, 22 (12), art. no. 6255
23. Maloberti, A., Bossi, I., Tassistro, E., et al. Uric acid in chronic coronary syndromes: Relationship with coronary artery disease severity and left ventricular

diastolic parameter (2021) *Nutrition, Metabolism and Cardiovascular Diseases*, 31 (5), pp. 1501-1508.

24. Moriggi, M., Belloli, S., Barbacini, P., et al. Skeletal muscle proteomic profile revealed gender-related metabolic responses in a diet-induced obesity animal model (2021) *International Journal of Molecular Sciences*, 22 (9), art. no. 4680

25. Gerussi, A., Natalini, A., Antonangeli, F., et al. Immune-mediated drug-induced liver injury: Immunogenetics and experimental models (2021) *International Journal of Molecular Sciences*, 22 (9), art. no. 4557

26. Saettini, F., Fazio, G., Moratto, D., et al. Case Report: Hypomorphic Function and Somatic Reversion in DOCK8 Deficiency in One Patient With Two Novel Variants and Sclerosing Cholangitis (2021) *Frontiers in Immunology*, 12, art. no. 673487

27. Maloberti, A., Bombelli, M., Vallerio, P., et al. Metabolic syndrome is related to vascular structural alterations but not to functional ones both in hypertensives and healthy subjects (2021) *Nutrition, Metabolism and Cardiovascular Diseases*, 31 (4), pp. 1044-1052.

28. Dal Magro, R., Vitali, A., Fagioli, S., et al. Oxidative stress boosts the uptake of cerium oxide nanoparticles by changing brain endothelium microvilli pattern (2021) *Antioxidants*, 10 (2), art. no. 266, pp. 1-16.

29. Piga, I., Capitoli, G., Clerici, F., et al. Ex vivo thyroid fine needle aspirations as an alternative for MALDI-MSI proteomic investigation: intra-patient comparison (2021) *Analytical and Bioanalytical Chemistry*, 413 (5), pp. 1259-1266.

30. Zambelli, V., Rizzi, L., Delvecchio, P., et al. Hexarelin modulates lung mechanics, inflammation, and fibrosis in acute lung injury (2021) *Drug Target Insights*, 15 (1), pp. 26-33.

31. Mulinacci, G., Palermo, A., Invernizzi, P., et al. Old and novel prognostic biomarkers in primary biliary cholangitis (2021) *Expert Opinion on Orphan Drugs*, 9 (4), pp. 123-131

32. Montali, L., Gragnano, A., Miglioretti, M., et al. Quality of life in patients with primary biliary cholangitis: A cross-geographical comparison (2021) *Journal of Translational Autoimmunity*, 4, art. no. 100081

33. Faverio, P., Piluso, M., De Giacomi, F., et al. Progressive Fibrosing Interstitial Lung Diseases: Prevalence and Characterization in Two Italian Referral Centers (2021) *Respiration*, 99 (10), pp. 838-845.

34. Cortesi, P.A., Maloberti, A., Micale, M., et al. Costs and effects of cardiovascular risk reclassification using the ankle-brachial index (ABI) in addition to the Framingham risk scoring in women (2021) *Atherosclerosis*, 317, pp. 59-66.

35. Luppi, F., Sebastiani, M., Silva, M., et al. Interstitial lung disease in Sjögren's syndrome: A clinical review (2021) *Clinical and Experimental Rheumatology*, 38 (4), pp. S291-S300.

36. Carbone, M., Milani, C., Gerussi, A., et al. Primary biliary cholangitis: a multifaceted pathogenesis with potential therapeutic targets (2020) *Journal of Hepatology*, 73 (4), pp. 965-966.

37. Rebor, P., Andreano, A., Triglione, N., et al. Association between uric acid and pulse wave velocity in hypertensive patients and in the general population: a systematic review and meta-analysis (2020) *Blood Pressure*, 29 (4), pp. 220-231.
38. Faverio, P., Kalluri, M., Luppi, F., et al. RA-ILD: does more detailed radiological classification add something to our knowledge of this condition? (2020) *Journal of Thoracic Disease*, 12 (6), pp. 2993-2995.
39. Maloberti, A., Bruno, R.M., Facchetti, R., et al. THE role of metabolic syndrome in blood pressure control and pulse wave velocity progression over a 3.5 years in treated hypertensive PATIENTS. (2020) *European Journal of Internal Medicine*, 76, pp. 107-109.
40. Bossen, L., Rebor, P., Bernuzzi, F., et al. Soluble CD163 and mannose receptor as markers of liver disease severity and prognosis in patients with primary biliary cholangitis (2020) *Liver International*, 40 (6), pp. 1408-1414.
41. Luppi, F., Sebastiani, M., Sverzellati, N., et al. Lung complications of Sjogren syndrome (2020) *European Respiratory Review*, 29 (157), art. no. 200021, pp. 1-17.
42. Arisido, M.W., Antolini, L., Bernasconi, D.P., et al. Joint model robustness compared with the time-varying covariate Cox model to evaluate the association between a longitudinal marker and a time-to-event endpoint (2019) *BMC Medical Research Methodology*, 19 (1), art. no. 222
43. Cerri, S., Fontana, M., Balduzzi, S., Clinical differences in sarcoidosis patients with and without lymphoma: A single-centre retrospective cohort analysis (2019) *European Respiratory Journal*, 54 (5), art. no. 1802470
44. Maloberti, A., Rebor, P., Andreano, A., et al. Pulse wave velocity progression over a medium-term follow-up in hypertensives: Focus on uric acid (2019) *Journal of Clinical Hypertension*, 21 (7), pp. 975-983.
45. Maloberti, A., Vallerio, P., Triglione, N., et al. Vascular Aging and Disease of the Large Vessels: Role of Inflammation (2019) *High Blood Pressure and Cardiovascular Prevention*, 26 (3), pp. 175-182
46. Faverio, P., De Giacomi, F., Bonaiti, G., et al. Management of Chronic Respiratory Failure in Interstitial Lung Diseases: Overview and Clinical Insights (2019) *International Journal of Medical Sciences*, 16 (7), pp. 967-980
47. Faverio P, Rebor P, Rossi E, et al. Impact of N-acetyl-L-cysteine on SARS-CoV-2 pneumonia and its sequelae: results from a large cohort study. *ERJ Open Res.* 2021 Feb 7;8(1):00542-2021
48. Luppi F, Sebastiani M, Salvarani C, Bendstrup E, Manfredi A. Acute exacerbation of interstitial lung disease associated with rheumatic disease. *Nat Rev Rheumatol.* 2022 Feb;18(2):85-96.
49. Dei G, Rebor P, Catalano M, et al. Functional Progression in Patients with Interstitial Lung Disease Resulted Positive to Antisynthetase Antibodies: A Multicenter, Retrospective Analysis. *J Clin Med.* 2020 Sep 21;9(9): E3033 NO SCOPUS
50. Cristoferi L, Calvaruso V, Overi D, et al; Italian PBC Registry. Accuracy of Transient Elastography in Assessing Fibrosis at diagnosis in Naïve Patients With

Primary Biliary Cholangitis: A Dual Cut-Off Approach. *Hepatology*. 2021 Sep;74(3):1496-1508

51. Maloberti A, Qualliu E, Occhi L, et al. Hyperuricemia prevalence in healthy subjects and its relationship with cardiovascular target organ damage. *Nutr Metab Cardiovasc Dis*. 2021 Jan 4;31(1):178-185.

52. Bianchi S, Maloberti A, Peretti A, et al. Determinants of Functional Improvement After Cardiac Rehabilitation in Acute Coronary Syndrome. *High Blood Press Cardiovasc Prev*. 2021;28(6):579-587.

53. Luppi F, Sebastiani M, Silva M, et al. Interstitial lung disease in Sjögren's syndrome: a clinical review. *Clin Exp Rheumatol*. 2020;38 Suppl 126(4):291-300.

54. Faverio P, Fumagalli A, Conti S, et al. Nutritional assessment in idiopathic pulmonary fibrosis: a prospective multicentre study. *ERJ Open Res*. 2022;8(1):00443-2021

55. Moriggi M, Belloli S, Barbacini P, Murtag V, Torretta E, Chaabane L, Canu T, Penati S, Malosio ML, Esposito A, Gelfi C, Moresco RM, Capitanio D. Skeletal Muscle Proteomic Profile Revealed Gender-Related Metabolic Responses in a Diet-Induced Obesity Animal Model. *Int J Mol Sci*. 2021 Apr 28;22(9):4680

In press:

56. Gerussi, A., Verda, D., Bernasconi, D.P., et al. Machine learning in primary biliary cholangitis: A novel approach for risk stratification (2022) *Liver International*

57. Rebora P, Centola M, Morici N, et al. Uric acid is associated with acute heart failure and shock at presentation in ACS patients (2022) *Eur J Intern Med*.

58. Maloberti A, Rebora P, Occhino G, et al. Prevalence of hypertension mediated organ damage in subjects with high-normal blood pressure without known hypertension as well as cardiovascular and kidney disease (2021) *J Hum Hypertens*.

59. Zeppellini A, Galimberti S, Leone BE, Changes in tumor microenvironment between primary tumor and metastasis in luminal a/b breast cancers: a pilot study. *BMC Cancer*

60. Harari, S., Pesci, A., Albera, C., et al Nintedanib in IPF: Post hoc Analysis of the Italian FIBRONET Observational Study (2022) *Respiration*

61. Efe, C., Lammert, C., Taşçılar, K., et al. Effects of immunosuppressive drugs on COVID-19 severity in patients with autoimmune hepatitis (2021) *Liver International*

Elenco dei lavori scientifici sottomessi con acknowledgment a PREMIA

62. Crespiatico I, Zaghi M, Mastini C, et al. SETBP1 mutations identify an aggressive subtype of Myelofibrosis. Submitted to *NEJM*

63. Murtag V, Penati S, Belloli S, et al. Brain sex-dependent alterations after prolonged high fat diet exposure. *Communication Biology*. Under revision

64. Monieri M, Rainone M, Sacchi A, et al. A stapled chromogranin A-derived peptide homes in on tumors that express $\alpha v\beta 6$ or $\alpha v\beta 8$ integrins. Preparation completed: under submission to Cancer Research.
65. Faverio P, Conti S, Madotto F, et al. Idiopathic pulmonary fibrosis mortality in the Italian epicenter of COVID-19 pandemic. Under submission to Respiratory Research.
66. Faverio P, Luppi F, Rebora P, et al. One-year pulmonary impairment after severe COVID-19: a prospective, multicenter follow-up study. Under submission to Respiratory Research.
67. Maloberti A, Sun J, Zannoni J, et al. Endothelial dysfunction in patients with advanced heart failure treated with levosimendan periodic infusion compared with optimal medical therapy. Submitted to American J Cardiology.
68. Cristoferi L, Porta M, Bernasconi D, et al. PSC radiomics score (PRS): A radiomics-based model for medium-term outcome prediction in primary sclerosing cholangitis. Under submission to J Hepatol.