TK216 FOR EWING SARCOMA- INTERIM PHASE 1/2 RESULTS

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TK216 FOR EWING SARCOMA- INTERIM PHASE 1/2 RESULTS

- TK 216 MOA
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- Patient Overview: Swimmers Plot
- Efficacy: Case Discussion (1/2)
- Efficacy: Case Discussion (2/2)
- Safety: Treatment Emergent AEs ≥ 20%
- Summary

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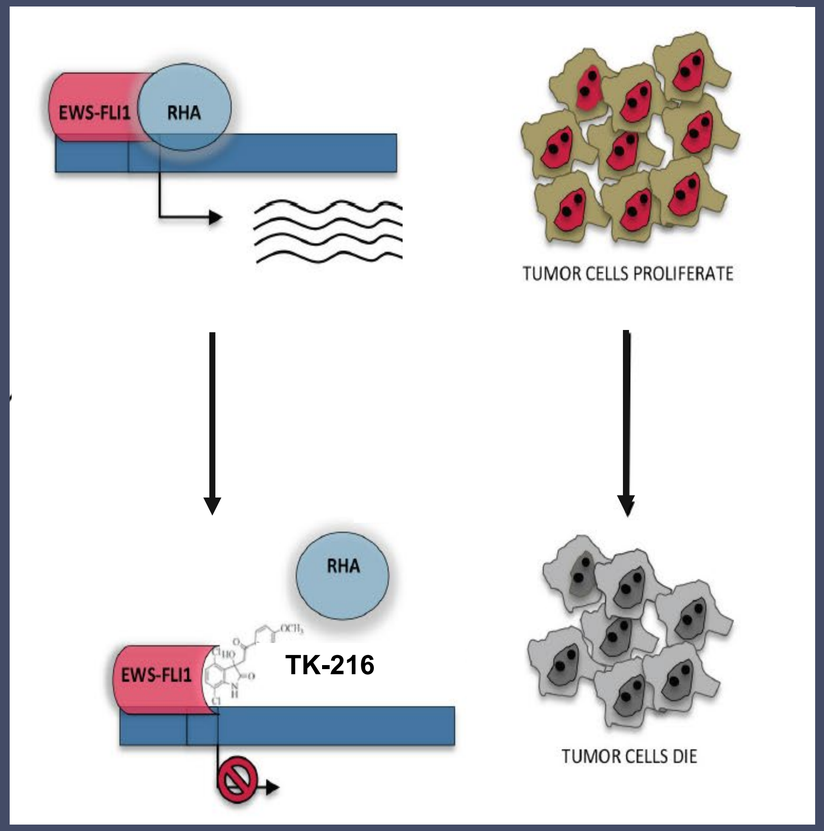
TK 216 MOA

Ewing sarcoma is a rare cancer affecting both children and adults with limited treatment options in the relapsed/refractory setting

- Fusions of the EWS gene and one of five different ETS transcription factors (e.g. EWS-FLI1) are dominant drivers of Ewing sarcoma
- Binding of EWS-FLI1 to RNA helicase A (RHA) is critical for its oncogenic function
- TK216 binds ETS proteins, disrupts protein-protein interactions, inhibits transcription factor function, leading to Ewing sarcoma cell death



Adapted from Fidaleo et al. Oncotarget, 2016

STUDY DESIGN

Phase 1 (Part 1 & 2) – COMPLETED

- DLT was primarily neutropenia

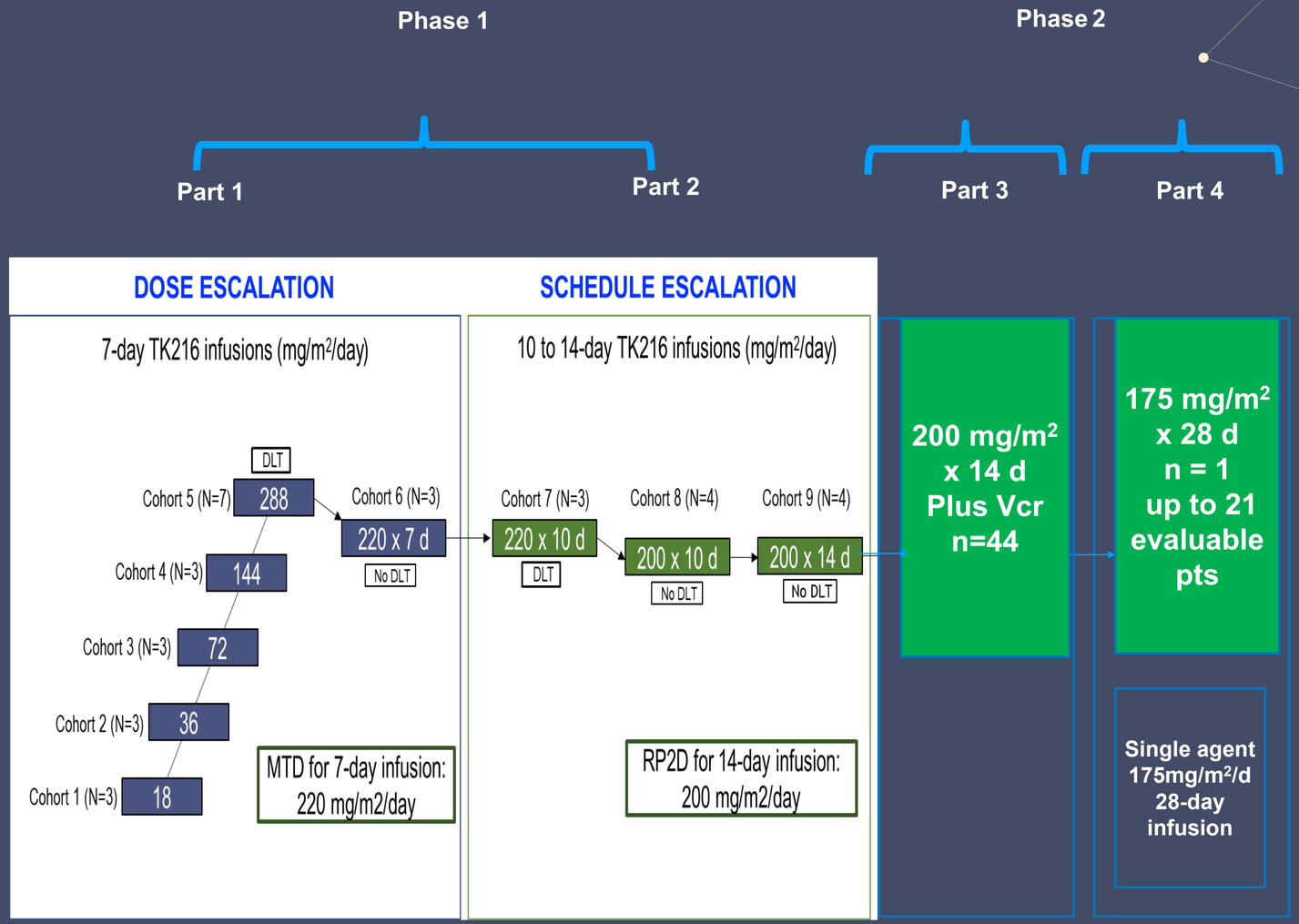
Phase 2

- Part 3 – ENROLLED (N=44)
- RP2D for 14-day infusion: 200 mg/m^2/day continuous IV infusion (Vincristine 0.75 – 1.5 mg/m^2 each cycle day 1)
- Part 4 – ENROLLING
- Objective: assess ORR of single agent TK216 at 175 mg/m^2 administered continuously for 28 days
- Key Eligibility :

  Metastatic disease

  ≥8 years old

  ≤ 5 prior systemic therapies



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DEMOGRAPHY AND BASELINE CHARACTERISTICS

	All Patients N=74	Cohort 9 & Expansion (RP2D**) N=45
Median Age (years) (min, max)	26.5 (11.0, 77.0)	26.0 (11.0, 77.0)
Male, n (%)	47 (63.5)	29 (64.4)
ECOG 0-1, n (%)	55 (96.5)	32 (94.1)
Median time from diagnosis to study start (years)	3.2 (0.4, 18.0)	2.7 (0.4, 18.0)
Prior surgery, n (%)	58 (78.4)	37 (82.2)
Prior radiotherapy, n (%)	60 (81.1)	37 (82.2)
Median number of prior systemic treatments	3.0 (1.0, 9.0)	3.0 (1.0, 8.0)
Metastases at study entry, n (%)	73 (98.6)	45 (100)
• Bone only	7 (9.5)	3 (6.7)
• Lung only	34 (45.9)	24 (53.3)
• Bone and Lung only	10 (13.5)	8 (17.8)
• Other location	22 (29.7)	10 (22.2)

Data Cut: 01OCT2021; Median estimates are shown with (min, max)
**RP2D = TK216 200 mg/m^2/d x14 + Vcr

Population: Heavily pre-treated with high disease burden

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EFFICACY: CLINICAL RESPONSE RATES

	All Subjects (N=60)	Cohort 9 & Expansion Cohort (RP2D) (N=37)
Overall Response (ORR), n (%)	3 (5.0%)	3 (8.1%)
Complete Response* (CR) , n (%)	2 (3.3%)	2 (5.4%)
Partial Response** (PR) , n (%)	1 (1.7%)	1 (2.7%)
Stable Disease (SD) , n (%)	14 (23.3%)	12 (32.4%)
Progressive Disease (PD) , n (%)	43 (71.7%)	22 (59.5%)
Disease Control Rate (DCR), n (%)	17 (28.3%)	15 (40.5%)
Duration of Response (months), median (95% CI)	14.7 (1.1, 28.6)	14.7 (1.1, 28.6)
6-month Progression-free-survival (PFS) rate (95% CI)	7.2% (2.4%, 15.8%)	12.0% (3.9%, 25.0%)

Data cut: 01OCT2021; All patients- include Cohorts 1-8, Cohort 9 & Expansion; Patients were considered evaluable for response if they completed 1-cycle of treatment and had 1-post baseline tumor assessment; * Two confirmed CRs: 1 completed 2-year treatment CR, 1 ongoing with no PD at 20 months on study.
** Unconfirmed PR observed in target lesion at Cycle 4 then PD observed at Cycle 6 in non-target lesions

Notable responses and disease control rates observed at the RP2D

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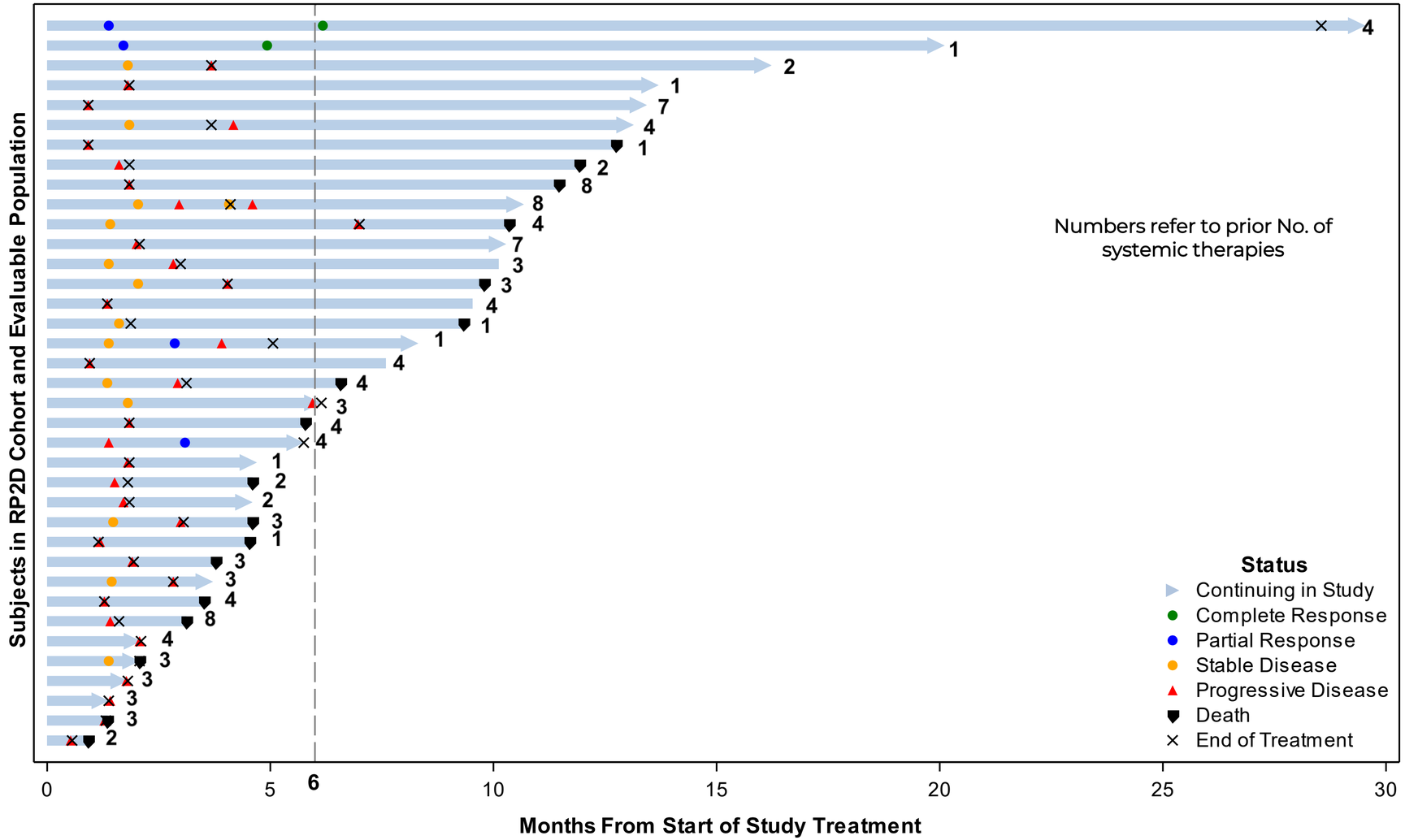
PATIENT OVERVIEW: SWIMMERS PLOT



Data cut: 01OCT2021; Patients were considered evaluable for response if they completed 1-cycle of treatment and had 1-post baseline tumor assessment; continuing in study includes long-term follow-up (survival);

37 evaluable patients have been treated with TK216 +/- vincristine at RP2D, durable treatment effect demonstrated on this heavily-treated patient population

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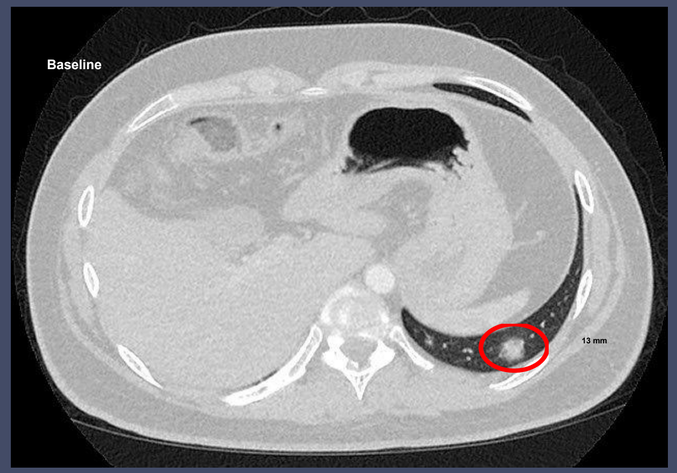
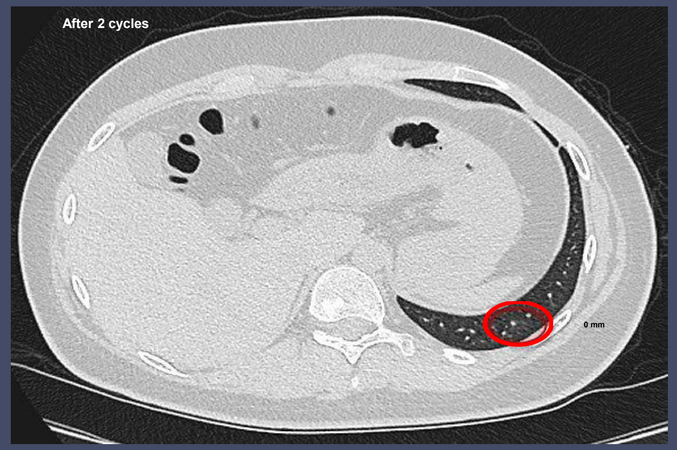
EFFICACY: CASE DISCUSSION (1 OF 2)

Sustained CR for >2 years in heavily pre-treated teenager with R/R Ewing sarcoma

Patient: 19-year-old male presented with Ewing sarcoma of the clavicle and multiple pulmonary metastases

- History:
  - Tumor genetics: EWSR1-FLI1 fusion
  - Prior Therapy: VDC/IE, surgical resection, RT 50.4 Gy
  - Relapsed 1.5 years after initial diagnosis
  - Multiple recurrences treated with: Whole lung RT, irinotecan/temozolomide, bevacizumab, pazopanib
  - Multiple progressing lung metastases at study entry
- TK216 Treatment Course: TK216 200 mg/m^2/day for 14-28 days
  - Regression of all target lesions after Cycle 2 (PR) without vincristine
  - Resection of residual non-target lung lesion at Cycle 6 (surgical CR)
  - Completed treatment with TK216 + Vincristine > 2 years on study with no evidence of disease





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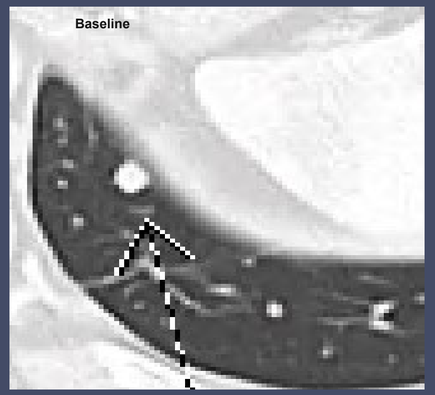
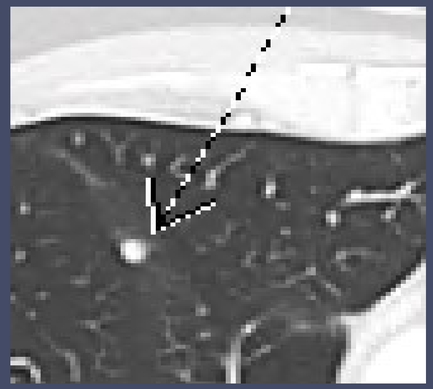
EFFICACY: CASE DISCUSSION (2 OF 2)

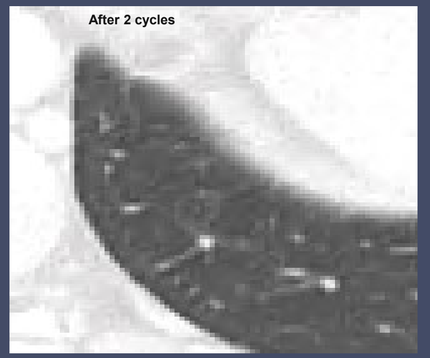
Sustained CR for >1.7 years in heavily pre-treated adult with R/R Ewing sarcoma

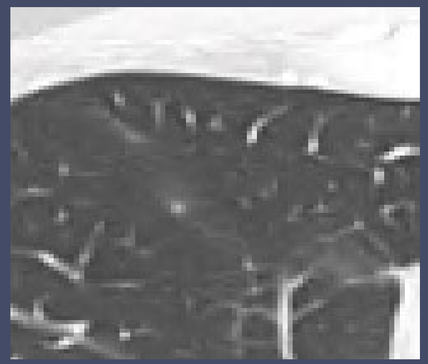
Patient: 51-year-old male presented with Ewing sarcoma of the kidney and multiple pulmonary metastases

- History:
  - Tumor genetics: EWSR1 translocation
  - Prior Therapy: VDC/IE, high-dose ifosfamide x1; surgical resection
  - Relapsed 1.6 years after initial diagnosis
  - Multiple progressing lung metastases at study entry
- TK216 Treatment Course: TK216 200 mg/m^2/day x 14 + vincristine 0.75 mg/m^2 day 1
  - Regression of 90% of target lesions at Cycle 2 (PR)
  - Regression of all target lesions at Cycle 6 (CR)
  - Remains on treatment with TK216 >20 months with no evidence of disease; No vincristine since month 3.7









SAFETY: TREATMENT EMERGENT AES ≥ 20% (REGARDLESS OF CAUSALITY)

	All Subjects (N=72)			Cohort 9 & Expansion Cohort (RP2D) (N=43)		
	All Grades (%)	Grades 1 or 2 (%)	Grades ≥3 (%)	All Grades (%)	Grades 1 or 2 (%)	Grades ≥3 (%)
No. of subjects with an event	72 (100.0%)	24 (33.3%)	48 (66.7%)	43 (100.0%)	13 (30.2%)	30 (69.8%)
Anaemia	36 (50.0%)	15 (20.8%)	21 (29.2%)	20 (46.5%)	7 (16.3%)	13 (30.2%)
Neutropenia	36 (50.0%)	9 (12.5%)	27 (37.5%)	25 (58.1%)	8 (18.6%)	17 (39.5%)
Leukopenia	30 (41.7%)	7 (9.7%)	23 (31.9%)	20 (46.5%)	5 (11.6%)	15 (34.9%)
Fatigue	29 (40.3%)	26 (36.1%)	3 (4.2%)	17 (39.5%)	16 (37.2%)	1 (2.3%)
Pyrexia	27 (37.5%)	27 (37.5%)	0 (0.0%)	14 (32.6%)	14 (32.6%)	0 (0.0%)
Alopecia	23 (31.9%)	23 (31.9%)	0 (0.0%)	18 (41.9%)	18 (41.9%)	0 (0.0%)
Nausea	23 (31.9%)	23 (31.9%)	0 (0.0%)	16 (37.2%)	16 (37.2%)	0 (0.0%)
Headache	18 (25.0%)	17 (23.6%)	1 (1.4%)	13 (30.2%)	13 (30.2%)	0 (0.0%)
Thrombocytopenia	16 (22.2%)	8 (11.1%)	8 (11.1%)	6 (14.0%)	4 (9.3%)	2 (4.7%)
Constipation	15 (20.8%)	14 (19.4%)	1 (1.4%)	10 (23.3%)	9 (20.9%)	1 (2.3%)

Data Cut: 01OCT2021; 1.4% (1/72) Grade ≥3 TEAEs led to drug discontinuation; Dose not changed was the action taken for TEAEs in 95.8% (69/72); SAEs occurred in 41.7% (30/72), of which 1.4% (1/72) led to drug discontinuation. RP2D = TK216 200 mg/m^2/d x14 + Vcr

TK216 +/- vincristine has a tolerable safety profile. Myelosuppression is the primary safety observation which is transient, reversible, and responsive to growth factors

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SUMMARY

- First in human study: TK216 targets ETS family of oncoproteins
- Phase 1 of study is complete and protocol-defined RP2D established
- Efficacy at RP2D is encouraging
    - 2 Complete responses are durable
    - Good disease control: DCR = 40.5% in Heavily pre-treated patients
- Safety profile is tolerable and manageable consisting of myelosuppression which is transient and reversible
    - Given ≥ Grade 3 neutropenia in 37.5% of patients at RP2D, increasing dose or duration at RP2D may be difficult
- Newly initiated Part 4 will investigate intensified dosing, with TK 216 dose of 175 mg/m^2/d given continuously for 28 days as single agent.

RP2D = TK216 200 mg/m^2/d x14 + Vcr

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