Research of Cancer Surgery: Progress in new cancer treatments is accelerating so rapidly that the standard of care for many cancer patients is changing right before our very eyes. Since 2017, the U.S. Food and Drug Administration (FDA) has approved a remarkable 53 therapies just to treat patients with blood cancers, and The Leukemia & Lymphoma Society (LLS) has helped advance 46 of these treatments. I have no reason to believe the next few years won't be as productive and groundbreaking as the last few. With that, here are some of my predictions for 2020: CAR T-cell Immunotherapy Continues to Amaze: Revolutionary advances in harnessing the body's immune system to seek out and destroy cancer cells, is creating excitement about chimeric antigen receptor (CAR) T-cell immunotherapy, a treatment that engineers the patient's own cells to fight cancer. While the treatment is currently FDA approved for two types of cancer - acute lymphoblastic leukemia (ALL) and large B-cell lymphoma - I predict we will see CAR-T approved this year for patients with mantle cell lymphoma and multiple myeloma. Compelling data for both of these blood cancers was presented at the American Society of Hematology meeting in December. I'm especially excited about so called "off-the-shelf immunotherapy" that doesn't require engineering individual patients' T cells, making manufacture of these cells less costly and time consuming. More Precision Medicine/Less Chemotherapy: Precision medicine - giving patients a drug based on their molecular profile rather than taking a one-size-fits-all approach - is showing great promise in acute myeloid leukemia (AML) and chronic lymphocytic leukemia (CLL). While chemotherapy, drugs that directly kill cells, remains an important component of many treatment regimens, I predict we will see less reliance on these types of drugs as more targeted therapies, drugs that work by interfering with molecules that help drive cancer growth, gain approval. More Help for Children with Cancer: For too long we've been treating children with acute leukemia with the same protocols developed more than 30 years ago. While most children with ALL survive with treatment, the harsh chemotherapy combinations leave many with lasting side effects. We can and will do better for these children. With the success of our Beat AML Master Clinical Trial, a precision medicine study for adults with AML, we are now planning a global precision medicine trial for children with AML. To develop new therapies for the 40% of children and young adults who don't respond to treatment, we aim to launch our trial – LLS PedAL – in the summer of 2020. While enormous progress has been made in the field of oncology this past decade, the most striking development has been the incredible growth of the field of immunotherapy. As highlighted in this recent post, the U.S. Food and Drug Administration (FDA) has approved immunotherapeutic regimens for two dozen cancer types so far, and thousands of clinical trials are currently evaluating immunotherapeutic approaches for the treatment of cancer. The field of precision medicine has also witnessed extraordinary advancements: Just this past year, the FDA approved 11 new anticancer therapeutics, and all of these are molecularly targeted agents. The breakthroughs in cancer research and treatment, however, do not benefit everyone equally. To educate both the public and Congress about cancer health disparities and to advocate for increased federal funding for this important area of research, the AACR is publishing its first ever report on cancer health disparities in 2020.

As a new decade begins to unfold, what advancements can we expect in the field of oncology? We talked with immunotherapy expert and AACR Women in Cancer Research (WICR) member Padmanee Sharma, MD, PhD; AACR board member, Fellow of the AACR Academy, and precision medicine expert Martine Piccart, MD, PhD; AACR treasurer, AACR Past President, Fellow of the AACR Academy, and cancer prevention and interception expert William Hait, MD, PhD; and AACR board member and cancer disparities expert Marcia Cruz-Correa, MD, PhD; to

discuss their unique perspective and to predict cancer research progress in 2020. IMMUNOTHERAPY ADVANCES IN 2020: Finding ways to unlock the immune system to better recognize and attack cancer cells has been a major focus in the oncology field in the past decade. Specifically, drugs that block the immune checkpoints CTLA-4 or PD-1/PD-L1, known collectively as immune checkpoint inhibitors, have been approved by the FDA to treat over a dozen different cancer types. "With the use of immune checkpoint inhibitors, we've been able to see that the immune system can treat many different types of cancer, regardless of where they originate," began Padmanee Sharma, MD, PhD, professor in the Department of Genitourinary Medical Oncology and Immunology at The University of Texas MD Anderson Cancer Center. "However, not all patients respond to this therapeutic strategy, and not every tumor type responds in the way that we expect," she said. "We must work diligently to improve the number of patients that can benefit from immunotherapeutic approaches."

One key area of research will focus on understanding why some tumor types – such as pancreatic cancer or glioblastoma – are more resistant to immune checkpoint inhibitors, predicts Sharma. While the field has centered on targeting T-cell pathways, which drive the antitumor response, many tumor types that do not respond to immune checkpoint inhibitors are infiltrated by myeloid cells rather than T cells, she explained. "Myeloid cells have alternative pathways that suppress the immune response, so targeting these cells and other immunosuppressive pathways may be the next step to improve immune checkpoint inhibitor efficacy," Sharma noted. Another research avenue that could increase the number of patients responding to immunotherapy is the investigation of combinatorial treatments. "Immune checkpoint inhibitors can be combined with a host of other therapeutic strategies," Sharma said. She highlighted the use of drugs that target tumor cells directly, such as chemotherapies, radiation therapies, or targeted therapies, as a "primer" for immune checkpoint blockade. "When tumor cells die, they are taken up by antigen-presenting cells, which present the offending antigen to the T cells as part of the immune response," she explained. "An immune checkpoint inhibitor can then enhance the T-cell killing of the remaining cancerous cells." Combinatorial immunotherapies, such as targeting both the CTLA-4 axis and the PD-1/PD-L1 axis simultaneously, are also being explored. "One might think that individual immune checkpoint inhibitors are interchangeable, but they're not," stressed Sharma. "Basic science has taught us that the CTLA-4 pathway works much earlier during an immune response compared with the PD-1/PD-L1 pathway. The combined inhibition of these immune checkpoints has been approved for multiple tumor types, such as melanoma and renal cell carcinoma, and we'll continue to see this approach used in other tumor types as well."

However, combinatorial approaches may be accompanied by increased toxicity. "The challenge is, once we unleash the immune response, we're releasing it throughout the entire body," Sharma noted. "As the immune system attacks the tumor cells and the tumor antigens, it may also attack self-antigens, which could be present in any part of the body, resulting in different inflammatory conditions." As such, a major area of research will focus on understanding and mitigating immune-related adverse events associated with checkpoint inhibitors, Sharma predicts. "We are trying to understand the underlying mechanisms of these adverse events and to determine the specific self-antigens that are being targeted by the immune system," she said. "We would then need to develop strategies to better manage these toxicities or develop drugs that minimize responses against self-antigens without comprising the antitumor effects of the checkpoint inhibitor."