Abstract #11516: Long-term follow-up for duration of response (DOR) after weekly *nab*-sirolimus (ABI-009) in patients with advanced malignant perivascular epithelioid cell tumors (PEComa): Results from a registrational open-label phase 2 trial, AMPECT

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] Erlinda M. Gordon, MD,[8] Jason L. Hornick, MD, PhD,[9] David J. Kwiatkowski, MD, PhD,[9] Heng Du, MD,[9] Berta Grigorian,[10] Anita N. Schmid, PhD,[10] Shihe Hou, PhD,[10] Katherine Harris, DrPH,[10] 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, Missouri; 6. University of Michigan; 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

Background

- Advanced malignant perivascular epithelioid cell tumor (PEComa) is a rare, aggressive sarcoma, with no approved treatments.
- The AMPECT phase 2 registration trial is the first prospective clinical trial and investigated the safety and efficacy of *nab*-sirolimus in advanced malignant PEComa (NCT02494570).

Methods

- **Key Eligibility:**
  - ≥18 years old, with ECOG PS 0, 1
  - Histologically confirmed malignant PEComa
  - Metastatic or inoperable locally advanced disease
  - No prior mTOR inhibitors
- **Sample Size:** ORR of ~30% in 30 evaluable patients to exclude the lower bound of the 95% CI of 14.7%
- **Key Endpoints:**
  - Primary – ORR by Independent Radiology Review
  - CT/MRI (RECIST v1.1) every 6 weeks for 1 year, then every 12 weeks thereafter
  - Secondary – DOR, median PFS, median OS, Safety
  - Exploratory – mutational analysis and biomarkers

Dosing & Administration

- *nab*-Sirolimus 100 mg/m^2 IV D1 and D8 q21d until progression or unacceptable toxicity

Variable	All 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)
Other/Unknown	4 (12)
Locally Advanced, n (%)	5 (15)
Metastatic, n (%)	29 (85)

Independent Review at the Primary Analysis of May 22, 2019	ABI-009 at 100 mg/m^2	95% CI
Best Response	N = 31	
Confirmed CR + PR	12/31 (39%)	21.8, 57.8
Stable Disease (SD)	16/31 (52%)	33.1, 69.8
Progressive Disease	3/31 (10%)	2.0, 25.8
Disease Control Rate (CR+PR+SD≥12 wks)	71%	52.0, 85.8
ORR in Metastatic Patients (All PR)	12/29 (46%)	26.6, 66.6
ORR in Locally Advanced Patients (All SD)	0/5 (0%)	--

1-year Follow-up

- The median duration of response (DOR) was not reached (>25.8 months, [5.6 – 42.4+]).
- 67% (8/12) of responders continue on treatment, with 58% (7/12) patients ongoing > 2 years, and 25% (3/12) patients ongoing >3 years.
- 1 PR converted to CR after the primary analysis and DOR is still ongoing at 17.6+ months
- Although all patients had a SD in the locally advanced subgroup, 2/5 (40%) underwent surgery following treatment (tumor reduction by 7.9% and 22.3%) and disease-free at 3 and 3.5 years.

Progression-free and Overall Survival at the Primary Analysis of May 22, 2019	ABI-009 at 100 mg/m^2	95% CI
PFS, Independent Review	N = 31	
PFS, median	8.9 months	5.5, —
PFS rate at 3 months	78.5%	58.5, 89.9
PFS rate at 6 months	69.5%	47.6, 83.7
PFS rate at 12 months	45.4%	22.6, 65.7
Overall Survival (OS)	N = 34	
OS, median, months	NR	22.2, —
OS rate at 6 months	93.2%	75.5, 98.3
OS rate at 12 months	88.8%	68.7, 96.3

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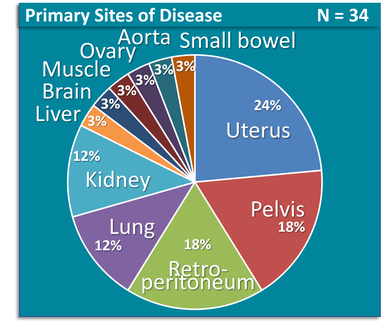
Corresponding author: Andrew_Wagner@dfci.harvard.edu

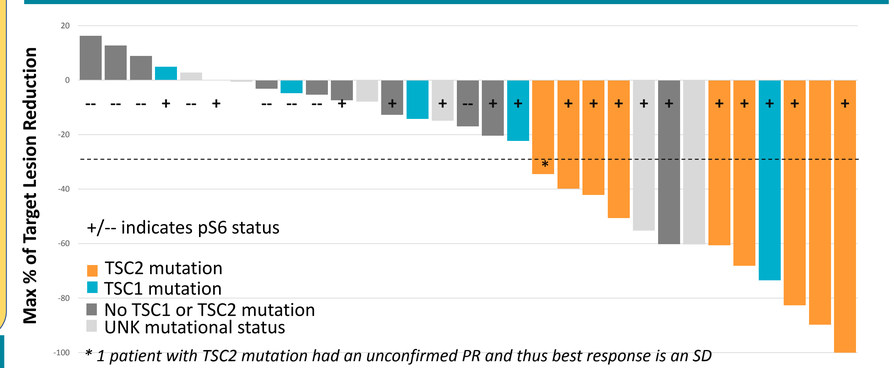
Results

Safety

- No grade 4 or 5 TR AEs
- No unexpected AEs
- Pneumonitis 6/34 (18%), all G1/G2
- Discontinuation due to AE: 2/34 (6%) (G2 anemia and G1 cystitis)
- *nab*-Sirolimus was safe and well tolerated as long-term treatment



Response vs Mutational Status and Biomarker Analysis



Conclusions and Future Direction

- Highly durable responses, with long-term median DOR not reached (>25.8 months)
- This registrational trial met its primary endpoint; the independently assessed ORR was 39% (95% CI 22% - 58%) and acceptable safety profile
- Patients with a *TSC2* mutation were significantly more likely to have a response to *nab*-sirolimus treatment (8/9 [89%] patients; *P* <0.001), and all patients with a TSC2 mutation had a target lesion response
- All *TSC2* mutations were found in the metastatic subgroup only
- A pan-tumor study focusing on *TSC1* and *TSC2* loss-of-function mutation is warranted