

MEETING HIGHLIGHTS: THE THIRD MARIE SKŁODOWSKA-CURIE SYMPOSIUM ON CANCER RESEARCH AND CARE AT ROSWELL PARK COMPREHENSIVE CANCER CENTER, BUFFALO, NY, SEPTEMBER 20-22, 2023

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ABSTRACT

Marie Skłodowska-Curie Symposia on Cancer Research and Care (MSCS-CRC) promote collaborations between cancer researchers and care providers in the United States, Canada and Central and Eastern European Countries (CEEC), to accelerate the development of new cancer therapies, advance early detection and prevention, increase cancer awareness, and improve cancer care and the quality of life of patients and their families. The third edition of MSCS-CRC, held at Roswell Park Comprehensive Cancer Center, Buffalo, NY, in September 2023, brought together 137 participants from 20 academic institutions in the US, Poland, Ukraine, Lithuania, Croatia and Hungary, together with 16 biotech and pharma entities. The key areas of collaborative opportunity identified during the meeting are a) creating of a database of available collaborative projects in the areas of early-phase clinical trials, preclinical development, and identification of early biomarkers; b) promoting awareness of cancer risks and efforts at cancer prevention; c) laboratory and clinical training; and d) sharing experience in cost-effective delivery of cancer care and improving the quality of life of cancer patients and their families. Examples of ongoing international collaborations in the above areas were discussed. Participation of the representatives of the Warsaw-based Medical Research Agency, National Cancer Institute (NCI) of the United States, National Cancer Research Institutes of Poland and Lithuania, New York State Empire State Development, Ministry of Health of Ukraine and Translational Research Cancer Center Consortium of 13 cancer centers from the US and Canada, facilitated the discussion of available governmental and non-governmental funding initiatives in the above areas.

KEY WORDS: cancer prevention, cancer care, clinical trials, education, training, research

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HISTORY, NEEDS AND GOALS

Marie Skłodowska-Curie (1867-1934) was a Polish expatriate and a pioneering scientist with groundbreaking contributions to the understanding and treatment of cancer. She was born in Warsaw, Poland, Nov 7, 1867. Studies and started her teaching and early laboratory work in Warsaw (1889-1891), before moving to Paris in 1891. Dr. Skłodowska-Curie was the first woman to earn Nobel Prize and the only person to win Nobel Prizes in 2 different disciplines (Physics, 1903; for work on radiation) and Chemistry (1911; discovery of Radium and Polonium). She trained 4 other Nobel Prize winners, including her daughter, Irène Joliot-Curie, and Frédéric Joliot-Curie, and founded Radium Institute of Paris (1914) and Warsaw Radium Institute (1932), which became the current Maria Skłodowska-Curie National Research Institute of Oncology (MSCI) in Warsaw, Poland.

When staying in Buffalo to meet her childhood friend, Dr. Francis Fronczak, a health commissioner of the Erie county in June 1921, Dr. Skłodowska-Curie visited New York State Pathological Laboratory of the University of Buffalo (now Roswell Park Comprehensive Cancer Center) first Cancer Center in the US, established in 1898 by a cancer surgeon, Dr. Roswell Park, known for his effectiveness in promoting private and governmental action in the area of health research (Wyrobek, 2022). Dr. Skłodowska-Curie's visit provided an important stimulus for early work on radiation biology and cancer treatment at Roswell, but also helped her to mobilize funds to support her work in Paris, and the Warsaw Radium institute. 1g of radium presented to Dr. Skłodowska-Curie by President Harding allowed her to advance her work on radioactivity applications in cancer and

other diseases. Her work fundamentally changed how we detect, treat and monitor the progress and effect of cancer treatments.

That success in leveraging the complementary expertise and resources available in the US and in Europe provided us with inspiration for the Marie Skłodowska-Curie Symposia on Cancer Research and Care (MSCS-CRC) initiative, started in May 2019, in conjunction the Buffalo-held 60 Million Congress/Global Polonia Summit, which brought together cancer researchers, educators and cancer care providers from the United States and Poland. After two years of Covid-related gap, the second edition of the MSCS-CRC, was held as a hybrid meeting in September 2022. The well attended meeting (112 participants) provided a platform for presentations by respected leaders of healthcare systems from Poland, Ukraine, Hungary, Czech Republic, Croatia, Canada and the United States. Basic and clinical oncology research, medical education and training, prevention, genetics, biomarkers, as well as oncology patient care were main topics discussed at the Meeting. The conference was very successful and showed opportunities for further international collaborations, to build stronger integrated research and healthcare systems in Eastern and Central Europe partnering with American institutions. The third edition was held as fully in-person meeting at the newly renovated Gaylord Cary Conference center of the Roswell Park Comprehensive Cancer Center on September 2023, brought together 137 participants from 20 academic institutions in US, Poland, Ukraine, Lithuania, Croatia and Hungary, and representatives of the Polish-American, Ukrainian-American, Romanian-American, Hungarian-American, Czech-American

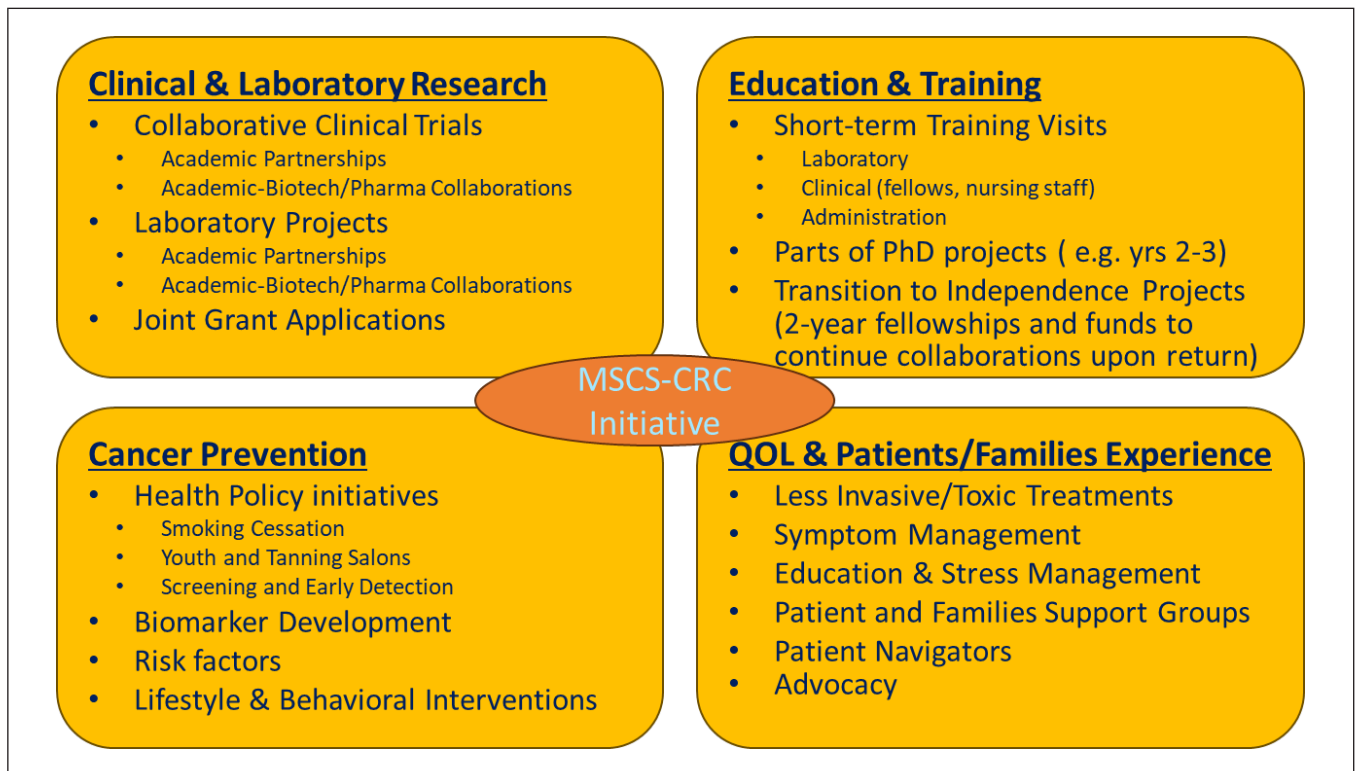


Fig. 1. Key areas of programmatic emphasis discussed during MSC-2023.

and Serbian-American research communities, as well as representatives from 16 biotech and pharma entities from the US and Poland (<https://www.roswellpark.org/msc-symposium>).

The overarching goal of the MSCS-CRC initiative is to promote collaborations between cancer researchers and care providers, biotech, pharma and policymakers from the US, Canada and Central and Eastern European Countries (CEEC). The 2023 Symposium focused on the needs and arising opportunities for research collaborations in the areas of joint laboratory and clinical research projects in cancer prevention, early detection and treatment, new health policy initiatives, education and training, as well as improvement of the quality of life of cancer patients and their families (Figure 1).

The development of the database connecting the parties interested in preclinical and clinical collaborations will be coordinated by the National Institute of Oncology, Warsaw Poland, and Roswell Park Comprehensive Cancer Center, Buffalo, NY.

Social events provided additional opportunities for networking and small group discussions (Figure 2).

Promoting collaborative clinical and laboratory research: Lower saturation with clinical trials performed in CEE Countries, combined with a strong clinical trials base and oversight (European Medicines Agency, a partner for the FDA and <https://www.biomapas.com/running-clinical-trials-in-eastern-europe/>), documented by multiple FDA audits, and approximately 50% lower costs of clinical trials, compared to the of the US, represents a unique opportunity to the US-CEE teams to accelerate early phase testing of new therapies developed in academic or commercial settings. Lower costs of the laboratory research in CEEC and high experience with many unique areas, such as novel drug delivery methods and mathematical approaches to biologic questions and image analysis, combined with the shortage of qualified research personnel in many parts of the US further creates a unique opportunity for the development of preclinical and translational projects involving partners from both continents, with opportunities for high impact publications, rapid clinical testing and commercialization. Dissemination of results from early phase trials of low-cost therapies with potential to enhance the effects of immunotherapy or radiotherapy (stress management, beta blockers, NSAIDs) and improve overall cancer outcomes conducted at Roswell and other institution, and their expansion into multi-center pivotal studies, was an example discussed in several presentations.

Education and training initiatives: Several of the speakers discussed their experience from training international clinicians and laboratory scientists in their labs. The challenges discussed included current difficulties in converting such short-term visits into career-building

programs and long-term collaborations, as a result of lack of suitable funding mechanisms.

Health policy initiatives, cancer awareness, prevention, early detection, and biomarkers represents another area of immediate opportunity to reduce cancer incidence, improve early diagnosis and initiation of treatment, with the overall goal to enhance survivorship and quality of life. Two of such areas discussed at MSC-2023 were smoking and vaping cessation and early-life UV exposure, relevant to, respectively, lung- and skin cancers.

Empowering patients and caregivers: Patient-centered care, survivorship, quality of life and advocacy. Empower patients and caregivers with knowledge, resources, and support systems to navigate the challenges of cancer, and actively involve them in discussions regarding research priorities and patient-centered care. Discuss new challenges of care treatment at the time of war and other disasters.

SCIENTIFIC SESSIONS OF MSC-2023: HIGHLIGHTS

The 2023 MSC Symposium was divided into an Opening Session and eight subject matter sessions, each involving individual presentations and panel discussions:

The Opening Session: The meeting was opened by **Pawel Kalinski, MD, PhD**, Senior Vice President for Team Science at Roswell, representing **Renier Brentjens, MD, PhD**, the Deputy Director of Roswell Park, and **Ms. Camille Brandon***, representing the General Pulaski Association of Western NYS. Welcome remarks were delivered by Elected Officials including **Karen Utz, JD**; WNY Regional Director, Empire State Development representing NYS **Governor Kathy Hochul** and **Jesse Prieto** representing **Congressman Nick Langworthy**. Other elected officials included NYS **Senator Timothy Kennedy**; Erie County Legislator **Hon. April Baskin**; Deputy Mayor of Buffalo, **Hon. Callie Johnson** and City of Buffalo Councilman **Hon. Bryan Bollman**. Roswell Park Board of Directors was represented by **Elyse NeMoyer**, herself a two-time cancer survivor, and **R. Buford Sears**, Senior Vice President for the Buffalo-based M&T Bank. The Session was concluded by Dr. Kalinski provided a historical perspective linking Dr. Skłodowska-Curie, Roswell Park and American Polonia, as well as the cultural and history of economic and political links between United States, Canada and Countries of Central and Eastern Europe, and an overview of the goals of the Symposium and its agenda.

Session 1: Ongoing Collaborations within the MSC-CRC Initiative was chaired by **Iwona Ługowska, MD, PhD** (NIO, Warsaw, Poland) and **Michael Nishimura,**

PhD (Loyola University, Chicago, Maywood, Illinois, USA). The goal of the session was to use the examples of the effective collaborations developed in the course of the past interaction between the members of the MCS-CRC Initiative to highlight the existing needs and immediate collaborative opportunities, encountered problems and ways of their elimination.

Michael Nishimura, PhD (Loyola University, Chicago, Maywood, Illinois, USA) provided an overview of his recent experience training medical scientists from Poland, Ukraine and Lithuania and transferring inexpensive CAR and TCR T Cell Technology to collaborating groups in Europe. He discussed the encountered roadblocks and experience overcoming them, as well as plan for extension of his collaborations to Ukraine.

Iwona Ługowska, MD, PhD (Maria Skłodowska-Curie National Research Institute of Oncology and the National Institute of Oncology, Warsaw, Poland) discussed her experience in establishing effective international collaborations in clinical research, especially early-phase trials with pharma partners. She highlighted the role of MSCI (originally founded in 1932 as the Radium Institute by Maria Skłodowska-Curie) as a comprehensive cancer center, encompassing both research and clinical aspects of oncology, as well as implementing high-quality patient care standards throughout Poland. In addition to the Warsaw HUB, MSCI has branches in Gliwice and Krakow, allowing it to provide care to patients for the 25% of cancer patients in Poland. This includes over 130,000 in-patients, 680,000 outpatient consultations and diagnosing 50,000 new patients annually. Currently, MSCI manages over 650 clinical trials (including 80 early-phase trials). Its Early Phase Clinical Trial Department, Center for Excellence in Precision Oncology, and the newly developed CAR-T Facility provide top-notch expertise and partnering opportunities for domestic and foreign collaborators. The Cancer Prevention Centre involved in many international projects, e.g. the Nordic-European Initiative on Colorectal Cancer, European Polyp Surveillance Trial and Era-NET Transcan). MSCI is a leader of the National Cancer Strategy, the National Oncology Network, and the National Coordinating Center for population screening and primary cancer prevention and runs the National Cancer Registry. Additional partnerships involved ESMO, ASCO, NCI, EORTC, NCCN, ASH, EURACAN, EuroBloodNet, EndoERN, Institute Curie, University of Leeds, MD Anderson's Sister Institution Network, EHA, WSN, EuMelaReg, EBMT, and different patient advocacy groups. Recently, MSCI signed Memorandums of Understanding (MOUs) with the National Comprehensive Cancer Network (NCCN) and the U.S. National Cancer Institute, leading to the implementation of NCCN guidelines in Poland and the

establishment of educational programs such as the School of Cancer Epidemiology.

Participation in research and infrastructure projects funded by the European Commission adds another dimension to MSCl's capabilities, propelling the development of innovative therapies and positioning Poland as a hub for cutting-edge technologies. With ongoing collaborative research projects, including JA JANE, JA, CRANE, CCI4EU, 4UNCAN, PCM4EU, PRIME-ROSE, CAN. Heal, MELCAYA, STRONG-AYA, ECHOS, and EUonQLQ, MSCl remains at the forefront of oncology research.

As a result of the 2nd MSC Symposium held in Buffalo in September 2022, MSCl has established collaborations with groups in Warsaw and Poznan, in Poland to transfer their gene therapy technology and establish a country-wide clinical gene therapy program with the goal of helping cancer patients in Poland. So far, three scientists from other centers have visited and trained at MSCl.

Leszek Kotula, PhD (Upstate Medical University, Syracuse, New York, USA) discussed the new collaboration with the NIO initiated at the MSC-2022 Symposium, which resulted in the establishment of a collaboration between Upstate Medical and NIO. Is focused on prostate cancer biomarker, ABI1 in advanced and therapy-resistant prostate cancer cases. ABI1 was identified as a biomarker by the group of Dr. Kotula at Upstate Medical University, while suitable patient cohorts for this study will be led by the NIO. The collaborating groups have already laid the groundwork for securing joint funding to support this initiative.

Pawel Kalinski, MD, PhD (Roswell Park) discussed his collaborative experience involving multiple academic centers, pharma and biotech partners in manipulating the induction and effector phase of immunity in tumor microenvironments (TME) and developing chemokine-modulating (CKM) regimen involving TLR3 ligand, rintatolimod and IFN α 2b (Muthuswamy et al., 2012; Muthuswamy et al., 2016; Muthuswamy et al., 2017; Muthuswamy et al., 2015; Obermajer et al., 2018; Theodoraki et al., 2018), which led to two recently-published positive clinical trials in ovarian cancer (local application of CKM) (Orr et al., 2022; Suarez Mora et al., 2022) and breast cancer (Gandhi et al., 2023), which demonstrated the ability of CKM to exert local effectiveness in advanced multi-focal disease even after its systemic application, due to its synergy with activated NF κ B, which cancers selectively activate local TME to promote their growth, vascularization and local immune suppression, but which can be utilized by the CKM to assure its local intratumoral selectivity even after its systemic application, converting immuno-resistant "cold tumors" into immuno-sensitive "hot"

tumors, without the need for local or targeted delivery. Dr. Kalinski discussed ongoing and upcoming trials of CKM in combination with chemotherapy, dendritic cell (DC) vaccines and PD1 blockade in melanoma, prostate, breast, ovarian and colorectal cancers, as well as in infectious diseases, and the opportunities for collaborations with partners in Poland and other CEE Countries, to address these questions in larger cohorts of patients. The final part of his talk discussed the logistic, fiscal and regulatory experience of the office of Scientific Programs Management, which he established at Roswell with importing foreign-produced drugs and obtaining FDA and local regulatory approval for their use as Investigational New Drugs in the clinical trials in the US.

Elizabeth Repasky, PhD (Roswell Park, Buffalo, NY, USA) discussed the role of psychologic stress and beta-adrenergic signaling pathway in promoting tumor growth, suppressing antitumor immunity and undermining the effectiveness of immunotherapy and radiation therapy in mice and cancer patients (Bucsek et al., 2017; Chen et al., 2020a; Eng et al., 2015; Gandhi et al., 2020; Gandhi et al., 2021; Kokolus et al., 2013; Kokolus et al., 2018; Mohammadpour et al., 2021). The recently published results of a phase I study in melanoma patients (Gandhi et al., 2021) indicate that beta blockers, such as propranolol can be used as safe low-cost enhancers of checkpoint blockade and potentially other forms of cancer. Ter retrospective analyses performed with **Anurag Singh, MD, PhD** at Roswell, provide rationale for similar intervention to enhance the effectiveness of cancer radiotherapy (Chen et al., 2020b; Farrugia et al., 2021a; Ma et al., 2021). Opportunities for partnering with CEEC collaborators were discussed, to advance the use of propranolol in wide groups of cancer patients.

Session 2: Opportunities for New Collaborations in Translational & Clinical Research was chaired by **Marcin Kortylewski, PhD** (City of Hope, Duarte, California, USA) and **Piotr Rutkowski, MD, PhD** (Medical Research Agency and Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland). The session on translational and clinical research in cancer presented a number of new opportunities for collaborations. The speakers focused on the potential of new approaches to cancer prevention, diagnostics and novel treatments based on cancer vaccination or CAR-based NK and T cell immunotherapies. The session provided an opportunity for networking and collaboration between scientists from different disciplines and institutions. As highlighted in the discussion by **Dr. Kortylewski**, effective cancer treatments need to combine strategies disrupting tolerogenic TME with expanding and armor-

ing immune effector cells against local suppression to ensure the long-term antitumor responses.

Gyorgy Paragh, MD, PhD (Roswell Park, Buffalo, NY, USA) discussed opportunities for prevention and treatment of squamous skin carcinoma by targeting early clonal mutations. He discussed their role in cancer progression and the feasibility of inducing immunity against these patient-specific mutational events as a pathway to skin cancer prevention. The theme of cancer vaccines was continued by **Wei-Zen Wei, PhD** (Karmanos Cancer Institute, Detroit, Michigan, USA) who presented her experience in targeting Her2 in the immunotherapy of breast cancer. Her presentation targeting new checkpoint molecules to enhance the clinical effectiveness of HER2 vaccination.

Sandro Matosevic, PhD (Purdue University, West Lafayette, Indiana, USA), discussed the role of cell-based immunotherapies utilizing natural killer (NK) cells in the treatment of cancer, and the existing challenges and opportunities for the broad deployment of these therapies to patients worldwide. NK cells, immune cells with innate ability to recognize and eliminate cancer cells, are powerful immune effectors, representing a widely applicable allogeneic immune cell. The dysfunction of endogenous NK cell function in the TME of solid tumors involves immune, epigenetic and metabolic mechanisms, both intrinsic and extrinsic to cancer and immunosuppressive immune cells, which dampens NK cell activation. These involve downregulation of NK activating receptors and upregulation of inhibitory receptors, as well as additional suppression involving other immune effector cells. The approaches to restore NK cell immuno-metabolic effector responses have involved pharmacological and genetic tools to regulate NK cell activation, their anti-tumor function, metabolism and enhancing their persistence in the TME by cytokine modulation. Dr. Matosevic discussed opportunities for using NK cells in immunotherapy, their novel genetic engineering approaches and therapeutic modulation strategies, with the ultimate goal to effectively and durably target the currently incurable cancers in patients in the US, Europe and beyond.

The last speaker in the session, **Renier Brentjens, MD, PhD** (Roswell Park, Buffalo, NY, USA), discussed Roswell Park's current expanding efforts to transfer his experience from the particularly successful CAR-T cell program in hematologic malignancies to solid cancers by the identification of the new antigenic targets relevant to highly heterogeneous solid tumors and the development of the next generation "armored" CAR T cells for solid tumor malignancies, able to overcome tumor heterogeneity and the highly immunosuppressive nature of the solid tumors TME.

Session 3: Opportunities for New Collaborations in Cancer Biomarkers & Prevention was chaired by

Leszek Kotula, PhD (Upstate Medical University, Syracuse, New York, USA) and **Sandro Matosevic, PhD** (City of Hope, Duarte, California, USA)

Petar Ozretić, PhD (Ruđer Bošković Institute and Croatian Association for Cancer Research (HDIR), Zagreb, Croatia) gave an overview of preclinical cancer studies carried out at the Institute, the largest basic research institution in Croatia. The work covers molecular mechanistic and functional in vitro analyses as well as molecular profiling of clinical samples, to better understand the signaling pathways involved in cancer development, such as the Hedgehog-Gli signaling pathway.

Daniel J. Powell, Jr, PhD (University of Pennsylvania, Philadelphia, Pennsylvania, USA; President of the Translational Research Cancer Centers Consortium, USA; <https://www.trccc.org/executive-board>) discussed the biomarkers of tumor-specific TILs which identify effector-like stem T cells with particularly high anti-tumor potential in adoptive T cell therapies. He emphasized the heterogeneity exists in intratumoral T cells in solid cancers and the role of CD137 as a reliable biomarker for identifying tumor-specific TILs. Biomarker based enrichment of TIL enhances their activity in adoptive T cell therapy of common epithelial cancers, permits TCR isolation, and deep interrogation of natural endogenous T cell immunity to cancer. Isolated CD137+ TILs contain T cells with stem-like properties which are still heterogeneous and include a non-canonical CD45RO+ Tcf-1+ stem-like TILs subset representing one of the earliest effector subsets in the TME. These unique cells maintain self-renewal capacity without a transcriptional commitment to exhaustion. Dr. Powell discussed the properties of this subset and other subsets of endogenous T cells relevant to controlling cancer progression in context of clinical trials of the TIL-based and transgenic-TCR-based adoptive T cell therapies (ACT).

Elżbieta Sarnowska, MD, PhD (Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland) discussed the character of T cell responses in kidney cancer and opportunities for their therapeutic manipulation. One of the hallmarks of cancer is immune system evasion. Proliferating tumor cells produce distinct suppressive cytokines and other molecules to inhibit the immune system attack. Prompted by the 2007 Polly Matzinger mouse study showing advantage of therapeutic use of CD4+ T cells, Dr. Sarnowska, demonstrated that, CD4+ TILs are predominant in clear cell renal cell carcinoma (ccRCC) TME compared to CD8+ TILs. CD4+ effector T cell become exhausted upon chronic activation and display PD-L1 and IDO1 as suppressive molecules, in addition to proinflammatory cytokine. Interestingly, the CD4/CD8 TILs ratio in primary tumors showed promise as a prognostic marker,

raising the need for larger prospective studies, which will benefit from collaborations.

Vita Pašukonienė, PhD (Vilnius Gediminas Technical University and National Cancer Institute, Vilnius, Lithuania) discussed her work development and use of a gene expression-based immune subtyping tool (IMSUBTOOL) for solid cancers, which utilizes a gene expression pattern maps as an algorithm for immune subtyping of high-grade serous ovarian carcinoma. The results allow to identify tumors with a better prognosis using only a few genes related to immune mechanisms and the TME, rather than the whole tumor genome. The group is interested in new collaborations to further develop immune subtyping tools to assess treatment efficacy in large prospective clinical trials and retrospective studies of immunotherapy.

Andrew Hyland, PhD (Roswell Park, Buffalo, NY, USA), presented his international collaborative efforts in reducing incidence of cigarette smoking, which is the leading cause of cancer death in the US, Poland, and many other countries. He discussed new initiatives to reduce cigarette smoking, including tobacco “quitlines”, as highly cost-effective health interventions. The Polish National Quitline and the New York State Smokers Quitline have been in operation for 20+ years and there are opportunities to apply successfully practices across borders to improve program success metrics. Five tangible areas of collaboration include: 1) strategies to increase marketing reach of tobacco cessation services; 2) improved protocols for telephonic delivery of tobacco treatment; 3) improved protocols for remote access to stop smoking medications; 4) increased training for health professions to treat tobacco dependence; and 5) enhanced digital services including evidenced-based text messaging programs tailored to different languages/populations.

Session 4: Opportunities for New Collaborations in Early Phase Clinical Trials was chaired by **Elizabeth Repasky, PhD** (Roswell Park, Buffalo, NY, USA) and **Daniel Powell, PhD** (University of Pennsylvania, Philadelphia, PA, USA).

The session was started by **Kęstutis Sužiedėlis, PhD** (National Cancer Institute, Vilnius, Lithuania) presenting his collaborative projects in search for more efficient modalities of cancer radiotherapy. **Brian Czerniecki, MD, PhD** (Moffitt Cancer Center, Tampa, Florida, USA) and **Gary K Koski, PhD** (Kent State University, Kent, Ohio, USA) discussed the role of DCs in cancer immunotherapy and the possibility of using the paradigms of natural infections to enhance their potency. They showed that human DCs loaded with synthetic tumor antigen peptides and activated with purified bacterial cell wall components *ex vivo*, and injected intratumorally, prime tumor-specific T cells, but also

promote local infiltration of multiple immune effector populations and create conditions for tumor elimination. Intratumoral delivery of such DCs combined with tumor-directed monoclonal antibodies resulted in dramatic tumor regressions in preclinical mouse models. A 12-subject phase I neoadjuvant clinical trial for locally advanced HER2 breast disease combining intratumoral DCs plus anti-HER2 monoclonal antibody drugs likewise showed dramatic regressions in most patients with no side effects, suggesting this approach should be further developed. Several multi-institutional clinical trials of different DC variants involving Moffitt Cancer Center and Roswell Park are currently accruing patients and can be extended to additional interested partners. In each trial, all autologous DC vaccines are produced at a single site (depending on the expertise with each specific DC type, either at Moffitt or at Roswell), to assure uniformity of the product. In case of patients from the other institution, the vaccine is prepared from the shipped leukapheresis material of each patient at the DC production institution (which holds the IND) and shipped back in a frozen form to the treating institution.

Iwona Ługowska, MD, PhD (National Institute of Oncology, Warsaw, Poland) discussed the impressive collaborative expertise of the Early Phase Clinical Trial Department and partnering opportunities for domestic and foreign collaborators resulting from the newly developed CAR-T Facility of the NIO’s Center for Excellence in Precision Oncology with. She also discussed the collaborative experience of the NIO’s Cancer Prevention Centre, already involved in many international projects, such as the Nordic-European Initiative on Colorectal Cancer, European Polyp Surveillance Trial and Era-NET Transcan). MSCI is a leader of the National Cancer Strategy, the National Oncology Network, and the National Coordinating Center for population screening and primary cancer prevention and runs the National Cancer Registry.

Waldemar Priebe, PhD (MD Anderson, Houston, Texas, USA) shared his experience connecting academic and biotech researchers in the US and in Poland in order to accelerate the development of novel cancer therapies. He discussed the feasibility of conducting clinical trials of the US-developed drugs in Poland and the value of seeking public - private partnerships in this area.

Session 5: Sources of Governmental Funding for International Collaborations was chaired by **Piotr Rutkowski, MD, PhD, and Mark Parascandola, PhD, MPH** (National Cancer Institute, Bethesda, Maryland, USA), and focused on the availability of state, federal and local governmental sources of funding available to support international collaborations in the area of cancer.

Piotr Rutkowski, MD, PhD, discussed the role of the Medical Research Agency (MRA) of Poland as the vehicle for development of new technologies in clinical medicine. MRA supports innovations in healthcare system, financing medical and health science research, and providing funding for non-commercial clinical trials. It supports the implementation of the National Oncology Strategy and responds to unmet medical needs of the society. Within the area of oncology, so far MRA funded 54 non-commercial clinical trials and 10 commercial clinical trial projects (at the level of 250,000,000 USD or 1 billion PLN) in the areas of non-commercial clinical trials and laboratory projects, R&D, head-to-head comparisons, rare diseases, targeted/personalized medicine, digital technologies, new pharmaceutical forms. MRA funds allowed for the establishment of 7 Oncology Clinical Trial Support Centers across Poland, contributing to creation of a structured and efficient organizational structure for cancer centers. They helped to increase the availability of clinical trials in oncology by increasing their overall number, standardization of operational processes related to their conduct, introduction of quality and other support systems, supporting adequate infrastructure and increased patient awareness of the importance of oncologic clinical trials. In 2024, new requests for proposals (RFP) to support innovative diagnostic and therapeutical solutions, targeted and personalized cancer therapies, digital technologies in healthcare, non-commercial clinical trials in cancer and a separate RFP for Regional Centers of Digital Medicine with Biobanking, will provide a strong background for multi-country collaborations including the CEE Region and the US.

Mark Parascandola, PhD, MPH (National Cancer Institute, Bethesda, Maryland, USA), provided overview of the role of the U.S. National Cancer Institute in supporting international collaborations to advance cancer research, through extramural grant funding, intramural research collaborations, and bilateral agreements. Over 10% of NCI extramural awards in 2022 involved a foreign collaborator. The NCI's Center for Global Health, established in 2011, supports global cancer research and training in low- and middle-income countries with a particular focus on the use of technology, implementation science, and health disparities (<https://www.cancer.gov/about-nci/organization/cgh/about>). The National Institutes of Health has also utilized bilateral funding agreements to support collaborative international cancer research, such as the Academy of Finland (AKA) –National Institutes of Health (NIH) Partnership Program (<https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-021.html>). In the ensuing discussion, Dr. Rutkowski, Dr. Kalinski and Dr. Mark Parandascola, PhD, from

the NCI (Bethesda, Maryland) discussed opportunities for potential bilateral collaboration between MRA and NCI in these areas.

Karen Utz, JD (Empire State Development; <https://esd.ny.gov/regions/western-new-york>), discussed the ESD's efforts at promoting healthcare & biotech Innovations in New York State. Ms. Utz discussed the individual tools aimed at promoting domestic and foreign investment in New York state, ranging from state grants, through matching funds to tax credits.

Session 6: Education & Training- Needs and Opportunities was chaired by **Adam Kisailus, PhD** (Roswell Park, Buffalo, NY, USA) and **Brian Czerniecki, MD, PhD** (Moffitt Cancer Center, Tampa, Florida, USA). The session addressed opportunities for undergraduate, graduate and post-graduate training available to domestic and international students. As highlighted by **Dr. Kisailus**, comprehensive cancer centers represent fertile grounds for education and training future cancer scientists and oncologists in an innovative, collaborative, and interdisciplinary environment. He highlighted the informal and formal educational opportunities to engage students as early as middle school in understanding cancer science, immerse college and health professional students in research experiences, to train graduate students through partnership with the University at Buffalo in the Roswell Park Graduate training programs in cancer sciences and prepare post-doctoral and graduate medical students for careers in academic research and oncology medicine. Several current faculty members at Roswell Park are alumni of these different programs and attest to their education and training at Roswell Park as confirming their pursuit of cancer careers and providing the preparation necessary to reach their career goals. The above sentiment was mirrored in the presentation of **Dr. Czerniecki**, who focused on his experience training of laboratory and clinical scientists at Moffitt. In the following discussion, **Drs. Sużiedėlis and Kalinski** argued for the need of programs allowing foreign trainees to complete fellowship (or a part of a PhD program) in another country and continue collaboration in the same area upon return to the home institution.

Session 7: National and International Collaborations with NGOs, Academia, Pharma & Biotech was chaired by **Pawel Kalinski, MD, PhD** and **Leigh Palladino, JD** from Roswell Park. Regulatory, fiscal & logistic arrangements needed to perform collaborative clinical trials with domestic and foreign academic & biotech partners were discussed by **Pawel Kalinski, MD, PhD** & **Donald Handley, MS, MBA** from Roswell. The presenters highlighted recent success of Roswell in replacing Intron-A, discontinued by Merck in 2019, with Argentinian produced generic version of IFNa2b,

Bioferon, which allowed for continuation of over 10 year-long NCI-funded program of Dr. Kalinski and colleagues performed at the University of Pittsburgh and Roswell Park, in collaboration with Merck and Florida-based AIM Immunotech, the supplier of rintatolimod (Ampligen, a TLR3 ligand). The positive results of the resulting phase I clinical trial combining systemic (i.v.) rintatolimod with IFN α 2b in patients with advanced breast cancer, manifested by the safety and average 10-fold in intratumoral CTL markers (Gandhi et al., 2023) can now be extended to the tests of the clinical efficacy of this combination when combined with PD1 blockade, thanks to the recent FDA approval of the use of Bioferon as a part of the experimental chemokine-modulating (CKM) regimen. Dr. Kalinski highlighted the collaborative opportunities for testing CKM in combinations with chemo-, targeted- and radiotherapy in additional cancer types. **Christopher McAleer, PhD** (AIM Immunotech, Ocala, FL) presented the overview of Ampligen's clinical progress in oncology and collaborative opportunities in the areas of the company in pancreatic, breast, ovarian and other cancers. **Rafal Obuchowicz, MD** (Raygenic, Warsaw, Poland) presented the company's unique platforms of image analysis and interests in collaboration with the US partners.

The presentation of **Katie Noyes, PhD, MPH** (State University of New York at Buffalo) addressed the burning topic of overcoming the urban-rural disparities in cancer care delivery. **Michał Mikula, MD, PhD** (NIO, Warsaw) provided an overview of the preclinical resources and unique models available at NIO for collaborative projects with academic, biotech and pharma partners. **Malgorzata Chalupowski, MD, PhD, JD**, and **Piotr Pierog, PhD** from the Copernicus Institute of New England (Cambridge, PA) presented their efforts at bringing together representatives of Biotech and STEM professionals from the Polish-American community. The session was concluded by **Daniel Powell, Jr, PhD** (University of Pennsylvania, Philadelphia, Pennsylvania), the President of the Translational Research Cancer Centers Consortium (<https://www.trccc.org/>) involving 14 cancer centers from North-eastern United States and Canada. Dr. Powell highlighted the history and mission of TRCCC as an organization successfully promoting multi-institutional collaborations between academic and biotech partners, aiming to accelerate the development of new cancer therapies. The next meeting of TRCCC will take place in Seven Springs, Pennsylvania February 21 - 23, 2024 (<https://www.trccc.org/annual-meeting/>), providing ample opportunities for the discussion of partnering options with the Consortium participants.

Session 8: Collaborative Efforts & Opportunities: Experience of Ukraine was chaired by **Mikhail**

Berezin, PhD (Washington University, St Louis, MO) and **Sergii Dubrov, MD, PhD** (First Deputy Minister of Health of Ukraine Kharkiv, Ukraine) and involved **Tetiana Orabina; MBA** (Ministry of Health, Kharkiv, Ukraine), and **Anna Titkova, MBA, MD, PhD** (Kharkiv National Medical University and Pratia Ukraine, Kharkiv, Ukraine).

Dr. Dubrov and colleagues discussed the extraordinary challenges faced by the current healthcare system of Ukraine amidst the war. Speakers presented the overview of the current situation and plans to restore and enhance Ukraine's healthcare infrastructure. The presentations provided prospective directions for the healthcare system reform as well as the past and the future of clinical trials. The presented approach aims to build a resilient and forward-looking healthcare system through collaborations with the neighboring countries and the US. The Ministry of Health of Ukraine has formulated a recovery plan tailored to the context of war and reconstruction. The plan emphasizes the ongoing transformation and improvement of the healthcare system and the continuation of health reforms. The primary objective is to deliver quality services to the public through financially sustainable mechanisms in the medium run. Both the Ministry of Health and local executive authorities are strategically planning to streamline the extensive and fragmented hospital network.

Ukraine has a strong record of clinical trials. Before the war, 794 clinical trials were approved, 2500 research centers were operating and more than 1000 researchers with ICH-GCP standards compliance were working in the country. 24th of February 2022 transiently stopped all clinical trial activities in the country, but that activity was restarted in the following months. The average clinical trials approval time decreased from 47 to 30 days. In 2023, 13 new clinical trials started, 20 studies resumed patient recruitment, 32 patients returned to clinical research sites.

Session 9: Reducing Treatment Burden and Improving Patient Experience was chaired by **Kara Eaton, MA, CPXP**, and **Kathleen Kokolus, PhD**, from Roswell Park. The session represented one of the key areas of focus of the MSCS-CRC Initiative, the quality of life (QOL) of cancer patients and their families, the area with significant differences in emphasis on between the United States and Europe.

Andras Perl, MD, PhD (Upstate Medical University, Syracuse, New York, USA) discussed the growing problem of Immune checkpoint inhibitor (ICI)-induced autoimmune phenomena, reported in 4.2-87.5% of ICI-treated cancer patients with preexisting genetic susceptibility. He discussed the pathogenesis and emerging treatment developed in his and other cen-



Fig. 2. MSC-2023 included unstructured time over meals and session breaks to provide opportunities for networking and small group discussions, similar to the past editions of the MSCS-CRC Symposia, which propelled the collaborative projects presented in Session 1.

ters. **Elizabeth Griffiths, MD** (Roswell Park, Buffalo, NY, USA) presented her experience with the clinical management of myelodysplastic syndrome (MDS), a clonal malignancy of aging patients associated with bone marrow failure, transfusion dependence, decreased life expectancy and risk for transformation to acute myeloid leukemia. The advanced age at presentation (typically in the mid-70s) and frequent existence of comorbidities, limit the application of the only proven curative intervention: allogeneic stem cell transplant. Additional therapies, including transfusion and chemotherapy are largely palliative and current response assessments suggest limited impact on survival for many patients. Since QOL is significantly lower for MDS patients compared to age matched controls and therapy is largely palliative, the ability of treatments to improve the symptoms is of a particular importance. Prior research suggests that QOL is prognostic, even corrected for performance status and conventional clinical staging, and offers an important novel endpoint for clinical trials. Routine application of the now internationally validated MDS-specific QALMs instrument (<https://qualms.dana-farber.org/>) for assessing QOL in MDS will improve our ability to quantify the QOL impact for established and novel

therapy in MDS and thereby maximize outcome for this underserved population.

Anurag Singh, MD (Roswell Park, Buffalo, NY, USA) discussed his highly collaborative work on the negative impact of beta-2 adrenergic stress (Chen et al., 2020a) on the effectiveness of radiation therapy and the patients' QoL. In addition, he presented data on how the baseline quality of life can impact outcomes in H&N (Farrugia et al., 2021a) and lung cancer (Farrugia et al., 2021b). In addition, the impact of financial stress on outcomes in H&N (Ma et al., 2021) and breast cancer (Ma et al., 2023) were discussed. Finally, research on smoking cessation, even if initiated directly prior to treatment, can modify stress in a simple, yet impactful way, influencing survival in H&N (Ma et al., 2022) and lung cancer (Dobson Amato et al., 2015). **Shipra Gandhi, MD** (Roswell Park, Buffalo, NY, USA) discussed the feasibility of replacing the currently used neoadjuvant chemotherapy/ICI combination in patients with high-risk triple-negative breast cancer (TNBC) with a less toxic combination of ICI with CKM regimen, combining IFN α 2b with rintatolimod. Her preliminary data from the clinical trial NCT04081389 investigating increasing doses of IFN along with fixed dose rintatolimod and celecoxib (CKM) in addition

to standard neoadjuvant chemotherapy (paclitaxel, doxorubicin, and cyclophosphamide) in stage I-II triple negative breast cancer showed residual cancer burden (RCB-0 and 1) rate of 66% (6/9 patients), comparable to the one expected on chemotherapy/ICI combination. No dose limiting toxicities were observed. Adverse events attributed to CKM were mostly limited to grade 1-2 toxicities. Future trials will test CKM and chemotherapy along with neoadjuvant pembrolizumab in triple negative breast cancer.

Kara Eaton, MA, CPXP (Roswell Park, Buffalo, NY, USA) concluded the session with the presentation of her data that making patients the center of care in hospitals is not only the right thing to do, but it also that leads to improved health outcomes, increased patient satisfaction, and more efficient healthcare delivery. This holistic approach to healthcare sees patients as more than their diagnosis, but rather unique individuals with physical, emotional, and social complexities. Recognizing the entire patient experience is fundamental in providing compassionate, safe and effective healthcare. The novel approaches to achieve this goal successfully introduced at Roswell can be rapidly implemented in other centers, representing a low-cost way to enhance both the satisfaction of pa-

tients and their families and to improve the outcomes of cancer patients' treatment.

ACTION ITEMS AND PLANS FOR MSC-2024

The discussions over MSC-2023 led the identification of the key areas of priorities (Figure 1) for MSCS-CRC Initiative to be pursued over the next year and the following year. The immediate efforts are a) the development of the data base helping our existing and new participants to identify collaboration partners for the existing and upcoming projects and the available sources of funding. The second area of our immediate efforts is the pursuit of stable funding to support the upcoming conferences, to allow increased involvement of junior faculty and trainees (travel grants for selected presenters) and invite high visibility speakers in the selected areas of priority. The next Symposium MSC-2024 will be held in Buffalo, September 22-25, 2024, with the 2025 event to be held at the NIO in Warsaw Poland, the 2026 meeting at Moffitt Cancer Center, Tampa, Florida. Prospective meetings hosted by additional institutions, are discussed with participants representing Washington University, Purdue University, City of Hope, as well as colleagues from Croatia and Ukraine.

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