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Early results from the first-in-human phase 1 study of WEE1 inhibitor APR-1051 in patients with advanced solid tumors (ACESOT-1051)

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INTRODUCTION

- WEE1 is a key cell cycle checkpoint tyrosine kinase regulator[1,2]
- Inhibiting WEE1 induces cell apoptosis, with promising efficacy observed in prior solid tumor studies. However, safety has been limited by grade 3 myelosuppression[1-5]
- APR-1051 is an orally bioavailable, potent, and selective small molecule WEE1 inhibitor with *in vivo* anti-tumor activity and favorable drug exposure and tumor concentrations in several cancer models[5]
- ACESOT-1051 is an ongoing first-in-human phase 1 study evaluating once-daily APR-1051 in advanced solid tumors harboring cancer-associated gene alterations
- As of May 6, 2026 (data cutoff), 28 patients have been enrolled in ACESOT-1051 up to dose level 300 mg (**Table 1**)

STUDY OBJECTIVES

Primary objective

- To characterize the safety profile, dose-limiting toxicity (DLT), maximum tolerated dose or maximum administered dose, and recommended phase 2 dose (RP2D) of APR-1051

Secondary objectives

- To characterize the PK of APR-1051
- To assess preliminary efficacy of APR-1051

METHODS

- APR-1051 is being evaluated as monotherapy with escalating dose levels using a combined accelerated titration and a Bayesian optimal interval (BOIN) design. One treatment cycle is 28 days (**Figure 1**)

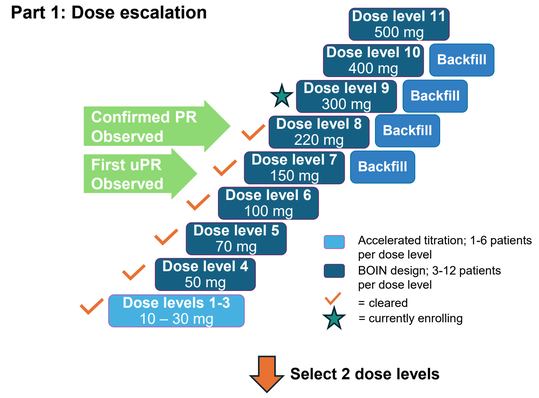
Inclusion criteria

- Age ≥ 18 years with advanced/metastatic solid tumor with specific types or cancer-associated gene alterations, such as:
  - Uterine serous carcinoma regardless of biomarker status
  - Amplification/overexpression of CCNE1 or CCNE2 regardless of tumor type
  - Deleterious mutations in FBXW7 or PPP2R1A regardless of tumor type
  - HPV-related oropharyngeal squamous cell carcinoma (OPSCC), cervical, vaginal, or vulvar carcinoma
  - Colorectal cancer with KRAS GLY12/13 and TP53 co-mutation
- Measurable disease per RECIST v1.1 (PCWG3 criteria for patients with mCRPC)
- ECOG PS 0 or 1 (or KPS ≥ 70)

Exclusion criteria

- Prior systemic anti-cancer therapy within 3 weeks or ≥ 5 half-lives prior to the first of day of treatment
- Prior therapy with a WEE1 inhibitor
- Concomitant treatment with other anti-cancer therapy

Figure 1. Study schema



RESULTS

Table 1. Baseline characteristics

Characteristic[a]	Study patients (N = 28)
Sex	
Male	12 (43)
Female	16 (57)
Median age (range), years	61.5 (40-86)
Race	
White	16 (57)
Black or African American	4 (14)
Asian	2 (7)
American Indian or Alaska Native	1 (4)
Unknown	5 (18)
ECOG PS	
0	7 (25)
1	21 (75)
Tumor types	
Colorectal	14 (50)
Uterine / endometrial	8 (29)
Pancreatic	2 (7)
Other[b]	4 (14)
Prior lines of systemic therapy	
1	2 (7)
2 or 3	15 (54)
≥ 4	11 (39)

a Data are n (%) unless otherwise indicated
b HPV+ OPSCC (n=2), breast (n=1), gastric (n=1)

As of May 6, 2026
Data not source verified

PLAIN LANGUAGE SUMMARY

- WEE1 is an important protein that controls how cells grow and divide
- WEE1 inhibition is clinically validated, but prior inhibitors have been challenged by narrow therapeutic windows
- Aprea is applying key insights to advance APR-1051 as a potentially best-in-class WEE1 inhibitor
- In this study, APR-1051 has shown manageable safety and early signs of tumor shrinkage and no substantial myelosuppression
- ACESOT-1051 is actively enrolling patients at three specialized sites in the U.S.

RESULTS (continued)

Safety

- A total of 26 (93%) patients had any TEAE at data cutoff
- TEAEs were mostly mild (Grade 1 or 2), not serious, and GI related (nausea [n=13; 46%], vomiting [n=10; 36%]) fatigue (n=7; 25%)
- Serious TEAEs were reported in 13 (46%) patients
- A total of 15 (54%) patients had TRAEs, which were mostly Grade 1 or 2 GI events (n=13; 46%) (**Table 2**)
- Two (7%) patients had Grade 3 TRAEs: lymphocyte decrease in one patient (dose level 50 mg) and increased AST and increased ALT in one patient (DLT, dose level 50 mg)
- No Grade 2 or greater related heme tox observed at doses ≥70 mg
- No Grade 4 or 5 TRAEs have been reported
- No patients withdrew from the study due to TEAEs (excluding disease progression)
- No study-treatment related deaths were reported

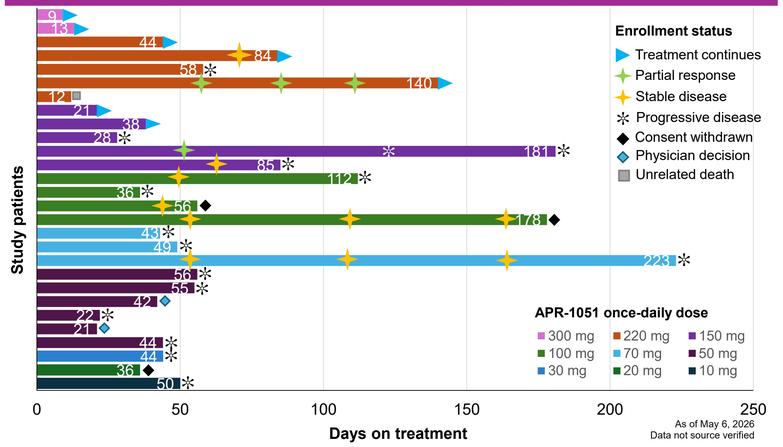
Table 2. Treatment-related AEs in patients treated with APR-1051

MedDRA Preferred Term	APR-1051 All dose levels (N = 28)	
Treatment-related AEs, n (%)[a]	**All Grades**	**Grade ≥ 3[b]**
Nausea	10 (36)	0 (0)
Fatigue	4 (14)	0 (0)
Vomiting	3 (11)	0 (0)
Alanine aminotransferase increased	1 (4)	1 (4)[c]
Anemia	1 (4)	0 (0)
Aspartate aminotransferase increase	1 (4)	1 (4)[c]
Blood bilirubin increased	1 (4)	0 (0)
Constipation	1 (4)	0 (0)
Dehydration	1 (4)	0 (0)
Dysgeusia	1 (4)	0 (0)
Dyspepsia	1 (4)	0 (0)
Eczema	1 (4)	0 (0)
Gastroesophageal reflux disease	1 (4)	0 (0)
Hypokalemia	1 (4)	0 (0)
Lymphocyte count decreased	1 (4)	1 (4)
Platelet count decreased	1 (4)	0 (0)

a A patient may have more than one AE and/or have the same AE more than once
b Grade 3 unless otherwise indicated
c Increased alanine aminotransferase and aspartate aminotransferase occurred in the same patient, was determined to be serious, and considered one DLT event

As of May 6, 2026
Data not source verified

Figure 2. Summary of duration of treatment and response (N = 28)



Pharmacokinetics

- A strong trend for dose proportionality (AUC, C_{max}) was observed (**Figures 3 and 4**)
- T_{max} average is 4 hours with relatively slow absorption, and the half-life averages 18 hours (C1D1), supporting once-daily dosing
- Drug accumulation is present between C1 and C2 with mean RA's (50-220 mg) 2.2 and 1.8-fold for AUC and C_{max}, respectively

Figure 3. APR-1051 conc. vs time at C1D1

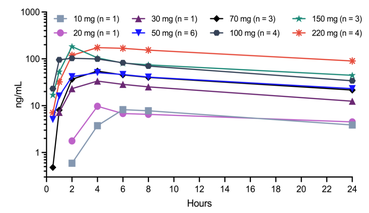
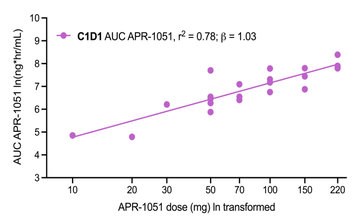


Figure 4. AUC_{0-24} by dose level at C1D1



CONCLUSION

- As of May 6, 2026, 28 patients with advanced solid tumors harboring specific cancer-associated gene alterations have been enrolled up to the 300 mg dose level
- Early signals of monotherapy activity across cohorts including uterine/endometrial cancer, CRC, and HNSCC
- Preliminary signs of clinical activity have been observed in 8 (29%) patients with partial responses (n=2) and disease stabilization (n=6)
- APR-1051 toxicity has been manageable to date with mostly mild to moderate GI AEs
- PK data support once-daily dosing with dose-proportional oral exposure
- These data suggest the potential for a more favorable therapeutic window
- This study is active enrolling at three sites in the U.S. (NCT06260514)

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Abbreviations: AE, adverse event; AUC, area under the curve; C, concentration; C1D1, Cycle 1 Day 1; CCNE, Cyclin E; CRC, colorectal cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; FBXW7, F-box and WD repeat domain containing 7; GI, gastrointestinal; Gly, glycine; HNSCC, head and neck squamous cell carcinoma; HPV, human papillomavirus; KPS, Karnowski Performance Scale; KRAS, Kirsten rat sarcoma viral oncogene homolog; mCRPC, metastatic castration-resistant prostate cancer; MedDRA, Medical Dictionary for Regulatory Activities; PCWG3, Prostate Cancer Clinical Trials Working Group 3; PK, pharmacokinetic; PPP2R1A, protein phosphatase 2 scaffold subunit alpha; PR, partial response; R, randomized; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; t, time; TEAE, treatment-emergent adverse event; TP53, tumor protein 53; TRAE, treatment-related adverse event; uPR, unconfirmed partial response; WEE1, Wee1-like protein kinase

References: 1. Elk CR et al. Mutate Res. 2020 Jan-Apr;819-820:111694; 2. de Jong MRW et al. Cancers. 2019; 11(11):1743; 3. Do K et al. J Clin Oncol. 2015 Oct 20;33(30):3409-15; 4. Fu S et al. J Clin Oncol. 2023 Mar 20;41(9):1725-1734; 5. Vacca J et al. Proceedings of the American Association for Cancer Research Annual Meeting 2025; Part 1 (Regular and Invited Abstracts); 2025 Apr 14-19; Orlando, FL. Philadelphia (PA): AACR; Cancer Res 2025;83(7_Suppl):Abstract nr 6177