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5 Studies Payers Need to Know

How FDA Decisions on the Horizon May Impact Your Cancer Spend

OncoHealth's **Senior Vice President for Clinical Strategy and Growth Laura Bobolts, PharmD, BCOP** summarizes 5 studies presented at the 2023 ASCO annual meeting that she anticipates will influence plan policy decisions and utilization management strategies. New scientific advances tend to increase financial toxicity at varying degrees of value, says Bobolts.

NATALEE

Kisqali with Positive Data in Early Breast Cancer

Key Points

We will soon see the second CDK4/6 inhibitor enter the adjuvant early breast cancer space.

NATALEE: The addition of Kisqali to adjuvant endocrine therapy lowered the risk of recurrence or death by 25% in HR-positive/HER2-negative early breast cancer patients.

The population of breast cancer patients eligible for adjuvant Kisqali could be 2- to 3-times larger than that for Verzenio if FDA approved irrespective of lymph node status.

Kisqali (ribociclib) is slated to be the second CDK4/6 inhibitor to enter the post-operative (adjuvant) early breast cancer space. In the NATALEE trial, the addition of Kisqali (ribociclib) to adjuvant endocrine therapy (ET) lowered the risk of recurrence or death by 25% in stage II/III hormone receptor-positive (HR+)/HER2-negative early breast cancer patients. The 3-year invasive disease-free survival (IDFS) was 90.4% with Kisqali plus ET versus 87.1% with ET alone (p=0.0014), for an absolute difference of 3.3%.

Adjuvant Kisqali per NATALEE is not published in full text yet, not listed in NCCN "yet", and not FDA approved yet, making broad off-label payer coverage uncommon until we have one of these supportive coverage sources. The manufacturer plans to file for FDA approval later this year. The dosage of adjuvant Kisqali was reduced from the metastatic dose of 600mg to 400mg and therapy continued up to 3 years, concurrently with 5-10 years of endocrine therapy.

While awaiting coverage support, the already FDA approved Verzenio (abemaciclib) is an alternative in lymph node positive stage II/III HR+/HER2- breast cancer patients. If FDA approved, the population of breast cancer patients eligible for Kisqali could be 2-3 times that of adjuvant Verzenio, given the NATALEE study included certain lymph node-negative patients where Verzenio has no available data. Spend for CDK4/6 inhibitors in breast cancer will increase with more adjuvant setting use, as will the complexity of how to treat those that progress to metastatic disease given CDK4/6 inhibitor-based therapy is standard of care first-line metastatic treatment.

KEYNOTE-671

Keytruda Likely First Peri-Op Immunotherapy in NSCLC

Key Points

Compelling data expands the use for Keytruda, a drug that is already top ten in spend for most payers.

KEYNOTE-671: 42% reduction in the risk of disease recurrence, progression, or death with adding Keytruda as perioperative treatment for early-stage resectable NSCLC.

The New England Journal of Medicine publication extends off-label coverage today for many patients across the United States and Puerto Rico.

A label expansion is on the horizon for Keytruda (pembrolizumab) as perioperative treatment for patients with resectable stage II, IIIA or IIIB non-small cell lung cancer (NSCLC) with a PDUFA date of October 16, 2023. This perioperative regimen includes adding Keytruda to platinum-based chemotherapy before surgery (neoadjuvant) and continued as single agent after surgery (adjuvant), up to one year total.

Data comes from the phase 3 KEYNOTE-671 trial where the addition of perioperative Keytruda to chemotherapy reduced the risk of disease recurrence, progression or death by 42%. Median event-free survival (EFS) was not reached with adding Keytruda versus 17 months with placebo (2-year EFS rate, 62.4% vs 40.6%). Keytruda's perioperative data may have outperformed a similarly designed trial, AEGEAN, where the addition of perioperative Imfinzi (durvalumab) to chemotherapy reduced the risk of disease recurrence, progression or death by 32% (median EFS not reached with adding Imfinzi versus 25.9 months with placebo). Imfinzi is anticipated to file for a similar perioperative NSCLC indication although the max total duration of therapy with Imfinzi is longer at roughly 15 months versus 12 months with Keytruda.

Perioperative Keytruda in NSCLC according to KEYNOTE-671 was presented at ASCO 2023 and simultaneously published in the New England Journal of Medicine, which extends off-label coverage for many patients across the United States and Puerto Rico according to CMS requirements.

PD-1/L1 inhibitors are already FDA approved with chemotherapy for use either before (Opdivo) or after (Keytruda; Tecentriq in PD-L1-positive disease) surgery in early-stage resectable NSCLC —now we have compelling data supporting both strategies with peri-operative Keytruda.

CARTITUDE-4

Carvykti to Move to Early Therapy in Multiple Myeloma

Key Points

Carvykti, under consideration by the FDA, slated to move up from fifth-line to second-line or later in multiple myeloma.

CARTITUDE-4: 74% reduction in risk of disease progression or death with Carvykti over current standard of care in lenalidomide-refractory multiple myeloma patients.

We expect CAR T-cell therapy to move to earlier line use in multiple myeloma soon, expanding eligible patient populations. Payers should prepare budgets accordingly.

FDA approval is sought to move the CAR T-cell therapy Carvykti (ciltacabtagene autoleucel; cilta-cel) up earlier in the treatment of relapsed multiple myeloma, from fifth-line to second-line or later. An application was submitted to the FDA for consideration of Carvykti in the treatment of adults with relapsed or refractory multiple myeloma who are refractory to lenalidomide and received at least one prior line of therapy including a proteasome inhibitor and an immunomodulatory agent.

Support comes from the phase 3 CARTITUDE-4 study, presented at ASCO 2023 and simultaneously published in the New England Journal of Medicine, where Carvykti reduced the risk of disease progression or death by 74% over Pomalyst-based therapy in patients with lenalidomide-refractory multiple myeloma who received one to three prior lines of therapy. Progression-free survival (PFS) at 12 months was 75.9% with Carvykti and 48.6% with standard therapy.

Carvykti has potential to be the new standard of care in lenalidomide-refractory multiple myeloma, as early as 2nd-line therapy once FDA approved. Of note, another CAR-T agent, Abecma (idecabtagene vicleucel; ide-cel), has a PDUFA date of December 16, 2023 to also move up earlier in therapy for the treatment of adults with relapsed/refractory multiple myeloma who received an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody. Abecma demonstrated positive results in the phase 3 KarMMA-3 study with a 51% reduction in the risk of disease progression or death over standard of care in the 3rd to 5th line treatment of relapsed/refractory multiple myeloma.

CAR T-cell therapy will move into earlier lines of treatment of multiple myeloma this year, significantly expanding the patient population eligible for CAR-T, which has the opportunity to drastically improve outcomes for our cancer patients, although at high costs to the healthcare system as a whole.

CAPItello-291

First AKT Inhibitor Coming in Breast Cancer

Key Points

Capivasertib will be the first oral AKT inhibitor, anticipated to enter the market in the fourth quarter of 2023.

CAPItello-291: 40% reduction in the risk of disease progression or death with the addition of investigational capivasertib to fulvestrant in previously HR-positive, HER2-negative metastatic breast cancer.

Therapy is expected to be FDA approved irrespective of biomarkers, expanding the eligible patient population.

Capivasertib is an oral investigational AKT inhibitor granted Priority Review in combination with fulvestrant for the treatment of adults with HR-positive, HER2-negative locally advanced/metastatic breast cancer following recurrence or progression on/after endocrine-based therapy, with an FDA decision anticipated fourth quarter of 2023.

Supportive data comes from the phase 3 CAPItello-291 trial which showed the combination of capivasertib plus fulvestrant reduced the risk of disease progression or death by 40% versus fulvestrant alone (median progression-free survival (PFS) 7.2 versus 3.6 months; p=<0.001) in locally advanced or metastatic HR-positive, HER2-low or negative breast cancer following aromatase inhibitor therapy.

Safety data from CAPItello-291 was presented at ASCO 2023. Common adverse effects with capivasertib plus fulvestrant include diarrhea (72%), rash (38%), and hyperglycemia (17%), most occurring within the first month. Risk factors for hyperglycemia included baseline history of diabetes and body mass index of 30 kg/m2.

Capivasertib plus fulvestrant will likely be a second line or later endocrine therapy option for HR+/HER2- metastatic breast cancer, irrespective of biomarkers or alterations in the AKT pathway (PIK3CA, AKT1 or PTEN genes).

COMMANDS

Reblozyl in ESA-Naive Lower-Risk MDS Anemia

Key Points

Reblozyl to expand use to the first-line treatment of anemia in ESA-naïve adults with lower-risk MDS who require red blood cell transfusions—PDUFA date, August 28, 2023.

We'll be watching for the FDA approval anticipated in late August to see whether use is restricted to those with ringed sideroblasts or not based on the benefit difference seen in the study.

The COMMANDS study demonstrated nearly twice as many patients experienced transfusion independence with Rebloyzl over the current standard of care, epoetin alfa, in the first-line treatment of adults with lower-risk MDS who require red blood cell transfusions.

Reblozyl (luspatercept) is anticipated to expand its use to the treatment of anemia in erythropoiesis-stimulating agent (ESA) naïve adults with very low- to intermediate-risk myelodysplastic syndromes (MDS) who require red blood cell (RBC) transfusions—PDUFA date, August 28, 2023.

Supportive data comes from the phase 3 COMMANDS study, presented at ASCO 2023, where Reblozyl was nearly twice as likely than the ESA Epogen/Procrit to result in transfusion independence for ≥12 weeks with a hemoglobin increase ≥ 1.5 g/dL in the first-line treatment of adults with very low-, low- or intermediate-risk MDS who require RBC transfusions. The transfusion independence rate was 58.5% for Reblozyl and 31.2% for Epogen/Procrit in the first 24 weeks of treatment.

Reblozyl may become a new standard of care in first-line treatment of anemia associated with lower-risk MDS, potentially replace ESAs, and may expand use beyond patients with ring sideroblasts (RS). Reblozyl is already FDA approved for low-risk MDS-associated anemia after failing an ESA, although only in RS-positive patients.

Will the FDA approve Reblozyl as first-line therapy in those with or without ringed sideroblasts? The positive effect in the COMMANDS study may have been primarily driven by RS-positive patients. Those who were RS-negative derived no significant benefit, with 12-week transfusion independence of 41.0% for Reblozyl versus 46.3% for Epogen/Procrit.