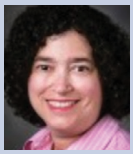
Other Solid Cancers: ASCO20 Virtual Scientific Program Highlights for the Advanced Practitioner




Elizabeth S. Waxman, RN, MSN, AOCN®, ANP-BC, of MD Anderson Cancer Center, evaluates a study showing activity by pralsetinib in patients with a variety of tumors harboring *RET* gene fusions, and **Abby Fuoto, DNP, ANP-BC, AOCNP®, ACHPN,** of University of Arizona Cancer Center, comments on the effect of deintensification in patients with intermediate-risk HPV-positive oropharyngeal cancer. Meeting coverage is provided by *The ASCO Post*.

Abstract 109

RET Kinase Inhibitor for Patients With Solid Tumors and *RET* Genetic Fusions

By The ASCO Post Staff

Visit https://meetinglibrary.asco.org/record/186874/abstract to read the full abstract and view author disclosures.

The RET inhibitor pralsetinib showed activity in patients with a broad variety of tumors harboring *RET* gene fusions, according to results from the phase I/II ARROW trial, presented by Vivek Subbiah, MD, and colleagues during the ASCO20 Virtual Scientific Program.

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"This trial shows that pralsetinib has broad and durable antitumor activity across multiple advanced solid tumor types, giving it the potential to address an unmet medical need for patients with RET fusion–positive cancers," said Dr. Subbiah, Associate Professor of Investigational Cancer Therapeutics at The University of Texas MD Anderson Cancer Center, in a statement. "The recent tumor-agnostic drug approvals have resulted in a paradigm shift in cancer treatment, away from organ-histology–specific indications to a biomarker-guided, tumor-agnostic approach. However, until recently, we haven't had any effective targeted therapies targeting RET alterations."

RET fusions occur when a portion of the chromosome containing the *RET* gene breaks off and joins with a gene on another chromosome, creating a fusion protein capable of fueling cancer development. *RET* alterations are most common in medullary thyroid cancers (approximately 90% of advanced cases), papillary thyroid cancers (approximately 10%–20% of cases) and non–small cell lung cancers (approximately 1%–2% of cases).

Study Details

The presentation included data for 13 patients with RET fusion–positive thyroid cancers and 14 patients with other RET fusion–positive cancers, including pancreatic cancer, cholangiocarcinoma, ovarian cancer, colon cancer, and others. Nearly all patients had stage IV disease that had progressed or relapsed on available standard therapies.

Among those patients with *RET* fusion–positive thyroid cancers, the duration of treatment ranged from 3 to 22 months, and 70% of responding patients remain on therapy.

Activity Seen in Multiple Tumor Types

In patients with RET fusion–positive thyroid cancer, pralsetinib achieved an overall response rate, indicating tumor shrinkage, of 91% and disease control rate, indicating tumor shrinkage or stable disease, of 100%. For all other tumor types included in the cohort, pralsetinib resulted in a 50% overall response rate and 92% disease control rate.

In other RET fusion–positive cancers, all patients with pancreatic cancer (n = 3) and cholangiocarcinoma (n = 2) in the trial had a partial response from treatment. The duration of treatment ranged from 2 to 21 months, and 67% of responding patients remain on therapy.

Further, treatment with pralsetinib was well tolerated across all patients in the cohort, explained Dr. Subbiah. "Pralsetinib was consistently safe across the overall population, and the majority of adverse events were low-grade. None of the patients in the basket cohort discontinued therapy due to treatment-related adverse events."

Additional Cohorts

Additional cohorts of the ARROW trial focus on patients with *RET* fusion–positive non–small cell lung cancers and RET-mutant medullary thyroid cancer. Data from the non–small cell lung cancer cohort, indicating an overall response rate of 65% and a disease control rate of 93%, were also in a poster discussion during the ASCO20 Virtual Scientific Program (Abstract 9515).

"This study stresses the importance of considering genomic testing for all patients regardless of tumor histology, so we can identify those that may benefit from targeted therapies such as pralsetinib," said Dr. Subbiah. "It's encouraging to be able to offer effective options to these patients and give them the gift of time." ●

The Advanced Practitioner Perspective

Elizabeth S. Waxman, RN, MSN, AOCN®, ANP-BC
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The drug pralsetinib showed activity against *RET* gene fusions in different malignancies. This is an interesting finding with targeted therapies. Pralsetinib, regardless of the site of disease—thyroid cancers, pancreatic cancer, cholangiocarcinoma, non–small cell lung cancer—showed benefit. The response rate and disease control rate for patients with *RET* fusion–positive cancers are impressive. The data for patients with non–small cell lung cancer showed an overall response rate of 65% and disease control rate of 93%, which is remarkable.

The findings from this study are interesting in that the drug pralsetinib benefitted patients with different malignancies but all with *RET* fusion mutations. This study also demonstrated the importance of mutation testing for all patients with cancer regardless of histology.

Disclosure: Ms. Waxman has no conflicts of interest to disclose.

Abstract 6500

Transoral Resection Followed by Low-Dose Radiation for Some Oropharyngeal Cancers

By The ASCO Post Staff

Visit https://meetinglibrary.asco.org/record/187340/abstract to read the full abstract and view author disclosures.

The final results of the randomized phase II ECOG-ACRIN E3311 trial were presented by Robert L. Ferris, MD, PhD, and colleagues during the ASCO20 Virtual Scientific Program (Abstract 6500). The trial, conducted in patients undergoing transoral robotic surgery, tested reduced postoperative radiation therapy in patients with human papillomavirus (HPV)-associated oropharyngeal squamous cell carcinoma at intermediate risk for recurrence.

"Transoral resection followed by low-dose radiation is safe in patients with intermediate-risk locally advanced oropharyn[geal] cancer, with very good oncologic outcome," said lead investigator Dr. Ferris, Director of the University of Pittsburgh Medical Center Hillman Cancer Center and a surgical oncologist specializing in head and neck cancer. "These results present a promising deintensification approach."

Study Background and Details

Most patients with oropharyngeal cancers caused by HPV have a very good outcome, and the cancer does not return or spread to other parts of the body after treatment. Dr. Ferris and colleagues sought to prove the benefits of using tumor pathologic features, obtained in specimens collected at surgery, to determine patients' risk of recurrence-low, -intermediate or -high disease. In particular, they sought to more clearly define the prognostic and predictive role of traditional pathologic biomarkers—such as extensive nodal or extranodal disease—to give the right amount of postoperative treatment for each risk group.

Patients at low risk of recurrence were observed. Patients at intermediate risk were randomly assigned to two arms of radiation alone, both at doses lower (50 or 60 Gy) than usual (60 to 66 Gy). At the time the trial opened in 2013, the optimal dose of radiation therapy was not defined. Patients at high risk were assigned to usual radiation therapy plus chemotherapy.

The primary endpoint was 2-year progression-free survival in patients determined to be at intermediate risk after surgical excision.

Findings

"Study E3311 met its primary endpoint," said Dr. Ferris. "For intermediate-risk patients—those with uninvolved surgical margins, less than five involved nodes, and less than 1 mm extranodal extension—reduced-dose postoperative radiation therapy without chemotherapy appears sufficient. In our study, this group had better outcomes than the group on usual high-dose radiation plus chemotherapy, showing that our patient stratification identified low- and intermediate-risk patients well, preserving patients' throat function and sparing them unnecessary short- and long-term toxicities."

For patients with low-risk disease, 2-year progression-free survival was favorable without postoperative therapy (observation alone). All arms had 2-year survival rates above 90%, and there was no excess of local recurrences with reduction in radiation or chemotherapy (arms B and C). Risk stratification appeared to appropriately select patients for observation (arm A).

The study authors concluded, "Transoral resection of p16-positive [oropharyngeal cancer] is safe and results in good oncologic outcome, presenting a promising deintensification approach. For patients with low-risk disease, 2-year progression-free survival is favorable without postoperative therapy. For those with uninvolved surgical margins, fewer than five involved nodes, and minimal extranodal extension, reduced-dose postoperative radiotherapy without chemotherapy appears sufficient. Transoral surgery plus 50 Gy should be compared to optimal nonsurgical therapy in a phase III trial."

Next Steps

The overall intent of E3311 was to gather essential data for the design of a future randomized phase III trial. The primary endpoint was to determine the feasibility and oncologic efficacy of a prospective multi-institutional study of transoral robotic surgery for HPV-associated oropharyngeal cancer followed by risk-adjusted adjuvant therapy.

"The tissue samples and imaging studies collected in the course of this trial are a rich resource for studying the biology of intermediate- and high-risk disease, in work that is ongoing," said ECOG-ACRIN Head and Neck Committee Chair Barbara A. Burtness, MD, Professor of Medicine and Co-Leader, Developmental Therapeutics Program, Yale Cancer Center and Yale School of Medicine. "ECOG-ACRIN plans to pursue the current data with a randomized phase III trial of transoral robotic surgery–based treatment deintensification compared with conventional chemoradiation."

The Advanced Practitioner Perspective

Abby Fuoto, DNP, ANP-BC, AOCNP®, ACHPN
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For several years, researchers have studied deintensification strategies due to concerns of overtreatment of patients diagnosed with p16-positive squamous cell carcinoma of the oropharynx. The phase II study, ECOG-ACRIN E3311, is another example of deintensification research. This study examined reduced postoperative therapy in patients with intermediate-risk p16-positive oropharynx cancer undergoing primary transoral surgical management. Intermediate risk features in this study include negative or close surgical margins, 2 to 4 positive lymph nodes, extranodal extension of 1 millimeter or less, and > 10-year tobacco history. The intermediate risk arms B and C received 50 and 60 Gy adjuvant radiation therapy, respectively, and progression-free survival was 95% and 95.9%, respectively. Dr. Ferris and colleagues concluded that reduced adjuvant therapy for those with intermediate-risk disease was safe and provided a good outcome. They recommend a phase III study comparing transoral surgery plus 50 Gy radiation to nonsurgical therapy as next steps.

As advanced practitioners, this study shows exciting promise for our patients with HPV-positive oropharyngeal cancer. Deintensification has been examined with the hopes of providing appropriate oncologic management with fewer late toxicities—specifically those related to swallow and shoulder function. However, patients sometimes express worry regarding deintensification due to the perception of receiving less therapy. A phase III clinical trial will help to definitively answer what the standard of care should be in the management of intermediate-risk p16-positive disease.

Disclosure: Dr. Fuoto has no conflicts of interest to disclose.