targeted immunotherapies have added an important new treatment approach to oncologists’ armamentarium, especially for melanoma, lung cancer, and blood cancers. Cancer immunotherapy is considered such an exciting area that the American Society of Clinical Oncology (ASCO) chose this field as its cancer advance of the year for 2016.

But many challenges remain in bringing treatments that harness the immune system to fight cancer fully into clinical practice, according to speakers at a workshop sponsored by the National Cancer Policy Forum (NCPF) of the National Academy of Medicine (formerly the Institute of Medicine). Issues that may be hampering the development of this field include physician training needs; the need for patient and family education; adverse events in immunotherapy treatment; and the high and escalating costs of these therapies, said workshop planning chair Samir N. Khleif, MD, Director of the Georgia Regents University Cancer Center and the Georgia Health Sciences University Cancer Center. Khleif noted that now, with immunotherapies being used in combination, it could cost up to $1 million per patient with this treatment approach, depending on how long that patient lives.

Studying the Possibilities
A number of groups are studying the challenges of realizing immunotherapy’s promise for cancer patients. The Friends of Cancer Research (FOCR) told OT it recently brought together a policy work group to develop a strategic plan to accelerate progress in immunotherapy across multiple cancers. The Society for Immunotherapy of Cancer (SITC) has established an immunotherapy biomarkers task force. In addition, the Association of Community Cancer Centers (ACCC) has established the Institute for Clinical Immunology to translate immunotherapies into practical application for cancer patients.

At the NCPF workshop, speakers stressed that years of building on advances in science have brought immunotherapy to the point of becoming another pillar in cancer treatment. “If you can induce a complete response, it is very likely to be durable,” said pioneering immunotherapy researcher Steven A. Rosenberg, MD, PhD, Chief of Surgery at the National Cancer Institute (NCI). Rosenberg has achieved exactly that kind of durable regression in patients who have metastatic melanoma by using the technique of autologous tumor-infiltrating lymphocytes (TILs). He also has seen marked tumor regression in patients with advanced sarcomas and lymphomas using this technique, which involves the adoptive transfer of genetically modified, cancer-fighting lymphocytes extracted from patients’ tumors and grown to very large numbers in vitro.

While “cell transfer therapy can mediate durable regressions in patients with metastatic cancer refractory to other treatments,” said Rosenberg, he acknowledged that “the problems are daunting.” In effect, each treatment is unique to each patient, so each patient is getting an individualized immunotherapy based on his or her own mutation profile. “The final common pathway of immunotherapy is the recognition of cancer mutations,” noted Rosenberg.

Now, said Rosenberg, these anti-tumor cells can be identified in peripheral blood as well as in the tumor tissue itself, which could lead to mechanization of TILs and a broader use of this technique of adoptive cell transfer therapy. “The key is to get those antigens from peripheral blood; that’s going to help get this into the clinic,” NCPF member Otis Brawley, MD, Chief Medical Officer and Executive Vice President of the American Cancer Society, told OT.

Several speakers stressed the promise of chimeric antigen receptor (CAR) T cell therapy to treat cancer patients. This therapy involves collecting T cells from a cancer patient, genetically programming them in the laboratory and infusing them back into the patient; the CAR cells are reprogrammed to make proteins which attack cancer cells. “This is a living drug,” said David L. Porter, MD, the Jodi Fisher Horowitz Professor in Leukemia
was no clinical experience with either product was proposed, then a
told Helms. But, she added, "If a first-in-human study where there
relevance can be an issue, “ said Whitney S. Helms, PhD, Supervisory
Products. Basically, an investigational immunotherapy can behave
present regulatory challenges for the agency. In preclinical studies,
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recurring theme at the NCPF workshop. Also, Porter cautioned that
toxicity and side effects can be significant, and may include tumor ly-
sis syndrome, cytokine release syndrome, high fever, nausea, hypoten-
sion, and hypoxia. Some patients may require admission to the ICU.

Regulatory Trials
Speakers from the FDA stressed that cancer immunotherapies can
present regulatory challenges for the agency. In preclinical studies, "even more frequently than with therapeutic antibodies targeting non-
immune associated targets (for example, VEGFR and EGFR), species
relevance can be an issue,” said Whitney S. Helms, PhD, Supervisory
Pharmacologist in FDA’s Office of Hematology and Oncology
Products. Basically, an investigational immunotherapy can behave
quite differently in another species than in humans.

Combination immunotherapies can also present a regulatory chal-
lenge. “In general, combination toxicology studies are not required,”
said Helms. But, she added, “If a first-in-human study where there
was no clinical experience with either product was proposed, then a

Friends of Cancer Research

Recommendations
The immunotherapy policy work group recently convened by the Friends of Cancer Research recommends

• aligning oncology review functions within the FDA;
• developing consensus around specific alternate immunoncology endpoints and definitions that are
  appropriate to immuno-oncology and have sufficient rigor to be acceptable to regulatory agencies;
• promoting opportunities to collect patient-reported outcomes, including symptoms and quality-of-life issues
from real-world patients;
• promoting novel trial designs in immuno-oncology, such as basket-type studies that attempt to match cancer
  patients with a rare mutation, regardless of tumor histology, to a drug expected to work through the mutated pathway;
• promoting a virtual bio-bank/common data platform that encourages and fosters data-sharing; and
• developing an education initiative for the full spectrum of care providers in a patient’s team within the community setting.

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academic centers are vital.

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Access to Data
In addition to cost, educational, regulatory and large-scale manufactur-
ing issues, moving the clinical use of immunotherapies forward is
being to require prudent use of large amounts of data, especially the
data in a cancer patient’s electronic health record (EHR), stressed Amy
P. Abernethy, MD, Chief Medical Officer and Senior Vice President
for Oncology at Flatiron Health, Professor in the Division of Medical
Oncology at Duke University School of Medicine, Director of the
Center for Learning Health Care at Duke and a member of the NCPF.

“EHRs are a massive file cabinet for the patient” with valuable
data, but much of the data is unstructured, said Abernethy. “A dataset
is an amalgamation of patient stories,” she added. Leveraging the valu-
able material in these patient-story datasets to advance the science of
immunotherapy will require organized data processing and linkage
and—most of all—interoperability, said Abernethy. “Policy solutions
should demand interoperability,” she emphasized.

To that end, ASCO recently made a pledge to the U.S. Department
of Health and Human Services (HHS) to improve health information
sharing. “Big data initiatives and future cancer care will depend on the
ability to electronically share clinical information between practitio-
ners,” said ASCO President Julie M. Vose, MD, MBA, the Neumann M.
and Mildred E. Harris Professorial Chair and Chief of the Oncology/ Hematology Division in the Department of Internal Medicine at the
University of Nebraska Medical Center, in a statement.

“However, EHRs often contain data that cannot easily be shared
among physicians or contribute to quality improvement, public
health reporting, or analytics,” said Vose. She noted that ASCO is ac-
tively working to develop interoperability standards and treatment
plans for sharing cancer information, has outlined steps Congress
should take to advance EHR interoperability and prevent information
blocking, and leads the development of CancerLinQ, ASCO’s cutting-
edge health information technology platform.

Peggy Eastman is a contributing writer for OT.