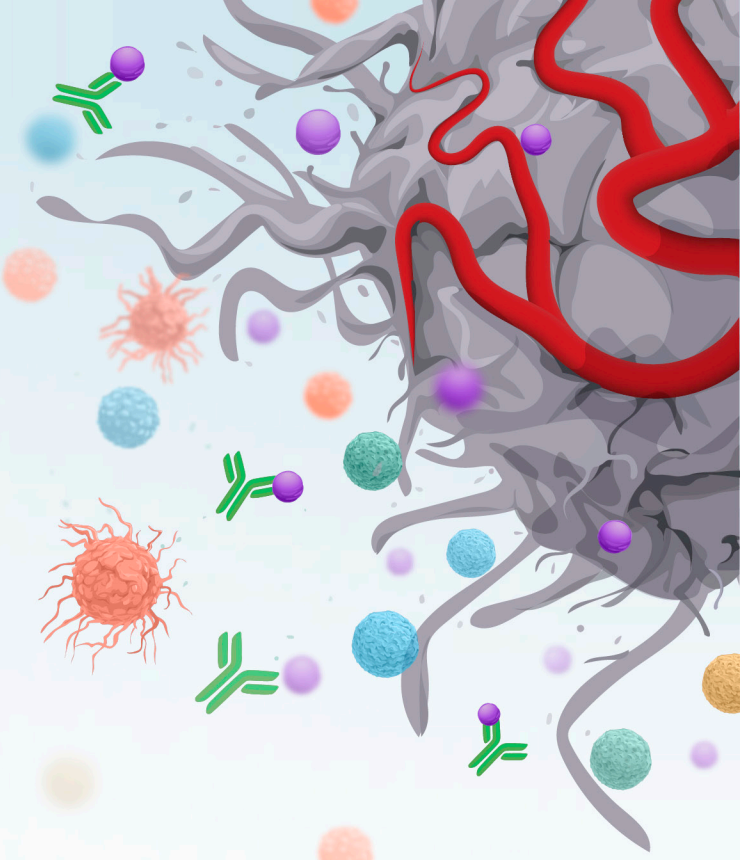
LEAP THERAPEUTICS
company presentation

ASCO 2022

DKN-01 Prostate Cancer Investigator-Initiated Study



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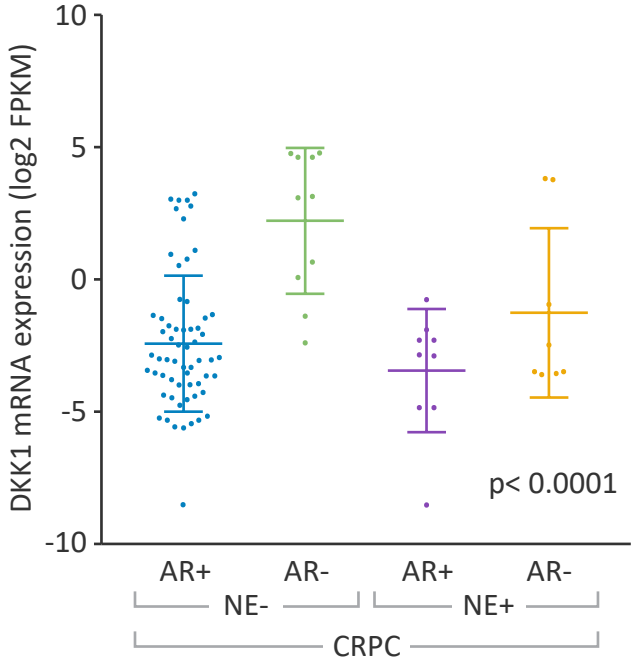
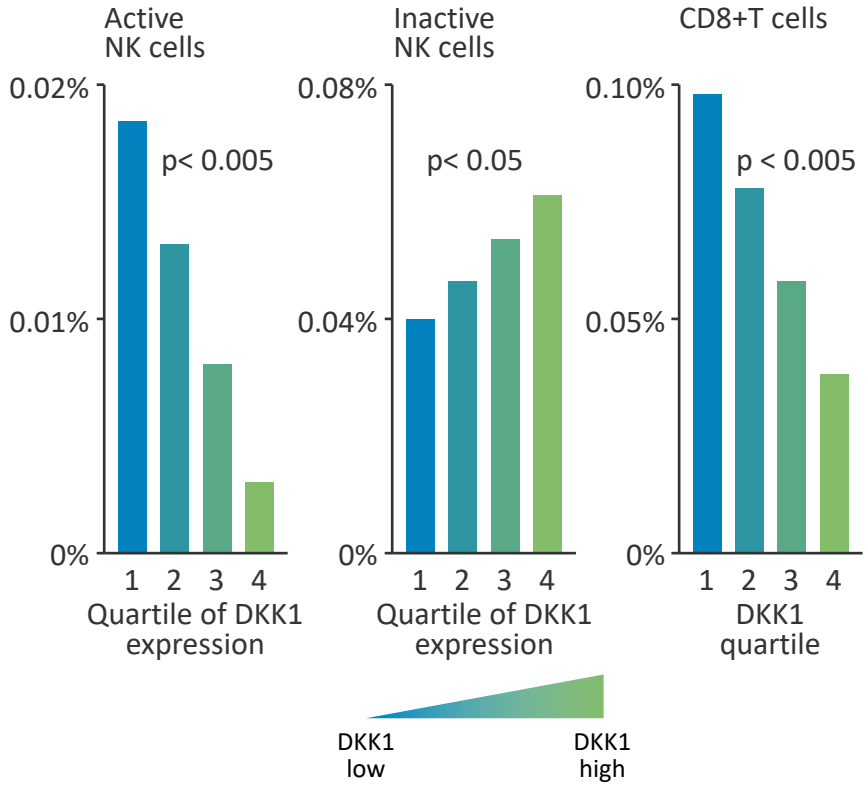
DKK1 and DKN-01 in prostate cancer

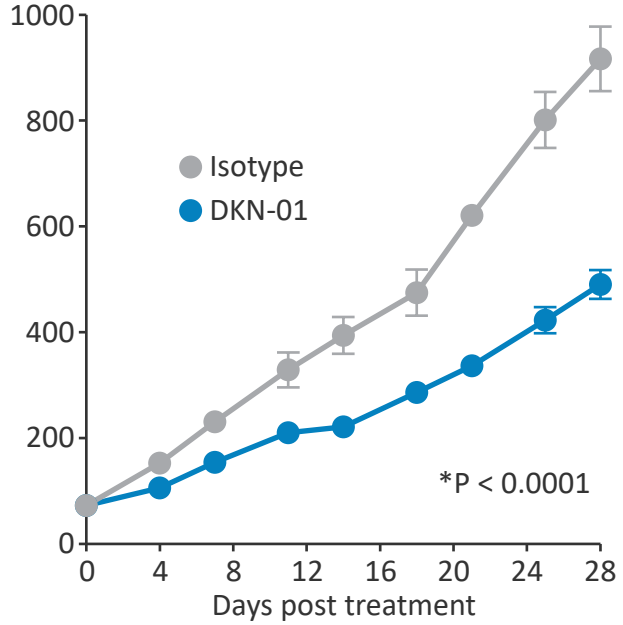
DKK1 expression is regulated by AR in CRPC tumor biopsies



CIBERSORT analysis shows DKK1 expression associated with reduced inflammatory infiltrate



DKN-01 has efficacy in a PC3 SCID xenograft



David Wise ASCO 2017

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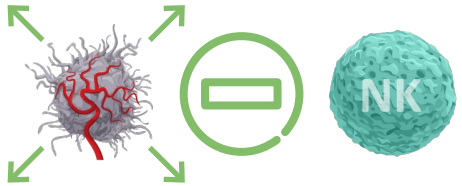
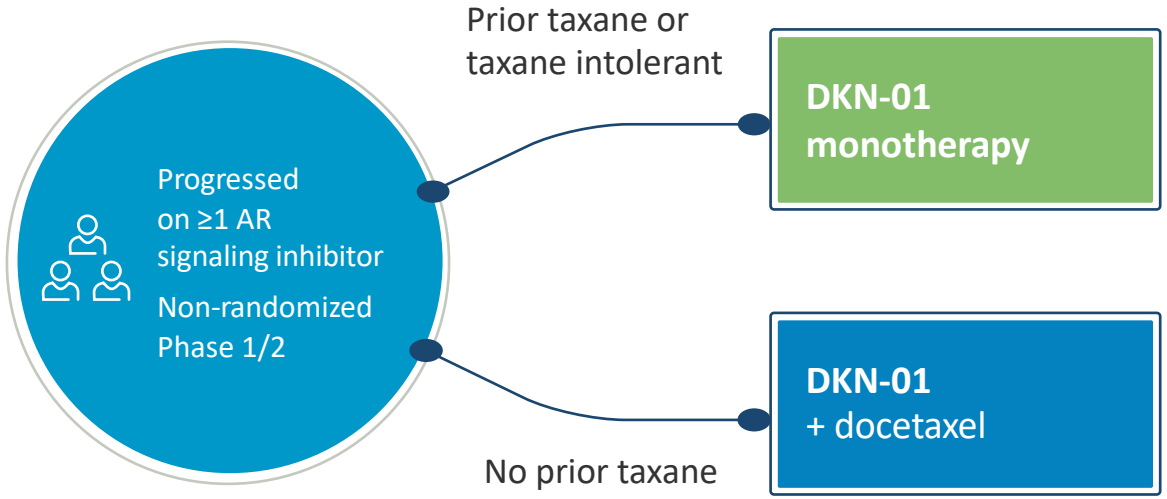
Investigator-initiated study in advanced metastatic castration-resistant prostate cancer (mCRPC)

Perlmutter Cancer Center
NYU Langone Health

DKK1 is upregulated in prostate cancers with low Androgen Receptor (AR) expression.



DKN-01 delays prostate cancer growth in pre-clinical models in an NK-cell dependent manner.



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Investigator-initiated study in advanced metastatic castration-resistant prostate cancer (mCRPC)

2L+ mCRPC
DKN-01
+ docetaxel

Perlmutter Cancer Center
NYU Langone Health

Baseline characteristics:

	DKN-01 + Docetaxel	300mg N/A	600mg N/A	300mg 75mg/m²	600mg 75mg/m²
		N=4	N=3	N=3	N=3
Age		64.5	74	66	68
Adenocarcinoma, n (%)		4 (100%)	3 (100%)	3 (100%)	1 (33%)
Neuroendocrine carcinoma, n (%)		0	0	0	2 (67%)
Aggressive variant (AVPC), n (%)		1 (25%)	0	1 (25%)	3 (100%)
APC mutation, n (%)		1 (25%)	1 (33%)	1 (33%)	0
CTNNB1 mutation, n (%)		0	2 (67%)	0	0

Safety data overview:

- No DKN-01 related Grade ≥ 3 adverse events occurred in either cohort
- No unexpected docetaxel-related Grade ≥ 3 AEs were observed

DKK1 expression in 42% of samples tested:

DKK1 expression	N=24
H-score 0	15 (58.3%)
H-score ≥1	10 (41.7%)
H-score ≥10	5 (20.8%)
H-score ≥35	3 (12.5%)

Primary endpoint: of the phase 1 dose escalation cohorts was safety, characterized by dose-limiting toxicity (DLT).

Secondary endpoints: of the study was to correlate anti-tumor activity, DKK1 expression (cutoff H-score ≥ 1), and clinical evidence of aggressive variant prostate cancer (AVPC).

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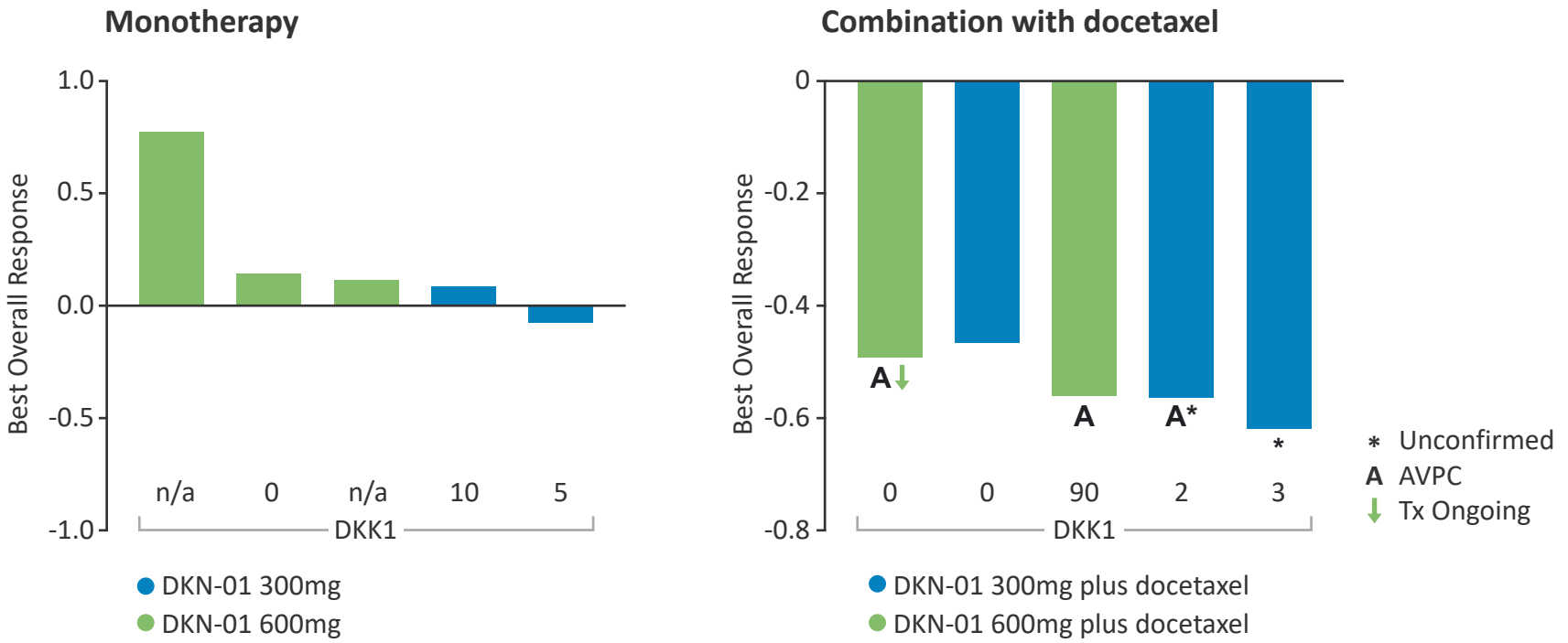
DKN-01 activity in advanced mCRPC patients

2L+ mCRPC
DKN-01
+ docetaxel

Perlmutter Cancer Center
NYU Langone Health



	Monotherapy N=7	Combination N=6
PR - partial response	0	5 (83.3%)
SD - stable disease	2 (28.6%)	0
PD - progressive disease	3 (42.9%)	0
NE - non-evaluable	2 (28.6%)*	1 (16.7%)*

1 NE patient in each group had no measurable disease at baseline

All 5 evaluable DKN-01 plus docetaxel patients had a RECIST partial response (3 confirmed, 2 unconfirmed)

Confirmed responses in 2 of 3 patients with AVPC

KEYNOTE-365 (cohort B), pembrolizumab plus docetaxel:

23% confirmed ORR by RECIST in evaluable patients

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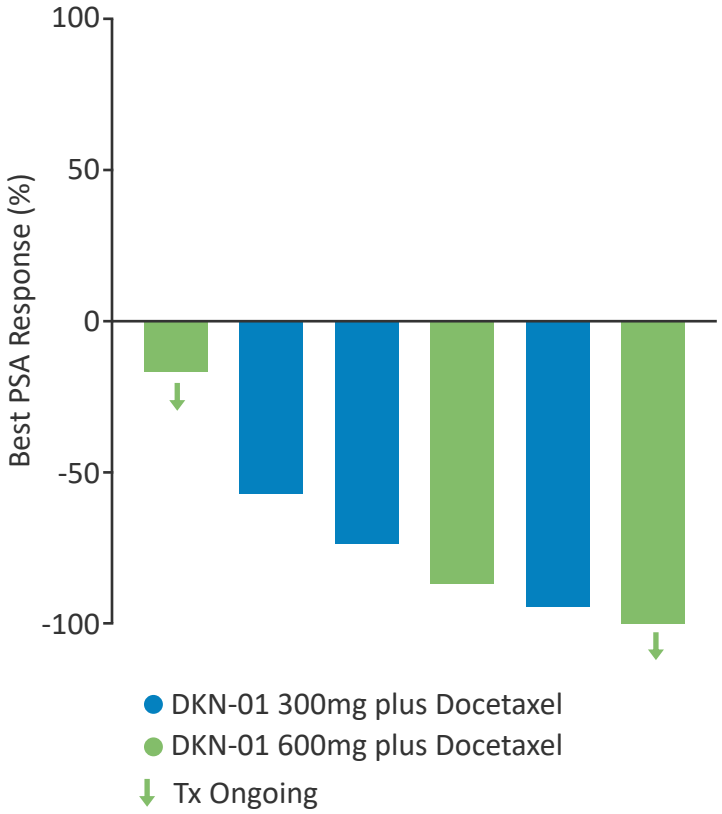
DKN-01 activity in combination with docetaxel

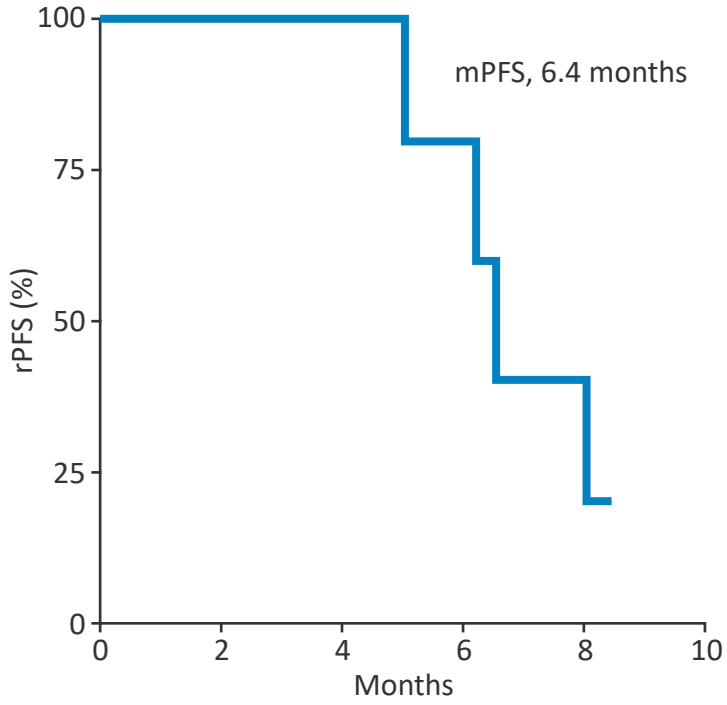
2L+ mCRPC
DKN-01
+ docetaxel

Perlmutter Cancer Center
NYU Langone Health

Best PSA Response



PFS



rPFS (n=6) pts treated with DKN-01 plus Docetaxel.

All 6 DKN-01 plus docetaxel patients have had a PSA50 response (6th patient PSA50 response post-data cut)

KEYNOTE-365 (cohort B), pembrolizumab plus docetaxel:

34% PSA50 response

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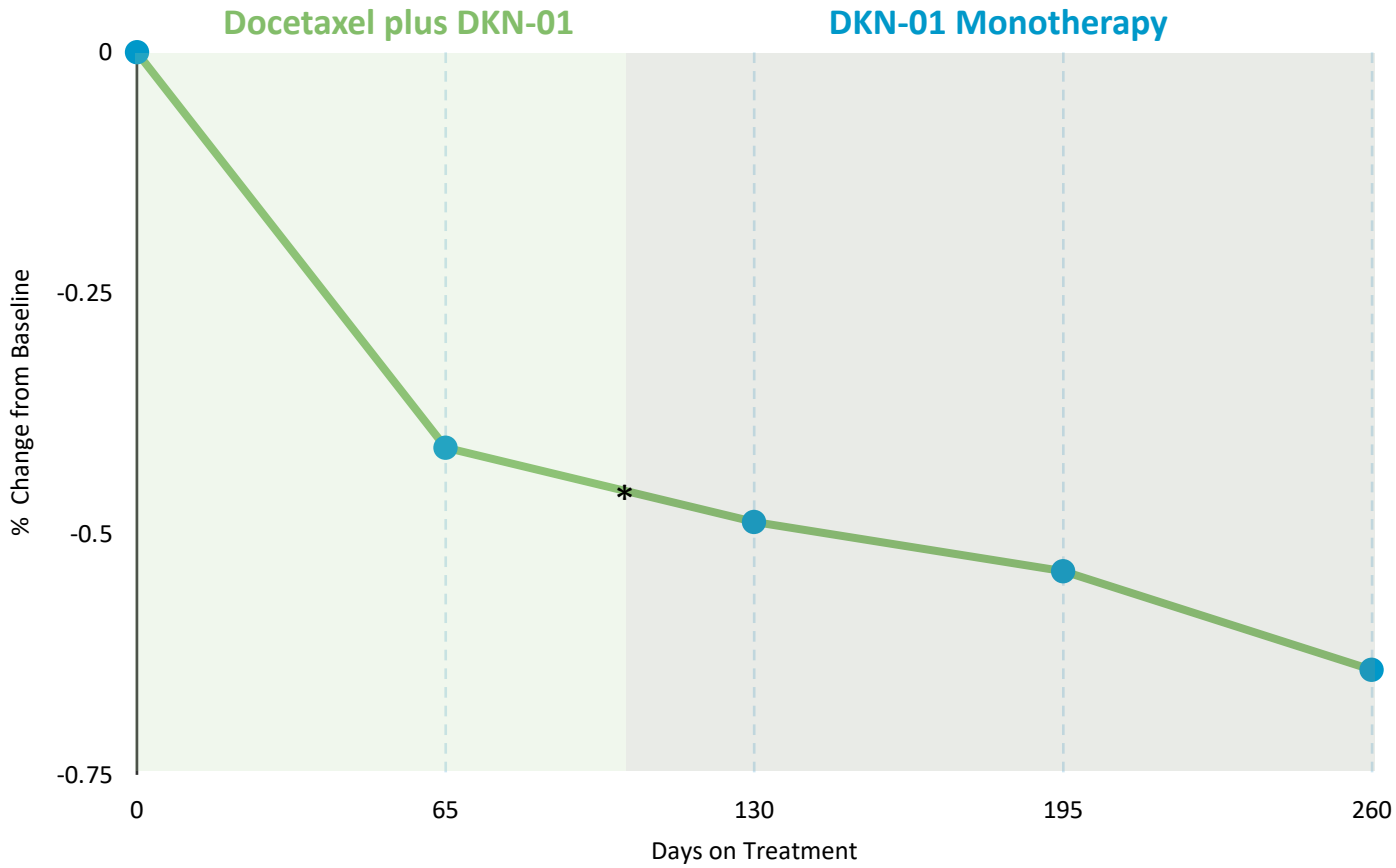
Confirmed partial response with deepening of response on monotherapy

Perlmutter Cancer Center
NYU Langone Health

- **Patient:** 69 yo male with metastatic castration resistant prostate cancer
- **Prior treatment:** Radical prostatectomy, pelvic RT, enzalutamide + 6 cycles of prostvac, bicalutamide, Lupron with immediate progression, darolutamide, sipuleucel-T with new liver lesions and biopsy proven prostate adenocarcinoma
- **Biomarkers:** NHTL1 mutation, DKK1 H-score = 0

Treatment:
DKN-01 plus docetaxel transitioned to DKN-01 monotherapy



Continued tumor regression with DKN-01 treatment observed after discontinuation of docetaxel

* Docetaxel discontinued due to toxicity

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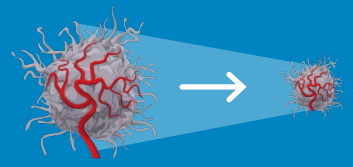
Conclusions

Non-clinical studies identified DKK1 as being upregulated in prostate cancers with low Androgen Receptor expression and that inhibition of DKK1 delayed prostate cancer growth

DKN-01 in combination with docetaxel showed promising clinical responses in unselected patients by both RECIST and PSA50 criteria



Clinical activity was particularly promising in patients with Aggressive Variant Prostate Cancer

Retrospective correlation of anti-tumor activity with biomarker status is ongoing