

# Other Solid Cancers: 2021 ASCO Annual Meeting Highlights for the Advanced Practitioner



**Abby Fuoto, DNP, ANP-BC, AOCNP®, ACHPN**, of University of Arizona Cancer Center, considers the implications of a novel monoclonal antibody for nasopharyngeal cancer, and **Mee-young Lee, MSN, ANP-BC**, of Monter Cancer Center, Northwell, discusses the design of a basket trial for tumors with HER2 amplification or over-expression. Meeting coverage is provided by *The ASCO Post*.

## Abstract LBA2

### Novel Monoclonal Antibody Emerges as Potential First-Line Standard in Nasopharyngeal Cancer

By Caroline Helwick

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**A** new first-line standard of care may be emerging for recurrent or metastatic nasopharyngeal carcinoma, based on the findings of the global phase III JUPITER-02 trial presented at the 2021 ASCO Annual Meeting by investigators from China.<sup>1</sup>

J Adv Pract Oncol 2021;12(6):629-632

<https://doi.org/10.6004/jadpro.2021.12.6.10> • © 2021 Harborside™

In the study, toripalimab, an anti-PD-1 monoclonal antibody, was given in combination with gemcitabine/cisplatin, the current standard treatment. In a previous study in the second line, POLARIS-2, toripalimab monotherapy conveyed a durable response duration of nearly 13 months.<sup>2</sup>

“The addition of toripalimab to gemcitabine/cisplatin as first-line treatment for recurrent or metastatic nasopharyngeal carcinoma showed better progression-free survival, objective response rates, and duration of response than chemotherapy alone,” said Rui-hua Xu, MD, President of Medical Oncology at Sun Yat-sen University Cancer Center, Guangzhou, China. “And though median overall survival is not mature in either arm, a 40% reduction in the risk of death was observed with toripalimab plus chemotherapy. These results suggest this regimen represents a new standard of care.”

### Breakthrough Status for Toripalimab

As Dr. Xu pointed out, nasopharyngeal carcinoma is an “endemic” malignancy in Southern China and Southeast Asia, with an incidence rate of 3.0 per 100,000, as compared with 1.2 per 100,000 elsewhere in the world. Treatment options for recurrent or metastatic disease have been limited.

“This is one of the first trials in recurrent and metastatic nasopharyngeal carcinoma to show the benefit of combining a PD-1 inhibitor with chemotherapy,” Julie R. Gralow, MD, ASCO Chief Medical Officer and Executive Vice President, said in a press briefing preceding the meeting.

Toripalimab is currently approved in China for several indications, including in the third-line setting for metastatic nasopharyngeal carcinoma. In the United States, it has received Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA) for recurrent or metastatic nasopharyngeal carcinoma as well as Fast Track and Orphan Drug status for other cancer types (mucosal melanoma, soft-tissue sarcoma). “With these study results, following FDA approval, these findings should prove to be practice-changing,” Dr. Gralow commented.

Ongoing or completed trials are evaluating toripalimab for a broad range of other tumor types, including cancers of the lung, esophagus, stomach, bladder, breast, liver, kidney, and skin.

### Significant Improvements in Disease-Free Survival

The double-blind, placebo-controlled phase III trial enrolled 289 treatment-naïve patients with recurrent or metastatic nasopharyngeal carcinoma; they were randomly assigned to receive gemcitabine at 1,000 mg/m<sup>2</sup> plus cisplatin at 80 mg/m<sup>2</sup> and toripalimab at 240 mg or placebo every 3 weeks for up to six cycles. The toripalimab arm also received maintenance toripalimab given every 3 weeks. The primary outcome was progression-free survival by blinded independent review.

Median progression-free survival was 11.7 months with toripalimab/chemotherapy vs 8.0 months with chemotherapy alone (hazard ratio [HR] = 0.52;  $P = .0003$ ); the 1-year progression-free survival rates were 49.4% and 27.9%, respectively. Per investigator assessment, median progression-free survival was not reached with toripalimab/chemotherapy and was 8.0 months with chemotherapy alone (HR = 0.41;  $P < .0001$ ). Benefit was seen across all key subgroups.

“The stopping boundary for efficacy was crossed at the progression-free survival analysis,” Dr. Xu said. “Therefore, the data safety monitoring committee recommended unblinding the study.”

Overall survival data remain immature. The 1-year overall survival rates were 91.6% in the experimental arm vs 87.1% in the control arm (HR = 0.603;  $P = .0462$ ). The objective response rate was 77.4% with the combination and 66.4% with chemotherapy alone ( $P = .033$ ), with median durations

of response of 10.0 vs 5.7 months, respectively (HR = 0.50;  $P = .0014$ ).

### Safety Profile

Aside from immune-related adverse events, the safety profiles of the experimental arm and control arm were similar. Adverse events grade 3 or higher related to the study drug were observed in 89% of each arm. The most common adverse events, for the experimental vs control arms, were leukopenia (62% vs 58%), anemia (47% vs 40%), neutropenia (57% vs 64%), and thrombocytopenia (33% vs 29%). Hypothyroidism of any grade, an immune-related effect, was more common with toripalimab (31% vs 17%).

### Similar Benefits Found With Camrelizumab

In the press briefing, Dr. Gralow indicated that toripalimab may not be the only new agent in recurrent or metastatic nasopharyngeal carcinoma. “Another PD-1 inhibitor being developed in China—camrelizumab—is showing similar results to toripalimab, so there is potentially an additional PD-1 inhibitor with very positive results,” she commented.

Li Zhang, MD, also of Sun Yat-sen University Cancer Center, and colleagues presented results from their first-line, phase III trial of camrelizumab (CAPTINE-1st study), with a design similar to JUPITER-02. Camrelizumab plus gemcitabine and cisplatin, by independent review, yielded a median progression-free survival of 10.8 months vs 6.9 months with placebo plus gemcitabine and cisplatin chemotherapy alone (HR = 0.51;  $P < .0001$ ) in patients with recurrent or metastatic nasopharyngeal carcinoma. Median overall survival was not reached with camrelizumab/chemotherapy and was 22.6 months with chemotherapy alone (HR = 0.67). Responses were observed in 88.1% and 80.6%, respectively, with median durations of response of 9.9 and 5.7 months, respectively.

Camrelizumab has been approved by the National Medical Products Association in China (formerly, the China FDA) for the indication of first-line treatment of advanced nasopharyngeal carcinoma in combination with the gemcitabine/cisplatin regimen based on this phase III study. It is also the first indication officially approved by drug regulatory authorities worldwide for this in-

dication. According to Dr. Zhang, the study has also been accepted for publication by *Lancet Oncology*.

## References

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### The Advanced Practitioner Perspective

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Since 2016, the standard-of-care first-line therapy for recurrent or metastatic nasopharyngeal cancer (NPC) has been cisplatin and gemcitabine. The findings of the JUPITER-02 phase III clinical trial may represent a paradigm shift in first-line treatment. Although immune checkpoint inhibitors have been approved in subsequent-line therapies, this study demonstrates superior progression-free survival (PFS) and overall response rate (ORR) combining toripalimab and chemotherapy in first line.

Patients with NPC often have tumors that stain strongly for PD-L1. This finding is consistent in the JUPITER-02 study population, where nearly three quarters of patients in both arms had PD-L1 positive tumors. PD-L1 positivity was defined as  $\geq 1\%$  PD-L1 expression of tumor cells or immune cell staining by immunohistochemistry. PD-L1 positivity indicates likely benefit for patients receiving immuno-

therapy. Interestingly, even patients who had low or no PD-L1 expression randomized to the toripalimab arm had improved PFS compared to the standard-of-care arm. One question this study provokes is whether the findings from China extend to other patient populations. As the standard of care for metastatic or recurrent NPC is generally uniform worldwide, and as these tumors often stain PD-L1 positive, it is probable that these findings will hold across other ethnicities and racial groups.

An important consideration for the advanced practitioner is that, to date, toripalimab has been granted fast track designation by the FDA to treat mucosal melanoma, but has not yet been approved to treat NPC. This limits the number of NPC patients who can receive therapy currently. Once FDA approved, advanced practitioners should anticipate toripalimab will become part of first-line therapy for NPC based on the findings of JUPITER-02.

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

## Abstract 3004

### Pertuzumab/Trastuzumab Demonstrates Activity in Tissue-Agnostic Trial for Patients With HER2-Positive Tumors

By The ASCO Post Staff

Visit <https://meetinglibrary.asco.org/record/196653/abstract> to read the full abstract and view author disclosures.

**R**esults from the phase II MyPathway basket trial found that the HER2-targeted therapies pertuzumab and trastuzumab demonstrated durable activity in patients with a wide variety of tumors

marked by HER2 amplification or overexpression, although responses were limited in those with *KRAS* mutations. These findings were presented during the 2021 ASCO Annual Meeting by Funda Meric-Bernstam, MD, and colleagues (Abstract 3004).

Pertuzumab and trastuzumab are antibody therapies that bind to HER2 and block its activity. HER2 is amplified or overexpressed in 2% to 3% of all solid tumors, but therapies against HER2 only are approved for breast, gastric, and gastroesophageal cancers.

### MyPathway Trial

The study enrolled 258 patients across a variety of tumor types, excluding those for which the ther-

apies already are approved. The most common cancer types enrolled were colorectal, biliary, and non–small cell lung cancers. Side effects recorded in the study were consistent with previous reports of these drugs.

Sixty patients (23.3%) had a confirmed objective response, indicating tumor shrinkage, including five complete responses. The disease control rate was 44.6%, and duration of response was 7.9 months. Notably, patients with *KRAS* mutations did not have a high response rate, with just one objective response reported among 26 patients.

“This trial truly demonstrated the value of the basket trial design in assessing efficacy across tumor types, as well as the impact of coalterations,” said Dr. Meric-Bernstam, Chair of Investigational Cancer Therapeutics at The University of Texas MD Anderson Cancer Center. “These agents were active in a wide variety of *KRAS* wild-type, *HER2*-amplified or -overexpressed tumor types, with notable activity in colorectal cancer and salivary tumors. However, there was limited activity in *KRAS*-mutant tumors, emphasizing that in precision oncology, we need to consider the full genomic profile in treatment selection.”

### The Advanced Practitioner Perspective

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Pertuzumab and trastuzumab is a standard *HER2*-targeted antineoplastic regimen for breast and gastric cancers. Unlike breast and gastric cancers, less than 2% of other solid tumors harbor *HER2* amplification/overexpression. The phase IIa MyPathway basket study examined pertuzumab and trastuzumab in nonindicated solid tumors that have *HER2* amplification/overexpression. Colorectal, biliary, non–small cell lung, ovarian, uterine, urothelial, salivary, pancreas, and other cancers were included in this study. The MyPathway trial showed durable response in these tumor types, and 23.3% (60/258 participants) had confirmed objective response and 5 patients with complete response.

With advancements in precision oncology, targeted therapy trials are aiming to capture multiple tumor types with common molecular alterations. Modern clinical trial designs such as basket and umbrella models are often used. Basket trials are prospective studies designed to evaluate one or more targeted therapies for multiple tumor types with common molecular alterations. Umbrella trials are also prospective clinical trials evaluating multiple targeted interventions for a single disease with predictive molecular alterations and stratified in multiple subgroups. These trial designs are conducted mostly in oncology trials where specific molecular biomarkers might make a difference in treatment plans and outcomes. We will encounter trial designs such as these more in the future as we move further in precision oncology.

**Disclosure:** Ms. Lee has no conflicts of interest to disclose.