

# Medical Oncology Redefined:

## A Conversation with the New Chief of the Medical Oncology Branch at CCR

Defining the discipline of medical oncology can be more difficult than one would initially think because it touches on so many aspects of cancer research and care. Most broadly, it can be defined as the care and study of adult cancers. Some categorize it as a subspecialty of internal medicine that provides chemotherapy and other non-radiation and non-surgical treatments, a definition that comes close to that of **Giuseppe Giaccone, M.D., Ph.D.**, Chief of the Medical Oncology Branch (MOB) at CCR. “Medical oncology is the medical treatment of cancer,” he noted, “which covers all that is not surgery or radiotherapy.”



(Image: Feinstein Kean Healthcare)

The Medical Oncology Branch brings resources, technologies, and people—researchers, clinicians, and patients—from across NCI and beyond together in ways that leverage the insights and capabilities of multiple clinical and scientific disciplines for the benefit of cancer patients worldwide.

That definition is changing, becoming more translational, more research oriented, and more reflective of the heterogeneity found among patients with the same or similar diagnoses. “Medical oncology also means understanding the range of treatments and identifying the best treatment for each unique patient,” Giaccone said. “It no longer means treating everyone the same, a shift in practice that really is only happening now.”

The nature of the research and organization of medical oncology is also changing to meet this new definition, a shift that is reflected in the efforts underway at CCR to revitalize the Medical Oncology Branch. Giaccone, a lung cancer specialist trained in the former NCI Medicine Branch, rejoined NCI last year as its Chief of Medical Oncology after 16 years at the Free University Medical Center in the Netherlands. His task: to revitalize the Branch as a translational research powerhouse by forging closer ties among the labs and sections comprising CCR’s medical oncology community; to recruit new leaders in key disease areas such as gastrointestinal (GI) and head and neck; to foster relationships between the MOB and extramural investigators; and to build effective partnerships with industry.

CCR Connections had a conversation with Giaccone about CCR’s vision for the new MOB and the Center’s goals for collaboratively leveraging the unique resources of CCR and the MOB to accelerate the national cancer research effort.

**Connections:** How was medical oncology research conducted within NCI in the past?

**Giaccone:** Until recently, cancer biologists were not involved in patient treatment; the provision of systemic therapy largely fell to trained medical oncologists. With the growing translation of biological insights into targeted therapies, many CCR labs and branches have become more interested and involved in bringing treatments to our patients. While this is a very positive development, it requires increased coordination within the MOB and between medical oncologists and our colleagues in the laboratory. In fact, I believe the MOB should be at the forefront of delivering new treatments to our patients.

There are attributes of the old NCI Medicine Branch, particularly its collaborative, multidisciplinary nature, that can serve us well in translating the scientific and medical advances—such as advanced technologies for genomic screening, tools for linking patients' clinical histories and outcomes with the molecular characteristics of their tumors, and enhanced techniques, including imaging, for investigating the efficacy and activity of new therapies, particularly targeted therapies—in clinical practice.

All of these advances, if they are to impact cancer prevention and care, require the contributions of multiple fields of expertise in their development and application. Based on this reasoning, we have thus far focused on facilitating greater integration and coordination across the different components of CCR that engage in medical oncology research.

**Connections:** Please define CCR's vision for the new MOB.

**Giaccone:** Medical oncology can only work when the strengths and expertise of numerous fields—immunology, molecular biology, translational medicine, etc.—are leveraged in an integrated, coordinated fashion. The MOB is the largest CCR branch practicing the discipline of medical oncology. As such, it will provide a framework for conducting all medical oncology research at CCR, bringing all of the sections, branches, and laboratories together to make joint strategic decisions about how to move forward in advancing cancer research.

**Connections:** Where do you see the new MOB fitting within the larger medical oncology community?



(Image: R. Baer)

Giuseppe Giaccone, M.D., Ph.D. (right), a thoracic oncologist by training, examines a patient at CCR.

**Giaccone:** We were once highly regarded for our cutting-edge capabilities in translational and clinical research, and for the resources we brought to the table. However, as our internal research efforts became fragmented, we lost this reputation. With the revitalization of the MOB, we want the cancer community to

to share additional and unique areas of expertise. The new MOB will be an interactive part of the oncology community, with active involvement in a broad portfolio of multicenter studies, where we can leverage our unique resources to carry out experiments that are not feasible outside of CCR.

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understand that we have an important role to play in translational cancer research: that of a high intensity clinical research center that is ideally suited to bring advanced treatments to patients in a highly integrated research setting.

Over the last few years, both NCI and CCR have recognized the need to remove barriers to both internal and external collaboration and have undertaken significant efforts to do so. We need to partner with other institutions in order

**Connections:** One of the main factors in the fragmentation of the old Medicine Branch was the concern that this intramural program was too similar in scope and activity to external programs. How are you addressing this concern now?

**Giaccone:** The new MOB needs to be able to differentiate itself significantly from what can be done in academia or industry and position itself as a complementary resource for such groups.

We have unique abilities in translational medical oncology research due in large part to our unique patient populations. From day one, CCR has focused on rare tumor types. It is relatively easy for CCR to gather patients with rare cancers from around the country and the globe and run complicated studies—such as molecular imaging studies over a regular timeframe or mechanism-of-action studies—that would be difficult and expensive to coordinate on the outside.

Because we are a clinical research center and not an academic or community hospital, we are able to take that relatively small number of patients and study them very intensively, allowing us to gain a deep understanding of these tumors from multiple points of view, including genomics and imaging, two critical areas of targeted treatment research that can be very resource-, infrastructure-, and time-intensive.

**Connections:** Do you see greater collaboration with industry as part of the branch's reformation?

**Giaccone:** Absolutely. This collaborative openness must extend to industry as much as to academia. Most drug development in oncology is conducted by industry these days. The MOB is working closely with the pharmaceutical industry to design and conduct studies that would not be feasible elsewhere or that require particular kinds of expertise. And we need to go further, to work with our industrial partners to identify important questions that must be answered but which cannot be studied in the context of industry-sponsored studies.

We are in a very good place to run very early Phase 0 clinical studies—extremely small trials where you give a new drug to a limited number of patients under an exploratory investigational new drug (IND) protocol and develop reliable, reproducible assays that help determine whether the drug's behavior in people mirrors that in preclinical models. Comprehensive molecular studies on biopsies or molecular imaging studies on patients are very hard to conduct and are resource-intensive. But if they can be conducted in near real-time in an exploratory context, the data that they generate can help quickly and accurately determine next steps and properly define patient populations before moving into larger, later phase trials.

**Connections:** Is there a role for the so-called “big four” tumors (lung, breast, prostate, and GI) in the new MOB?

**Giaccone:** While rare tumors form a core focus of CCR, the four major tumor families will be well represented in our efforts, for two reasons. First, from a population standpoint, these tumors are the most important, affecting larger numbers of patients and causing the greatest mortality and morbidity. Second, a critical part of our mission is to train the next generation of medical oncologists and physician-scientists. We have one of the largest fellowship programs in the nation here at CCR. For the fellows to have the best training and gain the most from their experience, they need to be able to understand the common tumors before they can be expected to understand the uncommon ones.

We also have to consider how the major and rare tumors relate to each other and to CCR's mission. The major tumors each have many rare subtypes. Generally speaking, rare tumor types are biologically less complex than the major tumors. They tend to have fewer genetic alterations, making them easier to study biologically and facilitating their use as models for understanding the biology underlying the major tumors. The work of [Urologic Oncology Branch Chief] W. Marston Linehan, M.D., on kidney cancer and the *VHL* gene is a prime example of how one can leverage discoveries from a rare condition—namely, von Hippel-Lindau syndrome—to advance the understanding and care of more common conditions.<sup>1</sup>

**Connections:** Can you give any other examples of the kinds of collaborative research you have been discussing?

**Giaccone:** CCR is now working with a researcher from Washington University in St. Louis, Samuel Wells, Jr., M.D., to conduct a trial here at the NIH Clinical Center focused on a rare hereditary form of thyroid cancer called hereditary medullary thyroid carcinoma (MTC).<sup>2</sup> MTC accounts for 2 to 3 percent of all thyroid cancers, and only 25 to 40 percent of MTCs are hereditary. Thus, it is very difficult to collect a cohort large enough to do a study with meaningful power. Dr. Wells has teamed up with Frank Balis, M.D. [NCI Clinical Director and Head of the Pharmacology and Experimental Therapeutics Section in CCR's Pediatric

Oncology Branch], to study a new targeted treatment option for patients with unresectable hereditary MTC, a study that likely would be impossible without CCR's research, resources, and reach.

**Connections:** What are the key elements for achieving this new strategic vision for the MOB?

**Giaccone:** Of all of the possible elements on the list, the most important is collaboration. You need a team approach and expertise from very different angles, from biology to patient care to symptom management, all combining to reach the best result. People in the different branches and sections recognize that we need to work together, not in isolation. But to bring us all back together, there needs to be a feeling that we all—all of the branches, all of the sections—are part of a larger enterprise.

**Connections:** What steps have been taken to make this vision of the MOB a reality?

**Giaccone:** Thus far, our efforts have primarily centered on bringing more integration and strategic planning into the clinical protocol development process. After consulting with the different MOB sections, my colleagues and I have developed a new planning step, called a concept review, designed to bring strategic consensus to protocol design. Before a protocol is written, we decide whether the question to be investigated is one that should be explored, and then we identify the resources needed, including those from other sections or branches. From there, we write the protocol collaboratively, ensuring that all details are addressed from the outset.

We also are actively involved in CCR's effort to reduce the time needed for protocol approval, with the goal of reducing that time to two months. This would make us extremely competitive with outside centers in terms of the speed with which we can translate discoveries into the clinic and also make us an attractive partner for collaborative efforts in clinical and translational research.

We are also actively reconstituting our lung, breast, prostate, and GI cancer programs. [MOB Investigator] William Dahut, M.D., has done well with the prostate cancer program for many years and will continue in his efforts to maintain its high standards. As head of the lung cancer program, I will be organizing



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the efforts of CCR's excellent team of lung cancer investigators. Leadership recruitment for the breast and GI programs, as well as our head and neck cancer program, is ongoing.

Lastly, CCR has initiated a Medical Oncology Center of Excellence (CoE). The CoE, which I am leading, is bringing collaborators inside and outside of NCI—people doing important work in areas related to translational medical oncology research like molecular diagnostics, molecular target development, early detection, tumor imaging, and early therapeutics development—together in a multidisciplinary way.

**Connections:** If there is any one message you would want to convey to our readership about CCR, the MOB, and how its reconstitution will affect translational cancer research nationally, what would it be?

**Giaccone:** The MOB is a cancer research resource that exists to complement the excellent and mission-critical research that is being conducted nationwide. The MOB is not here to compete with centers that participate in NCI's extramural program, but rather we exist to enrich their work by offering capabilities and expertise that are not available at the extramural centers, and we can leverage these capabilities in unique ways. As our transformation continues, we look forward to building closer ties to our colleagues in academia and industry, so that together we can make the best use of what the MOB and CCR as a whole have to offer.



(Image: R. Baer)

Giuseppe Giaccone, M.D., Ph.D., Chief of the Medical Oncology Branch (MOB) at CCR

The career path of Giuseppe Giaccone, M.D., Ph.D., has spanned a revolution in cancer research and care on two continents. He first came to the United States and to NCI from Italy in 1988 to work in the Medicine Branch laboratory of John Minna, M.D. (now Principal Investigator of the NCI-sponsored Specialized Program of Research Excellence [SPORE] in lung cancer at the University of Texas Southwestern Medical Center), in the early days of research efforts to understand the genomic component of lung cancer. After two years, he left to conduct doctoral work at the Free University Medical Center in Amsterdam, the Netherlands, where he eventually became a Professor of Medical Oncology and Head of the university's Department of Medical Oncology.

A year ago, Giaccone returned to NCI as Chief of the newly reconstituted Medical Oncology Branch. "I learned of the opportunity to come back to NCI and lead the branch, and I was quite interested, in part because of the challenge,

and in part because this is a unique place to work, with resources that you do not find anywhere else in the world."

Giaccone also returned to lead NCI's Lung Cancer Program. A thoracic oncologist by training, Giaccone will continue his research on targeted therapies for non-small cell lung cancer and how cancer cells regulate, or misregulate, apoptosis.

"I've now been back a little over a year, and while I feel that I'm still learning about the place, I have found very good people here. I am glad to be back and to contribute to CCR's efforts to advance translational cancer research."

To learn more about Dr. Giaccone and his work, please visit his CCR Web site at <http://ccr.cancer.gov/staff/staff.asp?profileid=12505>.

<sup>1</sup> To learn more about Dr. Linehan's work, see "A War on Kidney Cancer," CCR Connections, Vol. 1, No. 1.

<sup>2</sup> See "Staff News at CCR," p. 11.