Indication
KISQALI® (ribociclib) is indicated in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.

Important Safety Information

**QT interval prolongation.** KISQALI has been shown to prolong the QT interval in a concentration-dependent manner, with estimated mean increase in QTc interval exceeding 20 ms (22.9 ms [90% CI: 21.6-24.1]) at the mean steady-state C\textsubscript{max} following administration at the 600-mg once-daily dose. In MONALEESA-2, one patient (0.3%) had >500 msec postbaseline QTcF value (average of triplicate), and 9 of 329 patients (3.0%) had a >60 msec increase from baseline in QTcF intervals (average of triplicate). These electrocardiogram (ECG) changes occurred within the first 4 weeks of treatment and were reversible with dose interruption. There were no reported cases of Torsades de Pointes. Syncope occurred in 9 patients (2.7%) in the KISQALI + letrozole arm vs 3 patients (0.9%) in the placebo arm. In the KISQALI + letrozole treatment arm, there was 1 (0.3%) sudden death in a patient with grade 3 hypokalemia and grade 2 QT prolongation.

Assess ECG prior to initiation of treatment. Initiate treatment with KISQALI only in patients with QTcF values <450 msec. Repeat ECG at approximately day 14 of the first cycle, at the beginning of the second cycle, and as clinically indicated. Monitor serum electrolytes (including potassium, calcium, phosphorus, and magnesium) prior to the initiation of treatment, at the beginning of each of the first 6 cycles, and as clinically indicated. Correct any abnormality before starting therapy with KISQALI.

Avoid the use of KISQALI in patients who already have or who are at significant risk of developing QTc prolongation, including patients with:
- long QT syndrome
- uncontrolled or significant cardiac disease including recent myocardial infarction, congestive heart failure, unstable angina, and bradyarrhythmias
- electrolyte abnormalities

Avoid using KISQALI with drugs known to prolong the QTc interval and/or strong CYP3A inhibitors, as this may lead to prolongation of the QTcF interval. Based on the observed QT prolongation during treatment, KISQALI may require dose interruption, reduction, or discontinuation.

**Hepatobiliary toxicity.** In MONALEESA-2, increases in transaminases were observed. Grade 3 or 4 increases in alanine aminotransferase (ALT) (10% vs 1%) and aspartate aminotransferase (AST) (7% vs 2%) were reported in the KISQALI and placebo arms, respectively.

Among the patients who had grade ≥3 ALT/AST elevation, the median time to onset was 57 days for the KISQALI + letrozole treatment group. The median time to resolution to grade ≤2 was 24 days in the KISQALI + letrozole treatment group.

Concurrent elevations in ALT or AST >3 times the upper limit of normal (ULN) and total bilirubin >2 times the ULN, with normal alkaline phosphatase, in the absence of cholestasis occurred in 4 patients (1%) in MONALEESA-2, and all patients recovered after discontinuation of KISQALI.
Perform liver function tests (LFTs) before initiating therapy with KISQALI. Monitor LFTs every 2 weeks for the first 2 cycles, at the beginning of each of the subsequent 4 cycles, and as clinically indicated. Based on the severity of the transaminase elevations, KISQALI may require dose interruption, reduction, or discontinuation. Recommendations for patients who have elevated AST/ALT grade ≥3 at baseline have not been established.

Neutropenia. In MONALEESA-2, neutropenia was the most frequently reported adverse reaction (AR) (75%), and a grade 3/4 decrease in neutrophil count (based on laboratory findings) was reported in 60% of patients receiving KISQALI + letrozole. Among the patients who had grade 2, 3, or 4 neutropenia, the median time to grade ≥2 was 16 days. The median time to resolution of grade ≥3 (to normalization or grade <3) was 15 days in the KISQALI + letrozole treatment group. Febrile neutropenia was reported in 1.5% of patients receiving KISQALI and letrozole. Treatment discontinuation due to neutropenia was 0.9%.

Perform complete blood count (CBC) before initiating therapy with KISQALI. Monitor CBC every 2 weeks for the first 2 cycles, at the beginning of each of the subsequent 4 cycles, and as clinically indicated. Based on the severity of the neutropenia, KISQALI may require dose interruption, reduction, or discontinuation.

Embryo-fetal toxicity. Based on findings from animal studies and the mechanism of action, KISQALI can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, administration of KISQALI to pregnant rats and rabbits during organogenesis caused embryo-fetal toxicities at maternal exposures that were 0.6 and 1.5 times the human clinical exposure, respectively, based on area under the curve. Advise pregnant women of the potential risk to a fetus. Advise women of reproductive potential to use effective contraception during therapy with KISQALI and for at least 3 weeks after the last dose.

Adverse reactions. The most common ARs reported in the KISQALI + letrozole arm (frequency ≥20%) were neutropenia (75%), nausea (52%), fatigue (37%), diarrhea (35%), leukopenia (33%), alopecia (33%), vomiting (29%), constipation (25%), headache (22%), and back pain (20%). The most common grade 3/4 ARs (reported at a frequency >2%) were neutropenia (60%), leukopenia (21%), abnormal LFTs (10%), lymphopenia (7%), and vomiting (4%).

Laboratory abnormalities. The most common laboratory abnormalities occurring in patients receiving KISQALI + letrozole (all grades, incidence ≥20%) were leukocyte count decrease (93%), neutrophil count decrease (93%), hemoglobin decrease (57%), lymphocyte count decrease (51%), ALT increase (46%), AST increase (44%), platelet count decrease (29%), and creatinine increase (20%). The most common grade 3/4 laboratory abnormalities (incidence >2%) were neutrophil count decrease (60%), leukocyte count decrease (34%), lymphocyte count decrease (14%), ALT increase (10%), AST increase (7%), and phosphorus decrease (6%).

AI=aromatase inhibitor; CDK=cyclin-dependent kinase;
FDA=U.S. Food and Drug Administration.

For more information, contact your local Novartis representative or visit KISQALI.com.

Please see Brief Summary of Prescribing Information on adjacent pages.
KISQALI® (ribociclib) tablets, for oral use
Initial U.S. Approval: 2017

BRIEF SUMMARY: Please see package insert for full prescribing information.

1 INDICATIONS AND USAGE
KISQALI® is indicated in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.

4 CONTRAINDICATIONS
None.

5 WARNINGS AND PRECAUTIONS
5.1 QT Interval Prolongation
KISQALI® has been shown to prolong the QT interval in a concentration-dependent manner, with estimated mean increase in QTc interval exceeding 20 ms (22.9 ms [90% CI: 21.6, 24.1]) at the mean steady-state C_{ss} following administration at 800 mg once daily dose [see Clinical Pharmacology (12.2) in the full prescribing information]. In Study 1 (MONALEESA-2), one patient (0.3%) had >500 msec post-baseline QTcF value (average of triplicate), and nine patients out of 329 patients (3%) had a >60 msec increase from baseline in QTcF intervals (average of triplicate). These ECG changes occurred within the first four weeks of treatment and were reversible with dose interruption. There were no reported cases of Torsades de Pointes. Syncope occurred in 9 patients (2.7%) in the KISQALI plus letrozole arm versus 3 (0.9%) in placebo plus letrozole arm. On the KISQALI plus letrozole treatment group, there was one (0.3%) sudden death in a patient with Grade 3 hypokalemia and Grade 2 QT prolongation [see Adverse Reactions (6)].

Assess ECG prior to initiation of treatment. Initiate treatment with KISQALI only in patients with QTcF values less than 450 msec. Repeat ECG at approximately Day 14 of the first cycle and the beginning of the second cycle, and as clinically indicated.

Monitor serum electrolytes (including potassium, calcium, phosphorus and magnesium) prior to the initiation of treatment, at the beginning of the first 6 cycles, and as clinically indicated. Correct any abnormality before starting KISQALI therapy [see Dosage and Administration (2.2) in the full prescribing information].

Avoid the use of KISQALI in patients who already have or who are at significant risk of developing QTc prolongation, including patients with:
- long QT syndrome
- uncontrolled or significant cardiac disease including recent myocardial infarction, congestive heart failure, unstable angina and bradyarrhythmias
- electrolyte abnormalities

Avoid using KISQALI with drugs known to prolong QTc interval and/or strong CYP3A inhibitors as this may lead to prolongation of the QTc interval [see Clinical Pharmacology (12.3) in the full prescribing information].

Based on the observed QT prolongation during treatment, KISQALI may require dose interruption, reduction or discontinuation as described in Table 4 [see Dosage and Administration (2.2) in the full prescribing information and Drug Interactions (7.4)].

5.2 Hepatobiliary Toxicity
In Study 1, increases in transaminases were observed. Grade 3 or 4 increases in ALT (10% versus 1%) and AST (7% versus 2%) were reported in the KISQALI and placebo arms, respectively.

Among the patients who had Grade ≥ 3 ALT/AST elevation, the median time-to-onset was 57 days for the KISQALI plus letrozole treatment group. The median time to resolution to Grade < 3 was 24 days in the KISQALI plus letrozole treatment group.

Concurrent elevations in ALT or AST greater than three times the ULN and total bilirubin greater than two times the ULN, with normal alkaline phosphatase, in the absence of cholestasis occurred in 4 (1%) patients in Study 1 and all patients recovered after discontinuation of KISQALI.

Perform LFTs before initiating therapy with KISQALI. Monitor LFTs every 2 weeks for first 2 cycles, at the beginning of each subsequent 4 cycles, and as clinically indicated [see Dosage and Administration (2.2) in the full prescribing information].

Based on the severity of the transaminase elevations, KISQALI may require dose interruption, reduction, or discontinuation as described in Table 3 (Dose Modification and Management for Hepatobiliary Toxicity) [see Dosage and Administration (2.2) in the full prescribing information]. Recommendations for patients who have elevated AST/ALT Grade ≥ 3 at baseline have not been established.

5.3 Neutropenia
In Study 1, neutropenia was the most frequently reported adverse reaction (75%) and a Grade 3/4 decrease in neutrophil count (based on laboratory findings) was reported in 60% of patients receiving KISQALI plus letrozole. Among the patients who had Grade 2, 3, or 4 neutropenia, the median time to Grade ≥ 2 neutropenia was 16 days. The median time to resolution of Grade ≥ 3 neutropenia (to normalization or Grade < 3) was 15 days in the KISQALI plus letrozole treatment group. Febrile neutropenia was reported in 1.5% of patients receiving KISQALI and letrozole. Treatment discontinuation due to neutropenia was 0.9%.

Perform CBC before initiating therapy with KISQALI. Monitor CBC every 2 weeks for the first 2 cycles, at the beginning of each subsequent 4 cycles, and as clinically indicated.

Based on the severity of the neutropenia, KISQALI may require dose interruption, reduction or discontinuation as described in Table 2 [see Dosage and Administration (2.2) in the full prescribing information].

5.4 Embryo-Fetal Toxicity
Based on findings from animal studies and the mechanism of action, KISQALI can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, administration of ribociclib to pregnant rats and rabbits during organogenesis caused embryo-fetal toxicities at maternal exposures that were 0.6 and 1.5 times the human clinical exposure, respectively, based on area under the curve (AUC). Advise pregnant women of the potential risk to a fetus. Advise women of reproductive potential to use effective contraception during therapy with KISQALI and for at least 3 weeks after the last dose [see Use in Specific Population (8.1, 8.3) and Clinical Pharmacology (12.1) in the full prescribing information].

6 ADVERSE REACTIONS
The following adverse reactions are discussed in greater detail in other sections of the labeling:
- QT Interval Prolongation [see Warnings and Precautions (5.1)]
- Hepatobiliary Toxicity [see Warnings and Precautions (5.2)]
- Neutropenia [see Warnings and Precautions (5.3)]

6.1 Clinical Trial Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety data reported below are based on Study 1 (MONALEESA-2), a clinical study of 668 postmenopausal women receiving KISQALI plus letrozole or placebo plus letrozole. The median duration of exposure to the KISQALI plus letrozole was 13 months with 58% of patients exposed for ≥ 12 months.

Dose reductions due to adverse reactions (ARs) occurred in 45% of patients receiving KISQALI plus letrozole and in 3% of patients receiving placebo plus letrozole. Permanent discontinuations due to ARs were reported in 7% of patients receiving KISQALI plus letrozole and 2% in patients receiving placebo plus letrozole. The most common ARs leading to treatment discontinuation of KISQALI in patients receiving KISQALI plus letrozole were ALT increased (4%), AST increased (3%), vomiting (2%). Antiemetics and anti-diarrhea medications were used to manage symptoms as clinically indicated.

On-treatment deaths, regardless of causality, were reported in three cases (0.9%) of KISQALI plus letrozole treated patients vs. one case (0.3%) of placebo plus letrozole treated patients. Causes of death on KISQALI plus letrozole included one case each of the following: progressive disease, death (cause unknown), and sudden death (in the setting of Grade 3 hypokalemia and Grade 2 QT prolongation).

The most common ARs (reported at a frequency ≥ 20%) were neutropenia, nausea, fatigue, diarrhea, leukopenia, alopecia, vomiting, constipation, headache and back pain.

The most common Grade 3/4 ARs (reported at a frequency ≥ 2%) were neutropenia, leukopenia, abnormal liver function tests, lymphopenia, and vomiting.

ARs and laboratory abnormalities occurring in patients in Study 1 are listed in Table 6 and Table 7, respectively.
### Table 7: Laboratory Abnormalities Occurring in ≥ 10% of Patients in Study 1

<table>
<thead>
<tr>
<th>Laboratory parameters</th>
<th>KISQALI + Letrozole (N=334)</th>
<th>Placebo + Letrozole (N=330)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades %</td>
<td>Grade 3 %</td>
</tr>
<tr>
<td><strong>HEMATOLOGY</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukocyte count decreased</td>
<td>93</td>
<td>31</td>
</tr>
<tr>
<td>Neutrophil count decreased</td>
<td>93</td>
<td>49</td>
</tr>
<tr>
<td>Hemoglobin decreased</td>
<td>57</td>
<td>2</td>
</tr>
<tr>
<td>Lymphocyte count decreased</td>
<td>51</td>
<td>12</td>
</tr>
<tr>
<td>Platelet count decreased</td>
<td>29</td>
<td>1</td>
</tr>
</tbody>
</table>

### Table 8: Adverse Reactions Occurring in ≥ 10% and ≥ 2% higher than Placebo Arm in Study 1 (All Grades)

<table>
<thead>
<tr>
<th>Adverse drug reactions</th>
<th>KISQALI + Letrozole (N=334)</th>
<th>Placebo + Letrozole (N=330)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades %</td>
<td>Grade 3 %</td>
</tr>
<tr>
<td>Infections and Infestations</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>22</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>12</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>12</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>33</td>
<td>0</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>37</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Abnormal liver function tests</td>
<td>18</td>
<td>8</td>
</tr>
</tbody>
</table>

Grading according to CTC AE 4.03 (Common Terminology Criteria for Adverse Events)

1 abnormal liver function tests: ALT increased, AST increased, blood bilirubin increased

---

7 **DRUG INTERACTIONS**

7.1 Drugs That May Increase Ribociclib Plasma Concentrations

CYP3A4 Inhibitors

Coadministration of a strong CYP3A4 inhibitor (ritonavir) increased ribociclib exposure in healthy subjects by 3.2-fold [see Clinical Pharmacology (12.3) in the full prescribing information]. Avoid concomitant use of strong CYP3A4 inhibitors (e.g., boceprevir, clarithromycin, conivaptan, grapefruit juice, indinavir, itraconazole, ketoconazole, lopinavir/ritonavir, nefazodone, nefavir, posaconazole, ritonavir, saquinavir, and voriconazole) and consider alternative concomitant medications with less potential for CYP3A4 inhibition.

If coadministration of KISQALI with a strong CYP3A4 inhibitor cannot be avoided, reduce the dose of KISQALI to 400 mg once daily [see Dosage and Administration (2.2) in the full prescribing information].

Instruct patients to avoid pomegranate or pomegranate juice, grapefruit, all of which are known to inhibit cytochrome CYP3A enzymes and may increase the exposure to ribociclib [see Patient Counseling Information (17) in the full prescribing information].

7.2 Drugs That May Decrease Ribociclib Plasma Concentrations

CYP3A4 Inducers

Coadministration of a strong CYP3A4 inducer (rifampin) decreased the plasma exposure of ribociclib in healthy subjects by 89% [see Clinical Pharmacology (12.3) in the full prescribing information]. Avoid concomitant use of strong CYP3A4 inducers and consider an alternate concomitant medication with no or minimal potential to induce CYP3A (e.g., phenytoin, rifampin, carbamazepine and St John’s Wort [Hypericum perforatum]).

7.3 Effect of KISQALI on Other Drugs

CYP3A substrates with narrow therapeutic index

Co-administration of midazolam (a sensitive CYP3A4 substrate) with multiple doses of KISQALI (400 mg) increased the midazolam exposure by 3.8-fold in healthy subjects, compared with administration of midazolam alone [see Clinical Pharmacology (12.3) in the full prescribing information]. KISQALI given at the clinically relevant dose of 600 mg is predicted to increase the midazolam AUC by 5.2-fold. Therefore, caution is recommended when KISQALI is administered with CYP3A substrates with a narrow therapeutic index. The dose of a sensitive CYP3A substrate with a narrow therapeutic index, including but not limited to alfentanil, cyclosporine, dihydroergotamine, ergotamine, everolimus, fentanyl, pimozide, quinidine, sirolimus and tacrolimus, may need to be reduced as ribociclib can increase their exposure.

7.4 Drugs That Prolong the QT Interval

Avoid coadministration of KISQALI with medicinal products with a known potential to prolong QT such as antiarrhythmic medicines (including, but not limited to, amiodarone, disopyramide, procainamide, quinidine and sotalol), and other drugs that are known to prolong the QT interval (including, but not limited to, chloroquine, halofantrine, clarithromycin, haloperidol, methadone, moxifloxacin, bepridil, pimozide and ondansetron (i.v)) [see Warnings and Precautions (5.1) and Clinical Pharmacology (12.3) in the full prescribing information].

8 **USE IN SPECIFIC POPULATIONS**

8.1 Pregnancy

Risk Summary

Based on findings from animal studies and the mechanism of action, KISQALI can cause fetal harm when administered to a pregnant woman [see Clinical Pharmacology (12.1) in the full prescribing information].
There are no available human data informing the drug-associated risk. In animal reproduction studies, administration of ribociclib to pregnant animals during organogenesis resulted in increased incidences of postimplantation loss and reduced fetal weights in rats and increased incidences of fetal abnormalities in rabbits at exposures 0.6 or 1.5 times the exposure in humans, respectively, at the highest recommended dose of 600 mg/day based on AUC [see Data]. Advise pregnant women of the potential risk to a fetus.

The background risk of major birth defects and miscarriage for the indicated population is unknown. However, the background risk of major birth defects is 2-4% and of miscarriage is 15-20% of clinically recognized pregnancies in the U.S. general population.

Data

Animal Data

In embryo-fetal development studies in rats and rabbits, pregnant animals received oral doses of ribociclib up to 1000 mg/kg/day and 60 mg/kg/day, respectively, during the period of organogenesis.

In rats, 300 mg/kg/day resulted in reduced maternal body weight gain and reduced fetal weights accompanied by skeletal changes related to the lower fetal weights. There were no significant effects on embryo-fetal viability or fetal morphology at 50 or 300 mg/kg/day.

In rabbits at doses ≥ 30 mg/kg/day, there were adverse effects on embryo-fetal development including increased incidences of fetal abnormalities (malformations and external, visceral and skeletal variants) and fetal growth (lower fetal weights). These findings included reduced/small lung lobes, additional vessel on the aortic arch, small eyes, diaphragmatic hernia, absent accessory lobe or (partly) fused lung lobes, reduced/small accessory lung lobe, extra/rudimentary 13th ribs, misshapen hyoid bone, bent hyoid bone alae, and reduced number of phalanges in the pollex. There was no evidence of increased incidence of embryo-fetal mortality. There was no maternal toxicity observed at 30 mg/kg/day.

At 300 mg/kg/day in rats and 30 mg/kg/day in rabbits, the maternal systemic exposures (AUC) were approximately 0.6 and 1.5 times, respectively, the exposure in patients at the highest recommended dose of 600 mg/day.

8.2 Lactation

Risk Summary

It is not known if ribociclib is present in human milk. There are no data on the effects of ribociclib on the breastfed infant or on milk production. Ribociclib and its metabolites readily passed into the milk of lactating rats. Because of the potential for serious adverse reactions in breastfed infants from KISQALI, advise lactating women not to breastfeed while taking KISQALI and for at least 3 weeks after the last dose.

Data

In lactating rats administered a single dose of 50 mg/kg, exposure to ribociclib was 3.56-fold higher in milk compared to maternal plasma.

8.3 Females and Males of Reproductive Potential

Pregnancy Testing

Based on animal studies, KISQALI can cause fetal harm when administered to a pregnant woman [see Use in Specific Populations (8.1)]. Females of reproductive potential should have a pregnancy test prior to starting treatment with KISQALI.
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Brought to you as a service of the Academy of Managed Care Pharmacy.
The Role of the Oncology Pharmacist

In 2005, the American Society of Clinical Oncology commissioned the American Association of Medical Colleges Center for Workforce Studies to analyze the U.S. oncology workforce, and the findings indicated that an impending shortage of physicians, nurses, allied healthcare professionals, public health workers, social workers, and pharmacists would cause a crisis in the oncology workforce.

The report indicated that due to the rapidly growing U.S. population, an aging oncology workforce, and not enough newly trained practitioners coming into the field, the industry will be out of balance to supply healthcare providers and could threaten patient care, safety, and quality. The workforce study estimated a 48% increase in patient visit demand, but only a 14% increase in the number of oncologists by 2020. Thus, 9.4 million to 15.4 million visits will be missed annually due to 2,500 to 4,000 fewer oncologists.

During a presentation at the HOPA Annual Conference, Robert J. Ignoffo, PharmD, FASHP, FCSHP, professor Emeritus at Touro University and clinical professor Emeritus at the University of California at San Francisco, discussed the role of oncology pharmacists in filling these gaps in care in the coming years.

Dr. Ignoffo provided an overview of a study his team published in the Journal of Oncology Practice that examined the role of board certified oncology pharmacists (BCOPs) in reducing a shortfall in oncology visits. They conducted a literature review for existing oncology pharmacy programs providing clinical care.

Thirteen of 15 BCOPs accepted an invitation to participate in their study: 10 were from academic centers and 3 were from office-based centers. Nine patients completed a Postgraduate Year Two oncology residency. In the academic practice, there were 35 patient visits per week, while the office-based private practice saw 47 patient visits per week, for an average visit time of 30 minutes.

An expert panel came to a consensus on 8 clinical activities that BCOPs can perform that are distinctly different from other non-physician practitioners, such as nurse practitioners, and considered value-added services in the oncology setting (see TABLE).

The study also calculated how estimated BCOP 30-minute visits would help the impending physician shortage. Using a formula, they indicated that in 2015, the number of BCOPs was 1,863 and would reach 3,693 by 2020. In 2015, BCOP visits served 1.5 million patients and would reach 3 million by 2020, accounting for between 20% to 32% of the 9.4 million to 15.4 million visit deficit that is projected for that timeframe.

“Oncology practices should consider adding an oncology pharmacist to their team (preferably 0.5 full time equivalent or more) in a clinical role to produce greater efficiency,” said Dr. Ignoffo. He noted that future studies should evaluate the impact of oncology pharmacists, with a focus on increasing the efficiency and productivity of an oncology practice.

The study is limited in that it cannot predict the total BCOP Board of Pharmacy Services exam pass rate in the future. The study also potentially overestimates the total BCOP workforce and patient visit capacity by including those working outside the United States.


### TABLE. Clinical Activities Identified for BCOPs

<table>
<thead>
<tr>
<th>Services Reaching ≥80% Consensus</th>
<th>Fraction Reporting this Service Performed by BCOPs “Frequently or Often”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participating in clinical trials</td>
<td>100% (n=13)</td>
</tr>
<tr>
<td>Adjusting chemotherapy</td>
<td>92% (n=12)</td>
</tr>
<tr>
<td>Assessing chemotherapy response/toxicity</td>
<td>92% (n=12)</td>
</tr>
<tr>
<td>Managing nausea, vomiting, antiemetic therapy</td>
<td>92% (n=12)</td>
</tr>
<tr>
<td>Managing symptoms/providing supportive care</td>
<td>92% (n=12)</td>
</tr>
<tr>
<td>Providing patient counseling and education</td>
<td>92% (n=12)</td>
</tr>
<tr>
<td>Pain management</td>
<td>85% (n=11)</td>
</tr>
<tr>
<td>Participating in protocol-based initiatives</td>
<td>85% (n=11)</td>
</tr>
<tr>
<td>Services Not Reaching Consensus</td>
<td>Fraction Reporting this Service Performed by BCOPs “Frequently or Often”</td>
</tr>
<tr>
<td>Managing/administering growth factors</td>
<td>77% (n=10)</td>
</tr>
<tr>
<td>Assisting with new patient consults</td>
<td>62% (n=8)</td>
</tr>
<tr>
<td>Medication reconciliation</td>
<td>62% (n=8)</td>
</tr>
<tr>
<td>Managing anticoagulation therapy</td>
<td>46% (n=6)</td>
</tr>
<tr>
<td>Ordering routine chemotherapy</td>
<td>46% (n=5)</td>
</tr>
</tbody>
</table>

BCOPs: board-certified oncology pharmacists.
Making the Most of Pharmacy Changes Related to Care and Distribution Models

Treatment of multiple myeloma (MM) has evolved, as 7 new drugs were approved in the past 2 years. There is a lack of head-to-head data for available therapies, and sequencing is not well defined. Most regimens have supportive care considerations, and adherence to therapy remains an important treatment consideration.

During a presentation at the HOPA Annual Conference, Scott Wirth, PharmD, BCOP, a clinical pharmacist of hematology/oncology and a clinical assistant professor at the University of Illinois Hospital and Health Sciences System at the University of Illinois at Chicago College of Pharmacy, discussed the difficulty in MM care and the need for integration of specialized pharmacists into an ambulatory MM clinic.

MM treatment is complex in that treatment considerations must be considerate of adverse events, complex dosing schedules, adherence, transplant coordination, bone health, pain management, infection, anticoagulation, financial considerations, Risk Evaluation and Mitigation Strategies (REMS), and specialty pharmacy access.

Clinical pharmacists can have an impact on MM care in numerous ways, said Dr. Wirth, including:

- Therapeutic decision-making and monitoring
  - Knowledgeable in data regarding treatment options
  - Appropriate dosing, drug interactions, and monitoring
- Medication adherence
  - Management of oral therapies
  - Assistance in financial barriers
- Supportive care
  - Use of bisphosphonates
  - Immunizations
  - Toxicity monitoring and management (including nausea/vomiting, anemia, pain, and anticoagulation)
- REMS
  - Adhere to safety and documentation requirements
  - Coordinate authorizations, prescriptions, and deliveries
- Education
  - Provide medication education for multiple agents

Dr. Wirth then discussed the current practice at his facility – the University of Illinois at Chicago. Their organization has a 20-chair outpatient infusion center that sees approximately 30 patients daily. A specialty pharmacy is on-site, and clinical and staff pharmacists provide services across multiple disease states. In the MM clinic, patients are seen 2 days per week by a hematologist, oncology nurse, and 2 clinical pharmacists.

The workflow begins with a clinical pharmacist interviewing the patient on topics such as toxicity assessment, medication reconciliation, and disease control. The pharmacist then presents updates from the interview and recent treatment and/or laboratory results to the hematologist. As an interdisciplinary team, they finalize a plan for care and arrange for follow-up.

“Treatment of MM is different from many other disease states in that it requires complex oral anticancer administration schedules and intense REMS management.”

—Scott Wirth, PharmD, BCOP

She offered some potential solutions, such as increasing inventory, discussing changes with supply chain, increasing environmental services or changing time to accommodate delivery, exploring recycling options with facilities, and designating an employee to be in charge (reviewing patient treatments, ordering medications).

Dr. Fahrenbruch then discussed specialty oral oncology pharmacies. Specialty pharmacy has advantages such as inventory requirements, cost savings for payers and the specialty pharmacy, perception of...
The study was funded by Novartis Pharmaceuticals Corporation.

First-Line Ribociclib Plus Letrozole in an Effective Combination in Postmenopausal Women with Advanced Breast Cancer

Most patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2−) advanced breast cancer will receive endocrine therapy (ET) as first-line treatment; however, most patients will experience disease progression. Targeting the cyclin-dependent kinases 4 and 6 (CDK4/6) may delay endocrine resistance and enhance ET efficacy. Ribociclib – an oral selective inhibitor of CDK4/6 – has demonstrated anti-tumor activity in combination with ET in previous trials.

In the randomized, double-blind, placebo-controlled, international, phase III MONALEESA-2 study, researchers evaluated the safety and efficacy of ribociclib plus letrozole versus placebo plus letrozole as first-line therapy in patients with HR+, HER2− advanced breast cancer. The results of the study were presented at the HOPA Annual Conference during a poster session titled "Efficacy, Safety, and Pharmacokinetics of First-line Ribociclib Plus Letrozole in Postmenopausal Patients With Hormone Receptor-Positive, HER2-Negative Advanced Breast Cancer: MONALEESA-2 Trial."

Between January 24, 2014, and March 24, 2015, patients were randomized 1:1 to receive letrozole 2.5 mg per day plus ribociclib 600 mg per day for three weeks on and one week off (n=334) or placebo (n=334). At data cutoff (January 29, 2016), the median duration of follow-up was 15.3 months.

Ribociclib plus letrozole resulted in a clinically meaningful and significant increase in progression-free survival (PFS) compared to letrozole plus placebo (hazard ratio, 0.56; P=0.00000329), and outcomes were consistent across subgroup analyses (age, race, Eastern Cooperative Oncology Group performance status score, site of metastases, and prior therapy). Median PFS was not reached in the ribociclib plus letrozole group (95% CI, 19.3-not reached) and was 14.7 months in the placebo plus letrozole cohort (95% CI, 13.6-16.5).

The overall response rate was 40.7% in the ribociclib plus letrozole group and 27.5% in the placebo plus letrozole group (P=0.001). The clinical benefit for ribociclib plus letrozole was 79.6% compared to 72.8% for the placebo plus letrozole cohort (P=0.02).

The most common grade 3/4 adverse events (AEs) that occurred more frequently in the ribociclib treatment group than the placebo group were neutropenia (59.3% vs 0.9%, respectively), leukopenia (21% vs 0.6%), increased alanine aminotransferase (9.3% vs 1.2%), lymphopenia (6.9% vs 0.9%), and increased aspartate aminotransferase (5.7% vs 1.2%). Drug–drug interactions between ribociclib and letrozole were not reported. Dose interruptions occurred more frequently in the ribociclib treatment group (76.9%; n=257 vs 40.6%; n=134), as did dose reductions (50.6%; n=169 vs 42.2%; n=14).

More patients in the placebo cohort discontinued treatment than the ribociclib group (53.9%; n=180 vs 41.6%; n=139). Reasons for discontinuation in the ribociclib and placebo cohorts included disease progression (26%; n=87 vs 43.7%; n=146), AEs (7.5%; n=26 vs 21%; n=7), and patient/physician decision (6.6%; n=22 vs 7.8%; n=26).

Increased quality of patient management, specific U.S. Food and Drug Administration regulations, and an on-call pharmacist. The challenges, however, include demonstrating that additional services add value, inability to have some or next day delivery, technology, face-to-face interactions with patients, delays and interruptions in therapies, and operational efficiency.

She offered some potential solutions, such as implementing a pharmacy liaison for oral chemotherapy management to expedite prescriptions through insurance and specialty pharmacies, providing information on financial assistance and completing paperwork, and monitoring prescription refills as needed. Implementing a face-to-face interaction system, incorporating a better informatics system, engaging in comprehensive education for specialty pharmacy staff, and educating reasonable expectations for delivery can also help.

She concluded, “Be proactive and voice concerns with limited distribution models. Educate your staff regarding how to cope with changes.”


Comparing Targeted Therapies for Lung Cancer

One in 4 cancer deaths are expected to be from lung cancer, and an estimated 224,390 new cases of lung cancer were projected in 2016. A majority of lung cancers (80-85%) are non-small cell lung cancer (NSCLC), and molecular abnormalities in NSCLC dictate treatment options.

During a presentation at the HOPA Annual Conference, Eva M. Segal, PharmD, BCOP, a clinical oncology pharmacist from the University of Washington Medical Center/Seattle Cancer Care Alliance, discussed novel therapies for lung cancer.

See TABLE on next page for standard systemic therapies for patients with adenocarcinoma NSCLC. She then discussed targeted therapies that focus on receptors, genes, angiogenesis, and tumor pH.

Epidermal Growth Factor Receptor (EGFR) Inhibitors

These occur in 10% to 15% of all NSCLCs, with common mutations including exon 18 and exon 21 (L861Q) point mutation, exon 19 deletion, exon 20 insertion, and exon 21 L858R substitution.

Oral EGFR inhibitors include gefitinib, erlotinib, afatinib, and osimertinib.

In clinical trials comparing the EGFR tyrosine kinase inhibitors with platinum-doublet chemotherapy, gefitinib resulted in a higher response rate (RR; 71.2% vs 47.3% P<0.001), progression-free survival (PFS; 9.8 vs 6.4 months; P<0.001), and overall survival (OS; 18.6 vs 17.3 months; P=0.99) in the IPASS study. Erlotinib resulted in a higher RR (54.5% vs 10.5%; P<0.001) and PFS (9.7 vs 5.2 months; P<0.001), but not OS (19.3 vs 19.5 months; P=0.87) in the EURTAC trial. Afatinib resulted in a higher RR (71.2% vs 47.3% P<0.001), increased quality of patient management, specific U.S. Food and Drug Administration regulations, and an on-call pharmacist. The challenges, however, include demonstrating that additional services add value, inability to have some or next day delivery, technology, face-to-face interactions with patients, delays and interruptions in therapies, and operational efficiency.

She offered some potential solutions, such as implementing a pharmacy liaison for oral chemotherapy management to expedite prescriptions through insurance and specialty pharmacies, providing information on financial assistance and completing paperwork, and monitoring prescription refills as needed. Implementing a face-to-face interaction system, incorporating a better informatics system, engaging in comprehensive education for specialty pharmacy staff, and educating reasonable expectations for delivery can also help.

She concluded, “Be proactive and voice concerns with limited distribution models. Educate your staff regarding how to cope with changes.”

in higher RR (56% vs 23%; \( P = 0.001 \)) and PFS (11.1 vs 6.9 months; \( P < 0.001 \)), but the same OS (28.2 months each; \( P = 0.60 \)) in the LUX-Lung 3 trial.

The LUX-Lung 7 trial compared gefitinib versus afatinib in treatment-naïve patients with EGFR-mutated NSCLC and found that OS was longer with afatinib (70% vs 56%), but the median PFS was similar (11 vs 10.9 months; \( P = 0.017 \)). The time to treatment failure was 13.7 months with afatinib and 11.5 months with gefitinib (\( P = 0.0073 \)).

According to the National Comprehensive Cancer Network (NCCN) 2017 guidelines, if the patient is EGFR-positive and the mutation is discovered prior to first-line chemotherapy, erlotinib, afatinib, or gefitinib are preferred. If the mutation is discovered during first-line chemotherapy, patients should complete the planned chemotherapy, including maintenance therapy, or interrupt treatment and begin erlotinib, afatinib, or gefitinib.

Dr. Segal noted that treatment resistance can occur 8 to 16 months after treatment, and second-line options include local therapies, systemic chemotherapy or immunotherapy, continued EGFR therapy, or osimertinib.

**ALK Inhibitors**

These occur in 2% to 7% of NSCLCs, and currently approved agents for treatment include alectinib, ceritinib, and crizotinib.

In the PROFILE 1014 trial that included untreated patients with non-squamous NSCLC, crizotinib resulted in increased overall RR (ORR; 74% vs 45%; \( P < 0.001 \)) and median PFS (10.9 vs 7 months; \( P < 0.001 \)) compared to chemotherapy.

According to the NCCN 2017 guidelines, if the patient is ALK-positive and the mutation is discovered prior to first-line chemotherapy, crizotinib or ceritinib are preferred. If the mutation is discovered during first-line chemotherapy, patients should complete the planned chemotherapy, including maintenance therapy, or interrupt treatment and begin crizotinib or ceritinib.

Outcomes of the second-generation ALK inhibitors, alectinib and ceritinib, were then reviewed. In the NP28761 trial, alectinib resulted in an ORR of 48%, a median duration of response (DOR) of 13.5 months, and a median PFS of 8.1 months. In the NP28762 trial, alectinib resulted in an ORR of 49%.

In the ASCEND-1 trial, ceritinib resulted in an ORR of 56%, a median DOR of 8.3 months, and a median PFS of 6.9 months. In the ASCEND-2 trial, ceritinib resulted in an ORR of 39%.

**Immunotherapy**

Dr. Segal concluded by discussing programmed death-ligand 1 (PD-L1) agents, including pembrolizumab, nivolumab, and atezolizumab.

In the KEYNOTE-010 trial, median OS was 14.9 months with pembrolizumab 2 mg/kg (\( P < 0.001 \)), 17.3 months with pembrolizumab 10 mg/kg (\( P < 0.001 \)), and 8.2 months for docetaxel 75 mg/m². Median PFS was 5.2 months for both doses of pembrolizumab (\( P < 0.001 \) for both) and 4.1 months with docetaxel.

In the CheckMate-057 trial, nivolumab resulted in a median OS of 12.2 months compared to 9.4 months with docetaxel (\( P = 0.002 \)). The RR was 19% with nivolumab and 12% with docetaxel (\( P = 0.02 \)).

The OAK trial resulted in a median OS of 13.8 months for atezolozumab compared to 9.6 months with docetaxel (\( P = 0.0004 \)), while the POPLAR study resulted in 12.6 months and 9.7 months, respectively.


---

**TABLE. Selected Systemic Therapy for Advanced or Metastatic Disease for NSCLC Based on 2017 NCCN Guidelines**

<table>
<thead>
<tr>
<th>First-line Systemic Therapy Option for Patients with ECOG score 0-1</th>
<th>First-line Systemic Therapy Options for Patients with ECOG score 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevacizumab ± carboplatin/paclitaxel (category 1)</td>
<td>Albunin-bound paclitaxel</td>
</tr>
<tr>
<td>Bevacizumab ± carboplatin/pemetrexed</td>
<td>Carboplatin/alummin-bound paclitaxel</td>
</tr>
<tr>
<td>Bevacizumab ± cisplatin/pemetrexed</td>
<td>Carboplatin/docetaxel</td>
</tr>
<tr>
<td>Carboplatin/alummin-bound paclitaxel (category 1)</td>
<td>Carboplatin/etoposide</td>
</tr>
<tr>
<td>Carboplatin or cisplatin and docetaxel (category 1)</td>
<td>Carboplatin/gemcitabine</td>
</tr>
<tr>
<td>Carboplatin or cisplatin and etoposide (category 1)</td>
<td>Carboplatin/paclitaxel</td>
</tr>
<tr>
<td>Carboplatin or cisplatin and gemcitabine (category 1)</td>
<td>Docetaxel</td>
</tr>
<tr>
<td>Carboplatin or cisplatin and paclitaxel (category 1)</td>
<td>Gemcitabine</td>
</tr>
<tr>
<td>Carboplatin or cisplatin and vinorelbine (category 1)</td>
<td>Gemcitabine/docetaxel</td>
</tr>
<tr>
<td>Gemcitabine/docetaxel (category 1)</td>
<td>Gemcitabine/vinorelbine</td>
</tr>
<tr>
<td>Gemcitabine/vinorelbine (category 1)</td>
<td>Paclitaxel</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>Pemetrexed ± carboplatin</td>
</tr>
</tbody>
</table>

**Updates in Hemophilia Care**

Despite numerous approved treatment options for hemophilia (see **TABLE**), challenges persist, including the development of inhibitors, cost, access to factor products (particularly in less developed countries), and traditional factor products that have pharmacokinetic limitations.

During a presentation at the HOPA Annual Conference, Heidi Trinkman, PharmD, of Cook Children’s Medical Center in Texas, discussed advances in hemophilia treatment and new targets for the therapeutic management of bleeding.

“Research has been busy!” Dr. Trinkman noted. Better products with extended half-lives are available with pharmacokinetics and pharmacodynamics that improve the feasibility and compliance of prophylaxis (such as changing treatment from 3 times per week to once weekly), include less total factor used, and reduce hospital admissions.

New factor products include single chain recombinant factor VIII (FVIII), PEGylated products, and protein fusion products.

Dr. Trinkman then discussed gene therapy, which is the “only prospect for [a] definitive cure.” The goal with this therapy is to achieve factor activity level >1% to 5%. In addition to gene therapy, there is gene insertion, which corrects the defective gene in situ and uses nucleases designed to cleave DNA. Vectors carry the nucleases and the complementary DNA to be inserted, and the transgene remains for the life of the cell. Gene correction involves small base changes that can be affected by zinc-fingered nucleases, transcription activator-like effector nucleases, or clustered regularly interspersed palindromic repeat elements. “Animal studies are promising, but equivalent dose in humans would induce hepatic inflammation,” Dr. Trinkman warned.

“Factor replacement will soon become one of many options for treating hemophilia patients in the future,” Dr. Trinkman concluded.

---

**TABLE. Currently Available Factor Products for Hemophilia**

<table>
<thead>
<tr>
<th>Hemophilia A</th>
<th>Plasma Derived (pdFVIII)</th>
<th>Recombinant (rFVIII)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Full length</td>
<td>B-Domain Deleted</td>
</tr>
<tr>
<td>Alphanate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemophil M</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Humate P</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Koate DVI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wilate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monoclate P</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hemophilia B</th>
<th>Plasma Derived (pdFIX)</th>
<th>Recombinant (rFIX)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

FVIII: factor VIII; PK: pharmacokinetics; PD: pharmacodynamics; FIX: factor IX.

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**Younger Patients with Breast Cancer Present Challenge to Standard of Treatment and Management**

Although the median age at breast cancer diagnosis is 67 years, patients <40 years account for 7% to 10% of all breast cancer cases and present with a unique set of concerns that impact treatment and management. During a presentation at the HOPA Annual Conference, Neelam K. Patel, PharmD, BCOP, clinical pharmacy specialist at the University of Texas MD Anderson Cancer Center, discussed specific concerns related to caring for younger patients with breast cancer.

Premature menopause is a risk related to treatment for those <40 years old. Most women <35 years will resume menses within 2 years of completing chemotherapy, but Dr. Patel noted that if menses do not resume within 1 year of completion, premature ovarian failure may be considered.

“There is more data supporting ovarian suppression use during chemotherapy for ovarian preservation, but this is still not considered a standard, and risks need to be discussed with patients prior to review,” she said.

In addition to symptoms like hot flashes, sleep disturbances, vaginal dryness, dyspareunia, and changes in weight, it is also unclear if breast cancer survivors have a higher risk of cardiovascular disease than the general population.
Study Highlights SNPs Associated with PFS in Patients with DLBCL

Diffuse large B-cell lymphoma (DLBCL) is a common type of non-Hodgkin lymphoma that is often treated with first-line R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone). In a retrospective, cohort study, researchers sought to assess certain single nucleotide polymorphisms (SNPs) to determine an associated response to R-CHOP in this patient population. The results of the study were presented at the HOPA Annual Conference during a poster session titled “Pharmacogenomics of R-CHOP in Patients with Diffuse Large B-cell Lymphoma.”

The researchers assessed 166 patients (mean age, 53 years) with newly diagnosed DLBCL who were treated with R-CHOP between August 2007 and December 2010, most of whom (55%) had stage III/IV disease. Patients were excluded if they had unclear pathologic diagnosis (such as grey zone lymphoma), primary central nervous system DLBCL, and incomplete treatment records.

Eleven SNPs were selected for analysis: rs396991 (rituximab), rs3957357 and rs4880 (cyclophosphamide), rs8133052, rs1045642, rs25678, rs20572, rs9024, rs1800566, and rs1049255 (doxorubicin), and rs1870377 (angiogenesis).

The mean progression-free survival (PFS) was 957 days (range, 18-2,347 days), with 57% of patients (n=94) who were progression-free in June 2014.

After adjusting for International Prognostic Index score, molecular subtype, and disease stage, 2 SNPs were significantly associated with PFS: rs4880 and rs1870377 (see TABLE). For rs4880, the CC allele was associated with shorter PFS compared to TC (hazard ratio [HR], 3.63; 95% CI, 1.11-11.87; P=0.033) and TT (HR, 2.26; 95% CI, 0.79-6.49; P=0.128). For rs1870377, the AA allele was associated with longer PFS compared to TA (HR, 0.46; 95% CI, 0.22-0.98; P=0.043) and TT (HR, 0.57; 95% CI, 0.26-1.22; P=0.14).

<table>
<thead>
<tr>
<th>SNPs</th>
<th>Short-Term Efficacy (CR+PR achieved from R-CHOP)</th>
<th>Long-Term Efficacy (PFS at last follow-up)</th>
<th>Median PFS (in days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs4880</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TT</td>
<td>70.8%</td>
<td>52.5%</td>
<td>Not achieved (≥866)</td>
</tr>
<tr>
<td>TC</td>
<td>82.5%</td>
<td>72.5%</td>
<td>Not achieved (≥1,217)</td>
</tr>
<tr>
<td>CC</td>
<td>66.7%</td>
<td>33.3%</td>
<td>425</td>
</tr>
<tr>
<td>rs1870377</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TT</td>
<td>75%</td>
<td>55%</td>
<td>Not achieved (≥954)</td>
</tr>
<tr>
<td>TA</td>
<td>70.5%</td>
<td>471%</td>
<td>724</td>
</tr>
<tr>
<td>AA</td>
<td>76.3%</td>
<td>76.3%</td>
<td>Not achieved (≥1,286)</td>
</tr>
</tbody>
</table>

SNPs: single nucleotide polymorphisms; CR: complete response; PR: partial response; R-CHOP: rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; PFS: progression-free survival.

Preventing and Managing Chemotherapy-Induced Nausea and Vomiting

For patients receiving chemotherapy for cancer, the adverse event chemotherapy-induced nausea and vomiting (CINV) can occur in 70% to 80% of patients if the appropriate preventive treatment is not provided. For the majority of patients with CINV (95%), it can impact their daily life in the following ways:

- Cancel personal plans (56%)
- Change eating habits (46%)
- Avoid exercise or physical activity (43%)
- Call in sick to work (38%)
- Have a more negative outlook on prognosis (30%)
- Consider avoiding future cancer treatments (3 in 4 patients)

During a presentation at the HOPA Annual Conference, Carol C. Story, PharmD, BCOP, clinical pharmacy specialist in hematology/oncology, discussed how to prevent and manage CINV.

Patient risk factors that increase the likelihood of CINV include younger age, female gender, history of motion sickness, history of morning sickness, and low ethanol use. Modifications should be made based on a patient’s individual response and the severity of CINV can increase with repeated treatment cycles, Dr. Story cautioned. Delayed CINV is difficult to control and is more common than acute CINV. Delayed CINV is also less responsive to antiemetic therapy and is greater if acute CINV is poorly controlled, which can lead to dehydration, electrolyte imbalance, nutritional deficiency, esophageal tear, impact quality of life, lead to withdrawal from treatment, and increase the use of healthcare resources.

Dr. Story noted some treatment options for CINV, including:

- 5-HT₃ receptor antagonists (granisetron, ondasetron, dolasetron, palonosetron)
- Neurokinin-1-receptor antagonist
- Netupitant/palonosetron
- Rolapitant
- Olanzapine

Dr. Story noted that the pharmacist’s role in managing CINV is awareness of the complication and providing education to physicians, nurses, other pharmacists, and patients. It is also important to develop and adhere to institution-specific guidelines. The pharmacist should review the patient’s medication list, note potential drug–drug interactions, identify risk factors for CINV, and review and recommend a different class of an antiemetic and/or route of administration.

Source: Story CC. Updates on the Prevention and Management of Acute and Delayed Chemotherapy-Induced Nausea and Vomiting. Session 207. Presented at the HOPA 13th Annual Conference, March 30, 2017; Anaheim, California.

Study Assesses Long-Term Infusion Reactions Related to Chemotherapy Agents

Infusion-related and hypersensitivity reactions to chemotherapy are adverse events (AEs) that can lead to treatment interruption or discontinuation. In a study, researchers sought to describe the incidence rate of infusion-related reactions over a long-term period (7 years) at a single outpatient facility.

The results of the study were presented at the HOPA Annual Conference during a poster session titled “Incidence and Timing of Infusion and Hypersensitivity Reactions to Chemotherapy Over Seven Years at a Community Cancer Center.” Researchers from the Humphrey Cancer Center of North Memorial Health Care in Robbinsdale, Minnesota, conducted a retrospective chart review from continuously documented files between September 2009 and 2015. They collected data on:

- Inciting Agent
- Drug
- Dose
- Cycle
- Time to reaction
- Pre-medications
- Patient Information
- Gender
- Age
- Diagnosis
- Recorded allergies
- Previous exposures
- Results
- Common terminology criteria for AE grade
- Outcome

A total of 211 patients (median age, 61.7 years; 60.6% were female) were included in the study. They found that rituximab had the greatest number of reactions (mostly grade 1/2) and the highest reaction incidence (see TABLE). Reactions to rituximab were most common after first exposure, but were mild and rarely led to discontinuation. Rituximab was most likely to be re-initiated on the same day, rather than on a different day or discontinued permanently.

The authors noted, “Our observed reaction rates were lower than in package inserts, [and] most infusion reactions were manageable with interventional medications and did not progress to grade 3/4 reactions.”

Source: Hayes SM and Whalen J. Incidence and Timing of Infusion and Hypersensitivity Reactions to Chemotherapy Over Seven Years at a Community Cancer Center. Poster P22. Presented at the HOPA 13th Annual Conference, March 30-April 1, 2017; Anaheim, California.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Reaction Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituximab</td>
<td>4.7%</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>2.1%</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>1.23%</td>
</tr>
<tr>
<td>Oxaliplatin</td>
<td>0.99%</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>0.73%</td>
</tr>
<tr>
<td>Irinotecan</td>
<td>0.53%</td>
</tr>
</tbody>
</table>

TABLE. Reaction Incidence Between 2009 and 2015

Source: Story CC. Updates on the Prevention and Management of Acute and Delayed Chemotherapy-Induced Nausea and Vomiting. Session 207. Presented at the HOPA 13th Annual Conference, March 30, 2017; Anaheim, California.
Dose Rounding Results in Significant Cost Savings and Decreased Waste

As a pharmacist protocol, dose and vial rounding has demonstrated cost savings in previous trials. In a study, researchers at the University of California, San Francisco implemented an automated dose rounding algorithm and sought to assess cost savings and waste and address medications that are best for automated dose rounding.

The results of the study were presented at the HOPA Annual Conference during a poster session titled “Implementation of an Automated Dose Rounding Algorithm at UCSF Comprehensive Cancer Center: A Cost Savings and Value Analysis.”

The Epic Beacon© electronic medication records were built with automated dosing rules to round within a 5% or 10% window above and below a target dose. Four months pre- and post-implementation, the researchers assessed the following in adult patients being treated for hematology/oncology reasons:

- Doses dispensed, rounded, and average dose change
- Vials saved, cost savings, and average savings per dose dispensed
- Cost/milligrams of waste and adjusted waste per dose dispensed

During the study, 1,089 doses (72%) were rounded, which resulted in a total average wholesale price savings of $695,685 and average savings per dose ranging from $287 to $1,425 (see TABLE 1).

“Our study demonstrated significant cost savings and decrease in waste from automated dose rounding, but also identified that a large amount of excess drug continues to be left unutilized,” the authors concluded (see TABLE 2).


TABLE 1. Cost Savings

<table>
<thead>
<tr>
<th>Drug</th>
<th>Vials Saved</th>
<th>Cost Saving*</th>
<th>Average savings/dose dispensed*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevacizumab</td>
<td>86</td>
<td>$64,380</td>
<td>$287</td>
</tr>
<tr>
<td>Daratumumab</td>
<td>99</td>
<td>$54,957</td>
<td>$307</td>
</tr>
<tr>
<td>Elotuzumab</td>
<td>54</td>
<td>$116,811</td>
<td>$1,425</td>
</tr>
<tr>
<td>Nivolumab</td>
<td>175</td>
<td>$210,525</td>
<td>$545</td>
</tr>
<tr>
<td>Pembrolizumab</td>
<td>20</td>
<td>$110,700</td>
<td>$360</td>
</tr>
<tr>
<td>Rituximab</td>
<td>138</td>
<td>$138,312</td>
<td>$436</td>
</tr>
</tbody>
</table>

*Based on average wholesale price of smallest vial size available.

TABLE 2. Unutilized Costs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Total Waste cost (pre)*</th>
<th>Total Waste Cost (post)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevacizumab</td>
<td>$85,997</td>
<td>$124,038</td>
</tr>
<tr>
<td>Daratumumab</td>
<td>$36,468</td>
<td>$0</td>
</tr>
<tr>
<td>Elotuzumab</td>
<td>$42,496</td>
<td>$0</td>
</tr>
<tr>
<td>Nivolumab</td>
<td>$80,377</td>
<td>$23,217</td>
</tr>
<tr>
<td>Pembrolizumab</td>
<td>$263,442</td>
<td>$589,997</td>
</tr>
<tr>
<td>Rituximab</td>
<td>$81,438</td>
<td>$0</td>
</tr>
</tbody>
</table>

*Based on average wholesale price of smallest vial size available.
†Rounded to ±10% interval.

Leflunomide Plus Antiviral Therapy Effective for Cytomegalovirus Infection

Following allogeneic hematopoietic stem cell transplantation (alloHSCT), cytomegalovirus (CMV) can lead to morbidity and mortality, and despite prophylaxis or pre-emptive treatment, transplant recipients continue to develop refractory or recurrent CMV infection. Treatment toxicities compund the complexity of treating CMV.

In a retrospective analysis of adult alloHSCT recipients with refractory CMV infections, researchers assessed outcomes for leflunomide therapy. The results of the study were presented at the HOPA Annual Conference during a poster session titled “Leflunomide for Cytomegalovirus Infection in Stem Cell Transplant Recipients.”

The researchers assessed 14 patients who were treated at the University of Texas MD Anderson Cancer Center between January 1, 2005, and March 31, 2015, who were identified using a pharmacy database query. Medical history and laboratory values were collected from electronic medical records.

“The use of leflunomide with concurrent antiviral therapy for refractory CMV cases appears to be efficacious and safe,” the authors reported. The most common adverse events were cytopenia (n=8) and elevated liver function tests (n=4). Prospective, randomized trials are needed to confirm the results and determine an appropriate dosing schema.
