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**Background**

- **TSC1** and **TSC2** genes encode tumor suppressors in the mTOR pathway; mutated at low frequency across tumor types (~1–2%)
- Retrospective analyses did not show association between mutation status for **TSC1/TSC2/mTOR** and everolimus, an mTOR inhibitor (mTORi)
- In a Phase 2 study, patients with **TSC1** or **TSC2** mutations in advanced solid tumors treated with everolimus had a 7% (2/30) response rate
- In xenograft model, nab-sirolimus showed significantly higher tumor accumulation, target suppression (pS6), and antitumor activity versus everolimus or sirolimus
- Multinational Expanded Access Program (NCT03817515) with nab-sirolimus at 100 mg/m² given D1, D8 of a 21-day cycle

**Methods**

- **Study Design:** Multi-institutional Expanded Access for an Intermediate-size Population
- **Key Eligibility:**
  - ≥18 years old, with ECOG Performance Status 0–2
  - Histologically confirmed malignant PEComa OR any other malignancy harboring **TSC1** or **TSC2** mutations
  - No prior lines Rx with mutation in mTOR pathway genes
- **Response Analysis:** RECIST v1.1

**Results**

- **Patients with various malignancies bearing **TSC1** or **TSC2** mutations, most with progression on multiple prior therapies, showed evidence of response and manageable toxicities with nab-sirolimus**
  - 8 patients were treated, 6 were mTOR-naïve and 2 were previously treated with an mTORi; 7/8 were evaluable for response analysis:
    - 5 patients had confirmed PR – all of them were mTOR-naïve
    - 5 patients are still on therapy as of the data cutoff (March 2021)

**Conclusions and Future Directions**

- Encouraging preliminary results in patients with **TSC1** or **TSC2** mutations
- A tumor-agnostic study of nab-sirolimus in MTOR-naïve patients with **TSC1** or **TSC2** mutant malignancies is planned

**Acknowledgments**

The authors thank Kimberly Vela (Aadi Biosciences) for study management and data collection and Samson Biosciences for medical writing assistance.

**References**

3. Hou et al. AACR 2020 #300
4. Wagner et al. ASCO 2020 #415116
5. Wagner et al. CTOS 2020 #3483104

**Abstract #339405**

**Institutional experience with nab-sirolimus in patients with malignancies harboring **TSC1** or **TSC2** mutations**

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