# Study-end analysis from AMPECT, an open-label, phase 2 registration trial of patients with advanced malignant PEComa treated with *nab*-sirolimus, showing durability of response and long-term safety

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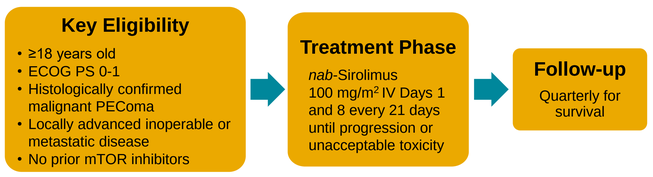
## BACKGROUND

- Malignant perivascular epithelioid cell tumor (PEComa) is an aggressive, rare sarcoma in which cytotoxic chemotherapies provide limited patient benefit
- *nab*-Sirolimus is a mTOR inhibitor that utilizes albumin-bound nanoparticle technology and is approved in the United States for the treatment of adult patients with locally advanced unresectable or metastatic malignant PEComas based on the primary analysis results of the AMPECT trial[1]
  - In preclinical animal models, treatment with *nab*-sirolimus resulted in significantly higher tumor uptake and tumor growth inhibition; and improved mTOR target (pS6) suppression, with a distinct pharmacokinetic profile, relative to oral mTORis[2,3]
- Results from the primary analysis, which was preplanned when the last enrolled patient had been treated for 6 months (May 2019, with 29% of patients ongoing at the time), and subsequent follow-up analyses from AMPECT have been previously reported; however, the median duration of response (DOR) was not yet reached after a median follow-up for response of 2.5 years after the last patient-initiated therapy (data cutoff June 30, 2021)[1]
- Here, we report the final data from study closure, which is a 3-year follow-up after the primary analysis of AMPECT data, including median DOR, through study completion (April 29, 2022)

## METHODS

- The AMPECT trial (NCT02494570) was an open-label, multicenter phase 2 registration study in adult patients (≥18 years) with histologically confirmed diagnosis of malignant PEComa and Eastern Cooperative Oncology Group performance status score of ≤1 (**Figure 1**)
- Patients received *nab*-sirolimus 100 mg/m$^2$ intravenously on Days 1 and 8 of a 21-day cycle until progression or unacceptable toxicity (**Figure 1**)

### Figure 1. Study Design




ECOG, Eastern Cooperative Oncology Group; IV, intravenously; mTOR, mammalian target of rapamycin; PEComa, perivascular epithelioid cell tumor; PS, performance status.

- The study sample size (approximately N=30) was calculated based on an estimated overall response rate (ORR) of 30%, excluding the lower bound of the 95% confidence interval (CI) of 14.7%
- The primary endpoint was ORR based on independent radiographic review using RECIST v1.1
- Confirmation of response was required per RECIST v1.1
- Secondary endpoints included DOR, progression-free survival (PFS) at 6 months, median PFS, median overall survival (OS), and safety
- Diagnosis of malignant PEComa was confirmed by a central pathology review
- Exploratory endpoints included a biomarker analysis evaluating the mutational profile using Next-Generation Sequencing and immunohistochemistry

## RESULTS

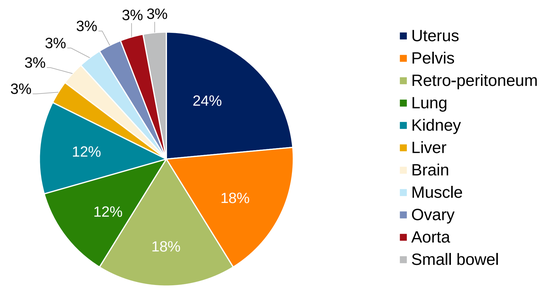
- A total of 34 patients were treated with at least 1 dose of *nab*-sirolimus in the study (safety-evaluable population; **Table 1** and **Figure 2**)
- The median duration on study at study closure, including survival follow-up, was 22 months (range, 1-66 months)

### Table 1. Baseline Characteristics

| Variable | All Treated Patients (N=34) |
|---|---|
| **Age, median (range), years** | 60 (27-78) |
| ≥65 years, n (%) | 15 (44) |
| **Sex female, n (%)** | 28 (82) |
| **Race, n (%)** | |
| White | 24 (71) |
| Black | 3 (9) |
| Asian | 3 (9) |
| Pacific Islander/Hawaiian | 1 (3) |
| Other/Unknown | 3 (9) |
| **ECOG PS, n (%)** | |
| 0 | 26 (76) |
| 1 | 8 (24) |
| **Disease status, n (%)** | |
| Metastatic | 29 (85) |
| Locally advanced, inoperable | 5 (15) |
| **Prior systemic therapy for advanced PEComa, n (%)[a]** | 4 (12) |

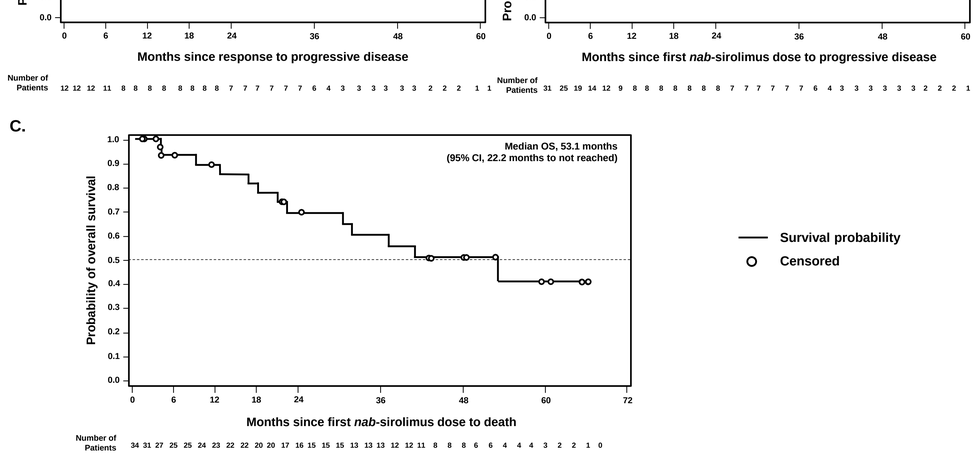
[a]Docetaxel, doxorubicin, gemcitabine, ifosfamide, and olaratumab.
ECOG, Eastern Cooperative Oncology Group; PEComa, perivascular epithelioid cell tumor; PS, performance status.

### Figure 2. Primary Site of Disease (N=34)

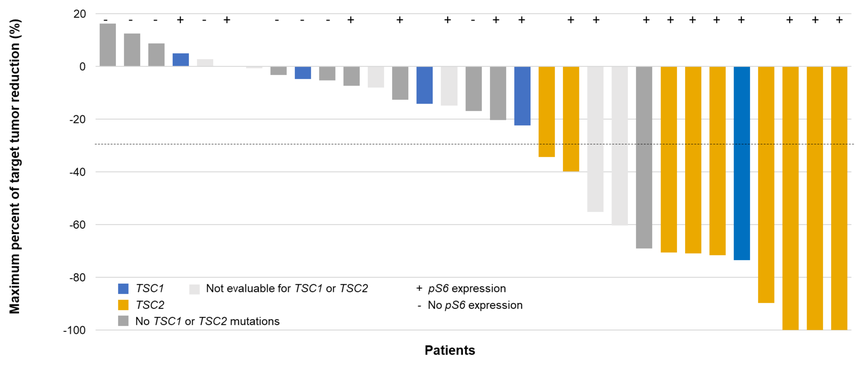



- Most patients in the safety population were female (82%, 28/34), white (71%, 24/34), and had metastatic disease (85%, 29/34); median age at baseline was 59.5 years (range, 27-78 years)
- The efficacy evaluable population included 31 patients with a PEComa diagnosis confirmed by central pathology review and received at least one dose of *nab*-sirolimus
- Among the 31 efficacy-evaluable patients, the independently assessed ORR at AMPECT study completion was 38.7% (95% CI, 21.8%-57.8%)
- Final results for best overall response included confirmed complete response in 2/31 (6.5%) patients, confirmed partial response in 10/31 (32.3%) patients, stable disease (SD) in 16/31 (51.6%) patients, and progressive disease in 3/31 (9.7%) patients
- Disease control rate (DCR; defined as the percentage of patients with a confirmed response or with SD of ≥ 12 weeks duration), was 71% (95% CI, 52%-85.8%)
- **Median DOR** was 39.7 months (95% CI, 6.5 months to not reached; **Figure 3A**)
- Median PFS remained at 10.6 months (95% CI, 5.5-41.2 months; **Figure 3B**)
- **Median OS** was 53.1 months (95% CI, 22.2 months to not reached; **Figure 3C**)

### Figure 3. Kaplan-Meier Estimates for (A) DOR, (B) PFS, and (C) OS



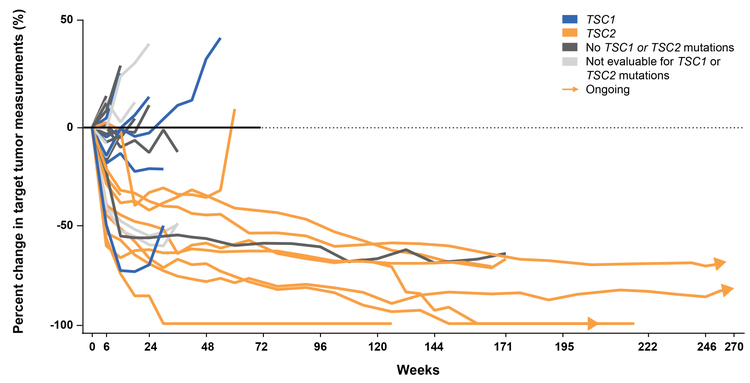

### Figure 4. Target Lesion Changes per Mutational Status




Target tumor reduction may not match best overall response assessment, which takes into consideration nontarget lesions and observations of new lesions per RECIST v1.1.

- In patients with *TSC2* mutations, 8/9 (89%) of patients had confirmed CR or PR (1/9 had an unconfirmed PR), with a DOR of 51.7 months (95% CI, 6.5 months to not reached; **Figures 4** and **5**)
- Response also occurred in some patients with *TSC1*, no *TSC1*/*TSC2*, or unknown mutational status (**Figures 4** and **5**)

### Figure 5. Rapid and Durable Responses




### Table 2. Common TRAEs Occurring in ≥ 25% of Patients With Any Event (N=34)

| TRAEs | Any grade >25%, n (%) | Grade 3, n (%)[a] |
|---|---|---|
| **Hematologic TRAEs** | | |
| Anemia[b] | 18 (53) | 5 (15) |
| Thrombocytopenia[b] | 12 (35) | 1 (3) |
| **Nonhematologic TRAEs** | | |
| Stomatitis[b] | 28 (82) | 6 (18) |
| Fatigue | 21 (62) | 1 (3) |
| Rash[b] | 21 (62) | 0 |
| Nausea | 16 (47) | 0 |
| Diarrhea[b] | 14 (41) | 1 (3) |
| Hyperglycemia[b] | 14 (41) | 3 (9) |
| Weight decreased | 14 (41) | 0 |
| Hypertriglyceridemia[b] | 12 (35) | 1 (3) |
| Edema[b] | 12 (35) | 1 (3) |
| Decreased appetite | 12 (35) | 0 |
| Hypercholesterolemia[b] | 11 (32) | 0 |
| Headache | 11 (32) | 0 |
| Dysgeusia[b] | 10 (29) | 0 |
| Pruritus | 9 (26) | 0 |
| ALT[b] | 9 (26) | 1 (3) |
| Vomiting | 9 (26) | 1 (3) |

[a]Additional G3 TRAEs were abdominal pain, increased AST, lymphopenia, pancytopenia (all 1 occurrence each), dehydration and hypokalemia (2 each). [b]Adverse Events of Special Interest and related referred terms are grouped. ALT, alanine aminotransferase; AST, aspartate aminotransferase; TRAE, treatment-related adverse event.

- There were no new or unexpected safety signals and no grade 4 or 5 treatment-related adverse events (TRAEs) throughout the study (**Table 2**)
- The most common nonhematologic TRAEs were stomatitis (28/34 [82%]) and fatigue and rash (21/34 [62%] each); there were no grade ≥4 TRAEs
- The most common hematologic TRAEs were anemia (18/34 [53%]) and thrombocytopenia (12/34 [35%])
- Noninfectious pneumonitis occurred in 7/34 (21%) patients and was grade 1 or 2 in all cases
- Out of 34 patients, 2 (6%) discontinued due to a TRAE, one of which was grade 2 anemia, and the other grade 1 cystitis
- Treatment-related serious adverse events occurred in 8 patients (24%), and included dehydration (6%), acute kidney injury, acute coronary syndrome, abdominal pain, diarrhea, edema, enteritis, and pancytopenia (3% each), all of which resolved

## CONCLUSION

- The AMPECT study met its primary endpoint and had a median DOR of over 3 years
- Compared to the previous data cut, ORR, DCR, and PFS essentially remained the same and DOR and OS have been updated
- The ORR, PFS, and OS at study completion, as well as the DOR of over 3 years highlight the clinical benefit of *nab*-sirolimus in the treatment of this aggressive, rare sarcoma
- The safety profile indicates that *nab*-sirolimus is tolerable for long-term treatment, without unexpected AEs or new safety signals at study closure
- A tumor-agnostic study (PRECISION 1: NCT05103358) is now recruiting for patients with pathogenic inactivating *TSC1* or *TSC2* alterations

## REFERENCES

1. Wagner AJ, et al. CTOS, November 10-13, 2021, Virtual. 2. Hou S, et al. AACR-NCI-EORTC, October 7-10, 2021, Virtual.
3. Hou S, et al. *Cancer Res.* 2019;79(13 Suppl):348.

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