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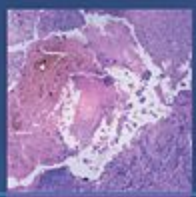
cancer TREATMENT AND RESEARCH COMMUNICATIONS





Impact of timing of administration of bone supportive therapy on pain palliation from radium-223

Next generation T-cell therapy for genitourinary malignancies, part A: Introduction and current state of the art

Next generation T-cell therapy for genitourinary malignancies, part B: Overcoming obstacles and future strategies for success

Bone turnover biomarkers identify unique prognostic risk groups in men with castration resistant prostate cancer and skeletal metastases: Results from SWOG S0421

Radiologic and autopsy findings in a case of fatal immune checkpoint inhibitor-associated pneumonitis

Lifetime physical inactivity is associated with lung cancer risk and mortality

Free sample of Editor's Choice articles

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AML, MDS, ALL, CML

Professor Matteo Lambertini, MD, PhD

University of Genoa, Genova, Italy

Breast cancer, BRCA, Oncofertility

Dr. Denis Ulises Landaverde, MD, MSc

Costa Rica University, San José, Costa Rica

Breast Cancer, Medical Oncology

Dr. Hun Ju Lee, MD

The University of Texas MD Anderson Cancer Center, Houston, Texas, United States of America

Hodgkin lymphoma, Mantle cell lymphoma

Dr. James Lee, MD, PhD

University of Pittsburgh, Pittsburgh, Pennsylvania, United States of America

Dr. Alessandro Leonetti, MD, PhD

University Hospital of Parma, Parma, Italy

Lung cancer

Dr. Daneng Li, MD

City of Hope Comprehensive Cancer Center Duarte, Duarte, California, United States of America

Hepatocellular carcinoma (HCC), Neuroendocrine tumors

Dr. Christopher Lieu, MD

University of Colorado Anschutz Medical Campus, Aurora, Colorado, United States of America

Dr. Stephanie J. Lim, MD

University of Hawai'i Cancer Center, Honolulu, Hawaii, United States of America

Pediatric Oncology, Immunotherapy, CAR T cell therapy, Pediatric leukemia, Pediatric lymphoma

Dr. Tiao Lin, MD, PhD

The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Osteoporosis, peri-prosthetic infection/bone loss, osteosarcoma, radiotherapy, chemotherapy

Dr. Luca Giovanni Locatello, MD

Friuli Centrale University Health Authority, Udine, Italy

head and neck cancer, laryngeal cancer, salivary gland cancer, oral cavity cancer, otolaryngology-head and neck surgery, otorhinolaryngology

Dr. Kristopher Lofgren, PhD

Gundersen Medical Foundation, La Crosse, Wisconsin, United States of America

Breast Cancer, Cell Signaling (growth factors, kinases, nuclear receptors), Mouse Models of Cancer, Mammary Gland Development

Assoc. Professor Chung Yeng Looi, PhD

Taylor's University School of Biosciences, Subang Jaya, Malaysia

Natural product, drug screening, molecular biology, cancer development, Pharmacology

Dr. Celso Abdon Lopes de Mello, MD, PhD

ACCamargo Cancer Center, Department of Medical Oncology, São Paulo, São Paulo, Brazil

Medical oncology, colorectal carcinoma, sarcoma, treatment, prognosis, circulating tumor cell

Dr. Jun Lu, MD

Beijing You'an Hospital Affiliated to Capital Medical University, Beijing, China

Hepatology and hepatocellular carcinoma, Cancer Biotherapy

Dr. Goran MARJANOVIĆ, MD, PhD

University of Niš, Niš, Serbia

Immuno hematology, Non hodgkin lymphomas, chronic lymphocitic leukemia

Dr. Ainhoa Madariaga, MD

University Hospital October 12th, Madrid, Spain

Ovarian cancer, Endometrial cancer, Cervical cancer, Vulvar cancer, Vaginal cancer, Drug development

Professor Makoto Maemondo, MD,PhD

Iwate Medical University, Department of Internal Medicine Division of Respiratory Medicine, Iwate, Japan

Translational oncology, Lung cancer research

Dr. Amita Maheshwari, MD

Tata Memorial Centre, Mumbai, India

Gynecologic oncology, cervical cancer, ovarian cancer, uterine cancer

Dr. Monica Malik, MD

Nizam's Institute of Medical Sciences, Hyderabad, India

Radiation Oncology, Palliative care and QOL

Dr. Saima Shakil Malik, PhD

Augusta University Medical College of Georgia, Augusta, Georgia, United States of America

Proteomics, Post translational modifications, Epigenetics, DNA repair mechanisms, Drugs associated cytotoxicity, Gene–environment interaction, Oncology, Pathology and Epidemiology, Genomics

Dr. Murali K. Mamidi, PhD

The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, United States of America

RTKs, BMPs, Transgenic mice, Cartilage, Bone, Blood cancer

Dr. Ankit Mangla, MBBS, MD

Case Western Reserve University School of Medicine, Cleveland, Ohio, United States of America

Soft-tissue Sarcoma, Melanoma, Merkel Cell Carcinoma, Cutaneous Squamous cell carcinoma, Basal cell carcinoma

Dr. Hitesh Mangukiya, PhD

Uppsala University Immunology Genetics and Pathology, Uppsala, Sweden

Tumor microenvironment, Tumor target discovery, Molecular signaling, Cancer metastasis, Antibody discovery, Cancer therapy, Glioblastoma, Cell migration, Glioblastoma invasion

Dr. Antonino Maniaci, PhD

University of Catania, Department of Surgical and Medical Sciences and Advanced Technologies 'G.F. Ingrassia', Catania, Italy

Head and Neck cancer, oral cancer, laryngeal cancer

Dr. Yariswamy Manjunath, PhD

University of Missouri, Columbia, Missouri, United States of America

Translational Oncology, Biomarkers in Cancer, Circualting Tumor Cells, non-small cell lung cancer

Dr. Francesco Mannavola, PhD

University of Bari, Bari, Italy

Liquid biopsy, Extracellular vesicles, Colorectal cancer

Dr. Luca Marinelli, MD

University of Rome La Sapienza, Roma, Italy

Radiation oncology

Dr. Benjamin L. Maughan, MD, PHARMD

The University of Utah, Salt Lake City, Utah, United States of America

genitourinary malignancies

Dr. Bradley McGregor, MD

Dana-Farber/Harvard Cancer Center, Boston, Massachusetts, United States of America

Medical Oncology For Gu Malignancies, Focus On Non-Prostate, ,

Professor Icro Meattini, MD

University of Florence, Firenze, Italy

Breast cancer, Clinical oncology, Radiation oncology

Dr. Quim Megías Barrera, PhD

University Clinic Hospital of Santiago de Compostela, Santiago de Compostela, Spain

Head and neck surgery, Head and neck reconstructive surgery

Dr. Rutika Mehta, MD, MPH

Moffitt Cancer Center, Tampa, Florida, United States of America

GI Medical Oncology

Dr. Yoav Messinger, MD

Children's Minnesota, Minneapolis, Minnesota, United States of America

Childhood Leukemia, Lymphoma, Rare Tumors, DICER1 Syndrome

Dr. Edoardo Migliori, PhD

Columbia University Irving Medical Center, New York, New York, United States of America

Cancer immunology, CAR-T, cell therapy, viral carcinogenesis, and breast cancer

Dr. Hamed Mirzaei, PhD

Kashan University of Medical Sciences, Institute for Basic Sciences, Kashan, Iran

MicroRNA, LncRNA, circular RNA, Natural compunds, Cancer

Dr. Kriti Mittal, MD

University of Massachusetts Chan Medical School, Worcester, Massachusetts, United States of America

Medical oncology, genitourinary oncology, renal cell carcinoma, urothelial carcinoma, prostate cancer, testicular cancer, adrenal cancer, GU oncology, immmunotherapy, patient reported outcomes

Dr. Mir Mohd Faheem, PhD

Council of Scientific & Industrial Research Indian Institute of Integrative Medicine, Jammu, India

Cancer cell signaling, EMT and metastasis, cancer drug discovery

Dr. Hengameh Mojdeganlou, MD, APCP

Urmia University of Medical Sciences, Urmia, Iran

Cancer/pathology

Dr. Mojtaba Mollaei

Tarbiat Modares University, Department of Immunology, Tehran, Iran

Cancer, Chemotherapy, Immunotherapy, Intracellular signaling, Apoptosis, Chemoresistance, The role of MicroRNAs and Long non-coding RNAs in cancer development

Dr. Floriana Morgillo, MD

University of Campania Luigi Vanvitelli, Caserta, Italy

Thoracic Head and Neck

Dr. Luca Moscetti, MD

University Hospital Modena, Modena, Italy

Breast Cancer

Dr. Pavlos Msaouel, MD, PhD

The University of Texas MD Anderson Cancer Center, Houston, Texas, United States of America

Renal cell carcinoma, Renal medullary carcinoma, SMARCB1 loss, Non-clear cell renal cell carcinoma

Dr. Eli Muchtar, MD

Mayo Clinic in Rochester, Rochester, Minnesota, United States of America

Multiple myeloma, AL amyloidosis, MGUS, Waldenström macroglobulinemia, CLL, hairy cell Leukemia, LGL Leukemia, general Hematology, stem cell transplantation , amyloidosis, light chain amyloidosis

Dr. Nupur Mukherjee, PhD

National Institute for Research in Reproductive Health, Department of Innate Immunity, Mumbai, India

Cancer Immunology, Molecular biology of Breast cancer, Translational Oncology, molecular therapeutics of cancer, Immunotherapy, transcription profiles of oncogenes, TSGs and pattern recognition receptors in cancer

Dr. Fahad Mukhtar, PhD

University of South Florida, Tampa, Florida, United States of America

Cancer epidemiology, lymphoma, multiple primary malignancies, cancer disparities , ,

Dr. Layth Mula-Hussain, MBChB, MS, EF, FRCP (Edin)

Dalhousie University, Faculty of Medicine, Halifax, Nova Scotia, Canada

Radiation oncology

Dr. Pashna N. Munshi, MD

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Stem Cell Transplant and Cellular Immunotherapy (autologous, allogeneic transplant, CAR T-cell therapies)

Dr. Masaki Nagaya, MD, PhD

Meiji University - Ikuta Campus, Kawasaki, Japan

GI cancer

Dr. Madhumathy Nair, Ph.D

St John's National Academy of Health Sciences Division of Molecular Medicine, Bengaluru, India

Breast cancer biology, MicroRNAs, Tumor microenvironment, Metastasis, Chemoresistance

Dr. Ranjit Nair, MD

The University of Texas MD Anderson Cancer Center, Houston, Texas, United States of America

Lymphoma/ Myeloma

Dr. Geeta Narayanan, MD

Vydehi Institute of Medical Sciences and Research Centre, Bangalore, India

Radiation oncology, Comparison of HPV genotype and response to chemo radiation in cervical cancer, Evaluation of telomerase as a tumor marker in head and neck cancer, Functional MRI imaging in cervical cancer brachytherapy, MRI adapted brachytherapy in cervical cancer, Evaluating the role of Neo adjuvant chemo therapy in various cancer sites

Dr. Azadeh Nasrazadani, MD, PhD

UPMC, Pittsburgh, Pennsylvania, United States of America

breast cancer

Dr. Loretta Nastoupil, MD

The University of Texas MD Anderson Cancer Center, Houston, Texas, United States of America

Lymphoma/Myeloma

Dr. Arash Navran, MD

Netherlands Cancer Institute, Amsterdam, Netherlands

Head and neck cancer, radiotherapy, chemoradiation, combined treatment, HNSCC, treatment toxicity, outcome, margin reduction, VMAT

Dr. Vahideh Nazari, PhD

Hamadan University of Medical Sciences, Hamedan, Iran

Medical physic, Dosimetry, Medical image processing, Adaptive radiotherapy, Patient-specific radiation treatment quality assurance, Radiation protection, Radiotherapy

Dr. Aziz Nazha, MD

Cleveland Clinic, Cleveland, Ohio, United States of America

leukemia

Assoc. Professor Ntokozo Ndlovu, MB ChB MMed

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Radiation/Clinical Oncology, Cancer, Cervical Cancer, Breast Cancer, HIV related Cancers, Prostate Cancer, Cancer Epidemiology

Professor Hovav Nechushtan, MD, PHD

Hadassah University Medical Center, Jerusalem, Israel

Signal Transduction, Lung Cancer, Personalized Medicine (Oncology)

Dr. Hema Negi, PhD

Shanghai Jiao Tong University, Shanghai, China

Clinical Oncology, Animal tumor models , molecular oncology

Dr. Erika A. Newman, MD

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Neuroblastoma and pediatric tumor biology, DNA repair, cancer xenograft models

Dr. Bikesh Kumar Nirala, PhD

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Tumor microenvironment, Immunology, Tumor immunotherapy, Paediatric tumor, Diabetes, Glycation biology

Dr. Gengming Niu, MD, PhD

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Gastrointestinal cancers

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Thoracic cancer, Lung cancer

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Gastrointestinal oncology

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pulmonary medicine

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Internal medicine, medical oncology, GU and Lung cancers

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Oak Lawn, United States of America

cancer and cancer treatment, Cancer Biology, Pharmacogenetics

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Urology And Urologic Oncology, Kidney Cancer, Bladder Cancer, Prostate Cancer, ,

Dr. Laura Paleari, PhD

ALiSa Health System of Liguria Region, Genova, Italy

Cancer prevention, molecular biology, drug repurposing, health technology assessment, pharmacoeconomics

Dr. Amit K Pandey, PhD

Amity University Amity Institute of Biotechnology, Noida, India

Non-coding RNA, Cancer Biology, Molecular and Cell Biology, Signaling Pathways

Dr. Parijat Pandey, PhD

Baba Mastnath University, Bohar, India

Nanotechnology, Oncology and Formulation Development

Dr. Alex Papachristodoulou, PhD

Columbia University Irving Medical Center, New York, New York, United States of America

Prostate Cancer, Glioblastoma, Mitochondria and Metabolism, ,

Dr. Mamta Parikh, MD, MS

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Genitourinary Oncology, Early Developmental Therapeutics

Dr. Sunil Pasricha, MD, FELLOWSHIP(ONCOPATHLOLOGY)

Rajiv Gandhi Cancer Institute and Research Centre, New Delhi, India

Oncopathology, ONCOPATHLOLOGY, HEAD AND NECK, BONE AND SOFT TISSUE, THORACIC PATHOLOGY

Dr. Sofia S. Pereira, PhD

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Adrenocortical tumors, obesity, endocrine tumors

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Thoracic oncology and genomic sequencing

Dr. Jason R. Pitarresi, PhD

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pancreatic cancer, tumor microenvironment, mouse modeling, metastasis, cellular plasticity, epithelial-to-mesenchymal transition (EMT)

Dr. Noam Falbel Pondé, MD, PhD

ACCamargo Cancer Center, SAO PAULO, Brazil

Breast cancer, Geriatric oncology

Dr. Kam Sheung Poon, MRCP, FHKCA, FANZCA

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General medicine, perioperative cancer medicine, cancer pain management

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neuroendocrine cancer, sarcoma, pancreatic cancer, rare tumors, colon cancer, liver cancer, biliary cancer, gastric cancer, esophageal cancer, head neck cancer

Dr. Sophie Postel-Vinay, MD, PhD

Gustave Roussy, Villejuif, France

lung cancer

Dr. Dinesh Pradhan, MD, FCAP, FASCP

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Melanoma, Cancer genetics and epigenetics, Vulvar cancer, Cutaneous lymphoma

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Palacky University Olomouc, Faculty of Medicine and Dentistry, Olomouc, Czechia

Lymphoma, biomarkers, imaging (PET), prognosis

Dr. Juan Qian, MD

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Hematology

Dr. Weiqiang Qiao, MD

Henan University of Science and Technology Affiliated First Hospital, Luoyang, China

Evidence-based medicine, Breast cancer, Meta-analysis

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Neuro-Oncology, Brain Tumors, Gliomas, Meningiomas, Brain metastases, Neurosurgery

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Head and neck cancer, skin cancers, radiation oncology

Dr. Elie Rassy, MD MSc MPH

Gustave Roussy, Villejuif, France

Precision oncology, early-stage cancer detection, cancer of unknown primary, urogenital cancers

Dr. Jun Ren, PhD

Harvard Medical School, Massachusetts General Hospital, Boston, Massachusetts, United States of America

Tumor microenvironment, Cancer immunotherapy, CAR T therapy, Vascular biology

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Clinical Veterinary, Gastroenterology, Endoscopy, Biochemistry, Reproduction science

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Austral University Cancer Immunobiology Laboratory, Buenos Aires, Argentina

Lung cancer, immunotherapy, real world data, tumor microenvironment, extracellular matrix, hyalurnic acid, clinical trial

Dr. Mersedeh Rohanizadegan, MD, MPH, FACMG

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Genetics and Pediatric Medicine

Dr. Graziana Ronzino, MD

Hospital Vito Fazzi, Lecce, Italy

Gynecologic oncology, Head and neck cancer, Familial cancer syndromes, Familial breast/ovarian cancer

Dr. Giovanni Rosti, MD

Foundation IRCCS Polyclinic San Matteo, Pavia, Italy

Testicular cancer, High dose chemotherapy, Supportive therapy

Dr. Sacha Rothschild, MD, PhD

University Hospital Basel, Basel, Switzerland

Thoracic oncology and Head and neck tumors

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Medical Oncology, Biomarkers, Epigenetics

Dr. Anwaar Saeed, MD

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Immunotherapy and Immune modulation in Gastrointestinal malignancies, Gastric and Esophageal Cancer, Colorectal cancer and Hepatocellular carcinoma

Dr. Kamal Sahu, MD

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prostate cancer, renal cancer, testicular cancer, bladder cancer, urothelial cancer, kidney cancer, genitourinary malignancies

Dr. Nasreena Sajjad, PhD

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Antioxidants, Antioxidant Activity, Reactive Oxygen Species, Phytochemicals, Natural Product Chemistry, Extraction, Chromatography, Bioactivity, Biomarkers, Food Chemistry

Dr. Ikuko Sakamto, MD

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Gynecologic oncology, endometrial cancer, ovarian cancer, cervical cancer

Dr. Maribel Salas, MD, DSc, MSc

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Internal medicine, pharmacoepidemiology, pharmacovigilance, patient safety

Dr. Alejandro Sanchez, MD

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Genitourinary Surgical Oncology , kidney cancer, obesity and cancer, translational research, ivc thrombectomy

Dr. Muzaffer Sanci, MD

Tepecik Education and Research Hospital Clinics, Konak, Turkey

Rare Genital Tumours

Dr. Alberto Sandri, MD

San Luigi Gonzaga University Hospital, Thoracic Surgery Unit, Orbassano, Italy

Thoracic oncology, minimally invasive surgery (uniportal VATS), technology applied to thoracic surgery, lung cancer, lung lobectomy, lung segmentectomy, NSCLC, lung function test, mesothelioma, neuroendocrine tumours of the lung and thymus

Dr. Jacob Sands, MD

Dana-Farber/Harvard Cancer Center, Boston, Massachusetts, United States of America

Small Cell Lung Cancer, Non-Small Cell Lung Cancer, Immunotherapy

Professor Daniele Santini, PhD, MD

Campus Bio-Medico University Hospital, Roma, Italy

GU cancers, GI Cancers, Supportive Therapy, Bone Metastases

Dr. Julien Sarkis, MD

University of Saint Joseph, West Hartford, Connecticut, United States of America

Translational oncology, Biomarkers, Prostate cancer, Kidney cancer

Prof. Dr. Yasushi Sasaki, MD, PhD

Sapporo Medical University, Sapporo, Japan

Molecular mechanisms of human carcinogenesis, Functional analysis of p53 family, Cancer genetics (Oral cancer, Gastrointestinal cancer, Pancreatic cancer)

Dr. Nicolas Sayegh, MD

University of Utah Health Huntsman Cancer Institute, Salt Lake City, Utah, United States of America

Genitourinary Oncology

Dr. Mohammad Sayyadi, PhD

Arak University of Medical Sciences, Arak, Iran

Cancer biology, Leukemic, Cell signalling, Drug efficiency in cancer

Dr. Daniele Scartoni, MD

Proton Therapy Center Trento, Trento, Italy

Radiotherapy, proton therapy, brain tumors, toracic tumors, GI tumors

Dr. Joel Segel, PhD

The Pennsylvania State University, Department of Health Policy and Administration, University Park, Pennsylvania, United States of America

Cancer health economics, Breast cancer and Genitourinary cancers

Dr. Alka Sehgal, MD, DNB, MNAMS

Government Medical College and Hospital, Chandigarh, India

Obstetrics and Gynecology

Dr. Benedict Seo, BDS, DClinDent, PhD, FICD

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Oral and maxillofacial pathology, histopathology, oral squamous cell carcinoma, unfolded protein response

Dr. Vinit Shanbhag, PhD

University of Missouri, Columbia, Missouri, United States of America

Biochemistry, Biology of cancer, Drug discovery, and development, Molecular biology and signaling

Dr. Aditi Shastri, MD

Albert Einstein College of Medicine, Montefiore Medical Center, Bronx, New York, United States of America

Acute myeloid leukemia, myelodysplastic syndromes, targeted therapies in hematologic malignancies, transcription factors/ signaling pathways

Dr. Zhiyong Shen, MD

Southern Medical University Nanfang Hospital, Guangzhou, China

The molecular mechanism of occurrence and development of colorectal cancer, Cancer metabolism, Transcriptional regulation, immune microenviroment) Minimally invasive treatment for gastrointestinal diseases, especially laparoscopic surgery for colorectal cancers.

Dr. Marisa Shiina, PhD

University of California San Francisco, San Francisco, California, United States of America

Drug resistance, epigenetic, cancer stem cells, neuroendocrine differentiation, biomarkers, cell signaling pathways, small molecule inhibitors

Dr. Nicholas Short, MD

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measurable residual disease, acute myeloid leukemia, acute lymphoblastic leukemia

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Hematologic malignancies

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NeuroOncology, Glioma biology, Stem Cell Biology, Organoid cancer models, Cancer Neuroscience

Dr. Charalampos Siotos, MD, PhD

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Breast cancer, mastectomy, breast reconstruction, oncoplastic surgery

Dr. Salvatore Siracusano, MD

University of L'Aquila, L'Aquila, Italy

Bladder and prostate cancer

Dr. Heloisa P. Soares, MD, PhD

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Neuroendocrine Tumors And Gastrointestinal Cancers, Clinical Trials

Prof. Dr. Carmino Antonio de Souza, MD, PhD

State University of Campinas, CAMPINAS, São Paulo, Brazil

Oncohematology and bone marrow transplantation, CML and malignant lymphomas, Bone Marrow, Stem Cell

Dr. Aris Spathis, PhD

General University Hospital Attikon, Athens, Greece

Molecular and cellular techniques with expertise in flow cytometry for diagnosis, typing, monitoring and treatment of malignancies

Assoc. Professor Carlo Sposito, MD, FEBS(HPB)

Foundation IRCCS National Cancer Institute, Milano, Italy

Hepatocellular carcinoma, Cholangiocarcinoma, Liver transplantation, Radioembolization, Chemoembolization, Liver surgery, Mini-invasive surgery, Laparoscopic surgery, Liver tumors, Pancreatic cancer, Gastric cancer, Esophago-gastric surgery

Prof. Dr. Czesław Stankiewicz, MD, PhD

Medical University of Gdansk, Gdansk, Poland

Otorhinolaryngology, head and neck cancer, parotid gland diseases and surgery, endoscopic laser treatment of vocal cord tumors

Raphael Eric Steiner, MD

The University of Texas MD Anderson Cancer Center, Houston, Texas, United States of America

Lymphoma

Dr. Michiel Strijbos, MD

University Hospitals Leuven, Leuven, Belgium

genitourinary malignancies

Dr. Tan Su-Ming, FRCS (Ed) (Surg), MMed (Surg)

Changi General Hospital, Singapore, Singapore

Breast Cancer

Dr. Dacita Suen, MBChB, FRACS,MS

The University of Hong Kong, Hong Kong, Hong Kong

Breast Surgery, Geriatric Oncology

Dr. Elgar Susanne Quabius, PhD

Kiel University, Kiel, Germany

Otorhinolaryngology, Head and neck surgery, Experimental oncology

Dr. Umang Swami, MD, MS

University of Utah Health Huntsman Cancer Institute, Salt Lake City, Utah, United States of America

Medical Oncology -- Genitourinary cancers (kidney, bladder, prostate and testicular cancers), melanoma, kidney

Em. Professor Argiris Symeonidis, MD, PhD

University of Patras, Patra, Greece

Gaucher disease, myelodysplastic syndromes, multiple myeloma, chronic myeloproliferative neoplasms, anemia, erythropoiesis, lymphoproliferative disorders, targeted treatments in hematology, Hematology

Dr. Weronika Maria Szejniuk, MD, PhD

Aalborg University Hospital, Department of Cardiology, Aalborg, Denmark

Lung cancer, NSCLC, SCLC, Radiation therapy of lung cancer, Radiation pneumonitis, Adjuvant chemotherapy, Radiation-induced lung injury, Mesothelioma

Dr. Marco Tagliamento, MD

Research Hospital San Martino, Genova, Italy

Thoracic Malignancies, Lung Cancer, Malignant Pleural Mesothelioma, Immunotherapy

Prof. Dr. Hiroyuki Takei, MD

Nippon Medical School, Bunkyo-Ku, Japan

Metastasis, Tumor Angiogenesis, Oncology, Endocrine therapy, Chemotherapy, Surgery, Breast cancer

Dr. Yuichi Tambo, MD, PhD

Kanazawa University Hospital, Kanazawa, Japan

Lung Cancer, NSCLC, SCLC, Immuno Oncology, Targeted Therapy, Translational Research, Clinical Trial

Dr. Daniel Tan, MD

National Cancer Centre Singapore, Singapore, Singapore

Thoracic, head and neck malignancies and drug development

Prof. Dr. Ozgur Tanriverdi, MD, MSc, PhD

Muğla Sıtkı Koçman University, Muğla, Turkey

Medical Oncology, Palliative Care, Psychooncology, Molecular Biology and Genetics, Gerontology

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Breast cancer

Dr. Monica Terenziani, M.D.

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Cancer survivorship, Pediatric germ cell tumors, Oncofertility and Pediatric Hodgkin Lymphoma

Dr. Nikolaos Thomakos, MD, PhD

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Perioperative care in Gyn/Oncology, Fertility sparing management in Gyn cancer

Dr. Elizabeth Thomas, PhD

University of Maryland School of Medicine, Baltimore, Maryland, United States of America

Oncogenic signaling, tumor progression & metastasis and cancer therapeutics

Prof. Dr. Anil Tombak, MD

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CLL, multple myeloma, lymphoma

Dr. Naoomi Tominaga, PhD

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Breast Cancer, Extracellular vesicles, Pathology, Cell-Cell Communication

Dr. Abhishek Tripathi, MD

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Clinical trials, genitourinary oncology, kidney, bladder and prostate cancer

Dr. Giuseppe Troiano, PhD

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Evidence-based Medicine, Meta-analysis, Prognostic Biomarker, oral squamous cell carcinoma

Dr. Emre Tuysuz, PhD

Lund University, Faculty of Medicine, Malmö, Sweden

Chordoma, miRNA, Cancer Stem Cell, Breast Cancer, Glioma, Role of Inflammation in Cancer Progression, Tumor Microenvironment , Complement System

Dr. Przemyslaw Twardowski, MD

Saint John's Cancer Institute, Santa Monica, California, United States of America

urologic oncology

Dr. Siddhartha Tyagi, MS

Baylor College of Medicine Verna and Marrs McLean, Department of Biochemistry and Molecular Biology, Houston, Texas, United States of America

Breast cancer, MYC, Splicing, Preclinical trials, Xenografts, Development of GEMM and PDX models, Molecular biology, Development and design new vectors, CRISPER, Development of in vivo screen technologies, Q PCR, ,

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Leukemia

Dr. Jeewan Ram Vishnoi, M.S., M.Ch., M.A.M.S.

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Surgical Oncology, Gastrointestinal Cancer, Head, and Neck Cancer, Breast Cancer, Cancer Epidemiology, Cancer Biomarkers, Translational Oncology

Dr. Mariza Vorster, PhD

University of Pretoria, Pretoria, South Africa

Nuclear medicine, theranostic, Ga-68-based PET, PET/CT, molecular imaging, targeted radionuclide therapy

Dr. Anderson Vulczak, PhD

University of São Paulo, SAO PAULO, Brazil

Tumor metabolism, Physical Exercise - Oncology, Breast Cancer, Exercise oncology

Dr. Mira Sudam Wagh, DNB

Regional Cancer Centre Thiruvananthapuram, Thiruvananthapuram, India

Upper Gastrointestinal malignancies, Lower Gastrointestinal malignancies, Hepaobiliary and Pancreatic cancers.

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Nikit Venishetty, Jessica Calderon-Mora, Navkiran K. Shokar, Pracheta Matharasi, ... Jennifer Molokwu

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Satoshi Endo, Takayuki Honda, Kazuaki Sato, Natsushi Kubota, ... Yoshikazu Tsukada

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Sanchay Jain, Vandana Dhingra, Bhavna Girdhani

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Lisa M. Hess, Patrick Peterson, Tomoko Sugihara, Naleen Raj Bhandari, ... Anthony Sireci

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Kamal Basri Siregar, Muhammad Al Anas

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Estrogen receptor and programmed death ligand-1 expression in type 1 endometrial cancer and its associated clinicopathological characteristics

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ABSTRACT

Background: This study aimed to determine the association of estrogen receptor (ER) and programmed death ligand-1 (PD-L1) expression with the clinicopathological characteristics of type 1 endometrial cancer.
Materials and methods: A total of 85 patients with type 1 endometrial cancer who underwent surgery at the Dr. Soetomo Hospital, Surabaya, Indonesia were retrospectively studied. Data about the age, menopausal status, body mass index, disease stage, cell differentiation, angiolymphatic invasion, myometrial invasion, and adjuvant therapy of the patients were collected from medical records. Immunohistochemistry with ER and PD-L1 antibodies was performed on all samples. The association between ER and PD-L1 expression and clinicopathological characteristics was statistically analyzed.
Results: The positivity rates of ER and PD-L1 in type 1 endometrial cancer were 68.2 % and 78.5 %, respectively. ER positivity was significantly correlated with body mass index (BMI) ≥25, premenopausal status, early stage of disease, <1/2 myometrial invasion, negative nodal metastasis, and lack of adjuvant therapy. It was also associated with age <55 years, low-grade cells, and angiolymphatic invasion, but the correlation was not significant. Meanwhile, PD-L1 positivity was significantly correlated with BMI <25, menopausal status, advanced stage of disease, high-grade cells, angiolymphatic invasion, and adjuvant therapy. It was also associated with age ≥55 years and nodal metastasis, but the correlation was not significant.
Conclusion: ER and PDL-1 positivity is associated with the clinicopathological characteristics of type 1 endometrial cancer.

1. Introduction

Endometrial cancer (EC) is the third leading cause of cancer-related deaths among women in Indonesia [1]. The incidence and death rates of this disease are predicted to increase by 20.3 % and 17.4 %, respectively, by 2025 [2]. The high percentage of cancer-related deaths indicates that research related to cancer therapy is still developing. The therapeutic paradigm has shifted with the advancement of research about EC and precision therapy. The National Comprehensive Cancer Network (NCCN) has recommended the use of immunotherapeutic agents, such as PD-1 inhibitors, for cancer therapy. However, PD-1 efficacy can be influenced by the expression of its ligands, such as PD-L1. The association of PD-L1 and estrogen receptor (ER) expression with EC is interesting and important for research.

ER, a member of the nuclear receptor superfamily, has two subtypes: estrogen receptor alpha (ERα) and estrogen receptor beta (ERβ). When estrogen binds to the binding domain, the ER ligand is activated, translocates to the nucleus, acts on the estrogen response element located in the upstream promoter of the target gene, and activates the transcription of the target gene. ERα and ERβ differ in expression and function during the progression of gynecologic cancer, such as EC [3]. For instance, ERα mediates estrogen-induced mitogenic signaling in

Abbreviations: EC, endometrial cancer; BMI, body mass index; ER, estrogen receptor; LVSI, lymphovascular space invasion; OS, overall survival; PD-L1, programmed death ligand-1; NCCN, National Comprehensive Cancer Network.

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cancer, whereas ERβ inhibits the proliferative effects of estrogen on cancer cells and reduces the phosphorylation of AKT and Cyclin D1 proteins, thereby inhibiting the cancer cell cycle and promoting apoptosis.

The endometrial tissue is sensitive to steroid hormones. Through its receptors, estrogen supports the development and growth of EC. Endometrioid-type EC is characterized by changes in the expression of various ER subtypes. Type 1 EC without ER expression is associated with aggressive tumors and a poor survival rate [4].

PD-L1 on the surface of tumor cells interacts with its receptors on T cells, triggering T cell dysfunction in tumor tissues and inhibiting T cell-induced antitumor immunity. 17b-estradiol (E2) increases PD-L1 expression in a dose-dependent manner [5]. Bioinformatics and cell line studies in cancer showed that PD-L1 expression is lower in ERα--positive breast cancer than in ERα-negative breast cancer [6,7].

Next-generation sequencing revealed that treatment with E2 affects PD-L1 expression in MCF-7 cells, indicating that estrogen regulates PD-L1 at the transcriptional level [8,9]. The checkpoint immunity of EC to PD-L1 and PD-1 is a concern. The positivity rates of PD-1 and PD-L1 in primary tumors are 59 % and 63 %, respectively [10].

PD-L1 positivity is associated with lympho-vascular space invasion (LVSI), histological type, myometrial invasion, and a good prognosis in EC survivors treated with immunotherapy [11,12]. A research in Egypt showed that the correlation of PD-L1 positivity with tumor and immune cells is stronger in older than in younger patients. Tumor and immune cells with PD-L1 expression are generally positive for LVSI, whereas those without PD-L1 expression are generally negative for LVSI [13]. High PD-L1 expression is a potential invasive mechanism against immune responses. PD-L1 increases the regulation of PD-1-positive tumor cells and is correlated with high tumor stages [14]. PD-L1 expression is also associated with LVSI, histology, myometrial invasion, and advanced stages [13].

Advanced gynecologic cancers have historically lacked effective treatment options. Immune checkpoint inhibitors (ICIs) have been approved by the US Food and Drug Administration for the treatment of cervical cancer and EC, offering durable responses for some patients [15]. The NCCN has recommended immunotherapeutic agents, such as PD-1 inhibitors (pembrolizumab), for the treatment of advanced EC with the microsatellite instability-high (MSI-H) or mismatch repair-deficient (MMRd) phenotype. MSI-H molecular subclasses are characterized by high numbers of CD3+/CD8+ tumor-infiltrating lymphocytes and an overexpression of PD-1 and PD-L1. Specifically, MSI-H/MMRd cancers are characterized by extremely high numbers of somatic mutations and have a relationship with MMR status and PD-1/PD-L1 expression in EC. EC cases with the MMRd phenotype have a higher cytotoxic T cell (CD8+) infiltration and PD-1/PD-L1 expression than those without this phenotype. The high immunogenicity of these tumors explains the strong rationale behind the use of immunotherapy in these subgroups of cancers [16].

In recent years, the MMRd phenotype has emerged as a predictive biomarker for immunotherapy, and ICIs such as pembrolizumab and dostarlimab have shown clinically meaningful activity as a monotherapy in patients with MMRd EC [17]. Moreover, ICIs and tyrosine kinase inhibitors have been extensively assessed, including tumors selected for DNA MMRd/MSI and PD-L1 expression status. Pembrolizumab plus lenvatinib is indicated for patients with unselected pretreated metastatic EC, whereas pembrolizumab monotherapy is a preferred option for patients with MMRd/MSI-H tumors [18].

2. Materials and methods

In this retrospective cross-sectional study, data about the age, menopausal status, body mass index (BMI), disease stage, cell differentiation, angiolymphatic invasion, myometrial invasion, and adjuvant therapy of patients with type 1 EC at Dr. Soetomo Hospital in Surabaya, Indonesia were obtained from medical records and histopathological results. Paraffin blocks from the Anatomical Pathology Laboratory of Dr. Soetomo Hospital containing a representative tumor mass collected from January 2018 to December 2022 were used to obtain ER and PD-L1 immunohistochemical data. PD-L1 expression was examined through immunohistochemical staining of endometrial tissue paraffin blocks using PD-L1 antibody from GenomeMe clone IHC411. ER expression was examined through immunohistochemical staining of endometrial tissue paraffin blocks using Biocare Medical ER. The tissues were examined using the LSAB II method and fixed using 10 % neutral buffered formalin (Fig. 2).

The association of ER and PD-L1 expression with the clinicopathological characteristics of patients with type 1 EC was analyzed using Fisher's exact, with $p < 0.05$ considered to indicate statistical significance (Fig. 3). This study was approved by the Research Ethics Committee of Dr. Soetomo Hospital Surabaya, Indonesia.

3. Results

A schematic of the patient selection is displayed in Fig. 1. A total of 105 patients with type 1 EC who underwent surgery in 2018–2022 were considered in this study. Among these patients, 20 were excluded because their paraffin blocks did not have a representative tumor to be assessed ($n = 12$) or their medical records were incomplete ($n = 8$). Thus, 85 eligible samples were included in this study (Fig. 1).

The clinicopathologic characteristics of the included patients are shown in Table 1. A total of 85 patients were eligible, of whom 41 (48.2 %) were aged <55 years and 44 (51.8 %) were aged >55 years. In terms of BMI, the patients were grouped as follows: underweight ($n = 6$, 7.1 %), normal ($n = 36$, 42.4 %), overweight ($n = 14$, 16.5 %), obesity class I ($n = 23$, 27.1 %), and obesity class II ($n = 6$, 7.1 %). In terms of menopausal status, they were classified as follows: premenopausal ($n = 39$, 45.9 %) and menopausal ($n = 46$, 54.1 %). In terms of disease stage, they were grouped as follows: early ($n = 45$, 52.9 %) and advanced ($n = 40$, 47.1 %). In terms of cell differentiation, they were classified as follows: low grade ($n = 54$, 63.5 %) and high grade ($n = 31$, 36.5 %). In terms of nodal metastasis, they were grouped into those without nodal metastasis ($n = 76$, 89.4 %) and those with nodal mestastasis ($n = 9$, 10.6 %). With regard LVSI, the patients were divided into those without LVSI ($n = 59$, 69.4 %) and those with LVSI ($n = 26$, 30.6 %). In terms of myometrial invasion, the patients were classified into those with < ½ myometrial invasion ($n = 22$, 25.9 %) and those with ≥½ myometrial invasion ($n = 63$, 74.1 %). In terms of adjuvant therapy, the patients either did not receive ($n = 19$, 22.4 %) or received ($n = 66$, 77.6 %) adjuvant therapy. (Table 1)

Association of ER and PD-L1 expression with the clinicopathological characteristics of type 1 EC

The ER expression in type 1 EC was higher in the patients aged <55 years than in those aged ≥55 years, but the difference was not statistically significant ($p = 0.050$). By contrast, the PD-L1 expression was higher in the patients aged ≥55 years than in those aged <55 years, but the difference was not statistically significant ($p = 0.067$; Table 2).

The ER positivity rates in the patients with BMI overweight, obesity class I, and obesity class II were 78.6 %, 95.7 %, and 100 %, respectively ($p = 0.0001$). By contrast, the PD-L1 positivity rates in the patients with BMI underweight and normal weight were 100 % and 97.2 %, respectively ($p = 0.0001$). The ER expression was higher in the premenopausal than in the menopausal patients with type 1 EC ($p = 0.034$), whereas the PD-L1 expression was significantly higher in the menopausal than in the premenopausal patients ($p = 0.042$; Table 2).

Based on disease stage, the ER expression was significantly higher in the early-stage group than in the advanced-stage group ($p = 0.0001$), whereas the PD-L1 expression was significantly higher in the advanced-stage than in the early-stage group ($p = 0.0001$). Based on myometrial invasion, the ER expression was significantly more prominent in the patients with <1/2 myometrial invasion than in those with ≥1/2 myometrial invasion ($p = 0.028$). Meanwhile, the PD-L1 expression was

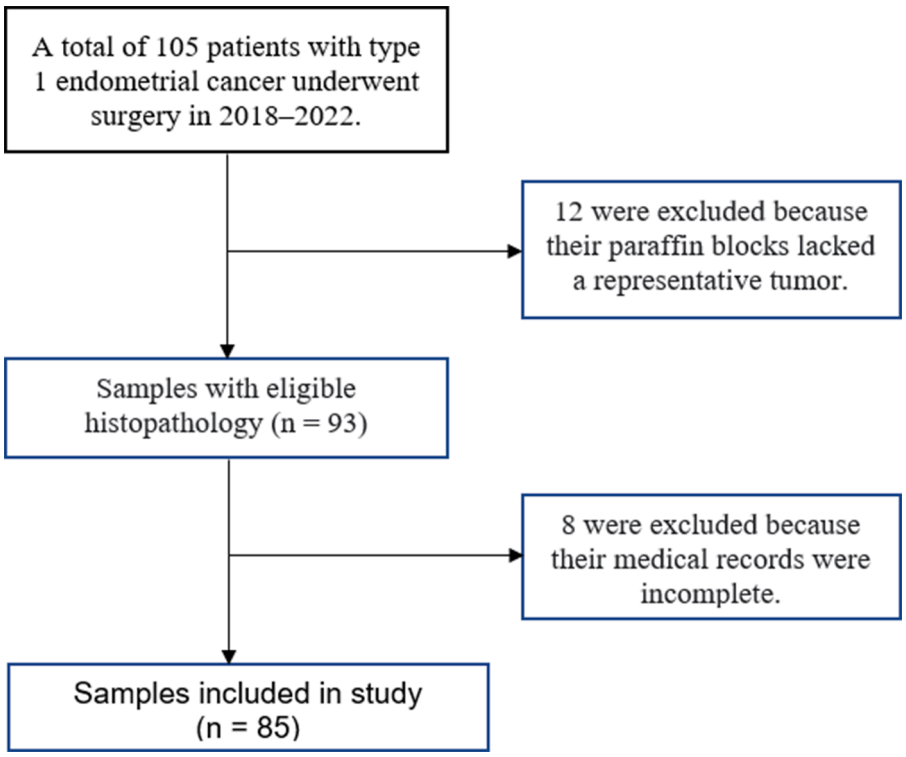

Fig. 1. Flowchart of sample selection.

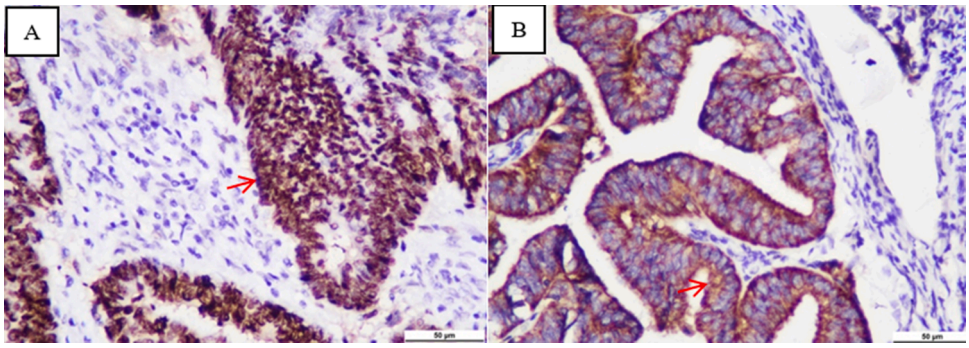

Fig. 2. Expression of ER in the cell nucleus (A). Expression of PD-L1 in the cell membrane (B) (magnification: 400×, scale bar: 50 mm).

significantly more prominent in the patients with ≥1/2 myometrial invasion than in those with <1/2 myometrial invasion. Based on the nodal metastatic group, the ER expression was higher in the non-nodal metastatic group than in the nodal metastatic group ($p = 0.0001$), whereas the PD-L1 expression was higher in the nodal metastatic group than in the non-nodal metastatic group, but the difference was not statistically significant ($p = 0.104$; Table 2).

The ER expression was higher in the patients with low-grade type 1 EC than in those with high-grade type 1 EC, but the difference was not statistically significant ($p = 0.201$). By contrast, the PD-L1 expression was significantly higher in the patients with high-grade type 1 EC than in those with low-grade type 1 EC ($p = 0.042$). Based on the LVSI group, the ER expression was higher in the group without LVSI than that with LVSI, but the difference was not statistically significant ($p = 0.129$), whereas the PD-L1 expression was higher in the group with LVSI than in that without LVSI ($p = 0.001$; Table 2).

The ER expression was significantly higher in the patients who did not receive or require adjuvant therapy than in those who received adjuvant therapy ($p = 0.019$), whereas the PD-L1 expression was significantly higher in the patients who received adjuvant therapy than in those who did not receive or require adjuvant therapy ($p = 0.0001$; Table 2).

4. Discussion

In the present study, the ER positivity rate in the patients with type 1 EC was 68.2 %, which is close to that (59.8 %) obtained by Wang et al. [19] in patients with EC in China. Meanwhile, the PD-L1 positivity rate in the patients with type 1 EC in the present study was 78.8 %, which is in accordance with that (70.15 %) obtained by Zhang et al. [20] in EC and that (63 %) obtained by Engerud et al. (2020) in primary tumors [10]. Gene expression analysis has shown that PD-L1 expression is upregulated in PD-1-positive tumor cells [21]. By contrast, Pasanen et al. [22] conducted a study in Finland and reported a PD-L1 positivity of only 8.58 %. This difference is likely due to the racial differences of the patients. However, whether a relationship exists between PD-L1 expression and race requires further research.

Association of ER and PD-L1 expression with the clinicopathological of type 1 EC

In the present study, the ER expression in type 1 EC was higher in the

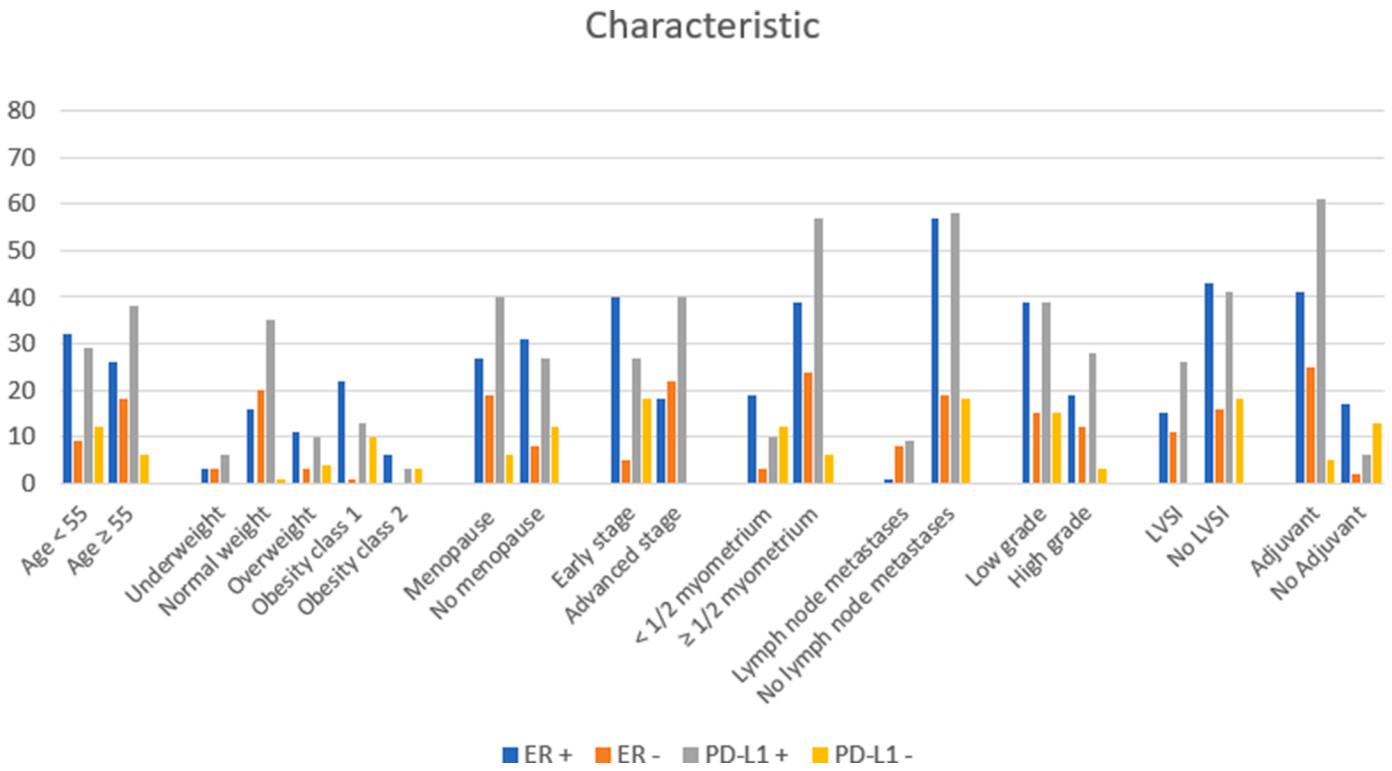

Fig. 3. Diagrams of association between ER and PD-L1 expression with clinicopathological characteristics of type 1 endometrial cancer.

patients aged <55 years than in those aged ≥55 years, but the difference was not statistically significant. Research by Shah et al. [23] in Pakistan suggested a significant relationship between age and ER expression. By contrast, other studies on the effect of young age on hormone receptors reported no significant association between age and ER or PR expression status. These differences may be due to the smaller sample sizes, racial variations, and different age groups in these studies [23].

In the present study, the PD-L1 expression was higher in the ≥55-year-old patient group than in the <55-year-old patient group with type 1 EC, but the difference was not significant. This result is in accordance with the findings of Zhang et al. [20] that PD-L1 expression is higher in women >60 years old than in those <60 years old. A study in Egypt found that patients positive for PD-L1 expression in tumor and immune cells are significantly older than those negative for PD-L1 expression [13].

The results of the present study showed that the ER expression was higher in the patients with a high BMI. This result is in accordance with the report of Chauhan et al. [24] that ER expression is higher in patients with BMI > 25. By contrast, PD-L1 expression was significantly higher in the patients with a normal or low BMI. Similarly, the study by Moreira et al. [25] in Brazil suggested that PD-L1 expression is higher in non-obese women than in obese women, but the difference is not significant.

In the present study, the patients in the premenopausal and non-menopausal groups significantly differed in ER expression. This result agrees with the findings of Milkov et al. [26] that menopause reduces ER expression because of low estrogen levels. Low estrogen levels in menopausal women decrease ER expression to capture estrogen. In the present study, PD-L1 expression was significantly higher in the menopausal group than in the premenopausal group. This result agrees with the report by Kim et al. [27].

In the present study, the ER expression was higher in the early-stage group than in the advanced-stage group. This result agrees with the findings of Wang et al. [19] in Shaanxi, China that ER expression is associated with low-disease-stage (stage I) EC. Meanwhile, the PD-L1 expression was higher in the advanced-stage group than in the early-stage group in the present study. This result agrees with the research findings of Kim et al. [27].

With regard myometrial invasion, the ER expression was higher in the group with <1/2 myometrial invasion than in that with ≥1/2 myometrial invasion. Wang et al. [19] found no significant difference between ER expression and myometrial invasion in patients with EC but reported ER negativity in patients with deep myometrial invasion and cervical invasion. Moreover, the present study showed that the relationship between PD-L1 expression and ≥1/2 myometrial invasion was significant, which is in accordance with the results of Kim et al. [27] that PD-L1 expression in EC is significantly associated with deep myometrial invasion.

In terms of nodal metastasis, the ER expression was higher in the group without nodal metastasis than in that with nodal metastasis. This result agrees with the report of Manan et al. [28] that loss of ER expression is significantly associated with lymph node metastasis in African and American women. Loss of ER independently predicts lymph node metastasis in women with EC. In the present study, PD-L1 expression was higher in the group with nodal metastasis than in that without nodal metastasis, but the difference was not significant. This result can be ascribed to the unbalanced distribution of samples. The results are in accordance with the findings of Li et al. [29] that PD-L1 levels are significantly higher in lymph node tumor cells. PD-L1 expression is also higher in tumor-positive lymph nodes than in tumor-negative lymph nodes. Disease-free survival and overall survival (OS) are worse in patients with lymph node metastasis.

In the present study, the ER expression was higher in the group with low-grade EC than in that with high-grade EC. Similarly, Jeffery et al. [30] conducted a study in Utah, USA and found that ER expression is associated with low cell differentiation. Moreover, the higher PD-L1 expression in the group with high-grade EC than in that with low-grade EC in the present study is consistent with the result of Kim et al. [27] that PD-L1 expression is associated with high cell differentiation.

In terms of LVSI, the ER expression was higher in the group without LVSI, but the difference was not significant, whereas the PD-L1

Table 1
Clinicopathological characteristics and ER and PD-L1 expression of patients with type 1 endometrial cancer.

Characteristics	Frequency	Percentage
Age	Mean: 53.42	
<55 years	41	48.2 %
≥55 years	44	51.8 %
BMI		
Underweight	6	7.1 %
Normal weight	36	42.4 %
Overweight	14	16.5 %
Obesity class 1	23	27.1 %
Obesity class 2	6	7.1 %
Obesity class 3	0	0 %
Menopausal status		
Yes	46	54.1 %
No	39	45.9 %
Cancer stage		
Early stage (I, II)	45	52.9 %
Advanced stage (III, IV)	40	47.1 %
Myometrial invasion:		
<1/2 myometrium	22	25.9 %
≥1/2 myometrium	63	74.1 %
Nodal metastasis:		
Yes	9	10.6 %
No	76	89.4 %
Cell differentiation (tumor grade):		
Low grades (I and II)	54	63.5 %
High grades (III and IV)	31	36.5 %
LVSI:		
Yes	26	30.6 %
No	59	69.4 %
Adjuvant therapy:		
Yes	66	77.6 %
No	19	22.4 %
Expression of ER:		
Positive	58	68.2 %
Negative	27	31.8 %
Expression of PD-L1:		
Positive	67	78.8 %
Negative	18	21.2 %

expression was higher in the group with LVSI than in that without LVSI. These results are in accordance with those of several studies, such as those conducted by Zhang et al. [20] in Tsukuba, which stated that PD-L1 is associated with LVSI positivity in EC and poor OS. Other studies have suggested that PD-L1 positivity is associated with LVSI, histological type, and myometrial invasion and is an effective immunotherapy [11, 12]. A research in Egypt demonstrated that tumor and immune cells expressing PD-L1 are mostly positive for LVSI, whereas those not expressing PD-L1 are mostly negative for LVSI [13].

In the present study, the ER expression was significantly higher in the patients who did not require adjuvant therapy than in those who did. This result can be ascribed to the association of ER expression with low risk factors for EC, such as age <55 years, early stage, low-grade cell, endometrioid cell, absence of lymph node involvement, and absence of LVSI. Meanwhile, the PD-L1 expression was significantly higher in the patients who required adjuvant therapy than in those who did not. This result is in accordance with the findings of Kim et al. [27] that PD-L1 expression is significantly related to the need for adjuvant therapy in EC.

The present study is the first to examine the correlation of ER and PD-L1 expression with the clinicopathological characteristics of type 1 EC. With the rapid development of EC therapy, anti-PD-1 immunotherapy has been introduced, and ligand expression (PD-L1) in immune and tumor cells has been proven to increase the effectiveness of this therapeutic strategy. The results of the present study can be used as a basis for further research on the roles of ER and PD-L1 in the prognosis and immunotherapy of EC. Considering that the future of cancer treatment is expected to rely on the combination of therapeutic strategies, several ongoing studies are evaluating the efficacy of ICIs used in combination with other immunotherapeutic agents, hormonal therapy, chemotherapy, radiotherapy, and targeted therapies.

Clinical evidence has suggested a strong correlation between ER and PD-L1 regulation in different types of cancer. Therefore, the combined use of ER inhibitors and anti-PD-L1 agents could exert synergistic effects. Further research is warranted to find novel combination therapy strategies and specific biomarkers for accurate immunotherapy response prediction. Hormonal and immune checkpoints have high potential as novel biomarkers or therapeutic agents in EC.

5. Conclusion

ER expression was significantly associated with BMI ≥ 25, premenopausal status, early-stage disease, <1/2 myometrial invasion, no nodal metastasis, and lack of adjuvant therapy. It was also associated with age <55 years, low-grade cells, and angiolymphatic invasion, but the relationship was not statistically significant. PD-L1 expression was significantly associated with BMI < 25, menopausal status, advanced disease stage, high-grade cell, angiolymphatic invasion, and adjuvant therapy. It was also associated with age ≥ 55 years and lymph node metastasis, but the relationship was not statistically significant.

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Consent

Studies on patients or volunteers require ethics committee approval and fully informed written consent which should be documented in the paper.

Authors must obtain written and signed consent to publish the case report from the patient (or, where applicable, the patient's guardian or next of kin) prior to submission. We ask Authors to confirm as part of the submission process that such consent has been obtained, and the manuscript must include a statement to this effect in a consent section at the end of the manuscript, as follows: "Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request".

Patients have a right to privacy. Patients' and volunteers' names, initials, or hospital numbers should not be used. Images of patients or volunteers should not be used unless the information is essential for scientific purposes and explicit permission has been given as part of the consent. If such consent is made subject to any conditions, the Editor in Chief must be made aware of all such conditions.

Even where consent has been given, identifying details should be omitted if they are not essential. If identifying characteristics are altered to protect anonymity, such as in genetic pedigrees, authors should provide assurance that alterations do not distort scientific meaning and editors should so note.

This was a retrospective study that used medical record for the data

Table 2
Association of ER and PD-L1 expression with clinicopathological characteristics of type 1 endometrial cancer.

Characteristic	Expression ER		p-value	Expression PD-L1		p-value
	ER negative	ER positive		PD-L1 negative	PD-L1 positive	
Age			0.050			0.067
<55 years	9 (22.0 %)	32 (78.0 %)		12 (29.3 %)	29 (70.7 %)	
≥55 years	18 (40.9 %)	26 (59.1 %)		6 (13.6 %)	38 (86.4 %)	
BMI	3 (50.0 %)	3 (50.0 %)	0.0001			0.0001
Underweight	20 (55.6 %)	16 (44.4 %)		0 (0.0 %)	6 (100 %)	
Normal weight	3 (21.4 %)	11 (78.6 %)		1 (2.8 %)	35 (97.2 %)	
Overweight	1 (4.3 %)	22 (95.7 %)		4 (28.6 %)	10 (71.4 %)	
Obesity class 1	0 (0 %)	6 (100 %)		10 (43.5 %)	13 (56.5 %)	
Obesity class 2				3 (50.0 %)	3 (50.0 %)	
Status menopause			0.034			0.042
Yes	19 (41.3 %)	27 (58.7 %)		6 (13.0 %)	40 (87.0 %)	
No	8 (20.5 %)	31 (79.5 %)		12 (30.8 %)	27 (69.2 %)	
Cancer stage			0.0001			0.0001
Early stage (I and II)	5 (11.1 %)	40 (88.9 %)		18 (40.0 %)	27 (60.0 %)	
Advanced stage (III and IV)	22 (55.0 %)	18 (45 %)		0 (0.0 %)	40 (100 %)	
Myometrial invasion:			0.028			0.0001
<1/2	3 (13.6 %)	19 (86.4 %)		12 (54.5 %)	10 (45.5 %)	
≥1/2	24 (38.1 %)	39 (61.9 %)		6 (9.5 %)	57 (90.5 %)	
Lymph node metastases:			0.0001			0.104
Yes	8 (88.9 %)	1 (11.1 %)		0(0.0 %)	9 (100 %)	
No	19 (25.0 %)	57 (75.0 %)		18 (23.7 %)	58 (76.3 %)	
Cell differentiation (tumor grade):			0.211			0.042
Low grades (I and II)	15 (27.8 %)	39 (72.2 %)		15 (27.8 %)	39 (72.2 %)	
High grades (III and IV)	12 (38.7 %)	19 (61.3 %)		3 (9.7 %)	28 (90.3 %)	
LVSI:			0.129			0.001
Yes	11 (42.3 %)	15 (57.7 %)		0(0.0 %)	26 (100 %)	
No	16 (27.1 %)	43 (72.9 %)		18 (30.5 %)	41 (69.5 %)	
Adjuvant treatment:			0.019			0.0001
Yes	25 (37.9 %)	41 (62.1 %)		5 (7.6 %)	61 (92.4 %)	
No	2 (10.5 %)	17 (89.5 %)		13 (68.4 %)	6 (31.6 %)	

Description: Statistical analysis with Fisher's exact test, with $p < 0.05$ indicating significance.

source.

The ethic of this study approved by the Research Ethics Committee of Dr.Soetomo General Academic Hospital Suabaya, Indonesia.

CRediT authorship contribution statement

Setyo Teguh Waluyo: Conceptualization, Methodology, Writing – original draft. **Brahmana Askandar Tjokroprawiro:** Conceptualization, Writing – review & editing. **Anny Setijo Rahaju:** Methodology, Formal analysis.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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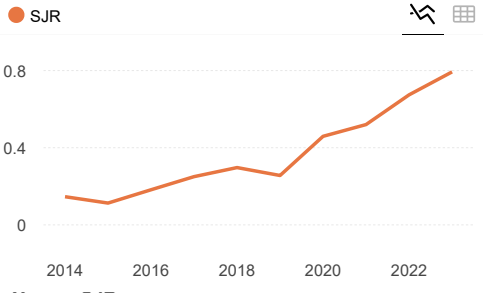

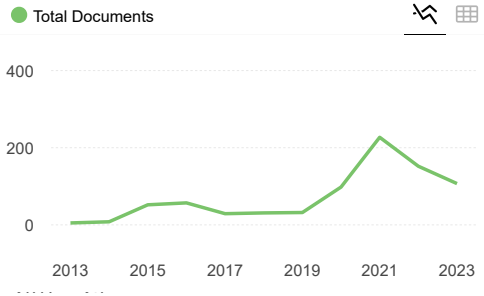

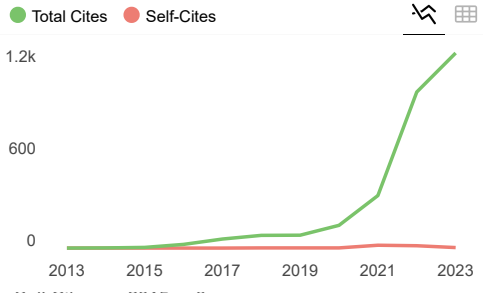

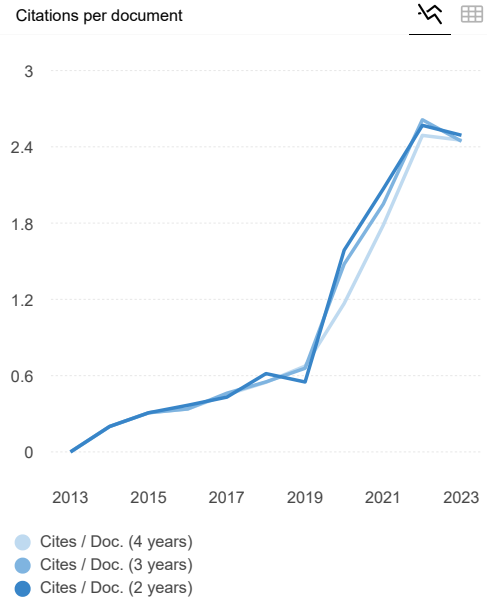

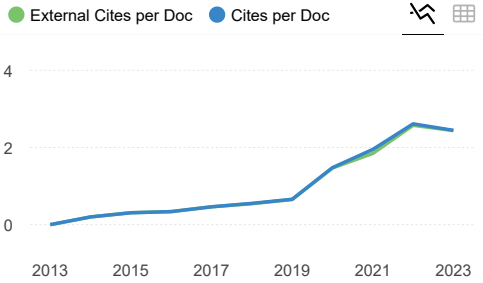

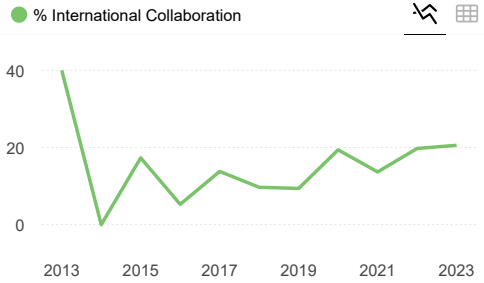

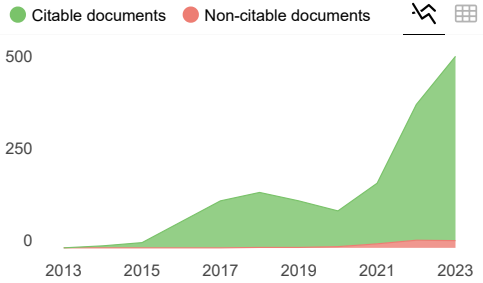

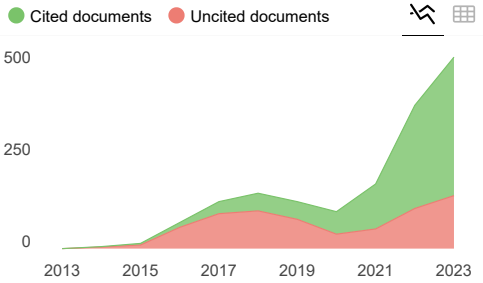

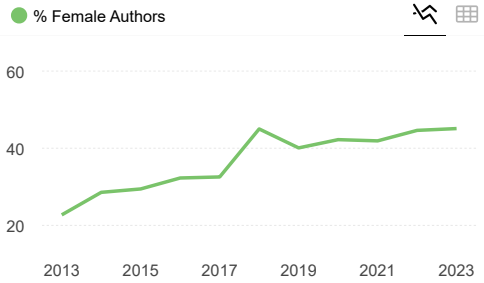

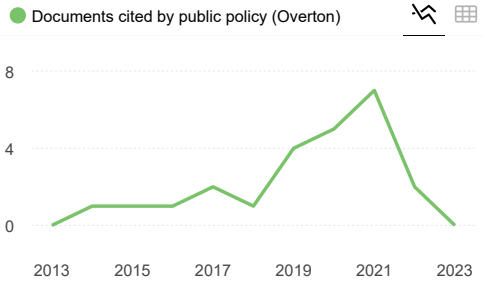

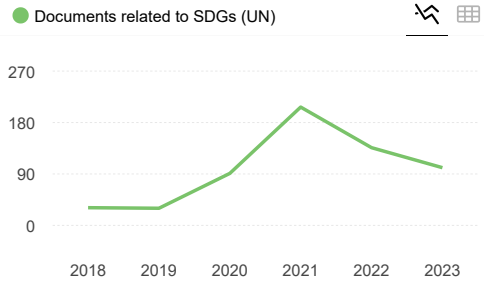

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PENELITI UTAMA : Dr. Brahmana Askanda Tjokroprawiro, dr., Sp.OG (K)

PENELITI LAIN : 1. Dr. Anny Setijo Rahaju, dr., Sp.PA (K)
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UNIT / LEMBAGA / TEMPAT PENELITIAN : RSUD Dr. Soetomo

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Berlaku dari : 27/02/2023 s.d 27/02/2024
Surabaya, 27 February 2023
KETUA

(Prof. Dr. Hendy Hendarto, dr., SpOG (K))
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