Abstract ID: 1080747
Session 8, Nov 12, 2021

FINAL ANALYSIS FROM AMPECT, an OPEN-LABEL PHASE 2 REGISTRATION TRIAL of *nab*-SIROLIMUS for PATIENTS WITH ADVANCED MALIGNANT PERIVASCULAR EPITHELIOID CELL TUMORS (PEComa)

Andrew J. Wagner, MD, PhD,[1] Vinod Ravi, MD,[2] Richard F. Riedel, MD,[3] Kristen N. Ganjoo, MD,[4] Brian A. Van Tine, MD, PhD,[5] Rashmi Chugh, MD,[6] Lee D. Cranmer, MD, PhD,[7] E. Maria Gordon, MD,[8] Jason L. Hornick, MD, PhD,[9] Heng Du, MD,[9] Berta Grigorian,[10] Anita N. Schmid, PhD,[10] Shihe Hou, PhD,10 Katherine Harris, DrPH, [10] David J. Kwiatkowski, MD, PhD,[9] Neil P. Desai, PhD,[10] Mark A. Dickson, MD,[11]

1. Dana-Farber Cancer Institute, Boston, MA
2. MD Anderson Cancer Center, Houston, TX
3. Duke Cancer Institute, Durham, NC
4. Stanford University, Stanford, CA
5. Washington University in Saint Louis, St. Louis, MO
6. University of Michigan, Ann Arbor, MI
7. Univ Washington/Fred Hutchinson Cancer Res Ctr, Seattle, WA
8. Sarcoma Oncology Center, Santa Monica, CA
9. Brigham and Women's Hospital, Boston, MA
10. Aadi Bioscience, Pacific Palisades, CA
11. Memorial Sloan Kettering Cancer Center, New York, NY

DISCLOSURES

- Consulting: Aadi Bioscience, Boehringer-Ingelheim, Cogent Biosciences, Daiichi-Sankyo, Deciphera, Eli Lilly, Foghorn Therapeutics
- Research Support to My Institution: Aadi Bioscience, Daiichi-Sankyo, Deciphera, Foghorn Therapeutics, Karyopharm, Plexxikon

- This study (NCT02494570) was sponsored by Aadi Bioscience
- This study was funded in part by FDA Office of Orphan Products Development (OOPD) Grant R01FD005749

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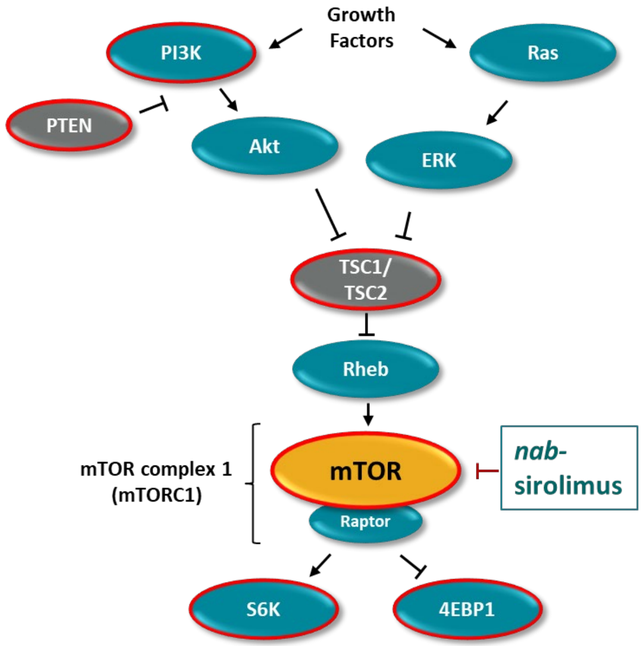
Rationale for *nab*-Sirolimus (ABI-009) for Patients with Advanced Malignant Perivascular Epithelioid Cell Tumors (PEComa)



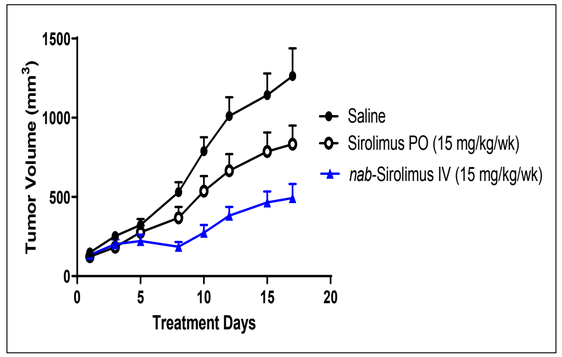
mTOR pathway activation is common in PEComa

- PEComas are associated with alterations of *TSC1* or *TSC2*, which are negative regulators of the mTOR signaling pathway [1]

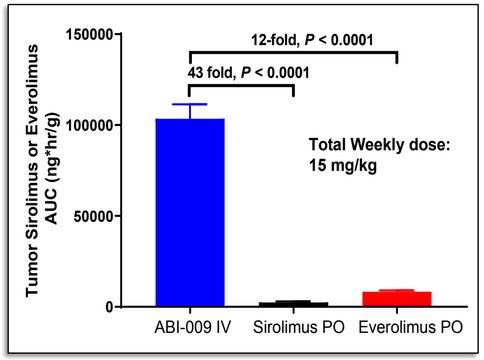
nab-Sirolimus

- *nab*-Sirolimus is an mTOR inhibitor with significantly higher anti-tumor activity, significantly higher intratumoral drug accumulation, and significantly higher mTOR target (pS6 and p4EBP1) suppression in preclinical models [2,3]

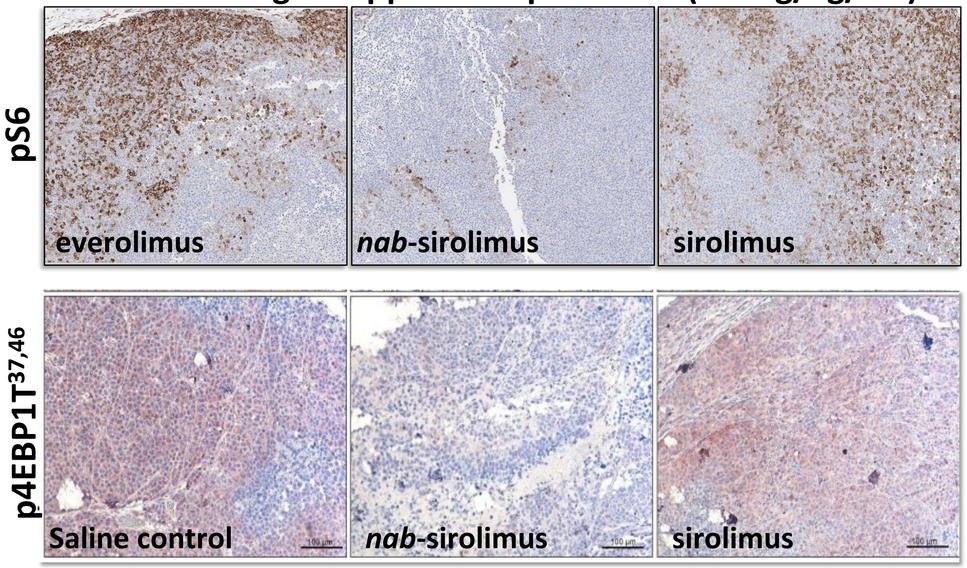
Tumor Growth [3]
(HCC, TSC-null)



Tumor drug accumulation [3]
(PTEN-loss, bladder cancer)



Tumor IHC Target suppression post dose (15 mg/kg/wk) [3]



1. *Gao et al., Signal Transduction 2015*
2. *Hou et al., AACR 2019 (Abstr#348)*
3. *Hou et al., AACR Molecular Targets 2021 (Abstr P138)*

AMPECT: *nab*-Sirolimus in Advanced Malignant PEComa
Phase 2 Registrational Open-label Multicenter Study Design

Key Eligibility
- ≥18 years old
- ECOG PS 0, 1
- Histologically confirmed malignant PEComa
- Locally advanced inoperable or metastatic disease
- No prior mTOR inhibitors

ClinicalTrials.gov: NCT02494570

→

Treatment Phase
nab-Sirolimus 100 mg/m^2 IV D1, 8 q 21d until progression or unacceptable toxicity

→

Quarterly Follow-up for survival

Sample Size: ORR of ~30% in 30 evaluable patients to exclude the lower bound of the 95% CI of 14.7%

Efficacy Evaluable Patients: Must receive ≥1 dose of *nab*-sirolimus; must have centrally confirmed PEComa

- **Primary Endpoint – ORR by Independent Radiology Review** (RECIST v1.1)
  - CT/MRI every 6 weeks for the 1st year, every 12 thereafter
- **Secondary Endpoints**
  - **DOR, PFS at 6 months, median PFS, median OS**
  - **Safety**
- **Key Exploratory Endpoints**
  - **Investigator response assessment**
  - **Biomarkers: mutational analysis (NGS, IHC, FISH)**

Presented here is the final analysis (June 2021), 2.5 years after the last patent initiated therapy

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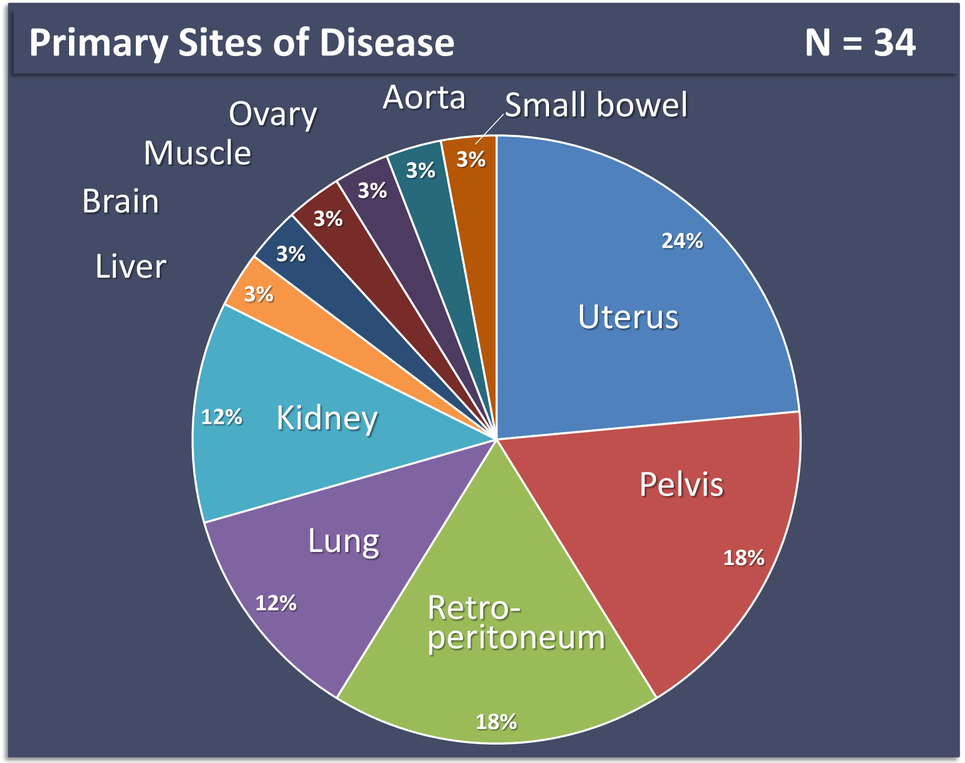
AMPECT: Baseline Demographics and Characteristics and Disposition

Variable	All Treated Patients (N = 34)
Age, median (range), years	60 (27, 78)
≥65 years, n (%)	15 (44)
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 0, n (%)	26 (76)
ECOG 1, n (%)	8 (24)
Metastatic, n (%)	29 (85)
Locally Advanced, inoperable, n (%)	5 (15)
Prior Systemic Rx for Advanced PEComa,* n (%)	4 (12)

** docetaxel, doxorubicin, gemcitabine, ifosfamide, olaratumab*



Patient Disposition as of June 30, 2021, Final Analysis

- Median Follow-up: 22 months (range 1, 58)
- 30 of 34 patients discontinued treatment. Main reasons off therapy was PD (59%), others included AE, surgery, withdrew consent, death
  - 4 patients have ongoing treatment (all responders)
  - 6 patients are in post-treatment on-study follow-up for survival

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AMPECT: Treatment-related Adverse Events (TRAEs) – Final Analysis

TRAEs	Any Grade >25% n (%)	Grade 3** n (%)
Patients with Any TRAEs	34 (100)	
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 (35)	--
Dysgeusia	9 (26)	--
Headache	10 (29)	--
ALT	9 (26)	1 (3)
Edema	9 (26)	--
Pruritus	9 (26)	--
Vomiting	9 (26)	1 (3)

- No grade 4 or 5 TRAEs
- No unexpected AEs or new safety signals
- Pneumonitis 7/34 (21%), G1/G2 only
- Discontinuation due to AE: 2/34 (6%) patients (grade 2 anemia and grade 1 cystitis)

- Treatment-related Serious Adverse Events were:
  - 6% dehydration and 3% each of acute kidney injury, acute coronary syndrome, abdominal pain, diarrhea, edema, enteritis, pancytopenia
    - All recovered / resolved

*Indicate Adverse Events of Special Interest and related preferred terms are grouped
** Additional G3 TRAEs were 6% hypokalemia each, and 3% each of AST/ALT, amylase ↑, hypophosphatemia, insomnia, lipase ↑, lymphocyte ↓, skin infection

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AMPECT: Best Responses and Duration of Response – Final Analysis

Variable	Independent Review
Best Overall Responses	**N = 31** [1]
Confirmed Overall Response Rate	**39% (12/31, 95%CI: 22, 58)**
Complete Response (CR)	7% (2/31)
Partial Response (PR)	32% (10/31)
Stable Disease	**52%**
Progressive Disease	**10%**
Disease Control Rate (CR, PR, SD ≥12 weeks)	**71%**
Duration of Response [2]	**n = 12**
Median DOR **Range: min - max, months**	**Not Reached** **5.6 — 55.5+**
DOR rate at 6 months	**92%**
DOR rate at 12 months	**75%**
DOR rate at 24 months	**66%**
DOR rate at 36 months	**66%**

Total may exceed 100% due to rounding

[1] **3/34 treated patients were not evaluable - 2 pts confirmed as 'not PEComa' (misdiagnosis), 1 pt had no tissue for central confirmation of PEComa**

[2] **Duration of response median and rates are based on KM estimates "+" indicate ongoing value.**

- **2 patients converted from a PR to CR after 11 months and 34 months of treatment, respectively**
- **Median DOR has not been reached, 50% of patients had a DOR of 36.1+ months (range 5.6, 55.5+ months)**

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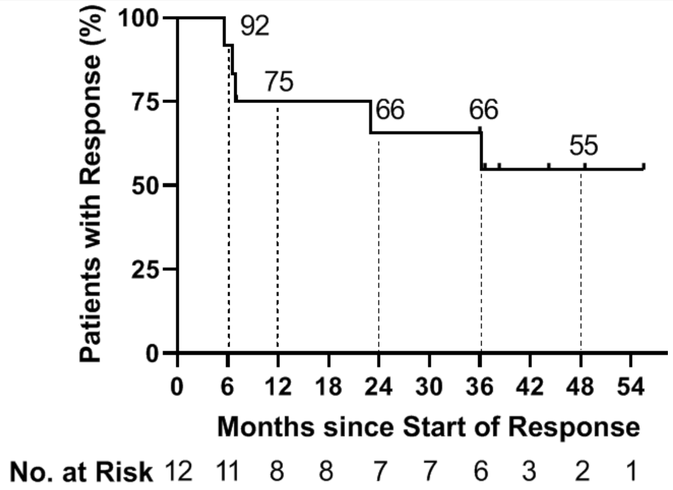
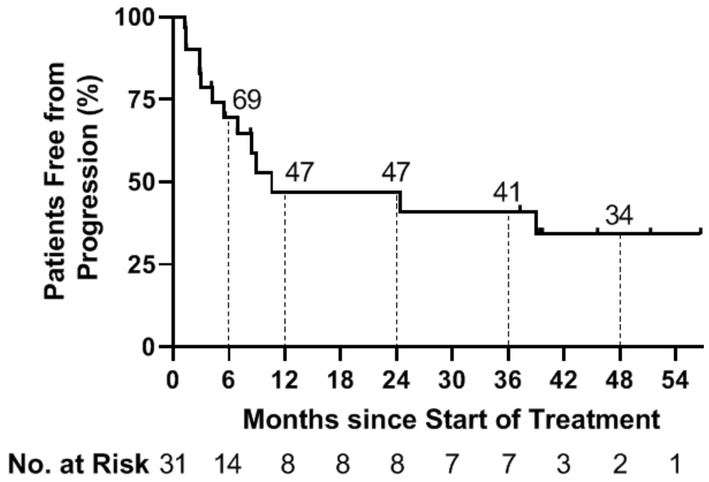
AMPECT: Kaplan-Meier Estimates for DOR, PFS, and OS – Final Analysis

DOR for Responders
n = 12



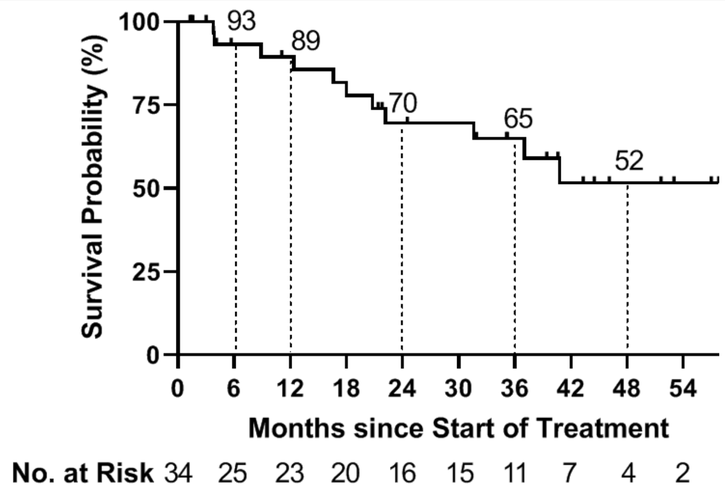
Median DOR: not reached

PFS for Efficacy evaluable patients
n = 31



Median PFS: 10.6 mo

OS for Treated Patients
N = 34



Median OS: 40.8 mo

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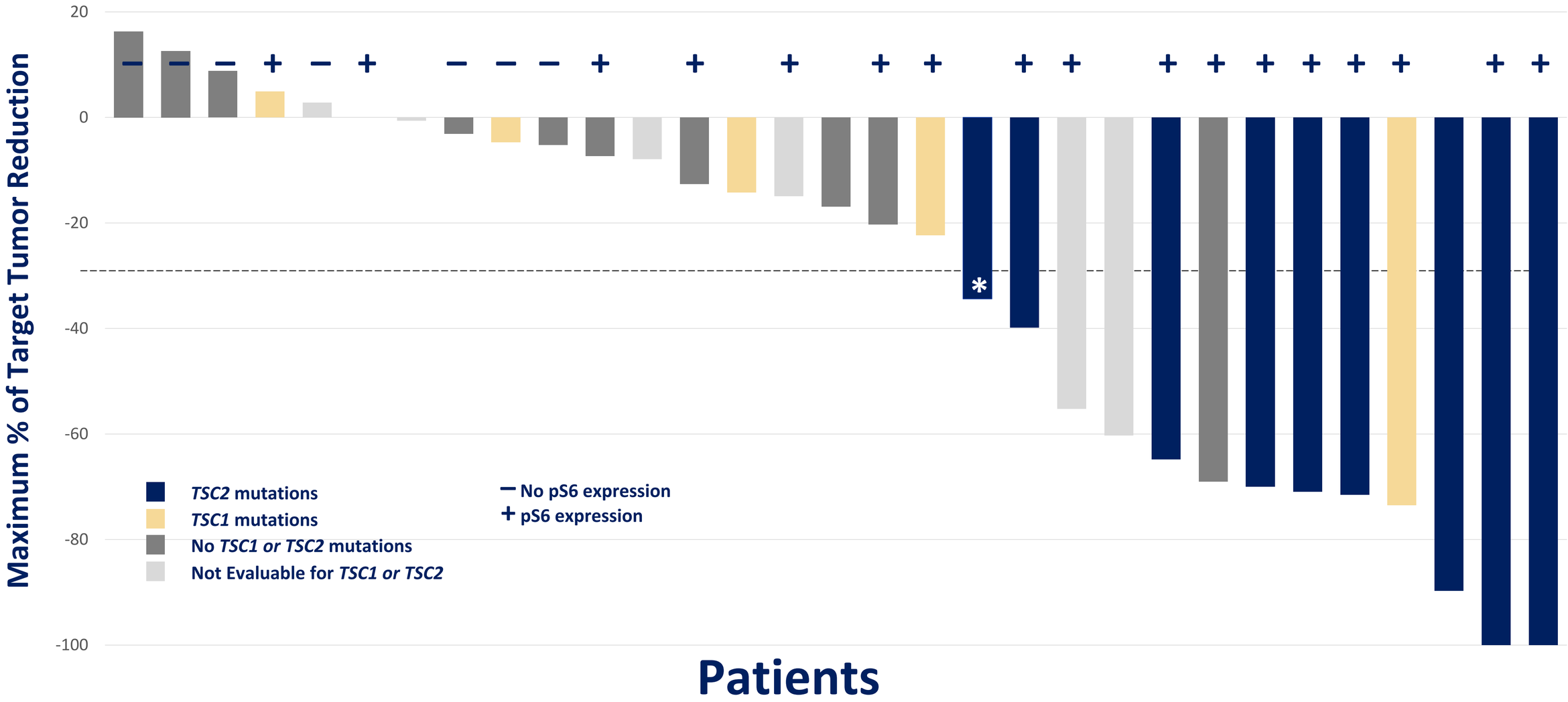
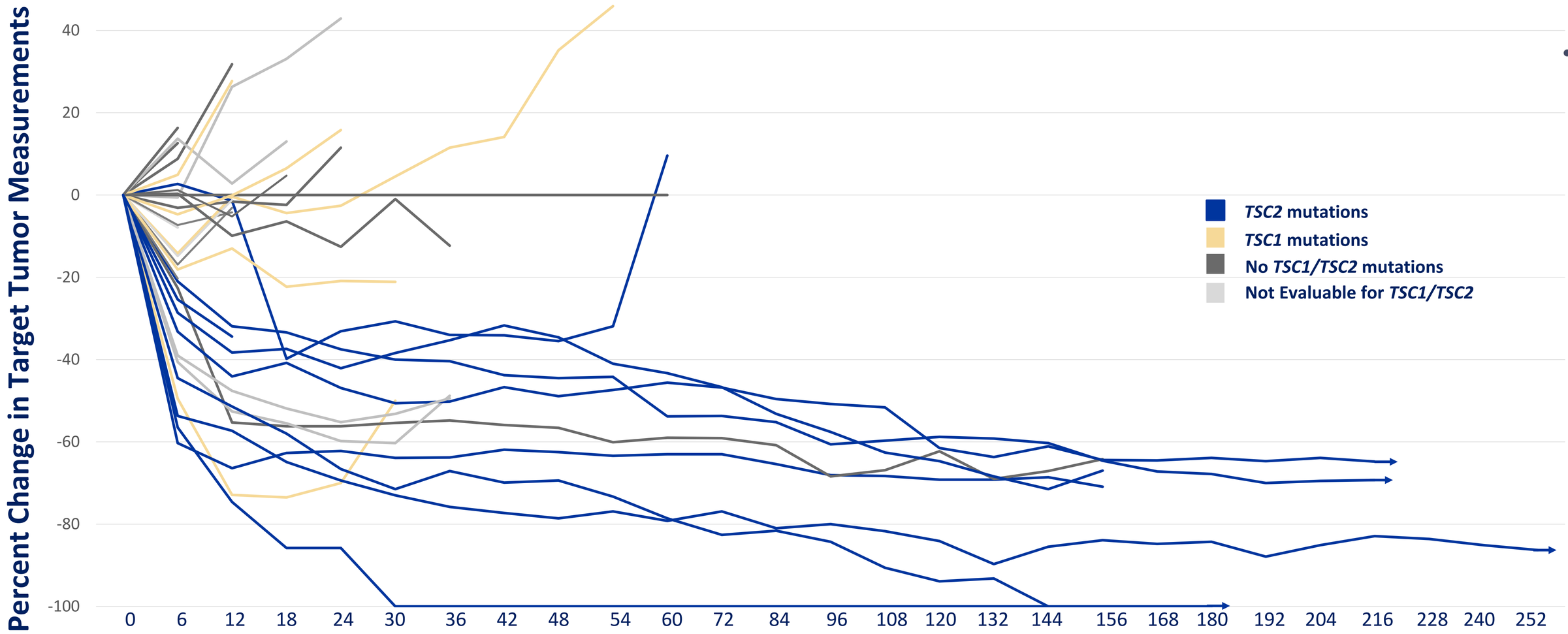
AMPECT: Target Lesion Changes Per Mutational Status – Final Analysis



* 1 patient had an unconfirmed partial response and thus best response is stable disease as per RECIST v1.1

AMPECT: Rapid and Durable Responses – Final Analysis



2.5-year Follow Up Final Results From AMPECT: *nab*-sirolimus in Advanced Malignant PEComa

- This registrational trial met its primary endpoint; the independently assessed confirmed ORR was 39% (95% CI 22% - 58%), 2 CRs and 10 PRs, with durable responses and acceptable safety profile
- Median DOR has not been reached, 50% of patients had a response exceeding 36+ months (range: 5.6, 55.5+)
- Disease control (CR/PR/SD ≥12 weeks) was achieved in 71% of patients
- No new safety signals observed despite relatively high doses of nab-sirolimus compared to other mTORi

Mutational Analysis vs Response:

- *TSC2* mutations: 89% (8/9) patients had confirmed ORR (1/9 had an unconfirmed response)
- Responses also occurred in some patients with *TSC1* or *no TSC1 / TSC2* or unknown mutational status
- This first prospective study in advanced malignant PEComa suggests that *nab*-sirolimus is active in a rare and aggressive sarcoma for which there are no approved therapies
- A tumor-agnostic study is planned for patients with pathogenic inactivating *TSC1* or *TSC2* alterations

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A ‘Thank you’ to the Patients and Families, and to the Study Teams!