Biologics

Clinical Therapeutic Intelligence Report: Special Edition

Biologics' Clinical Therapeutic Intelligence Office was established to advance the company's clinical expertise efforts as it continues to distinguish itself as a leader in pharmacy services, specifically within the oncology sector.

Nine new orals have been approved in the oncology space in 2015 year to date, with seven new indications for previously approved therapies[i]. The approvals span multiple indications, routes of administration and mechanisms of action, and include orphan and breakthrough therapies.

"The continued development of effective therapeutics based on our understanding of cancer biology and the ability through the use of biomarkers to personalize therapies have lead to further expand options for patients across multiple malignancies," said Dr. Mark Socinski, Director, Lung Cancer Section, Division of Hematology/Oncology at the University of Pittsburgh.

FDA Approval Designations

Fast Track Designation

Designation of the U.S. FDA that facilitates the development, and expedites the review, of drugs which treat a serious or life-threatening condition and fill an unmet medical need.

Breakthrough Therapy

A new drug may be designated as a breakthrough therapy by the U.S. FDA if it is intended to treat a serious or life-threatening disease and preliminary clinical evidence suggests it provides a substantial improvement over existing therapies.

Priority Review

A Priority Review designation directs overall attention to the evaluation of drugs that, if approved, would be significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications.

Accelerated Approval

A drug that treats a serious condition and generally provides a meaningful advantage over available therapies, and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit.

See full list of oncology drug approvals on pages 3-4.

Focus: Non-Small Cell Lung Cancer

In 2015 alone, an estimated 221,200 people will develop some form of lung or bronchus cancer, which will account for about 13 percent of all cancer diagnoses[ii]. While the incidence rate has been steadily declining in recent years, lung cancer continues to account for more deaths than any other cancer in both men and women.

Non-small cell lung cancer (NSCLC) represents 83 percent of the lung cancer population. Large cell carcinoma, squamous cell carcinoma and adenocarcinoma are the most common subtypes, though there are many others which occur less frequently[iii].

Currently, there are 95 phase II and III trials in the pipeline focusing on lung cancer, with a majority specifically targeting non-small cell lung cancer. Many drugs previously approved for other disease states, such as the poly-ADP ribose polymerase (PARP) inhibitor **olaparib**, are being tested for efficacy in NSCLC.

About 15 percent of patients with NSCLC have epidermal growth factor receptor mutations[iv]. Within this population, EGFR T790M mutation is the most common mechanism of drug resistance to EGFR tyrosine kinase inhibitors, which are commonly used to treat NSCLC[v]. AstraZeneca's **osimertinib**, approved in early November 2015, was proven effective against T790M resistance, as well as EGFR tyrosine kinase inhibitor-sensitizing mutations.

Osimertinib was granted Fast Track, Breakthrough Therapy, Priority Review and Accelerated Approval status by the U.S. Food and Drug Administration[vi]. Approval was based on data from two AURA PHase II studies, which demonstrated efficacy in EGFRm T790M non-small cell lung cancer patients that had progressed while on or after EGFR TKI therapy. Overall objective response rate was 59%.

Immunotherapies such as **nivolumab** and **ipilimumab**, previously approved for melanoma, were also expanded for use in lung cancer in 2015.

Nivolumab, a PD-1 inhibitor, was approved under the FDA's Priority Review program for the treatment of advanced metastatic squamous non-small cell lung cancer[vii]. In studies, patients receiving nivolumab lived an average of 3.2 months longer than those receiving the other trial agent, docetaxel.

Results of safety and effectiveness studies showed that 15% of study participants treated with nivolumab's tumors shrank or disappeared completely, and about half of people who responded to the drug had responses lasting six months or longer.

More Information

To sign up to receive additional information about the Oncology Pipeline, please email info@biologicsinc.com

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Sources

i "Hematology/Oncology (Cancer) Approvals & Safety Notifications," 2015. U.S. Food and Drug Administration.

ii "Cancer Facts & Figures 2015," American Cancer Society.

iii "General Information About Non-Small Cell Lung Cancer (NSCLC)," August 6, 2014, National Cancer Institute.

iv "Epidermal Growth Factor Receptor (EGFR) Testing for Advanced Non-Small Cell Lung Cancer," American Society of Clinical Oncology.

v "AZD9291 in EGFR Inhibitor-Resistant Non-Small Cell Lung Cancer," April 30, 2015, N Engl J Med 2015.

vi "TAGRISSO™ (AZD9291) approved by the US FDA for patients with EGFR T790M mutation-positive metastatic non-small cell lung cancer," November 13, 2015.

vii "FDA Approves Opdivo (Nivolumab) for Lung Cancer," March 5, 2015.

2015 Drug Approval Breakdown

Drug Name	*Manufacturer*	*Indication*	*Genetics*	*Route of Administration*	*Mechanism*	*Clinical Trial Results*	*Biologics Availability*
IMBRUVICA® (ibrutinib)	Janssen	Waldenström's macroglobulinemia (WM)	N/A	PO	BTK inhibitor	62% of patients had cancer shrink for 2.8 - 18.8 months (WM)	Yes
IBRANCE® (palbociclib)	Pfizer, Inc.	ER-positive, HER2-negative advanced breast cancer	ER, HER2	PO	CDK4/6 inhibitor	20.2 months of progression free survival, compared to 10.2 months	Yes
LENVIMA® (lenvatinib)	Eisai, Inc.	Radioactive iodine-refractory differentiated thyroid cancer	N/A	PO	Multi-kinase inhibitor	Median of 18.3 months of progression free survival, compared to median of 3.6 months	Yes
FARYDAK® (panobinostat)	Novartis Pharmaceuticals	Multiple myeloma	N/A	PO	HDAC inhibitor	10.6 months of progression-free survival, compared to 5.8 months	Yes
OPDIVO® (nivolumab)	Bristol-Myers Squibb	Metastatic squamous non-small cell lung cancer	BRAF	IV	PD-1 blocking antibody	15% experienced objective response rate, 59% had response durations of 6 months or longer	No
UNITUXIN® (dinutuximab)	United Therapeutics Corporation	Pediatric high-risk neuroblastoma	N/A	IV	GD2-binding monoclonal antibody	Three year estimate of overall survival was 80%, compared to 67%	No
CYRAMZA® (ramucirumab)	Eli Lilly and Company	Metastatic colorectal cancer (mCRC)	VEGFR2	IV	VEGFR2 antagonist	Median overall surival was 13.3 months, compared to 11.7 months with placebo	Yes
IRESSA® (gefitinib)	AstraZeneca	Metastatic non-small cell lung cancer	EGFR mutation-positive	PO	EGFR inhibitor	70% overall response rate, with a median duration of response of 8.3 months	Yes
ODOMZO® (sonidegib)	Novartis Pharmaceuticals	Locally advanced basal cell carcinoma	N/A	PO	Hedgehog signaling pathway inhibitor	58% overall response rate, with a duration of 1.9 to 18.6 months	No
Kyprolis® (carfilzomib)	Onyx Pharmaceuticals, Inc.	Multiple myeloma	N/A	IV	Proteasome inhibitor	22.9% overall response rate, with a median duration of 7.8 months	No
ADCETRIS® (brentuximab vedotin)	Seattle Genetics	Classical Hodgkin lymphoma, Systemic anaplastic large cell lymphoma	N/A	IV	CD30-directed antibody-drug conjugate	73% of patients achieved either a complete or partial response to treatment, responses lasted on average 6.7 months	No
LONSURF® (trifluridine/ tipiracil)	Taiho Oncology, Inc.	Metastatic colorectal cancer	N/A	PO	Nucleoside metabolic inhibitor, thymidine phosphorylase inhibitor	Median overall survival lasted an average of 7.1 months compared to 5.3 months	Yes
KEYTRUDA® (pembrolizumab)	Merck Sharp and Dohme Corporation	Metastatic non-small cell lung cancer	PD-L1	IV	PD-1-blocking antibody	Tumors shrank in 41% of patients, and effect lasted between 2.1 and 9.1 months	No

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ONIVYDE® (irinotecan liposome injection)	Merrimack Pharmaceuticals, Inc.	Metastatic adenocarcinoma of the pancreas	N/A	IV	Topoisomerase inhibitor	Median overall survival of 6.1 months for patients who received irinotecan liposome in combination with 5FU and LV	No
YONDELIS® (trabectedin)	Janssen Biotech	Unresectable or metastatic liposarcoma or leiomyosarcoma	N/A	IV	Alkylating drug	Median overall survival lasted 13.7 months, with median progression free survival of 4.2 months	No
YERVOY® (ipilimumab)	Bristol-Myers Squibb	Cutaneous melanoma	N/A	IV	CTLA-4-blocking antibody	Median recurrence-free survival of 26 months	Yes
COTELLIC® (cobimetinib)	Genentech, Inc.	Unresectable or metastatic melanoma	BRAF	PO	MEK inhibitor	Median progression free survival of 12.3 months	Yes
TAGRISSO™ (osimertinib)	AstraZeneca	Metastatic EGFR T790M-positive non-small cell lung cancer	EGFR	PO	EGFR-TKI inhibitor	Two studies showed overall response rates of 57% and 61%, respectively	Yes
DARZALEX™ (daratumumab injection)	Jannsen Biotech	Multiple myeloma	N/A	IV	Human CD38-directed monoclonal antibody	Objective response rate of 29% with a median response duration of 7.4 months	No
NINLARO® (ixazomib)	Takeda Pharmaceuticals	Multiple myeloma	N/A	PO	Proteasome inhibitor	Median progression free survival of 20.6 months, compared to 14.7 months	Yes
OPDIVO® (nivolumab)	Bristol-Myers Squibb	Advanced renal cell carcinoma	N/A	IV	PD-1 blocking antibody	Median overall survival of 25 months, with a median response duration of 23 months	No
PORTRAZZA™ (necitumumab)	Eli Lilly and Company	Metastatic squamous non-small cell lung cancer	N/A	IV	EGFR antagonist	Median overall survival of 11.5 months, with median progression free survival of 5.7 months	Yes
EMPLICITI™ (elotuzumab)	Bristol-Myers Squibb	Multiple myeloma	SLAMF7	IV	SLAMF7-directed immunostimulatory antibody	Median progression free survival of 19.4 months, with an overall response rate of 78.5%	No