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NCOA ONCOLOGY DRUG NEWSLETTER

FDA APPROVALS

Capivasertib (Truqap) and Fulvestrant (Faslodex) Combination

The FDA granted approval to the combination of **capivasertib (Truqap)** and **fulvestrant (Faslodex)** for the treatment of adult patients with hormone receptor–positive, HER2-negative, locally advanced or metastatic breast cancer that harbors 1 or more PIK3CA, AKT1, or PTEN alterations as detected by an FDA-approved test following progression on 1 or more endocrine-based regimens in the metastatic setting or recurrence on or within 12 months of completing adjuvant therapy.[1]

Data from the phase 3 CAPItello-291 trial (NCT04305496) support this approval. Tumors of 289 patients had AKT pathway alterations. In all, among 155 patients in this group who were treated with the combination, the median progression-free survival (mPFS) was 7.3 months (95% CI, 5.5-9.0 months). In comparison, among 134 patients given placebo plus fulvestrant, the mPFS was 3.1 months (95% CI, 2.0-3.7 months) (hazard ratio, 0.50; 95% CI, 0.38-0.65; P=.0001).[1,2]

In the overall population, 335 patients were treated in the capivasertib arm; they had an mPFS of 7.2 months (95% CI, 5.5-7.4 months). In comparison, 353 patients treated with placebo plus fulvestrant had an mPFS of 3.6 months (95% CI, 2.8-3.7 months) (hazard ratio, 0.60; 95% CI, 0.51-0.71; P=.001).[2]

Enzalutamide (Xtandi)

Enzalutamide (Xtandi) received FDA approval for the treatment of patients with nonmetastatic castration-sensitive prostate cancer with high-risk biochemical recurrence. With this approval, it becomes the first

and only androgen receptor signaling inhibitor approved by the FDA for use in this population.[3]

The regulatory decision is supported by findings from the phase 3 EMBARK trial (NCT02319837), which demonstrated that enzalutamide plus the androgen deprivation therapy (ADT) leuprolide given to 355 patients reduced the risk of metastasis or death by 58% when compared with results among 358 patients given leuprolide alone (HR, 0.42; 95% CI, 0.30-0.61; P=.0001).[4,5]

At a median follow-up of 60.7 months for patients given the combination of enzalutamide plus ADT and 60.6 months for the placebo group, the median metastasis-free survival (MFS) was not reached (NR) (95% CI, NR to NR) with enzalutamide and NR (95% CI, 85.1 to NR) with placebo. At 3 years, the MFS rates in the enzalutamide plus ADT arm and in the placebo arm were 92.9% and 83.5%, respectively; the 5-year rates were 87.3% and 71.4%, respectively.

Pembrolizumab (Keytruda)

The FDA approved **pembrolizumab (Keytruda)** used with fluoropyrimidine- and platinum-containing

chemotherapy for the treatment of patients with locally advanced, unresectable, or metastatic gastric or gastroesophageal junction adenocarcinoma (GEJ).[6]

Findings from the phase 3 KEYNOTE-859 (NCT03675737) support this regulatory decision, as the combination demonstrated a significant improvement in overall survival (OS) vs chemotherapy alone. These results were independent of PD-L1 expression and were noted in patients who were HER2-negative (HER2–). The combination was previously approved for patients with HER2-positive gastric or GEJ adenocarcinoma.[7]

The randomized, double-blind study had an enrollment of approximately 1579 patients with HER2–, previously untreated, unresectable or metastatic gastric or GEJ adenocarcinoma. At a median follow-up of 31.0 months (range, 15.3-46.3 months), the median OS was 12.9 months (95% CI, 11.9-14.0 months) with pembrolizumab plus chemotherapy vs 11.5 months (95% CI, 10.6-12.1 months) with placebo plus chemotherapy (HR, 0.78, 95% CI, 0.70-0.87; P =.0001). The median PFS was 6.9 months (95% CI, 6.3-7.2 months) vs 5.6 months (95% CI, 5.5-5.7 months), respectively (HR, 0.76, 95% CI, 0.67-0.85; P=.0001). The survival results were consistent in the subgroup populations.

Repotrectinib (Augtyro)

The FDA granted approval to **repotrectinib (Augtyro)**, a tyrosine kinase inhibitor (TKI), for the treatment of patients with ROS1-positive, locally advanced or metastatic non–small cell lung cancer.[8]

Data from the phase 1/2 TRIDENT-1 study (NCT03093116) showed that patients who were TKI-naive or TKI-pretreated (including patients who had ROS1 resistance mutations and were treated with repotrectinib) had a high response rate and a clinically meaningful duration of response (DOR).[9]

After a median follow-up of 18.1 months for the TKI-naive patients, the overall response rate (ORR) was 78.9% (95% CI, 67.6%-87.7%), and the 12-month landmark DOR was 86.1%. For patients who were previously treated with 1 prior ROS1 TKI and no prior chemotherapy, the ORR was 37.5% (95% CI, 24.9%-51.5%) with a 6-month landmark DOR of 79.5% after a median follow-up of 15.5 months.[10]

Fruquintinib (HMPL-013; Fruzaqla)

The FDA approved **fruquintinib (HMPL-013; Fruzaqla)** for the treatment of patients with metastatic colorectal cancer (mCRC) who were previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy; an anti-VEGF therapy; and, if the tumor was RAS wild-type and it was medically appropriate, an anti-EGFR therapy.[11]

Data from the FRESCO-2 (NCT04322539) study showed that treatment with fruquintinib reduced the risk of death by 34% in patients with refractory mCRC; the median overall survival with fruquintinib plus best supportive care (BSC) was 7.4 months and with placebo plus BSC was 4.8 months, representing a significant improvement (HR, 0.66; 95% CI, 0.55-0.80; P=.0001).[12]

The randomized, double-blind, placebo-controlled, phase 3 study enrolled 691 patients with refractory mCRC. The median duration of treatment in the study was 11.3 months in the fruquintinib/BSC arm and 11.2 months in the placebo/BSC arm. The median progression-free survival (PFS) was 3.7 vs 1.8 months, respectively (HR, 0.32; 95% CI, 0.27-0.39; P=.001). At 6 months, the PFS was 24% vs 1%.13 For the other efficacy end points, use of fruquintinib resulted in an overall response rate of 1.5% vs 0%. Notably, the disease control rate with fruquintinib/BSC was 56%.

Pembrolizumab (Keytruda)

The FDA granted approval to **pembrolizumab (Keytruda)** combined with gemcitabine and cisplatin for the treatment of patients with locally advanced, unresectable or metastatic biliary tract cancer (BTC). Results from the phase 3 KEYNOTE-966 trial (NCT04003636) support the regulatory decision, as patients treated with the combination had significantly improved overall survival (OS) rates compared with patients given chemotherapy alone. The median OS was 12.7 months (95% CI, 11.5-13.6 months) among patients given pembrolizumab plus chemotherapy vs 10.9 months (95% CI, 9.9-11.6 months) for those treated with chemotherapy alone.[14]

KEYNOTE-966 is a multicenter, double-blind, randomized, placebo-controlled trial that enrolled 1069 patients with locally advanced, unresectable or metastatic BTC. Eligible patients had no prior systemic treatment for advanced disease. Once enrolled, patients were randomly assigned 1:1 to receive either intravenous placebo (n = 536) or 200 mg of pembrolizumab (n = 533) on day 1; members of each group also received 1000 mg/m^2 of gemcitabine and 25 mg/m2 of cisplatin on days 1 and 8 every 3 weeks.

According to previous data reported from the prespecified final analysis for PFS and objective response rate (ORR), pembrolizumab plus chemotherapy led to a numerical—but not statistically significant—improvement in PFS compared with chemotherapy alone in patients with BTC.[15]

In the pembrolizumab arm, the median PFS was 6.5 months (95% CI, 5.7-6.9 months) vs 5.6 months (95% CI, 5.1-6.6 months) with chemotherapy alone

(HR, 0.86; 95% CI, 0.75-1.00). The ORR in the pembrolizumab plus chemotherapy arm was 29% (95% CI, 25%-33%) vs 29% (95% CI, 25%-33%) among patients given chemotherapy alone. Of patients who responded to pembrolizumab with chemotherapy, 2.1% achieved a complete response (CR), and 27% experienced a partial response (PR). With chemotherapy alone, the rates of CR and PR were 1.3% and 27%, respectively. Patients received pembrolizumab for a median duration of 6 months (range, 1 day to 28 months).

Toripalimab-tpzi (Loqtorzi)

The FDA granted approval to combined use of **toripalimab-tpzi (Loqtorzi)** with cisplatin and gemcitabine for the first-line treatment of adult patients with metastatic or recurrent locally advanced nasopharyngeal carcinoma; this agent was also approved as a monotherapy for the treatment of adult patients with recurrent, unresectable, or metastatic nasopharyngeal carcinoma with disease progression during or after platinum-containing chemotherapy.[16]

Findings from the phase 3 JUPITER-02 trial (NCT03581786) and the phase 2 POLARIS-02 trial (NCT02915432) support this regulatory decision. Highlights from JUPITER-02 revealed that the first-line treatment combination of toripalimab with chemotherapy reduced the risk of disease progression or death by 48% vs chemotherapy alone (HR, 0.52; 95% CI, 0.36-0.74; P < .0003) in patients with recurrent or metastatic nasopharyngeal carcinoma.[17,18]

For progression-free survival (PFS) in JUPITER-02, benefits were observed irrespective of PD-L1 status. A median PFS of 11.7 months (95% CI, 11.0 months to not evaluable) was noted among 146 patients treated with the combination vs 8.0 months (95% CI, 7.0-9.5 months) among 143 patients in the control arm.

Ivosidenib (Tibsovo)

The FDA approved use of **ivosidenib (Tibsovo)** tablets for adult patients with relapsed/refractory myelodysplastic syndromes (R/R MDS) with a susceptible IDH1 mutation as detected by an FDA-approved test. Data from the open-label, single-arm, multicenter, AG120-C-001

(NCT02074839) trial, which included 18 adult patients with R/R MDS that harbored an IDH1 mutation, were the basis for this approval.[19]

All the responses observed among patients in the trial were complete responses (CRs). The CR rate was 38.9% (95% CI, 17.3%-64.3%), the median time to CR was 1.9 months (range, 1.0-5.6 months), and the median duration of CR was not estimable (range, 1.9-80.8 months or longer).

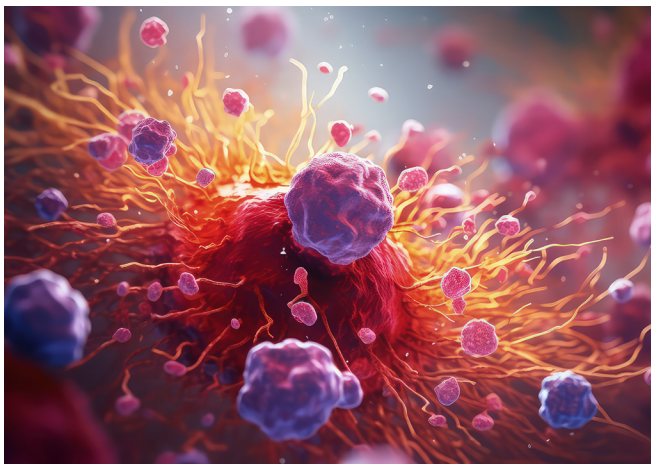
Enrollment was open to patients who were 18 years or older with documented IDH1 R132 gene–mutated, advanced hematologic malignancy based on local or central evaluation, and patients must be have been amenable to serial bone marrow biopsies, peripheral blood sampling, and urine sampling during the study.20 Patients had to have an ECOG performance status of 0 to 2, a platelet count of at least 20 × 103/μL or greater, and adequate hepatic and renal function; they also had to recover from any clinically relevant toxic effects of any prior surgery, radiotherapy, or other therapy intended to treat cancer.

The median treatment duration was 9.3 months.19 One patient underwent a stem cell transplant following treatment with ivosidenib. Efficacy was established by CR or partial remission (PR) rate, CR plus PR durations, and conversion rate from transfusion dependence to independence.

Entrectinib (Rozlytrek)

The FDA granted accelerated approval to **entrectinib (Rozlytrek)** for the treatment of pediatric patients 1 month and older with solid tumors that harbor a NTRK gene fusion without an acquired resistance mutation and that are metastatic; further, treatment is intended for those who are not favorable candidates for surgical resection and who have disease progression following treatment.[21]

The FDA accelerated approval program facilitates an advanced approval timeline for drugs that treat serious conditions or fill an unmet medical need. The approval is based on findings from the



phase 1/2 STARTRK-NG trial (NCT02650401) and the phase 2 TAPISTRY trial (NCT04589845). The efficacy of entrectinib was evaluated in 33 pediatric patients. The most common tumors among treated patients were primarily central nervous system tumors and infantile fibrosarcoma.[22,23]

NEW DRUG APPLICATION

Tovorafenib (DAY 101)

The FDA accepted the new drug application (NDA) for the oral, highly selective, type 2 RAF kinase inhibitor **tovorafenib (DAY 101)** as a single-agent treatment for patients with relapsed or progressive pediatric low-grade glioma, according to Day One Biopharmaceuticals.[24]

The NDA is based on findings from the open-label, phase 2 FIREFLY-1 trial (NCT04775485).[25] Among 69 evaluable patients treated with tovorafenib, an overall response rate of 67% per Response Assessment for Neuro-Oncology high-grade glioma (RANO-HGG) criteria was reached, along with a clinical benefit rate of 93%. This included a complete response rate of 17%, a partial response rate of 49%, and a stable disease rate of 26%. The median duration of response was 16.6 months (95% CI, 11.6 months to not estimable) per RANO-HGG criteria.

MB-109

The FDA accepted the investigational new drug application for **MB-109** for the treatment of recurrent glioblastoma multiforme (GBM) and high-grade astrocytoma, according to Mustang Bio.

MB-109 is a novel combination of MB-108 (used to reshape the tumor microenvironment and make cold tumors hot) and MB-101 (a chimeric antigen receptor T-cell therapy that targets interleukin 13 Rα2 [IL13Rα2]). With this acceptance, a phase 1 multicenter clinical trial at City of Hope and the University of Alabama at Birmingham will begin to assess the safety, tolerability, and efficacy of MB-109 in adult patients with recurrent GBM and high-grade astrocytomas that express IL13Rα2 on the surface of the tumor cells.[26]

BIOLOGICS LICENSE APPLICATION

N-803 (Anktiva) Plus Bacillus Calmette-Guérin

The FDA accepted the biologics license application resubmission for **N-803 (Anktiva)** and **Bacillus Calmette-Guérin (BCG)** for the treatment of BCG-unresponsive, non–muscle invasive bladder cancer (NMIBC) in situ with or without Ta or T1 disease. The FDA has issued a target action date of April 23, 2024.[27]

Two clinical trials are evaluating N-803 and BCG for the treatment of NMIBC.

QUILT-2.005 (NCT02138734) is a phase 1/2 trial investigating N-803 and BCG in patients with BCG-naive NMIBC.[28] The trial has an estimated enrollment of 596 patients. The primary end points are complete response and disease-free survival. The secondary end points are progression-free survival, overall survival, disease-specific survival, time to disease worsening, time to cystectomy, and safety profile. There is also the phase 2/3 QUILT-3.032 trial (NCT03022825) in patients with BCG-unresponsive NMIBC.

FAST TRACK DESIGNATION

SLS009 (formerly GFH009)

The FDA granted **SLS009 (formerly GFH009)**, a novel CDK9 inhibitor, a fast track designation from the FDA for the treatment of relapsed or refractory peripheral T-cell lymphomas (R/R PTCLs), according to SELLAS Life Sciences Group. The fast track designation is designed to expedite the development of investigational agents that fill a serious, unmet medical need. [29]

A phase 1 dose-escalation trial of SLS009 in R/R hematologic malignancies was recently completed. Four of 11 patients (36.4%) with acute myeloid leukemia or PTCL had complete or partial responses. Belinostat (Beleodaq), the current standard-of-care treatment for PTCL, demonstrated a 25.8% response rate in a similar patient population.

An open-label, single-arm, phase 1b/2 trial (NCT05934513) of SLS009 will further evaluate its safety and efficacy in patients with R/R PTCL. The recommended phase 2 dose is 100 mg given once weekly. This study will enroll up to 95 patients. The primary end points are adverse events in phase 1b and objective response rate in phase 2.[30]

ONCT-534

The FDA gave **ONCT-534** a fast track designation for the treatment of patients with relapsed or refractory, metastatic, castration-resistant prostate cancer that is resistant to androgen receptor (AR) pathway inhibitors. ONCT-534 interacts with the N-terminal and ligand-binding domains of ARs to inhibit cell growth and induce AR degradation. Preclinical data of ONCT-534 show activity in prostate cancer models against unmutated and mutated ARs.[31]

ONCT-534 is being investigated in a phase 1/2 study (NCT05917470) with an estimated enrollment of 59 patients. Phase 1 investigators are investigating the maximum tolerated dose (MTD) of ONCT-534, and phase 2 investigators are evaluating the agent's antitumor activity at tolerable doses.[32]

The trial's primary end points are MTD of ONCT-534, safety and tolerability, reduction of prostate-specific antigen (PSA) level by more than 50% and time to this reduction, reduction of PSA level by more than 90% and time to this reduction, overall response rate, complete response rate, duration

of response, and progression-free survival. Secondary end points include maximum plasma concentration, area under the curve, and antitumor activity with the AR phenotype.

ORPHAN DRUG DESIGNATION

TTX101

The FDA granted an orphan drug designation (ODD) to the nanoformed drug candidate **TTX101** for potential use in patients with malignant gliomas.[33] TTX101 uses a hydrogel nanoformulation and enables a 200-fold increase in drug load compared with bulk and a 5-fold increase in drug load compared with nanomilling. This agent is designed to release the active substance over a period of weeks to cover the wound healing period between surgery and radiotherapy.[34] This ODD for TTX101 follows the generation of preclinical data that showed a survival advantage with use of this nanoform-enabled medicine candidate.[33]

CLINICAL HOLD UPDATE

NX-2127

The FDA placed a partial clinical hold on the phase 1 **NX-2127-001** study (NCT04830137) of NX-2127 for the treatment of various B-cell malignancies. The placement of this hold follows Nurix Therapeutics' communication with the FDA regarding its intention to transition to an improved manufacturing process.[35]

Roginolisib (IOA-244)

The FDA granted permission for clinical investigations of **roginolisib (IOA-244)** in the United States to proceed, according to iOnctura. Roginolisib is currently being developed for patients with solid and hematologic malignancies, including uveal melanoma. Roginolisib is the first novel allosteric modulator of PI3K; its high selectivity for PI3Kδ and unique binding mode may offer greater safety and tolerability than do earlier generation inhibitors.[36]

CHANGES IN LABELED INDICATIONS

Tbo-filgrastim (Granix)

Tbo-filgrastim treatment is approved for use in adults and children 1 month and older. Before starting tbo-filgrastim treatment, the diagnosis of severe chronic neutropenia (SCN) must be confirmed. In cases of congenital neutropenia, there have been instances of

myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML) occurring naturally, even without cytokine therapy. Patients treated with tbo-filgrastim for SCN have shown cytogenetic abnormalities, transformations to MDS, and AML. However, available data suggest that the risk of developing MDS and AML appears to be specific to patients with congenital neutropenia. Abnormal cytogenetics and MDS have been linked to the eventual development of myeloid leukemia.[37]

The impact of tbo-filgrastim on the development of abnormal cytogenetics and the continuation of tbo-filgrastim treatment in patients with abnormal cytogenetics or MDS remains unknown. Therefore, patients in such scenarios must be monitored for signs and symptoms of MDS/AML. Careful consideration should be given to the risks and benefits of continuing tbo-filgrastim treatment if a patient diagnosed with SCN exhibits abnormal cytogenetics or myelodysplasia.

Please refer to the drug label update for further information.

Nab-Paclitaxel (Abraxane)

The safety and efficacy of paclitaxel protein-bound particles for injectable suspension (albumin-bound) (nab-paclitaxel) in pediatric patients have not been established. In an open-label, dose escalation, and dose expansion study (NCT01962103) involving 96 patients with recurrent or refractory pediatric solid tumors, the pharmacokinetics, safety, and antitumor activity of the medication were evaluated. No new safety concerns were identified in these pediatric studies.[38] In addition, pediatric patients had greater

exposure of nab-paclitaxel normalized by dose than did the adults.

Cyclophosphamide (Cytoxan)

Clinical studies and postmarketing reports have highlighted certain adverse events (AEs) linked to the use of cyclophosphamide. Due to the voluntary reporting of these reactions from a population of uncertain size, accurate estimation of their frequency or establishment of a direct link to drug exposure may be challenging.[39]

Among the most prevalent AEs reported were neutropenia, febrile neutropenia, fever, alopecia, nausea, vomiting, and diarrhea. Gastrointestinal-related AEs now include vomiting, nausea, and diarrhea; general disorders now include febrile neutropenia, according to the latest updates.

The inclusion of etanercept alongside cyclophosphamide treatment resulted in an increased occurrence of noncutaneous malignant solid tumors among patients diagnosed with Wegener granulomatosis.

Fatal harm can develop from cyclophosphamide injection when administered to pregnant women.

Consider the alcohol content present in cyclophosphamide injection when using in patients with hepatic impairment.

Advise the patient about possible bone marrow failure and to inform the physician about known or suspected pregnancy.

Triptorelin Pamoate (Trelstar)

Use of gonadotropin-releasing hormone (GnRH) agonists can result in metabolic alterations (eg, hyperglycemia, diabetes mellitus, hyperlipidemia). Postmarketing data for triptorelin reported nonalcoholic fatty liver disease, including cirrhosis, associated with use of these drugs. Regularly observe patients receiving a GnRH agonist for alterations in serum lipids and blood glucose levels and address these changes following institutional protocols. In most patients, there was an initial rise in testosterone levels above baseline that was followed by a subsequent decline to castrate levels (< 50 ng/dL) within a span of 4 weeks.40

Please refer to the drug label update for further information on treatment-related adverse events related to use of triptorelin.

Tazemetostat (Tazverik)

The safety profile of tazemetostat was assessed in cohorts 4 and 5 of the E7438-G000-101 study (NCT01897571), which included patients with relapsed or refractory follicular lymphoma. In all, 99 patients were given tazemetostat, 800 mg, orally twice daily. Among these patients, 68% were exposed for 6 months or more, 39% for 12 months or more, and 21% for 18 months or more.[41]

The median age of participants was 62 years (range, 36-87 years); 54% of the patients were male, and 95% had an ECOG performance status of 0 or 1. The median number of prior therapies was 3 (range, 1-11 therapies). Patients were required to have a creatinine clearance of at least 40 mL/min according to the Cockcroft and Gault formula.

Please refer the drug label update for further information on treatment related adverse events tazemetostat hydrobromide.

Enzalutamide (Xtandi)

Additional information now appears for adverse events related to the use of enzalutamide, including muscle pain, unusual fatigue, bleeding issues, falls, fractures of the bone, and headaches. Other updates to the trials evaluating enzalutamide can be found on the drug label update.[42]

Methotrexate Sodium (preservative-free)

Updates include additional experiences observed, such as injection-site necrosis and reaction.[43]

Pembrolizumab (Keytruda)

The safety profile of pembrolizumab was assessed in 1572 patients with HER2-negative (HER2–) gastric or gastroesophageal junction (GEJ) cancer enrolled in the KEYNOTE-859 (NCT03675737) study. This study included 785 patients treated with pembrolizumab, 200 mg, given in combination with FP (fluorouracil plus cisplatin) (n = 106) or CAPOX (capecitabine [Xeloda] plus oxaliplatin [Eloxatin]) (n = 674) every 3 weeks; outcomes were compared with those noted in 787 patients who received placebo and FP (n = 107) or CAPOX (n = 679) every 3 weeks [refer to Clinical Studies (14.9)]. The median duration of exposure to pembrolizumab was 6.2 months.[44]

Please refer the drug label update for further information regarding the KEYNOTE-859 trial updates evaluating pembrolizumab in patients with HER2– gastric or GEJ cancer.

Asciminib (Scemblix)

Asciminib is an inhibitor of OATP1B and BCRP. The impact of simultaneously using asciminib with OATP1B and BCRP substrates has not been determined in clinical studies. Nevertheless, based on the understanding of the elimination mechanism of asciminib and its inhibitory potential in vitro, concurrent use of asciminib elevates the maximum concentration and area under the curve of OATP1B and BCRP substrates, thereby potentially increasing the risk of adverse events (AEs) associated with these substrates.[45]

It is advisable to avoid administering asciminib at all recommended doses with rosuvastatin and atorvastatin (Lipitor). Vigilantly monitor for AEs in patients receiving asciminib at all recommended doses who are using other OATP1B or BCRP substrates concurrently. When used alongside asciminib at all recommended doses, consider reducing the dosage of other OATP1B or BCRP substrates in accordance with the recommendations provided in their prescribing information.

Olaparib (Lynparza)

In the updated analysis of results from the SOLO-1 trial (NCT01844986) involving patients diagnosed with newly advanced BRCA mutated ovarian cancer, the incidence of myelodysplastic syndrome/acute myeloid leukemia (MDS/AML) was 1.9% among those given olaparib compared with an incidence of 0.8% among the placebo group. Similarly, in the PAOLA-1 trial (NCT02477644), among patients diagnosed with newly advanced ovarian cancer with homologous recombination deficiency–positive status, the incidence of MDS/AML was 1.6% for individuals treated with olaparib and 2.3% among those in the control arm.[46]

In the SOLO2 trial (NCT01874353) involving patients with BRCA-mutated, platinum-sensitive, relapsed ovarian cancer, the incidence of MDS/AML was 8% for those receiving olaparib vs 4% among the placebo group. The duration of olaparib treatment before the diagnosis of MDS/AML varied from 0.6 to 4.5 years.

Larotrectinib (Vitrakvi)

Patients receiving larotrectinib (Vitrakvi) have experienced hepatotoxicity, including drug-induced liver injury, including in individuals experiencing increases (grade 2 or greater) of alanine aminotransferase and/or aspartate aminotransferase and bilirubin levels. It is important to conduct liver function tests prior to initiation and to monitor them throughout larotrectinib treatment. If increases in liver function values occur, a dose reduction or temporary hold is recommended.[47]

Ripretinib (Qinlock)

In the INVICTUS trial (NCT03353753), adverse events reported in less than 10% of patients receiving ripretinib include sensory neuropathy, dermatitis acneiform, and rash. Photosensitivity is also a potential risk in patients receiving ripretinib.[48]

Ivosidenib (Tibsovo)

In the monotherapy clinical trial AG120-C-001 (NCT02074839), 11% of patients diagnosed with relapsed or refractory myelodysplastic syndrome and treated with ivosidenib (Tibsovo) encountered

differentiation syndrome. Both patients who experienced differentiation syndrome recovered after receiving treatment or following a pause in ivosidenib dosage. Differentiation syndrome was observed in some patients as early as 1 day after the initiation of ivosidenib; it persisted for up to 3 months. This syndrome manifested irrespective of concomitant leukocytosis in some instances.[49]

Please refer the drug label update for further information.

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