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ANNUAL MEETING
ON WOMEN'S CANCER

San Diego, CA • 2024

Response to Treatment with *nab*-Sirolimus in Patients with Perivascular Epithelioid Cell Sarcoma (PEComa) of Gynecologic or Peritoneal Origin: Subgroup Analysis from AMPECT

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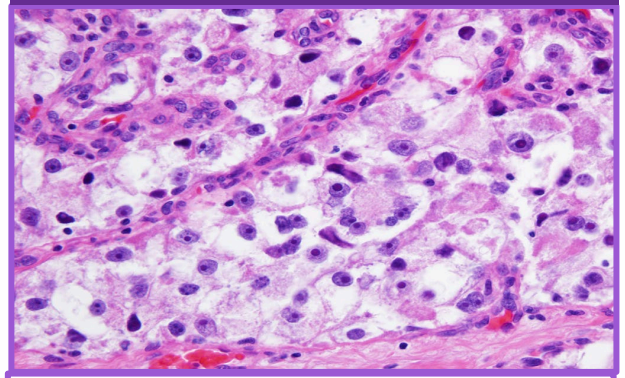
Unlabeled/Investigational Uses

I will not be discussing any unlabeled or investigational uses of any pharmaceutical products or medical devices.

Disease Overview: Advanced Malignant PEComa

HISTOLOGY



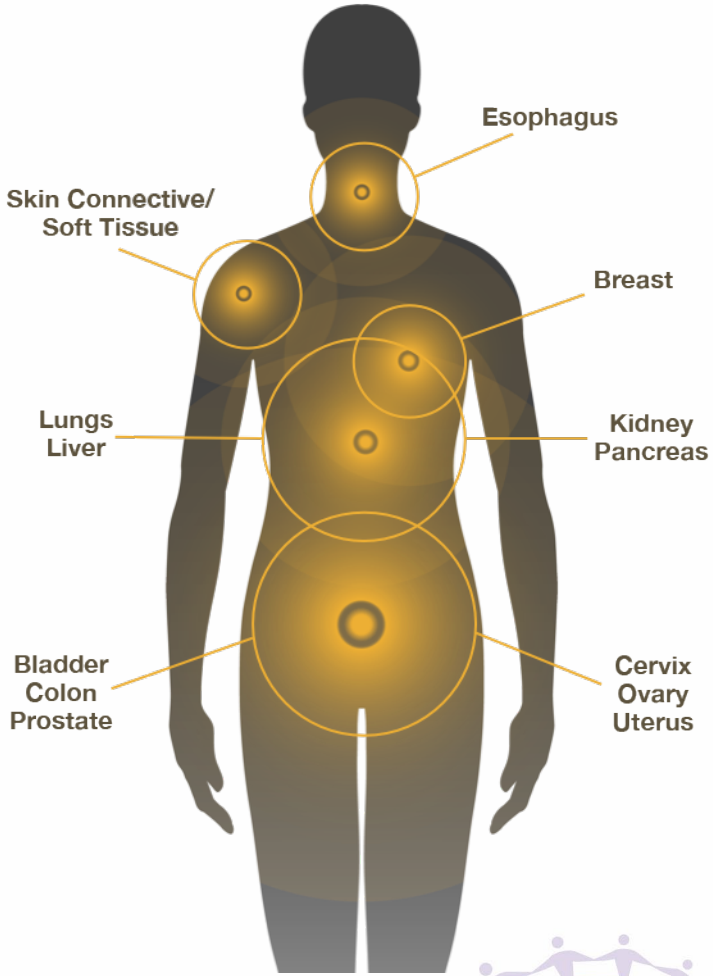
- Mesenchymal tumor (sarcoma) consisting of perivascular epithelioid cells[1]
- Distinctive cells with focal association with blood vessel walls
- Often misdiagnosed as leiomyosarcoma, clear cell sarcoma, metastatic melanoma[2,3]

PRESENTATION

- Aggressive soft tissue sarcomas originating in tissues from diverse anatomic locations[4]
- Rare sarcomas that disproportionately affect females[4–6]
- In the phase 2 registrational AMPECT trial, over **80%** of the patients were female[7,8]

PROGNOSIS

- Advanced malignant PEComa associated with poor prognosis[6]
- Malignant PEComas demonstrate local invasion and/or metastatic spread[6]
- In the metastatic/ unresectable setting, median OS ranges from 16 months with cytotoxic chemotherapy to 29 months with targeted therapy[4,9]



OS, overall survival; PEComa, perivascular epithelioid cell tumor.

1. Data on file. Aadi Bioscience, Inc.; 2021. **2**. National Organization for Rare Disorders. https://rarediseases.org/rare-diseases/perivascular-epithelioid-cell-neoplasm. Accessed January 11, 2023. **3**. Tirumani SH, et al. *AJR.* 2014;202(2):252-2587. **4**. Bleeker JS, et al. *Sarcoma*. 2012;541626. **5**. Sanfilippo R, et al. *Clin Cancer Res.* 2019;25:5295–5300. **6**. Armah HB and Parwani AV. *Arch Pathol Lab Med.* 2009;133:648-654. **7**. Wagner AJ, et al. *J Clin Oncol.* 2024 (in press). **8**. Wagner AJ, et al. *J Clin Oncol.* 2021;39(33):3660-3670. **9.** Benson C, et al. *Anticancer Res*. 2014;34(7):3663-3668.

Objective

- *nab*-Sirolimus is the first and only US FDA-approved treatment for locally advanced unresectable or metastatic malignant PEComa[1,2]
- In the phase 2 registrational AMPECT trial (NCT02494570) in patients with malignant PEComa[3]
  - *nab*-sirolimus demonstrated: ORR=38.7%; median DOR=39.7 mo; median OS=53.1 mo

Herein we report the AMPECT subgroup analysis in female patients with malignant PEComas originating in the uterus, ovary, pelvis, or retroperitoneum

DOR, duration of response; ORR, overall response rate.

1. Hou S, et al. *Cancer Res.* 2019;79:13_suppl, 348. **2**. FYARRO® Package insert. Aadi Bioscience, Inc.: Pacific Palisades, CA; December 2021. **3**. Wagner AJ, et al. *J Clin Oncol.* 2024 (in press). Data cutoff: 29 April 2022.

Phase 2 AMPECT Study Design[1]

Key Eligibility

- ≥18 years old
- ECOG PS 0–1
- Histologically confirmed malignant PEComa
- Locally advanced inoperable or metastatic disease
- ≥1 measurable target lesion by CT or MRI
- No prior mTOR inhibitor

Treatment Phase

- *nab*-Sirolimus 100 mg/m^2 IV on Days 1 and 8 of a 21-day cycle
- Continued until progression or unacceptable toxicity

Endpoints

- Primary Endpoint
  - ORR by independent radiology review (by RECIST v1.1)
- Secondary Endpoints
  - DOR, DCR, and safety/tolerability

ECOG, Eastern Cooperative Oncology Group; IV, intravenously; mTOR, mechanistic target of rapamycin; PS, performance status; RECIST, Response Evaluation Criteria in Solid Tumors.

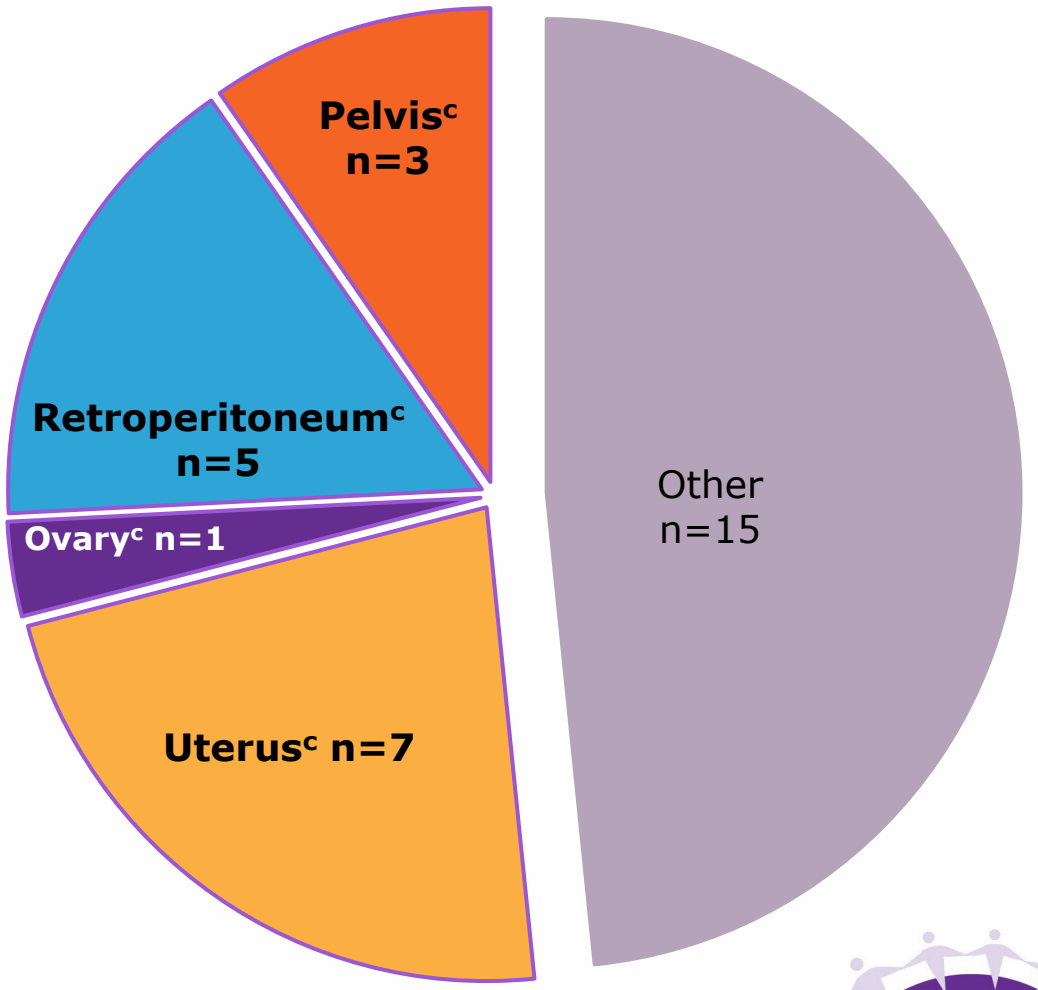
1. Wagner AJ, et al. *J Clin Oncol.* 2024 (in press).

Baseline characteristics

Gynecologic or peritoneal site of PEComa origin subgroup

Baseline characteristic	Female patients in subgroup (n=16)
Age in years, median (range)	61.5 (39–78)
≥65 years, n (%)	7 (44)
Race, n (%)	
White	9 (56)
Black	3 (19)
Other[a]	4 (25)
Ethnicity, n (%)	
Not Hispanic or Latino	12 (75)
Hispanic or Latino	3 (19)
Not reported	1 (6)
ECOG performance status, n (%)	
0	13 (81)
1	3 (19)
Prior treatment for PEComa, n (%)	
Any surgery	14 (88)
Any systemic treatment	2 (13)
Any radiation	1 (6)
None	2 (13)
Number of metastatic sites[b] , n (%)	
1	5 (31)
2	7 (44)
≥3	3 (19)

Primary site of PEComa origin in AMPECT (N=31, all patients)



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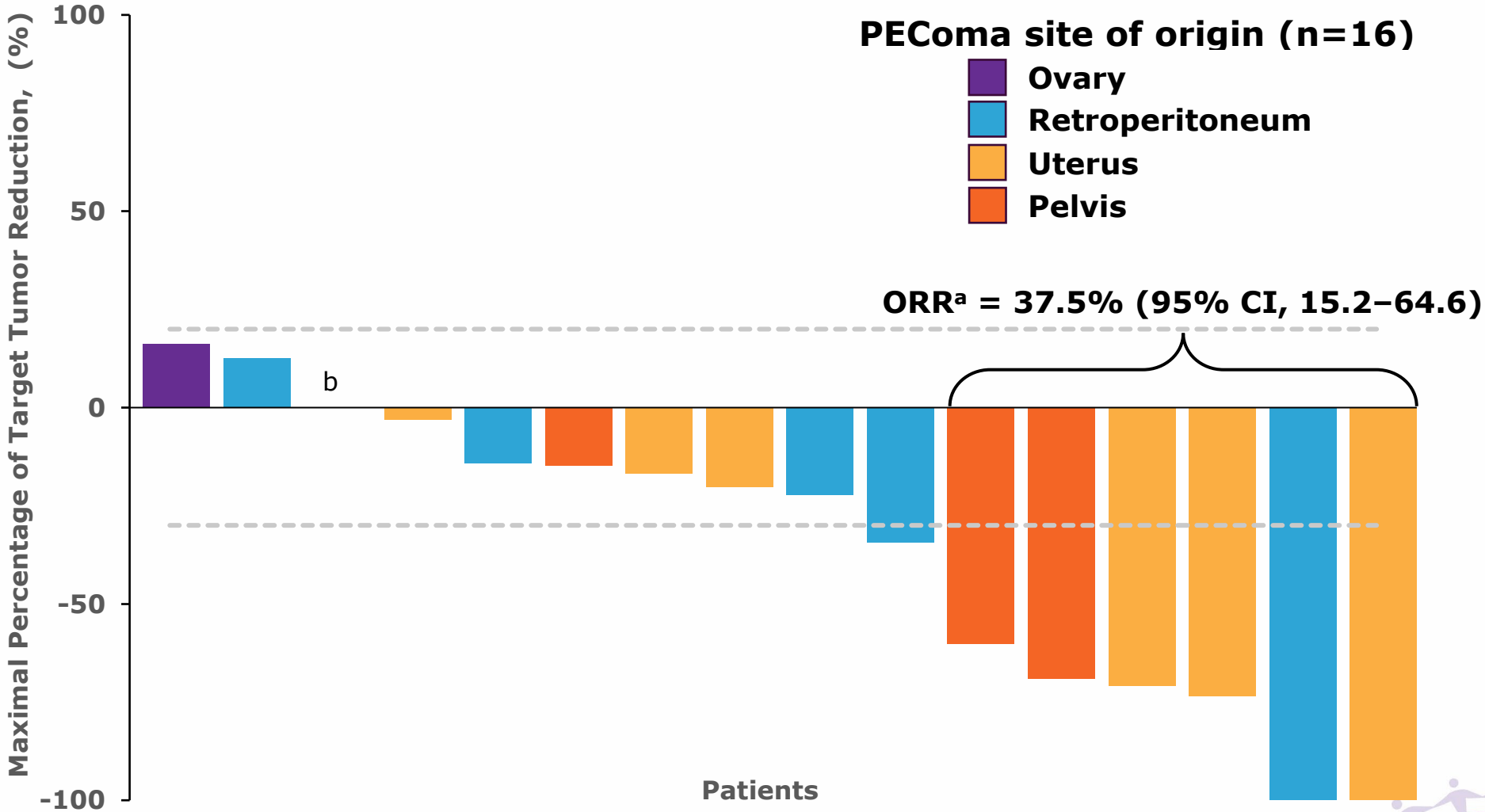
ECOG, Eastern Cooperative Oncology Group.
[a]Includes n=1 each for Asian and Native Hawaiian/other Pacific Islander; n=2 not reported. [b]One patient did not have metastatic disease. [c]Numbers correspond to female patients with these PEComa origin sites. Data cutoff: 29 April 2022.

Best overall response

Gynecologic or peritoneal site of PEComa origin subgroup

- ORR = 37.5% (6/16 pts)
  - All confirmed PR
- DCR = 62.5%
  - SD for ≥12 weeks, 25% (4/16 pts)
- Results consistent with overall AMPECT population[1] (ORR = 38.7%, DCR = 71%)



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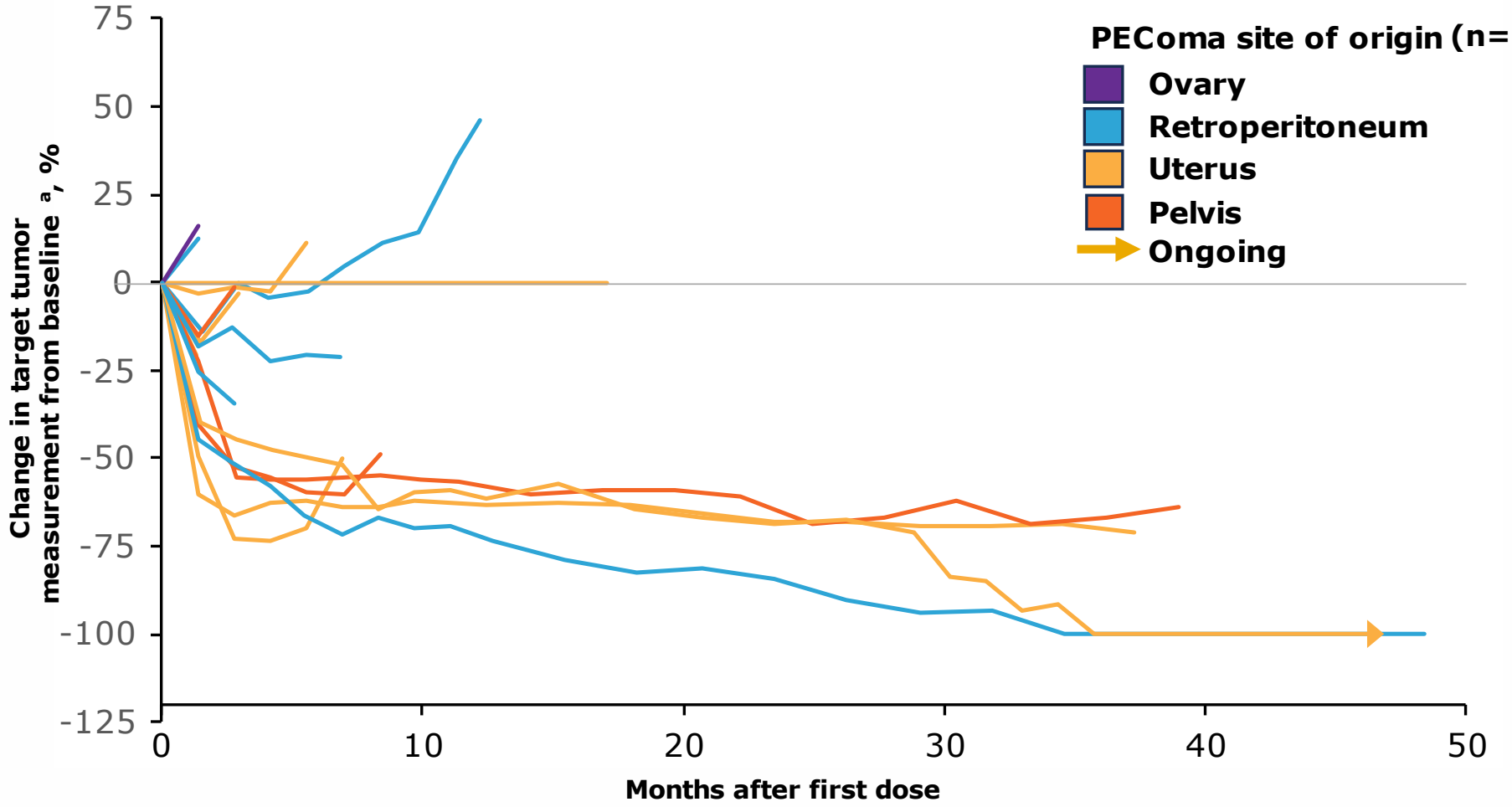
CI, confidence interval; DCR, disease control rate; ORR, overall response rate; PD, progressive disease; PR, partial response; pts, patients; SD, stable disease. **1**. Wagner AJ, et al. *J Clin Oncol.* 2024 (in press).
[a]Overall response rate was determined by independent radiology review per RECIST v1.1. [b]This patient (PEComa of uterine origin) had no baseline target tumor based on independent radiology review. Data cutoff: 29 April 2022.

Tumor responses to *nab*-sirolimus

Gynecologic or peritoneal site of PEComa origin subgroup

The median time to response among the 6 responders was 1.4 months and the median DOR was 36.2 months



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DOR, duration of response; PD, progressive disease; PR, partial response; SD, stable disease.
[a]One patient had no baseline target tumor based on independent radiology review (flat line displayed here).
Data cutoff: 29 April 2022

Safety

Gynecologic or peritoneal site of PEComa origin subgroup

- **Most TRAEs were grade 1 or 2**
- **Other grade 3 TRAEs:**
  - Lipase increased (n=1, 6%)
  - Dehydration (n=2, 13%)
  - Hypophosphatemia (n=1, 6%)
  - Enteritis (n=1, 6%)
- **No grade 4 or 5 TRAEs**
- **3 patients had serious TRAEs**
- **TRAEs led to:**
  - Dose delay, n=10 (63%)
  - Dose reduction, n=5 (31%)
  - Treatment discontinuation, n=1 (6%, due to grade 2 anemia)

TRAEs occurring in ≥25% of patients[a]	Any grade	Grade 3
Patients with any TRAE	**16 (100)**	**10 (63)**
Non-hematologic TRAEs		
Stomatitis[b]	**13 (81)**	**4 (25)**
Fatigue	**10 (63)**	**0**
Edema[b]	**9 (56)**	**0**
Rash (maculo-papular)[b]	**9 (56)**	**0**
Diarrhea[b]	**8 (50)**	**1(6)**
Hyperglycemia[b]	**8 (50)**	**2 (13)**
Nausea	**8 (50)**	**0**
Decreased appetite	**7 (44)**	**0**
Vomiting	**7 (44)**	**1 (6)**
Hypercholesterolemia[b]	**6 (38)**	**0**
Taste disorder[b]	**5 (31)**	**0**
Hypokalemia[b]	**5 (31)**	**2 (13)**
Pruritus	**5 (31)**	**0**
Weight decreased	**5 (31)**	**0**
Alopecia	**4 (25)**	**0**
Amylase increased	**4 (25)**	**1 (6)**
Constipation	**4 (25)**	**0**
Headache	**4 (25)**	**0**
Pneumonitis[b]	**4 (25)**	**0**
Hematologic TRAEs		
Anemia[b]	**9 (56)**	**3 (19)**

TEAE, treatment-emergent adverse events; TRAE, treatment-related adverse events.
[a]Two grade 5 TEAEs (upper gastrointestinal hemorrhage and atelectasis), both unrelated to *nab-sirolimus*, were reported.
[b]Preferred terms were grouped for mTOR inhibitor class effects. Data cutoff: 29 April 2022

Conclusions

- ORR of 37.5% observed (irrespective of *TSC1*/*TSC2* mutation status) among 16 female patients with malignant PEComas originating from uterine, ovarian, pelvic, and retroperitoneal sites
  - Results similar to ORR of 38.7% for the overall AMPECT efficacy population (n=31)[1]
  - This subgroup of patients comprised over half of the evaluable AMPECT study population
- Responses to *nab*-sirolimus were rapid and durable
- A manageable safety profile was observed in the subgroup, and was consistent with that of the full AMPECT population
- Studies are underway investigating utility of *nab*-sirolimus (current SOC and NCCN-preferred regimen to treat malignant PEComa[2]) in mTOR-driven cancers of gynecologic origin

NCCN, National Comprehensive Cancer Network; ORR, overall response rate.

1. Wagner AJ, et al. *J Clin Oncol.* 2024 (in press). **2.** FYARRO® Package insert. Aadi Bioscience, Inc.: Pacific Palisades, CA; December 2021.

Acknowledgments

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