Penn Medicine

A SUMMARY OF 20 ONCOLOGY DRUGS

from Penn Medicine's Abramson Cancer Center Receiving FDA-Approval between 2017 - 2022

Penn Medicine, comprising the Perelman School of Medicine (PSOM), the Abramson Cancer Center (ACC) of the University of Pennsylvania, and their affiliated facilities, is a global leader in basic, translational and clinical research and an epicenter for the development of novel therapeutic agents and technologies. Since 2017, the achievements of investigators at the ACC have contributed — directly or through foundational research — to 20 FDA approvals related to oncology.

EIGHT OF THESE APPROVALS WERE FIRST-IN-CLASS WITHIN THEIR RESPECTIVE INDICATIONS. THEY INCLUDE:

- **TISAGENLECLEUCEL**
  The first personalized gene therapy approved in the United States
- **IOBENGUANE I 131**
  The first and only treatment option for adults and adolescents with malignant, recurrent, or unresectable pheochromocytomas and paragangliomas
- **GILTERITINIB**
  The first tyrosine kinase-inhibitor (TKI) drug for the treatment of patients with relapsed/refractory acute myeloid leukemia (AML) and mutation of *FMS-like tyrosine kinase 3* (FLT3)
- **SELINEXOR**
  The first oral, selective exportin 1 (XPO1) inhibitor for combined use with dexamethasone to treat relapsed/refractory multiple myeloma (RRMM)
- **BELANTAMAB MAFODOTIN-BLMF**
  The first antibody–drug conjugate that selectively targets and kills myeloma cells
- **BELZUTIFAN**
  The first oral hypoxia-inducible factor (HIF)-2α inhibitor for treating tumors associated with von Hippel-Lindau disease
- **PAFOLACIANINE**
  The first receptor-targeted, intraoperative, fluorescence-imaging agent capable of illuminating ovarian cancer and detection of lung cancer lesions
- **TECLISTAMAB-CQYV**
  The first bispecific T cell engager antibody for the treatment of patients with relapsed or refractory multiple myeloma

The ACC and PSOM continue to drive basic science discoveries and are committed to translating the latest innovations in genetics, immunology, and cell and gene therapy into additional approved therapeutic strategies.

A GLOSSARY OF COMMON ACRONYMS USED IN THIS GUIDE

- ACC | Abramson Cancer Center
- ALL | Acute Lymphoblastic Leukemia
- AML | Acute Myeloid Leukemia
- CAR | Chimeric Antigen Receptor
- CHOP | Children's Hospital of Philadelphia
- CR | Complete Remission
- CRS | Cytokine Release Syndrome
- DLBCL | Diffuse Large B-cell Lymphoma
- ER | Estrogen Receptor
- MM | Multiple Myeloma
- NSCLC | Non-Small Cell Lung Cancer
- ORR | Overall Response Rate
- OS | Overall Survival
- PET | Positron Emission Tomography
- PFS | Progression-Free Survival
- PSOM | Perelman School of Medicine
- RR | Recurrent/Refractory
- VHL | Von Hippel-Lindau

2017

TISAGENLECLEUCEL

Tisagenlecleucel (Kymriah), the first cancer gene therapy available in the United States, was approved for the treatment of children and young adults with relapsed/refractory B-cell acute lymphoblastic leukemia (ALL) based on studies led by Drs. Carl June, David Porter, Stephan Grupp, Bruce Levine, and colleagues at the PSOM, ACC, and Children's Hospital of Philadelphia (CHOP).

Generally considered a principal accomplishment of modern cancer research and a foundational achievement in cancer immunotherapy, tisagenlecleucel is an autologous therapy in which a patient's T cells are genetically engineered with a chimeric antigen receptor (CAR) that allows the detection and elimination of leukemia cells expressing the surface molecule CD19.

ALL is the most common childhood cancer in the United States. Before tisagenlecleucel, patients with relapsed and refractory ALL had few treatment options and an overall poor prognosis. Initiation studies of CAR therapy at the ACC demonstrated sustained remission; in the definitive study at CHOP that was the basis for FDA approval, the overall remission rate was 81% within 3 months, with all patients showing treatment response also negative for minimal residual disease. Furthermore, the rates of event-free survival and overall survival (OS) were 73% and 90%, respectively, at 6 months and 50% and 76%, respectively, at 12 months.

In May 2018, tisagenlecleucel was further FDA approved for appropriate patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) based on the JULIET trial led by Dr. Stephen Schuster at the ACC. In this trial, patients with relapsed and refractory aggressive DLBCL demonstrated a best overall response rate (the combined percentage of patients who had a complete or partial response) of 52%, with 40% showing complete response, and 12% partial response.

At 12 months after initial response, the rate of relapse-free survival in all patients was projected to be 65% (79% among patients with a complete response). A 5-year follow-up study of patients in the JULIET trial revealed a progression-free survival (PFS) rate of 31% (median duration of response: 61.4 months) among patients with DLBCL with 60% of patients having a sustained response.

Dr. Schuster and colleagues at the ACC also studied tisagenlecleucel in patients with relapsed/refractory follicular lymphoma. Among patients in this population, 71% had a complete remission. Of follicular lymphoma patients who had any response to therapy, 89% maintained this response at 28.6 months, and a sustained response was evident in 60% of patients at 5 years. On the basis of these data, ***tisagenlecleucel received an additional FDA approval in May 2022 for adults with relapsed/refractory follicular lymphoma.***

Among CAR T studies ongoing at the ACC, several are designed to overcome impediments to the therapy in solid tumors, including glioblastoma. The latter contain few unique antigen targets for T cells and exist in a hostile microenvironment defined by the predominance of infiltrative and immunosuppressive macrophages. To address these challenges, CAR T cell technology is being combined with gene-editing technologies (including CRISPR) to initiate a new and promising era in immunotherapy.

TOCILIZUMAB

Tocilizumab (Actemra) is a monoclonal interleukin (IL)-6 receptor antagonist for the treatment of CAR T cell-induced cytokine release syndrome (CRS; also known as "cytokine storm"). Previously approved for the treatment of rheumatoid arthritis, tocilizumab was co-labeled as part of an emergency use authorization related to tisagenlecleucel's FDA approval in 2017 on the basis of studies performed at the ACC and CHOP. These trials were the first to investigate tocilizumab in CRS, a critical, life-threatening condition characterized by an acute, uncontrolled, systemic inflammatory response that manifests as the activation and expansion of immune cells and hyperproduction of cytokines. Untreated CRS correlates with multi-organ failure and death, whereas treatment with tocilizumab effectively turns off the IL-6-specific cytokine response by blocking IL-6 receptors.

2018

OLAPARIB

In December 2014, the orally administered poly(ADP-ribose) polymerase (PARP) inhibitor olaparib (Lynparza) was FDA approved as monotherapy for the treatment of patients with deleterious or suspected deleterious germline *BRCA*-mutated advanced ovarian cancer previously treated with three or more lines of chemotherapy. The approval was based on the findings of an international single-arm clinical trial led by Dr. Susan Domchek of the Basser Center for *BRCA* and the ACC. Previously, Dr. Domchek contributed to the 2010 trial for olaparib in the United Kingdom that provided proof of concept of the efficacy and tolerability of genetically targeted treatment with olaparib in *BRCA*-mutated advanced ovarian cancers.

Dr. Domchek then co-led a clinical trial that resulted in FDA approval of olaparib for the treatment of patients with metastatic breast cancer and tumors harboring a *BRCA* mutation. **This marked the first FDA approval in 2018 for a for a PARP inhibitor for the treatment of breast cancer and the first approval of any drug to treat certain patients with BRCA-positive metastatic breast cancer.**

In March 2022, the FDA approved olaparib as an adjuvant therapy for high-risk, early stage BRCA-associated breast cancer based on the OlympiA study, a Phase 3, double-blind, randomized trial involving patients with HER2-negative early breast cancer with *BRCA1* or *BRCA2* germline pathogenic or likely pathogenic variants and high-risk clinicopathological factors and who had received local treatment and neoadjuvant or adjuvant chemotherapy. Dr. Domchek co-authored the published report and was on the executive committee for this trial.

IOBENGUANE I 131

The ACC was among the leading sites for the clinical trial leading to FDA approval of iobenguane I 131 (Azedra), which received fast-track approval for use in adults and adolescents aged ≥ 12 years with malignant (metastatic), recurrent or unresectable pheochromocytomas and paragangliomas. This is the first and remains the only drug therapy approved for pheochromocytoma/paraganglioma.

Neuroendocrine tumors arising from adrenal glands (pheochromocytomas) or outside the adrenal glands (paragangliomas) frequently increase the production of epinephrine and norepinephrine, leading to malignant (uncontrollable) hypertension. Although surgery is the standard of care, 10% to 35% of cases are metastatic or locally invasive at diagnosis, and post-surgery recurrence may not be resectable. Moreover, the 5-year survival rate for unresectable pheochromocytoma may be as low as 12%.

Iobenguane I 131 efficacy was demonstrated in a single-arm, open-label clinical trial involving 68 patients. The principal investigator for the trial at the ACC was Dr. Daniel Pryma, chief of the Division of Nuclear Medicine Imaging and Therapy at PSOM and co-leader of the ACC Radiobiology and Imaging Program. Dr. Pryma presented the study findings at the 2018 meeting of the American Society for Clinical Oncology and was first author for the published findings.

Trial endpoints included the number of patients experiencing a ≥50% reduction in all antihypertensive medications lasting at least 6 months and overall tumor response measured by traditional imaging criteria. Overall, 25% of evaluable patients met these endpoints, with objective tumor response achieved in 22% of patients.

GILTERITINIB

The FDA approved gilteritinib (Xospata) as the first TKI drug for the treatment of patients with FLT3-mutated relapsed/refractory AML. The approval was granted based on the multi-center ADMIRAL trial led by Dr. Alexander Perl at the ACC.

FLT3 is expressed in normal bone marrow cells and regulates the orderly growth of blood cells in response to daily demands. It is the most commonly mutated gene in AML and results in the uncontrolled growth of cancer cells. Patients with mutations in FLT3 and relapsed/refractory AML have very low response rates to chemotherapy at the time of relapse, resulting in a poor prognosis.

Gilteritinib inhibits FLT3 activity in AML patients with tumors expressing the two most common types of FLT3 mutations. The first is FLT3 internal tandem duplication (FLT3-ITD) associated with aggressive disease behavior, frequent relapse and short remission duration. Historically, patients with relapsed/refractory FLT3-ITD AML have an average OS of ~4 months. To lower relapse risk, oncologists often recommend the most aggressive chemotherapeutic approaches for FLT3-ITD AML patients, including high-dose chemotherapy and stem cell transplantation.

The second FLT3 mutation targeted by gilteritinib affects the tyrosine kinase domain of the translated protein and is associated with resistance to a number of previously developed FLT3 inhibitors.

An interim analysis from the ADMIRAL trial showed significantly higher rates of complete remission (CR) or CR with partial hematologic recovery among gilteritinib-treated patients relative to those receiving standard chemotherapy. Furthermore, the final results from the ADMIRAL trial showed significantly longer survival among patients in the gilteritinib-treatment group (9.3 months) as compared with those receiving standard chemotherapy treatments (5.6 months), with long-term follow-up confirming improvements in sustained OS.

Dr. Perl was also the lead author of a 2017 publication presenting results from a first-in-human Phase 1 and 2 trial (CHRYSALIS). In this trial of 252 patients with relapsed/refractory FLT3-mutated AML, 49% of patients responded to gilteritinib treatment, with a subsequent median survival rate of >7 months instead of chemotherapy. Only 12% of patients without FLT3-mutated AML in this trial responded to the drug, providing evidence that gilteritinib acts as a selective inhibitor of mutated FLT3.

Although the terms of the current FDA approval limit gilteritinib to therapeutic applications for patients with relapsed/refractory FLT3-mutated AML, studies have demonstrated the feasibility of regimens combining gilteritinib with other novel chemotherapeutic agents for these patients. Ongoing clinical trials at the ACC are also evaluating whether adding gilteritinib to first-line therapy for newly diagnosed FLT3-mutated AML patients can prevent relapse and improve remission rates and survival.

2019

TRANSORAL ROBOTIC SURGERY (TORS)

TORS, created by Drs. Gregory S. Weinstein and Bert W. O'Malley, Jr., at PSOM's Department of Otorhinolaryngology–Head and Neck Surgery, altered the landscape of head and neck surgery.

TORS combines the capacities of a magnified, high-resolution endoscope and a set of robotic surgical instruments small enough to enter the confined environment of the head and neck. Prior to TORS, operating in this space often required a mandibulotomy to access the target lesion, followed by extensive reconstruction surgery and consequent effects on talking, swallowing, and eating during recovery.

TORS first received FDA approval in December 2009 for transoral procedures involving selected benign and malignant T1 to T2 tumors in adults, with a second approval granted in March 2019, expanding the indications for use in procedures targeting benign tumors at the tongue base. Based on additional investigations at PSOM, TORS is now widely used to address obstructive sleep apnea by increasing the size of the air space leading from the mouth to the trachea, as well as for radical tonsillectomy and resection of palatal and skull-base tumors, hemiglossectomy and tumors of the larynx.

Drs. Weinstein and O'Malley founded the world's first TORS program in 2004 to develop and research a variety of robotic surgical neck approaches for both malignant and benign tumors of the mouth, larynx, tonsils, tongue and throat. In 2005, the TORS training program was initiated at Penn, leading to the subsequent rapid adoption of TORS by surgeons in the United States, Europe and Asia. Following FDA approval of TORS in 2009, the Department of Otorhinolaryngology–Head and Neck Surgery established a dedicated state-of-the-art robotic surgery training facility where hundreds of surgeons have been trained. The program combines case observation with hands-on surgical education.

Together, these efforts have taught TORS techniques to surgeons from 14 countries and qualified surgeons in the United States, who were encouraged to begin their own clinical research programs.

The benefits of TORS are reflected in the reported improvements in patient OS, recurrence-free survival, functional outcomes, and quality of life. Further innovations are being studied at PSOM and worldwide.

SELINEXOR

The FDA granted accelerated approval to selinexor (Xpovio), a first-in-class, oral, selective XPO1 inhibitor for use in combination with dexamethasone for the treatment of adult patients with RRMM who have received at least four prior therapies, and whose disease is resistant to several other forms of treatment, including at least two proteasome inhibitors, at least two immunomodulatory agents and an anti-CD38 monoclonal antibody. Overall survival (OS) in patients with myeloma refractory to these classes is brief. Myeloma patients refractory to the anti-CD38 monoclonal antibody daratumumab, for example, have a median OS of 1.7 to 3.0 months.

The FDA approval was based on results of the multi-center STORM Part 2 trial led by Dr. Dan Vogl at the ACC. Dr. Vogl was first author on the report presenting the study findings and second author on the subsequent report, both of which supported FDA approval.

Selinexor is a selective inhibitor of XPO1, which is involved in the transport of macromolecules from the cell nucleus to the cytoplasm. MM progression is accompanied by XPO1 overexpression, which is sustained throughout the course of the disease and correlates with poor survival.

Findings in STORM Part 2 revealed a ORR of 25.3%. The median time to first response was four weeks; the median duration of response was 3.8 months.

A subsequent randomized Phase 3 trial (BOSTON) confirmed the clinical benefit of selinexor, showing improved progression-free survival (PFS) from a combination of selinexor, bortezomib, and dexamethasone as compared with bortezomib and dexamethasone (Vd) alone. In this trial, patients in the selinexor arm had a median PFS of 13.9 months vs. 9.5 months for Vd, as well as a 30% reduction in risk of progression of death. The results of BOSTON led to full approval of selinexor in 2020 (in combination with bortezomib and dexamethasone) for the treatment of adult patients with MM who have received at least one prior therapy.

2020

ENTRECTINIB

The FDA granted approval to entrectinib (Rozlytrek) for adults and pediatric patients aged ≥12 years with neurotrophic tyrosine receptor kinase (TRK)-fusion-positive solid tumor cancers and for adults with ROS proto-oncogene 1 (ROS1)-positive non-small cell lung cancers (NSCLCs).

Rozlytrek is an oral medication that acts as a potent anaplastic lymphoma kinase (ALK) inhibitor active on ALK-dependent cell lines capable of efficiently penetrating the blood–brain barrier to target key genetic drivers of cancer rather than a specific type of tumor. It was approved based on findings from the STARTRK-1 clinical trial in adults and an ancillary trial (STARTRK-NG, NCT02650401) initiated in 2016 that included children.

The 2016 trial was preceded by a Phase 1 study of entrectinib in children, adolescents and young adults with recurrent/refractory solid tumors co-authored by Drs. Garrett Brodeur and Elizabeth Fox, members of the ACC Pediatric Oncology Program who were subsequently instrumental in ensuring that the approval terms included children. Evidence that entretinib could inhibit activated TRK receptors in the central nervous system was reported in a pre-clinical trial conducted at CHOP and PSOM in 2016.

FLUOROESTRADIOL F 18, OR $^{[18]}$F FES)

$^{[18]}$F FES (Cerianna) was approved in combination with positron emission tomography (PET) scans for the visual detection of estrogen receptor (ER)-positive lesions in patients with recurrent or metastatic breast cancer. Approximately 75% of all breast cancers in women and 99% in men are ER-positive.

Although $^{[18]}$F FES approval was based on data from a number of trials, including a clinical trial in the Republic of Korea, foundational studies on the metabolism and pharmacokinetics of PET $^{[18]}$F FES regarding its role as an ER tracer in breast cancers were conducted by Dr. David Mankoff, who joined the ACC faculty >20 years ago.

Dr. Mankoff and colleagues published the first report on human metabolites in tracer-FES uptake in breast tumors in 1997, demonstrating the rapid clearance and metabolism of FES and its optimal arrival time for imaging and visualization of estrogen-containing tissues. Subsequently, a clinical study conducted by Dr. Mankoff and colleagues, including Erin Schubert in the PSOM PET Center, provided early evidence of the efficacy of FES in predicting breast cancer response to endocrine therapy that has been widely cited and was a key factor in FDA review and approval. This team also developed and performed a prospective clinical trial that was the basis for a National Cancer Institute Investigational New Drug Application allowing the establishment of protocol template components and general requirements for studies employing $^{[18]}$F FES in prospective trials and provided foundational data for the FDA approval of $^{[18]}$F FES.

2021

BELANTAMAB MAFODOTIN-BLMF

Belantamab mafodotin-blmf (Blenrep) was approved by the FDA for the treatment of patients with RRMM who have received at least four prior therapies, including anti-CD38 therapy. The approval was based on the pivotal findings of the multicenter DREAMM-2 study, for which Dr. Adam Cohen at the ACC was principal investigator and a senior author of the published findings.

MM remains largely incurable and accounts for 10% of all hematologic malignancies. The depth and duration of response to the three standard MM therapies (proteasome inhibitors, immunomodulatory agents and monoclonal antibodies) typically diminish over time, until none is effective. The prognosis for these patients, now defined as having refractory disease, is poor (median OS: 9.3 months).

Belantamab mafodotin-blmf is a first-in-class antibody–drug conjugate that binds to B-cell maturation antigen, a protein on the surface of myeloma cells, leading to internalization and release of a toxic drug that kills the cells. The DREAMM-2 study enrolled patients with RRMM demonstrating disease progression after four or more therapies and who were refractory to immunomodulatory drugs and proteasome inhibitors and refractory or intolerant to an anti-CD38 monoclonal antibody.

The study found that the OS rate at the FDA-approved intravenous dose of 2.5 mg/kg every 3 weeks was 31%, with 73% of responders showing a response duration of ≥6 months. In a subsequent report at a 13-month median follow-up, the median estimated duration of response, OS, and PFS were 11.0 months, 13.7 months, and 2.8 months, respectively.

CRIZOTINIB

The FDA approved crizotinib (Xalkori) for pediatric patients aged ≥1 year and young adults with relapsed/refractory systemic anaplastic large-cell lymphoma (ALCL) that is ALK-positive. The approval was based on the findings of ADVL0912, a multicenter, single-arm, open-label trial in patients aged 1 to 21 years directed by Dr. Yael Mossé at CHOP.

Crizotinib inhibits ALK and ROS1 activities, which are dysfunctional in various cancers, including ALCL, inflammatory myofibroblastic tumors, NSCLC and neuroblastoma. A study led by investigators at CHOP and PSOM in 2011 first demonstrated that heritable mutations of *ALK* cause familial neuroblastoma and identified ALK as a tractable therapeutic target for this malignancy. These findings also provided the first example of a pediatric cancer arising because of mutations in an oncogene and served as the impetus for developing therapeutic strategies aimed at inhibiting ALK-mediated signaling.

In July 2022, the FDA approved crizotinib for a second indication: adult and pediatric patients aged ≥1 year with unresectable, recurrent or refractory inflammatory ALK-positive myofibroblastic tumors.

BELZUTIFAN

The FDA approved belzutifan (Welirig) as a first-in-class oral HIF-2α inhibitor for treating certain types of VHL disease-associated tumors, including renal cell carcinoma (RCC), CNS hemangioblastomas and pancreatic neuroendocrine tumors.

VHL is a rare, hereditary disorder characterized by elevated levels of HIF-2α, and a significant contributor to cancer tumorigenesis, angiogenesis, and metastasis via hypoxia induction. Individuals with VHL have visceral cysts and benign tumors capable of malignant transformation, including those related to clear-cell RCC, pancreatic neuroendocrine tumors and hemangioblastomas in the CNS and retina. Belzutifan works by selectively blocking HIF-2α activity.

Among the largest VHL programs in the country, the ACC was a major participant in the definitive clinical trial, with ACC members Dr. Vivek Narayan participating as a co-author of the manuscript reporting the study's findings, and Dr. Katherine Nathanson acting as a member of the national study group.

The approval of belzutifan followed more than a decade of basic science research to understand cancer hypoxia by Dr. M. Celeste Simon at the ACC, with findings from two publications from Drs. Simon and Nathanson particularly valuable to the research that led to drug approval.

In 2019, the Nobel Prize in Physiology or Medicine was awarded to Dr. William Kaelin, Sir Peter Ratcliffe, and Dr. Gregg Semenza for their work on another HIF family transcription factor, HIF-1. Dr. Semenza completed his MD and PhD at the University of Pennsylvania.

CABOZANTINIB

The FDA approved cabozantinib (Cabometyx) based on findings from COSMIC-311, a global Phase 3 clinical trial in patients aged ≥16 years with radioiodine-refractory differentiated thyroid cancer (DTC). Cabozantinib is a multi-kinase inhibitor that blocks hepatocyte growth factor receptor, vascular endothelial growth factor receptor 2 and the tyrosine kinase receptor known as rearranged during transfection (RET).

DTC includes papillary thyroid carcinoma, follicular thyroid carcinoma (FTC) and the FTC variant Hürthle cell carcinoma. Standard therapy for DTC includes thyroidectomy and removal of associated lymph nodes, followed by radioactive iodine (RAI) ablation (thyroid cancer cells are generally RAI-avid) and thyroid hormone suppression. Many patients with DTC will eventually develop RAI non-avid (or RAI-refractory) disease. Prior to the advent of the TKIs, there were no efficacious FDA-approved therapies for RAI-refractory thyroid cancers.

The ACC participated in the COSMIC-311 study, in which Dr. Marcia Brose served as national principal investigator and the first author of the published findings. An early advocate of TKIs for treatment of advanced thyroid cancer, Dr. Brose also played a fundamental role in the DECISION trial that led to the 2013 FDA approval of sorafenib, the first TKI approved for radioactive iodine-refractory metastatic DTC.

PAFOLACIANINE

Following successful Phase 2 and 3 trials by the national principal investigator, Dr. Janos Tanyi, a member of the ACC, Pafolacianine (Cytalux) is the first FDA-approved substance to illuminate ovarian cancer (2021) and lung cancer (2022) lesions during surgery.

Complete removal of malignant tissue is the single most important prognostic indicator for survival in ovarian cancer, but identifying all lesions can be challenging. Pafolacianine binds to folate receptors that are over-expressed in most epithelial ovarian cancers, and, when used with a near-infrared imaging system, allows surgeons to remove malignant tissues undetectable by visualization and palpation under normal light.

In the pafolacianine Phase 3 intraoperative molecular imaging study, 27% of patients had at least one evaluable ovarian cancer lesion detected with pafolacianine that was not observed by the surgeons' standard visual or tactile inspection, thereby demonstrating the efficacy of pafolacianine to help surgeons identify malignant lesions that might otherwise be missed during surgery. Simultaneously, a national randomized multi-center Phase 3 study of pafolacianine was subsequently completed at the ACC by the national principal investigator, Dr. Sunil Singhal, to compare the performance of folate-receptor-targeted intraoperative molecular imaging of pulmonary adenocarcinomas.

In December 2022, the FDA approved a second indication for pafolacianine for the detection of lung cancer lesions in adult patients with known or suspected lung cancer. The label expansion was based on the safety and efficacy findings of the phase 3 ELUCIDATE trial (NCT04241315), which evaluated pafolacianine in patients scheduled to undergo thoracic surgery for confirmed or suspected lung cancer. Of the 110 patients in ELUCIDATE who received a dose of pafolacianine and were evaluated under normal and fluorescent light during surgery, 24% had at least 1 cancerous lesion detected that was not identified by standard visual or tactile inspection. The principal investigator for ELUCIDATE, a randomized, single dose, multi-center study, was Sunil Singhal, MD, Director of the Center for Precision Surgery at Penn Medicine. Dr. Singhal was joined in this effort by investigators from the ACC and On Target Laboratories.

One of the most prominent research centers for intraoperative molecular imaging in the world, the PSOM is engaged in other recent and ongoing clinical trials of intraoperative fluorescence imaging at the ACC. These include assessment of the technology in pulmonary nodules and adenocarcinomas, solid tumors, lung cancers, pituitary adenomas, thoracic malignancies, breast cancer, renal nodules, the parathyroid, colorectal neoplasms, and glioblastomas.

TECLISTAMAB-CQYV

A T cell-redirecting bispecific antibody, teclistamab-cqyv (Tecvayli) is an off-the-shelf first-in-class therapy for adult patients with relapsed or refractory multiple myeloma who previously received four or more prior lines of therapy, including a proteasome inhibitor, immunomodulatory drug and anti-CD38 monoclonal antibody. Multiple myeloma patients who have had disease progression after receiving these agents have generally limited options and poor outcomes.

Teclistamab-cqyv mediates T cell activation and lysis of BCMA+ myeloma cells by targeting CD3 expressed on the surface of T cells and BCMA expressed on the surface of myeloma cells. FDA approval of the agent was based upon the conclusions of the multicenter pivotal Phase 2 MajesTEC-1 clinical trial conducted at the Abramson Cancer Center by Alfred L. Garfall, MD, a co-author for the study findings report.

In MajesTEC-1, teclistamab-cqyv resulted in a high rate of deep and durable response in patients with triple-class–exposed relapsed or refractory multiple myeloma, indicating the potential for substantial clinical benefit to a broader population of patients. Among participants, the overall response rate was 61.8%. Among responders, the estimated duration of response was 90.6% at 6 months and 66.5% at 9 months. The median duration of progression-free survival was 11.3 months. Cytopenias and infections were common; toxic effects that were consistent with T cell redirection, including cytokine release syndrome, were mostly grade 1 or 2.

FY23 36837 1/23