AUGUST 2023

TACOS ONCOLOGY DRUG NEWSLETTER

The Arizona Clinical Oncology Society

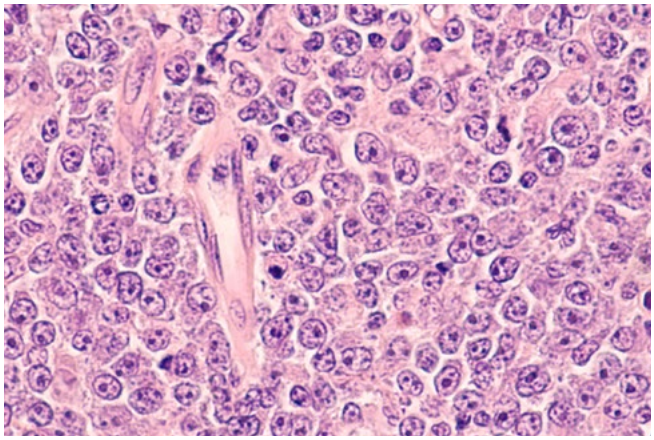
FDA APPROVALS

Glofitamab-gxbm (Columvi)

The FDA granted accelerated approval to glofitamab-gxbm (Columvi) for adult patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified or large B-cell lymphoma arising from follicular lymphoma, after at least 2 lines of systemic therapy.

In the phase 1/2 NP30179 trial (NCT03075696), glofitamab generated a 56% overall response rate (ORR) and 43% complete response (CR) rate with 68.5% of patients who achieved a response continuing to respond for at least 9 months (95% CI, 56.7-80.3). Moreover, the median duration of response was 18.4 months (95% CI, 11.4-not estimable).

In the multicenter, open-label, dose-escalation, and dose-expansion NP30179 trial, 132 patients with relapsed/refractory DLBCL received glofitamab as a fixed course for 8.5 months. A total of 30% of patients had received prior chimeric antigen receptor (CAR) T-cell therapy and 83% were refractory to their most recent treatment.



The primary end point of the trial is CR rate by an independent review committee, and secondary end points include ORR, duration of response, progression-free survival, safety, and tolerability.

REFERENCES

1. FDA approves Genentech's Columvi, the first and only bispecific antibody with a fixed-duration treatment for people with relapsed or refractory diffuse large B-cell lymphoma. News release. Genentech. June 15, 2023. Accessed June 16, 2023. https://tinyurl.com/3hwsvvrb
2. Dickinson MJ, Carlo-Stella C, Morschauser F, et al. Glofitamab for relapsed or refractory diffuse large B-cell lymphoma. N Eng J Med. 2022;387(24):2220-2231. doi:10.1056/NEJMoa2206913

FoundationOne Liquid CDx

The FDA has approved FoundationOne Liquid CDx to be used as a companion diagnostic with encorafenib (Braftovi) in combination with cetuximab (Erbitux) to identify patients with BRAF V600E alterations in metastatic colorectal cancer (mCRC).[1]

FoundationOne Liquid CDx is a qualitative next-generation sequencing–based in vitro diagnostic test for patients with advanced solid tumors. Using circulating cell-free DNA, the test analyzes 324 genes. The FDA has approved the diagnostic to report short variants in 311 genes.

In 2021, the agency approved the 2-drug combination of encorafenib (Braftovi) and cetuximab (Erbitux) for adult patients with previously treated mCRC who harbor a BRAF V600E alteration. Findings from the phase 3 BEACON CRC study (NCT02928224) support this indication.

The median overall survival (OS) among patients who received cetuximab plus encorafenib was 8.4 months (95% CI, 7.5-11.0) vs 5.4 months (95% CI, 4.8-6.6) in the control arm. For the 3-drug combination, the objective response rate (ORR) was 20% (95% CI, 13%-29%) compared with 2% in the control arm (95% CI, 0%-7%). The partial response rate was 15% with the 2-drug combination arm vs 2% in the control arm, and the median duration of response for the experimental group was 6.1 months (range, 4.1-8.3) vs not reached (NR) in the control group (2.6-NR).[2]

REFERENCES

1. U.S. Food and Drug Administration (FDA) approves FoundationOne LiquidCDx as a companion diagnostic for Pfizer's Braftovi (encorafenib) in combination with cetuximab to identify patients with BRAF V600E alterations in metastatic colorectal cancer. News release. Foundation Medicine Inc. June 9, 2023. Accessed June 9, 2023. https://tinyurl.com/2p9568nx

2. Study of encorafenib + cetuximab plus or minus binimetinib vs. irinotecan/cetuximab or infusional 5-fluorouracil (5-FU)/folinic acid (FA)/irinotecan (FOLFIRI)/cetuximab with a safety lead-in of encorafenib + binimetinib + cetuximab in patients with BRAF V600E-mutant metastatic colorectal cancer (BEACON CRC). ClinicalTrials.gov. Updated May 6, 2023. Accessed June 9, 2023. https://clinicaltrials.gov/ct2/show/NCT02928224

ODAC (ONCOLOGIC DRUGS ADVISORY COMMITTEE) MEETING

New Drug and Biologic Products

The FDA's Oncologic Drugs Advisory Committee (ODAC) met on June 16, 2023, to discuss considerations for dose optimization of new drug and biological products for pediatric patients with cancer.

Considerations discussed during the meeting include the potential need for collecting and interpreting pharmacology data, using trial designs that compare multiple dosages of drugs, and further safety and tolerability assessments. Dosage optimization is an integral aspect of oncology drug development as it helps to maximize the safety, efficacy, and tolerability of new drugs, especially regarding pediatric patients with cancer. Currently, the majority of pediatric cancer drug development occurs with drugs being developed for adult patients with cancer.

A full report of the meeting is available online at TargetedOnc.com/link/2178.

REFERENCES

1. Oncologic Drugs Advisory Committee (ODAC) meeting. FDA. June 16, 2023. Accessed June 16, 2023. https://www.fda.gov/advisory-committees/advisory-committee-calendar/june-16-2023-pediatric-oncology-subcommittee-oncologic-drugs-advisory-committee-meeting-announcement

NEW DRUG APPLICATION

Nirogacestat (Ogsiveo)

The FDA has extended the Prescription Drug User Fee Act decision date by 3 months for the new drug application (NDA) seeking the approval of nirogacestat (Ogsiveo) in the treatment of adult patients with desmoid tumors, according to SpringWorks Therapeutics.[1]

In February 2023, the FDA granted priority review to the NDA and set an action date of August 27, 2023, based on findings from the phase 3 DeFi trial (NCT03785964).[2] In the study, treatment with nirogacestat reduced the risk of disease progression or death by 71% vs placebo in this patient population (HR, 0.29; 95% CI, 0.15-0.55; P < .001).

Among patients treated with nirogacestat (n = 70), the Kaplan-Meier-estimated median progression-free survival (PFS) could not be estimated as there were a low number of events. However, those who received placebo (n = 72) had a median PFS of 15.1 months (95% CI, 8.4-not estimable), and the likelihood of being event free at 1 year was higher for those who received

nirogacestat vs placebo, at 85% (95% CI, 73%-92%) and 53% (95% CI, 40%-64%), respectively. Moreover, the rates for being event free at 2 years were 76% (95% CI, 61%-87%) and 44% (95% CI, 32%-56%).[3]

REFERENCES

1. SpringWorks Therapeutics announces PDUFA date extension for nirogacestat NDA. News release. SpringWorks Therapeutics, Inc. June 5, 2023. Accessed June 13, 2023. https://tinyurl.com/5yeh3mck

2. SpringWorks Therapeutics announces FDA acceptance and priority review of new drug application for nirogacestat for the treatment of adults with desmoid tumors. News release. SpringWorks Therapeutics. February 27, 2023. Accessed June 12, 2023. https://tinyurl.com/237snj7n

3. Gounder M, Ratan R, Alcindor T, et al. Nirogacestat, a γ-secretase inhibitor for desmoid tumors. N Engl J Med. 2023;388(10):898-912. doi:10.1056/NEJMoa2210140

NALIRIFOX (liposomal irinotecan [Onivyde], 5-fluorouracil, leucovorin, and oxaliplatin

FDA has accepted a supplemental new drug application (sNDA) for NALIRIFOX (liposomal irinotecan [Onivyde], 5-fluorouracil, leucovorin, and oxaliplatin) as a first-line treatment for patients with metastatic pancreatic ductal adenocarcinoma (PDAC).[1]

Findings from the phase 3 NAPOLI 3 trial (NCT04083235) support the sNDA because treatment with NALIRIFOX led to a statistically significant improvement in overall survival (OS) and progression-free survival (PFS) vs nab-paclitaxel (Abraxane) plus gemcitabine in this patient population.[2]

At a median follow-up of 16.1 months (95% CI, 15.3-16.8), patients treated with NALIRIFOX (n = 383) had a median OS of 11.1 months (95% CI, 10.0-12.1) compared with 9.2 months (95% CI, 8.3-10.6) for those who received nab-paclitaxel and gemcitabine (n = 387; HR, 0.83; 95% CI, 0.70-0.99; P = .04). In the NALIRIFOX arm, the median PFS was 7.4 months (95% CI, 6.0-7.7) vs 5.6 months (95% CI, 5.3-5.8) in the nab-paclitaxel/gemcitabine arm (HR, 0.69; 95% CI, 0.58-0.83; P < .0001).[3]

REFERENCES

1. Ipsen announces US FDA submission acceptance of its supplemental new drug application for Onivyde regimen in first-line metastatic pancreatic ductal adenocarcinoma. News release. Ipsen Biopharmaceuticals. June 14, 2023. Accessed June 15, 2023. https://tinyurl.com/2my9cvyk

2. Wainberg ZA, Melisi D, Macarulla T, et al. NAPOLI 3: a randomized, open-label phase 3 study of liposomal irinotecan + 5-fluorouracil/leucovorin + oxaliplatin (NALIRIFOX) versus nab-paclitaxel + gemcitabine in treatment-naïve patients with metastatic pancreatic ductal adenocarcinoma. J Clin Oncol. 2023;41(suppl 4):LBA661. doi:10.1200/JCO.2023.41.3_suppl.LBA661

3. A study to assess the effectiveness and safety of irinotecan liposome injection, 5-fluorouracil/leucovorin plus oxaliplatin in patients not previously treated for metastatic pancreatic cancer, compared to nab-paclitaxel+gemcitabine treatment (NAPOLI 3). ClinicalTrials.gov. Updated March 13, 2023. Accessed June 15, 2023. https://clinicaltrials.gov/ct2/show/NCT04083235

BIOLOGICS LICENSE APPLICATION

Pembrolizumab (Keytruda)

The FDA has set a Prescription Drug User Fee Act target action date of February 7, 2024, to decide on the approval application for pembrolizumab (Keytruda) plus standard chemotherapy for advanced biliary tract cancer (BTC).[1]

The application is supported by results from the phase 3 KEYNOTE-966 study (NCT04003636).

The FDA has also accepted the supplemental biologics license application for the combination of pembrolizumab (Keytruda) and the standard-of-care (SOC) chemotherapy doublet, gemcitabine (Gemzar) and cisplatin (Platinol, Platinal–AQ), for the treatment of patients with locally advanced, unresectable, or metastatic BTC.

With the KEYNOTE-966 trial, a significant improvement in overall survival (OS) was achieved when pembrolizumab was added to SOC chemotherapy compared with SOC chemotherapy alone in patients with locally advanced,

unresectable, or metastatic BTC who received treatment in the first line.

Specifically, at a median follow-up of 25.6 months (range, 18.3-38.4), gemcitabine and cisplatin plus pembrolizumab achieved a 17% reduction in the risk of death as first-line treatment for patients with locally advanced, unresectable, or metastatic BTC compared with gemcitabine and cisplatin alone (HR, 0.83; 95% CI, 0.72-0.95; P = .0034). The median OS observed was 12.7 months (95% CI, 11.5-13.6) with the addition of pembrolizumab vs 10.9 months (95% CI, 9.9-11.6) without.[2]

REFERENCES

1. FDA accepts application for Merck's Keytruda (pembrolizumab) plus chemotherapy as treatment for advanced or unresectable biliary tract cancer. News release. Merck. June 8, 2023. Accessed June 9, 2023. https://tinyurl.com/ycxwjn29

2. 2. Merck's Keytruda (pembrolizumab) plus chemotherapy significantly improved overall survival compared to chemotherapy alone in patients with advanced or unresectable biliary tract cancer. News release. Merck, April 16, 2023. Accessed June 9, 2023. https://tinyurl.com/yarnm55x

Ciltacabtagene Autoleucel (cilta-cel ; Carvykti)

A biologics license application (BLA) has been submitted to the FDA for ciltacabtagene autoleucel (cilta-cel; Carvykti), a potential treatment option for adult patients with relapsed or refractory multiple myeloma (RRMM) who have received at least 1 prior line of therapy including a proteasome inhibitor, an immunomodulatory agent, and are refractory to lenalidomide (Revlimid) .[1]

The announcement of the BLA comes from the phase 3 CARTITUDE-4 study (NCT04181827). In the study, treatment with cilta-cel led to a significant improvement in progression-free survival (PFS) over standard-of-care (SOC) pomalidomide (Pomalyst), bortezomib (Velcade) and dexamethasone (PVd), or daratumumab (Darzalex) , pomalidomide, and dexamethasone (DPd), in patients with lenalidomide-refractory multiple myeloma who had received 1 to 3 prior lines of therapy.[2]

At a median follow-up of 15.9 months (range, 0.1-27), patients in the cilta-cel arm (n = 208) had a median PFS that was not yet reached (NR; 95% CI, 22.8 months-not estimable [NE]) compared with 11.8 months (95% CI, 9.7-13.8) in the SOC arm (n = 211; HR, 0.26; 95% CI, 0.18-0.38; P < .0001). The 12-month PFS rate was 76% in the cilta-cel arm vs 49% in the SOC arm.[2]

The PFS benefit was observed across all prespecified subgroups, including those with 1 prior line of treatment (HR, 0.35; 95% CI, 0.19-0.66) and those with 2 or 3 prior lines of therapy (HR, 0.24; 95% CI, 0.16-0.37).[2]

REFERENCES

1. Janssen submits supplemental biologics license application to U.S. FDA seeking approval of Carvykti for the earlier treatment of patients with relapsed or refractory multiple myeloma. News release. The Janssen Pharmaceutical Companies of Johnson & Johnson. June 6, 2023. Accessed June 7, 2023. https://shorturl.at/flyB4

2. Dhakal B, Yong K, Harrison SJ, et al. First phase 3 results from CARTITUDE-4: cilta-cel versus standard of care (PVd or DPd) in lenalidomide-refractory multiple myeloma. J Clin Oncol. 2023;41(suppl 17):LBA106. doi:10.1200/JCO.2023.41.17_suppl.LBA106

CHANGES IN LABELED INDICATIONS

Pralsetinib (Gavreto)

The changes relate to the inclusion of this drug for patients with RET fusion–positive thyroid cancer as well as the original use for those with RET fusion–positive thyroid cancer according to the ARROW study (NCT03037385).

REFERENCES

1. Drug safety-related labeling changes. FDA. Revised July 20, 2023. Accessed July 31, 2023. https://bit.ly/3rWZUzJ

Cabazitaxel (Jevtana Kit)

For male patients undergoing treatment with cabazitaxel (Jevtana Kit), and who have female partners, their partners should use effectual contraception during treatment and 4 months after the last dose.

REFERENCES

1. Drug safety-related labeling changes. FDA. Revised July 7, 2023. Accessed July 31, 2023. https://bit.ly/3OiPWAr