nab-Sirolimus for patients with advanced malignant PEComa with or without prior mTOR inhibitors: Biomarker results from AMPECT and an expanded access program



Data Collection

(when available)

Post-hoc evaluation of

response via electronic

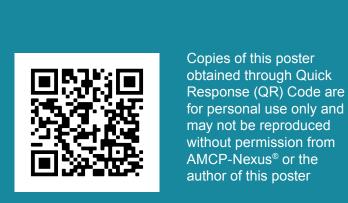
medical record review

Tumor molecular profile by

next generation sequencing

Mark A Dickson, MD¹; Vinod Ravi, MD²; Richard F Riedel, MD³; Kristen N Ganjoo, MD⁴; Brian A Van Tine, MD, PhD⁵; Rashmi Chugh, MD¹; Lee D Cranmer, MD, PhD⁵; Rashmi Chugh, MD¹; Lee D Cranmer, MD, PhD⁵; Rashmi Chugh, MD¹; Vinod Ravi, MD¹; Martina C Murphy, MD¹¹; Anita N Schmid, PhD¹¹; Neil Desai, PhD¹¹; Norma Alonzo Palma, PhD¹¹; David J Kwiatkowski, MD, PhD¹²; Andrew J Wagner, MD, PhD¹³

¹Memorial Sloan Kettering Cancer Center, New York, NY; ²The University of Texas MD Anderson Cancer Center, Houston, TX; ³Duke Cancer Institute, Duke University of Washington/Fred Hutchinson Cancer Research Center, Durham, NC; ⁴Stanford University, Stanford University, Stanford University of Michigan, Ann Arbor, MI; ¹University of Florida, Gainesville, FL; ¹¹Aadi Bioscience, Pacific Palisades, CA; ¹²Brigham and Women's Hospital, Boston, MA; ¹³Dana-Farber Cancer Institute, Boston, MA



INTRODUCTION

- ► Inactivating alterations in *TSC1* or *TSC2* are considered targetable biomarkers for mTOR inhibition¹
- nab-Sirolimus is an albumin-bound mTOR inhibitor (mTORi) approved for the treatment of adult patients with locally advanced unresectable or metastatic malignant PEComa, a tumor that frequently has inactivating alterations in *TSC2* or *TSC1*^{2,3}
- The AMPECT trial (NCT02494570) of *nab*-sirolimus efficacy and safety was the first prospective study in advanced malignant PEComa⁴
- In exploratory biomarker analyses, known inactivating alterations in TSC1 or TSC2 were associated with response
- To allow access to *nab*-sirolimus treatment for patients with serious conditions who were excluded from AMPECT⁴, an expanded access program⁵ (EAP; NCT03817515) bridged the gap between closure of enrollment in the AMPECT trial and *nab*-sirolimus market access
- We report data from the final analysis of AMPECT patients, who were naïve to mTORi, and from patients with malignant PEComa with prior mTORi exposure treated with *nab*-sirolimus in the EAP

SAFETY

- ► There were no Grade 4 or 5 treatment-related AEs (TRAEs) in AMPECT
- ► The most common TRAEs in AMPECT were mucositis, fatigue, and rash (**Table 1**) Four patients with a response had TRAEs that were managed with dose reduction; these patients maintained response on the lower dose
- AEs reported by the treating physician in the EAP were consistent with what was reported in AMPECT

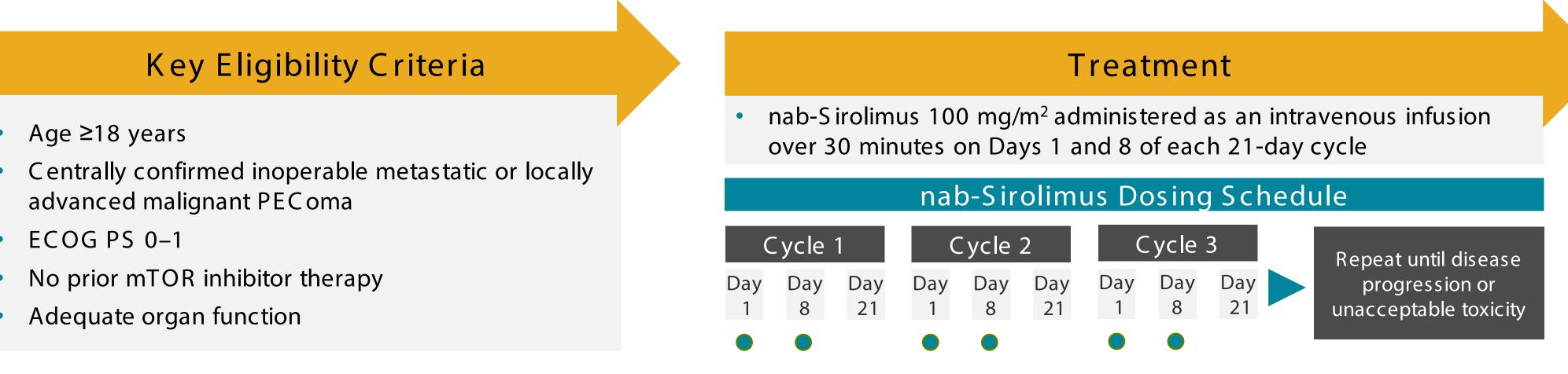
Table 1. Most frequent TRAEs and Grade 3 TRAEs in AMPECT

TRAEs	Any grade (>25%)	Grade 3
Hematologic TRAEs		
Anemia	18 (53)	5 (15)
Thrombocytopenia	12 (35)	1 (3)
Nonhematologic TRAEs		
Mucositis	27 (79)	6 (18)
Fatigue	21 (62)	1 (3)
Rash	21 (62)	
Nausea	16 (47)	
Diarrhea	14 (41)	
Hyperglycemia	14 (41)	3 (9)
Weight decreased	14 (41)	
Dermatitis	12 (35)	
Hypertriglyceridemia	11 (32)	1 (3)
Hypercholesterolemia	11 (32)	
Decreased appetite	12 (33)	
Dysgeusia	9 (26)	
Headache	10 (29)	
ALT	9 (26)	1 (3)
Edema	9 (26)	
Pruritus	9 (26)	
Vomiting	9 (26)	1 (3)

METHODS

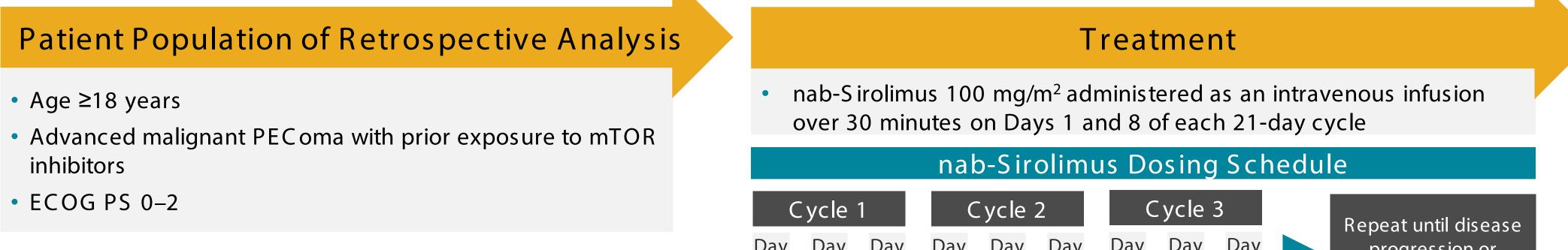
AMPECT

> AMPECT was a phase 2, open-label, single-arm, multicenter study in patients with advanced malignant PEComa to determine the efficacy and safety of *nab*-sirolimus through intravenous infusion (data cutoff as of June 2021)



Expanded Access Program

> Based on early signal of clinical benefit from the AMPECT study, this expanded access protocol bridged between the closure of the enrollment in AMPECT and the regional marketing approval of the product in order to allow patients with malignant PEComa to be treated with nab-sirolimus



EFFICACY

- > 31 patients with malignant PEComa and no prior mTORi exposure are shown as of June 2021
- ► ORR was 39% (12/31 patients), including 2 CRs, and DCR was 71% Median DOR was not reached after 3 years of follow-up, indicating
- that >50% of patients will have a DOR >36 months
- No clinically relevant differences by baseline characteristics were noted

baseline had successful resection after treatment with *nab*-sirolimus

Patients obtained benefit regardless of TSC1 and TSC2 alteration status During long-term follow-up, 2 patients ineligible for tumor resection at

Table 2. Best overall response in all evaluable patients and patients with known inactivating alterations in *TSC1* or *TSC2* in AMPECT

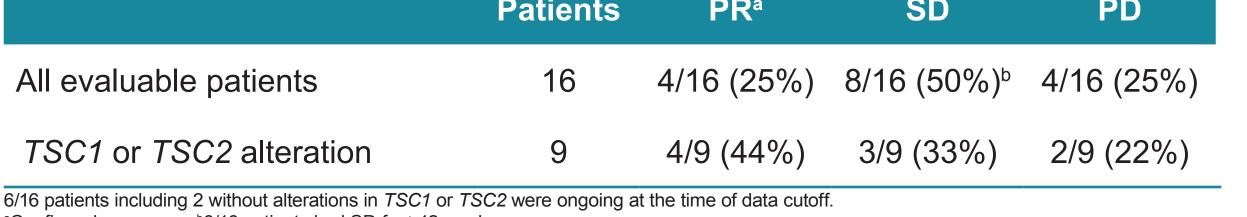
	Patients	CR or PR ^a	SD	PD
All evaluable patients	31	12/31 (39%)	16/31 (52%)	3/31 (10%)
TSC1 or TSC2 alteration	14	9/14 (64%)	4/14 (29%)	1/14 (7%)

CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease

16 patients with malignant PEComa and prior mTORi exposure were treated on the EAP from July 2019–July 2021; prior mTORi included sirolimus, everolimus, temsirolimus, and sapanisertib; 12 patients had exposure to 1 prior mTORi and 4 patients had exposure to ≥2 prior mTORis; and 50% had had progressive disease as best response on previous mTORi

The DCR was 63% (10/16)

Table 3. Best overall response in all evaluable patients and patients with known inactivating alterations in *TSC1* or *TSC2* on the EAP



^aConfirmed responses. ^b6/16 patients had SD for ≥12 weeks. EAP, expanded access program; PD, progressive disease; PR, partial response; SD, stable disease.

REFERENCES

- . Huang J, et al. *Biochem J.* 2008 ; 412(2) :179–90. FYARRO (sirolimus albumin-bound particles for injectable suspension). Package insert. Pacific Palisades, CA. Aadi Bioscience, Inc.; 2021. Martignoni G, et al. Virchows Arch. 2008;452:119–132.
- 4. Wagner AJ, et al. *J Clin Oncol*. 2021;39(33):3660–70. 5. Dickson MA, et al. Connective Tissue Oncology Society Meeting November 10-13, 2021 [Oral Presentation]

This study was funded by Aadi Bioscience, Inc. Editorial support was provided by Hilary Durbano, PhD, of AlphaBioCom, LLC, King of Prussia, PA, USA, and funded by Aadi Bioscience, Inc.



Primary Endpoint

Other Endpoints

ORR by central review per RECIST v1.1

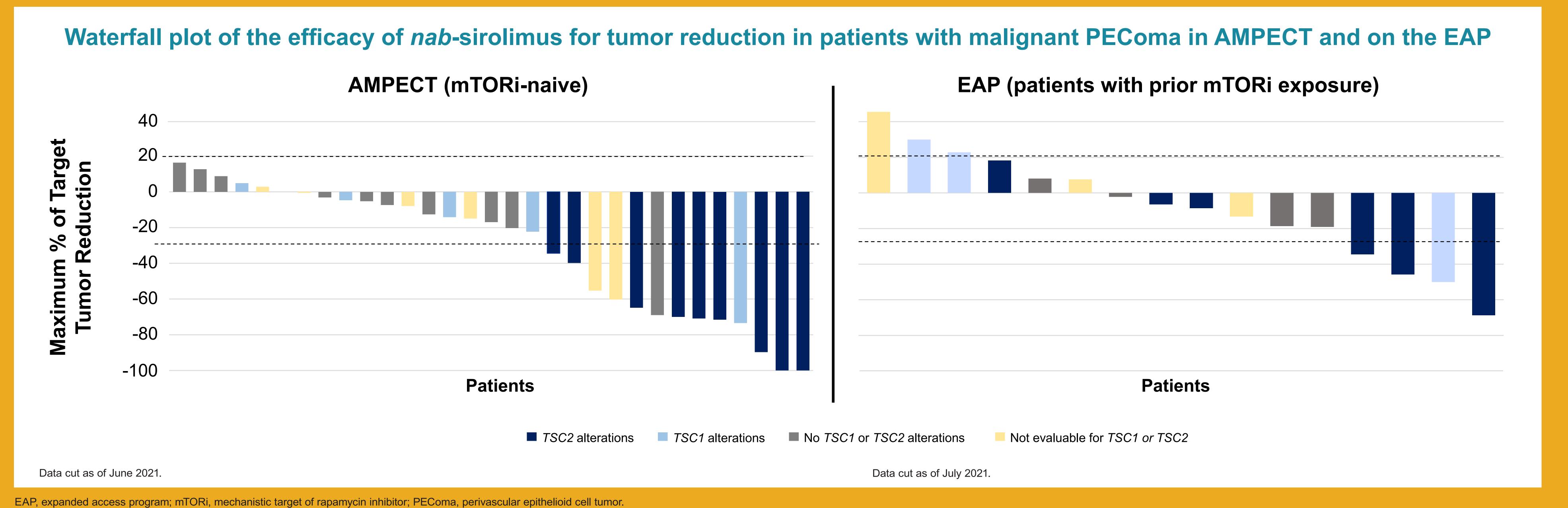
DOR, DCR (CR, PR, or SD of ≥12 weeks'

duration), safety/tolerability, and

sequencing (when available)

subgroup analyses based on tumor

molecular profiling by next generation



CONCLUSIONS

- nab-Sirolimus provided clinical benefit in mTORi-naïve patients with malignant PEComa in the AMPECT trial and in patients with malignant PEComa with prior mTORi therapy in an EAP
- Although AMPECT and the EAP cannot be directly compared, response rates showed similar trends regardless of prior mTORi exposure and in patients with TSC1 or TSC2 alterations
- > Based on the emerging biomarker results, a tissue-agnostic pan-tumor Phase 2 study in patients with TSC1 and TSC2 alterations has been initiated and is currently enrolling patients (NCT05103358)