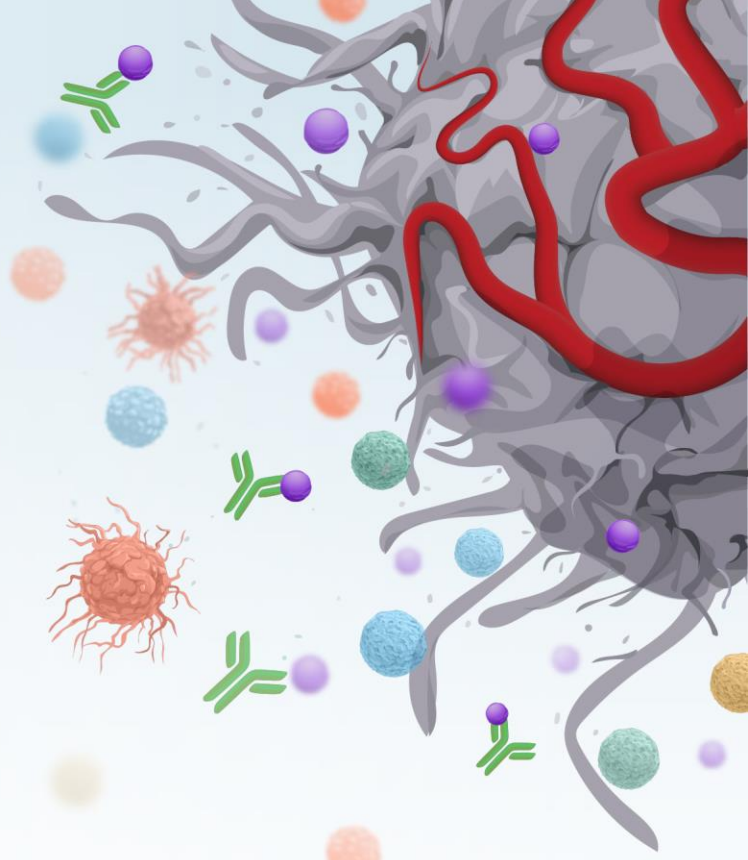
LEAP THERAPEUTICS

company presentation

DKN-01 R&D Day

July 12, 2022



leaptherapeutics

Forward looking statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding our strategy, future operations, clinical trials, collaborations and partnerships, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements within the meaning of U.S. securities laws. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based only on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions.

Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. These and other risk factors are listed from time to time in reports filed with the Securities and Exchange Commission, including, but not limited to, our Annual Reports on Form 10-K and our Quarterly Reports on Form 10-Q. We assume no obligation to update any forward-looking statements, except as required by applicable law.

This presentation does not constitute an offer to sell, or the solicitation of an offer to buy, any securities.

leaptherapeutics

Agenda

DKK1 Biology and DKN-01 Mechanism of action

Gastric cancer:

Samuel Klempner, MD
Massachusetts General Hospital

Colorectal cancer:

Zev Wainberg, MD
UCLA

Endometrial cancer:

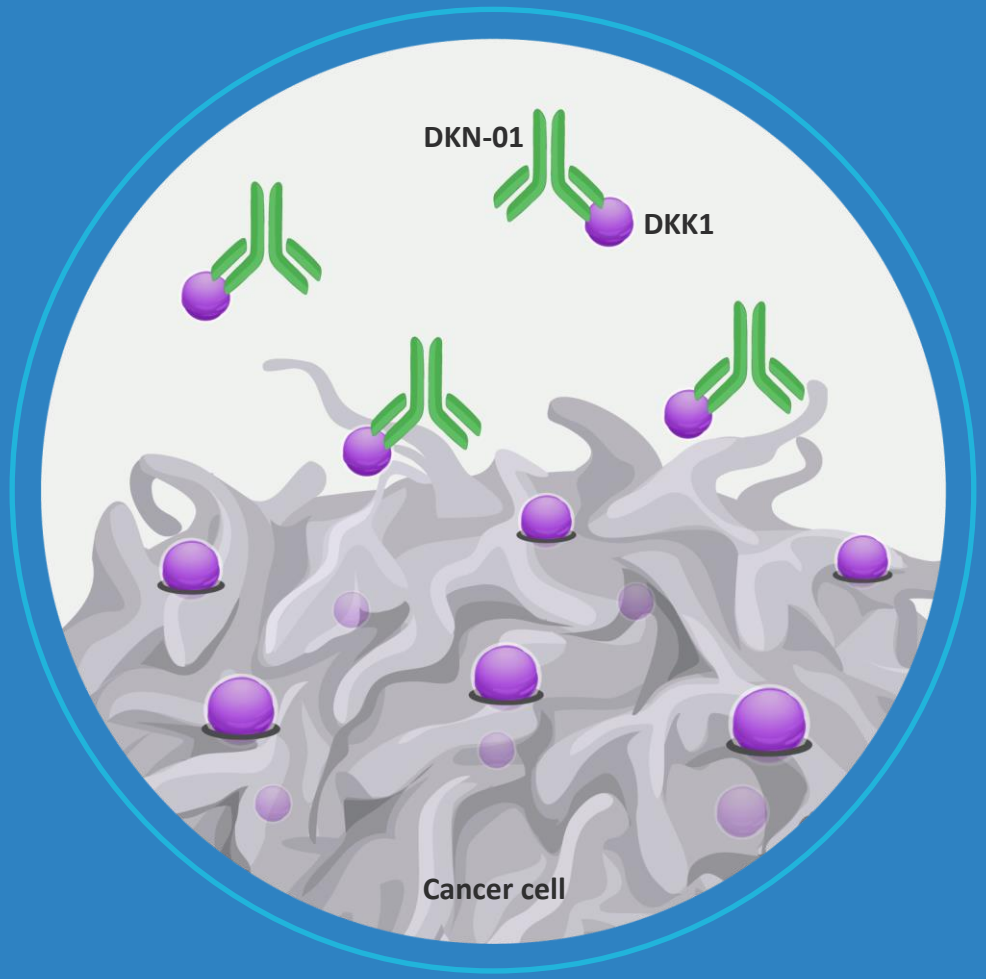
Rebecca Arend, MD
University of Alabama at Birmingham

Prostate cancer:

David Wise, MD, PhD
New York University

leaptherapeutics

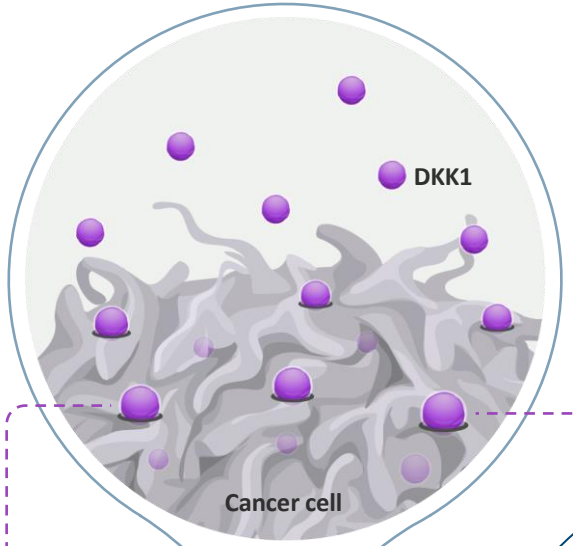
DKN-01 Overview



- Biomarker-targeted development
- Single agent activity in three indications
- Combinations with checkpoint inhibitors and chemotherapy
- Strategic partnership with BeiGene
- Important milestones in 2022 and 2023

leaptherapeutics

The role of DKK1 in cancer



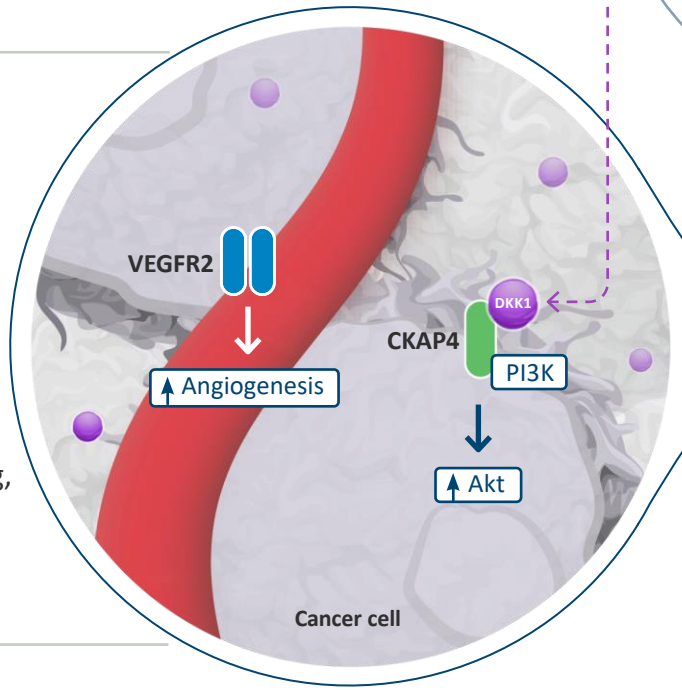
DKK1 is produced and secreted by cancer cells, functions on several tumor pathways and nearby immune cells

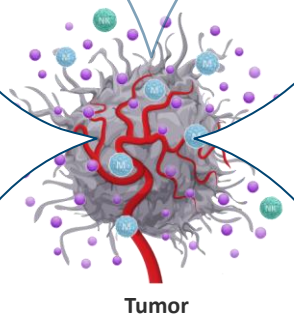
Angiogenesis

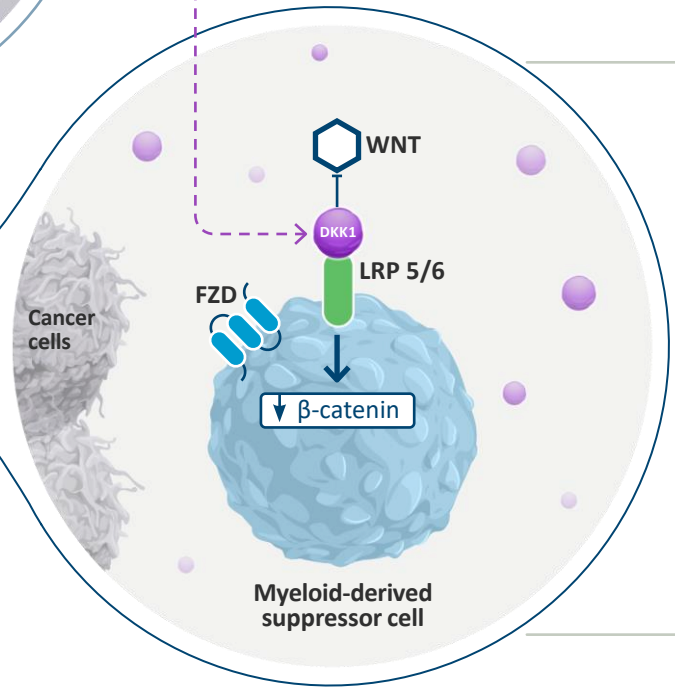
Upregulates VEGFR2, increases formation of tumor blood vessels

Cell proliferation

Blocks Wnt signaling, signals through CKAP4 and PI3K to activate Akt







Enhances MDSC cells

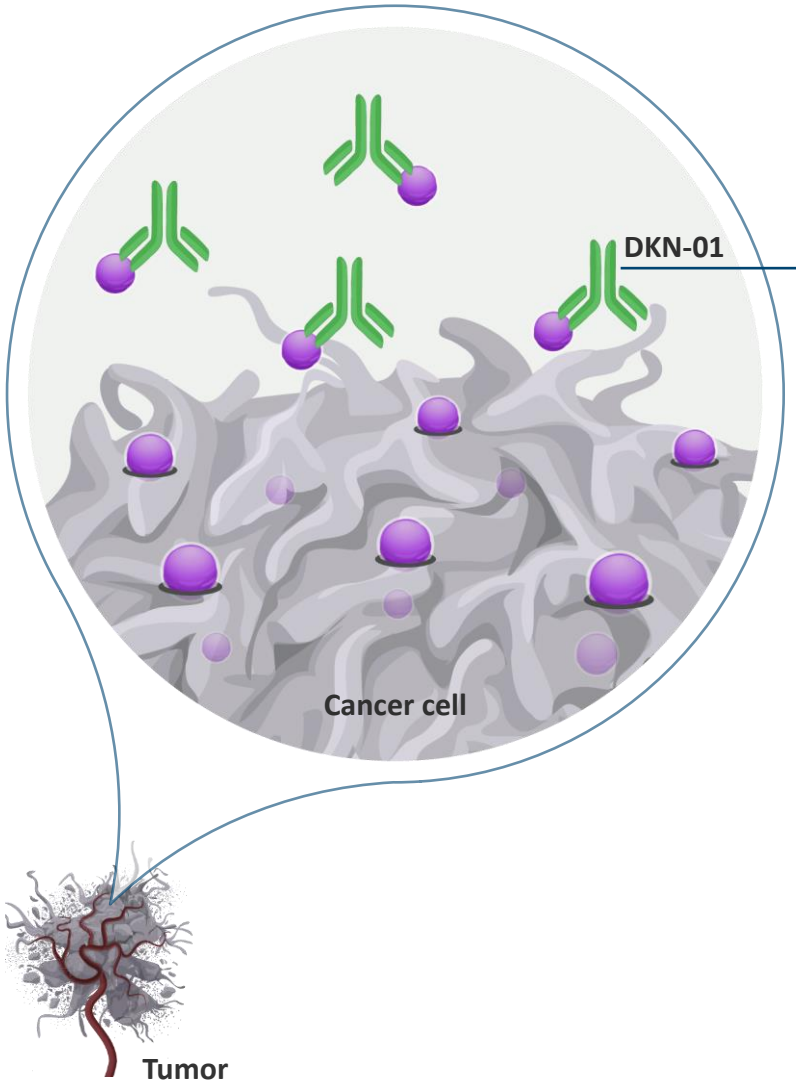
Inhibits β-catenin dependent Wnt signaling to enhance suppressive activity

Suppresses NK cells

Helps tumor cells escape NK cells

leaptherapeutics

DKN-01 - an anti-DKK1 antibody



DKN-01 binds and removes free DKK1 from the TME:

Reduces cell proliferation

Blocks signaling through CKAP4 and PI3K to downregulate akt

Suppresses MDSC cells

B-catenin dependent Wnt signaling reprograms MDSCs and reduces immunosuppressive activity

Reduces angiogenesis

Reduces blood vessel formation, upregulates key cytokines, IFNy, IL-15 and IL-33

Activates NK cells

Upregulates NK cell ligands on tumor, production of Granzyme B by activated NK cells

Single agent and combination activity demonstrated in three different tumor types. Well-tolerated as monotherapy and in combination with chemotherapy or checkpoint inhibitors.

leaptherapeutics

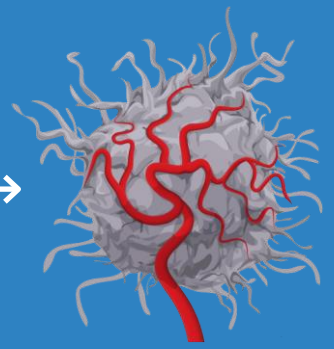
DKN-01 + anti-PD-1 combination

DKN-01 stimulates innate immune system:

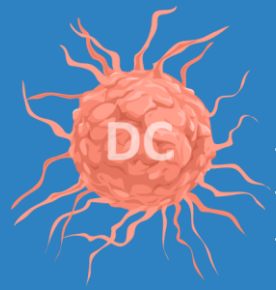
Stimulates activity of NK cells

Induces pro-inflammatory tumor microenvironment

Upregulates PD-L1 (the target for anti-PD-1 antibodies)



Anti-PD-1 stimulates CD8 T cell adaptive immunity:

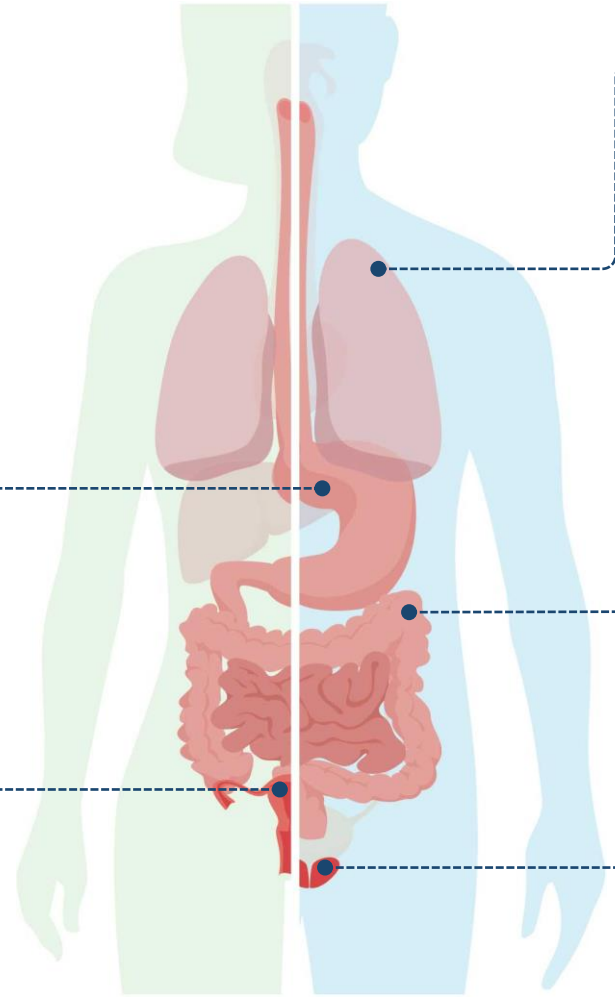


Enhances tumor microenvironment for immune cells to target and clear the tumor

Activates CD8 T cells

leaptherapeutics

Pipeline



Gastric/GEJ cancer

DKN-01
+ anti-PD-1 tislelizumab
+ chemotherapy (1L)

DKN-01
+ anti-PD-1 tislelizumab (2L)

- 1L PFS data, 2L initial data Q1 2022
- Final 1L data expected in Q3 2022
- 1L Randomized Controlled Trial FPI Q4 2022

Endometrial cancer

DKN-01
+ anti-PD-1 pembrolizumab

- Investigator-initiated study
- FPI Q4 2022

Lung cancer

DKN-01

Colorectal cancer

DKN-01
+ bevacizumab
+ chemotherapy

- FPI Q3 2022

Prostate cancer

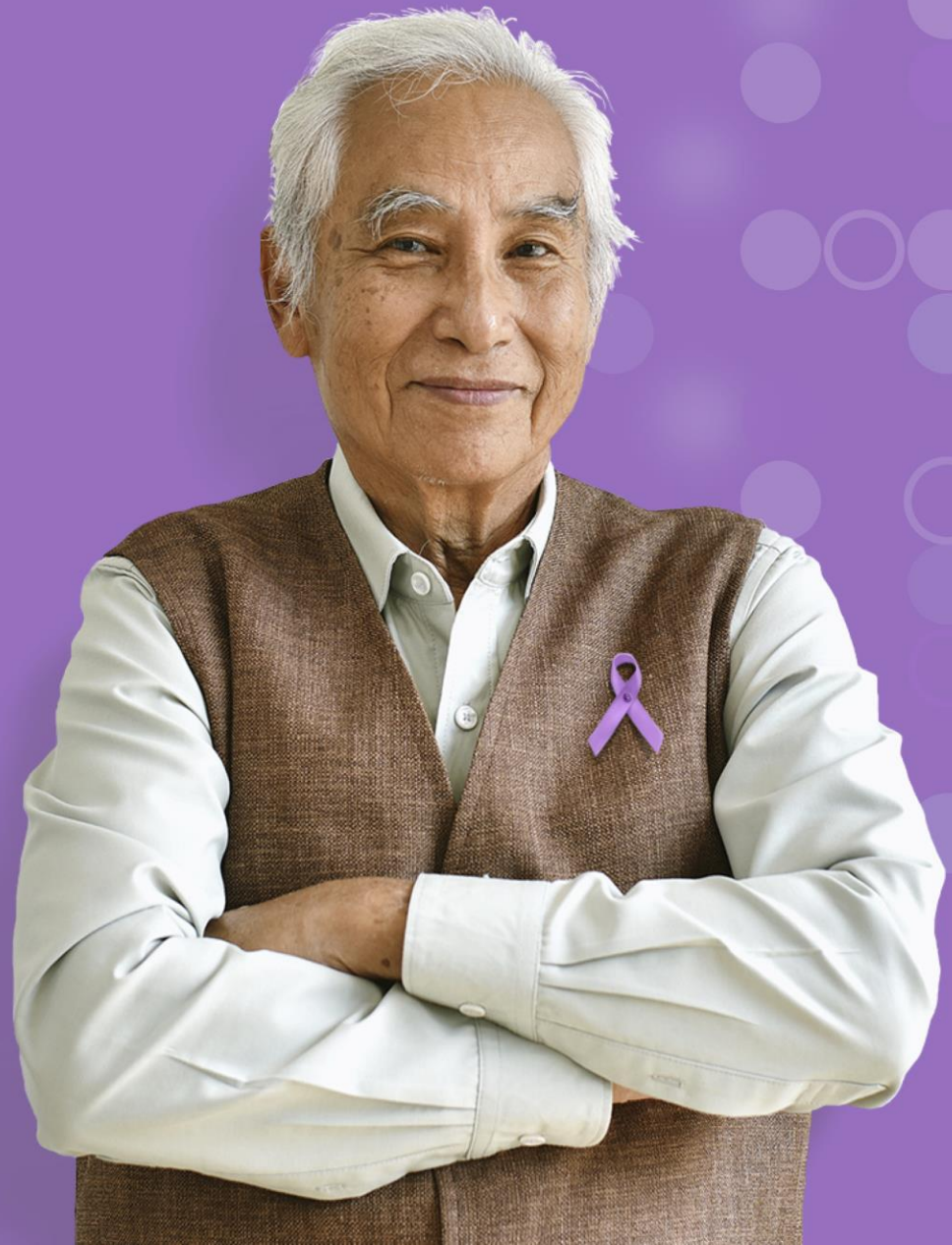
DKN-01
+ docetaxel

- Investigator-initiated study
- Initial data Q2 2022

leaptherapeutics

DKN-01

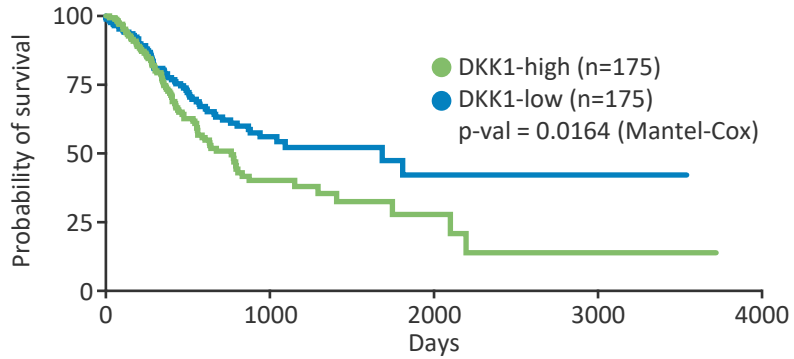
Gastric cancer development



DKK1-high levels are associated with poor survival

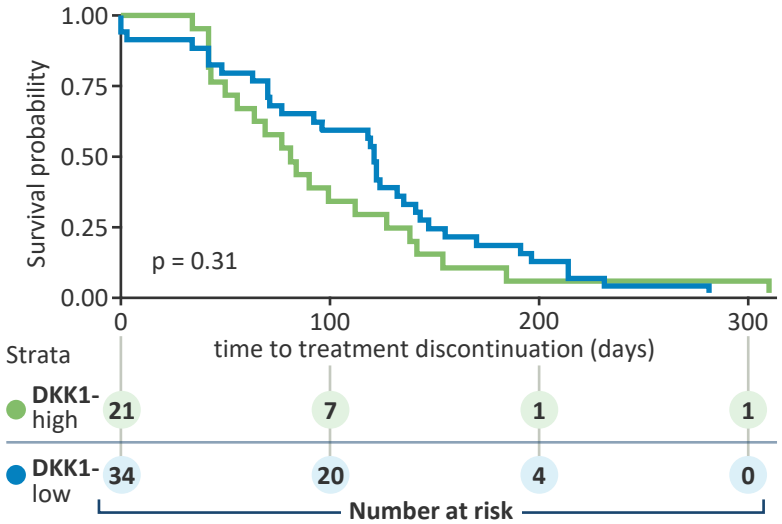
High levels of DKK1 correlate with shorter overall survival In gastric cancer

TCGA STAD dataset

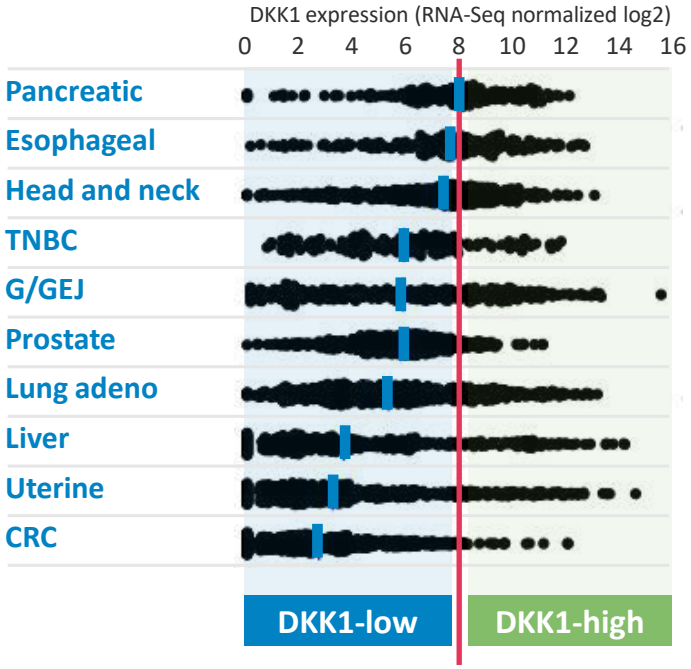


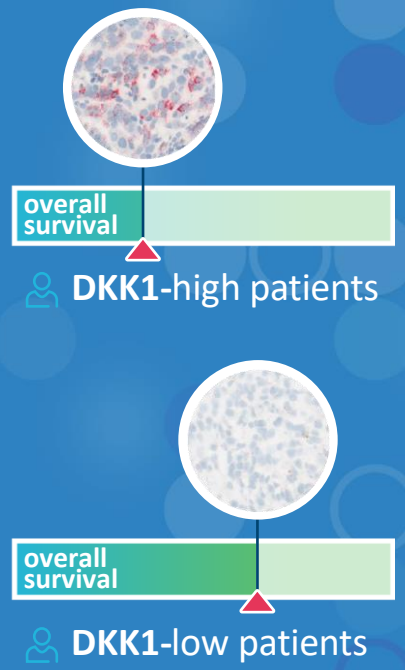
DKK1-high is associated with poor response to first-line platinum + fluoropyrimidine based therapies in GEJ/gastric cancer patients

Collaboration with Tempus



DKK1 expression data (TCGA):

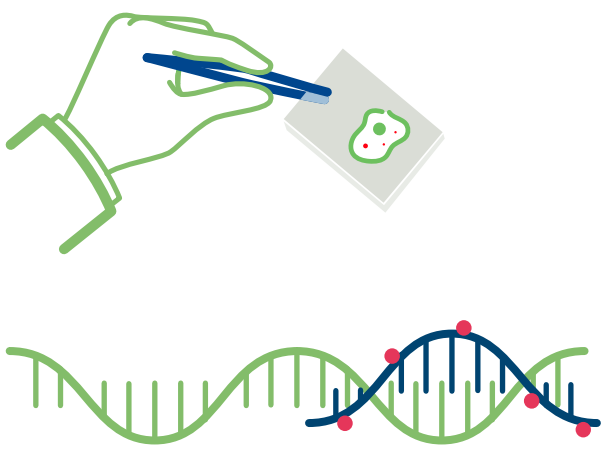


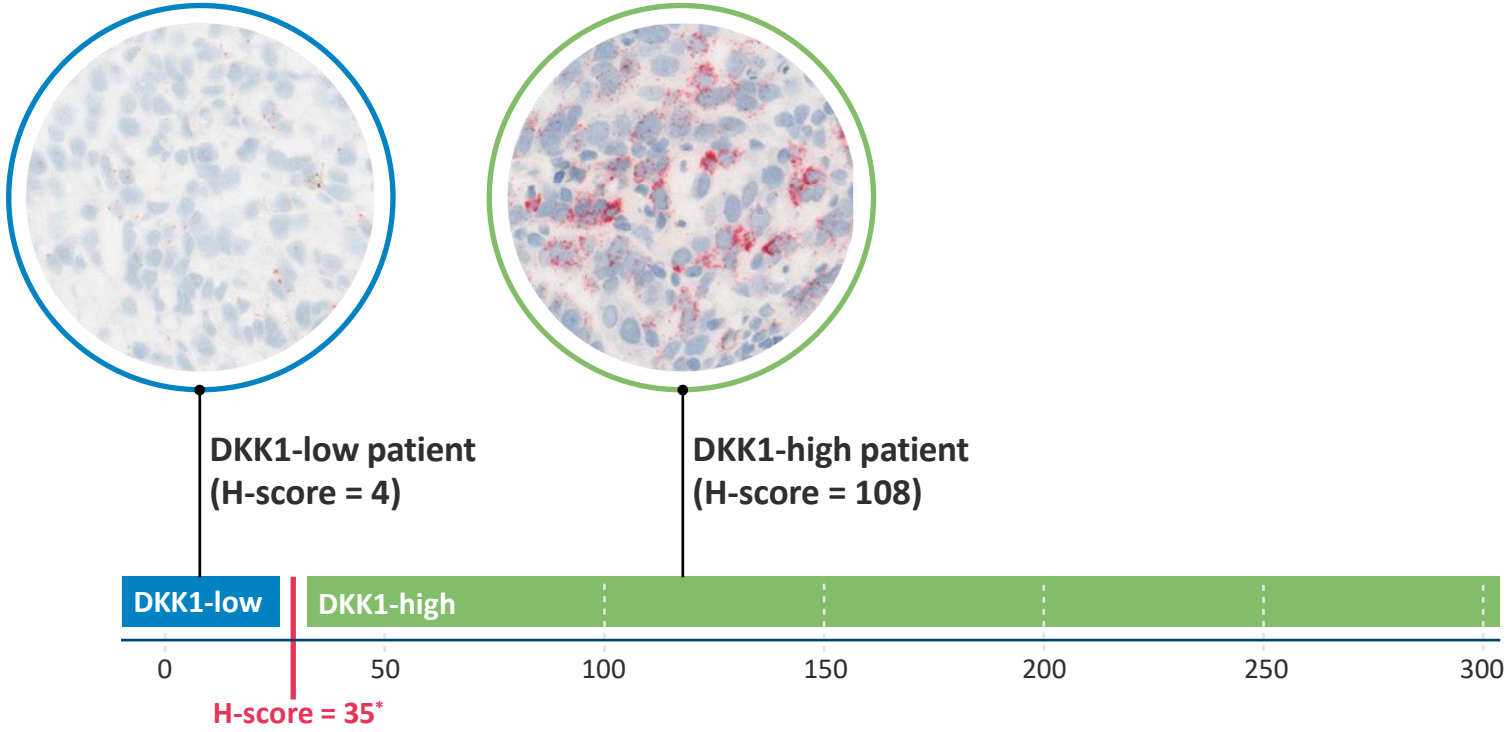


~2.5 years shorter OS in DKK1-high patients

leaptherapeutics

DKK1 expression determined using RNAscope





Chromogenic *in situ* hybridization RNAscope

The biopsy sample is stained to identify DKK1 mRNA

Pathologist determines histology score (H-score), measuring DKK1 expression rather than protein itself

Each red dot is an individual mRNA for DKK1
Number of cells and intensity of staining is converted to H-score

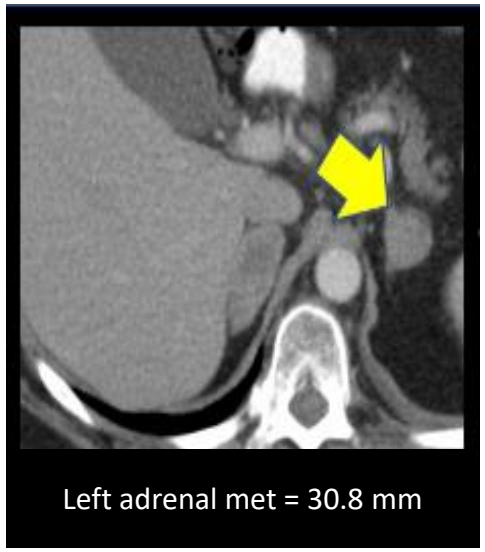
* H-score cut-off at 35 (equating to TPS 20) was identified for gastric cancer from our study of DKN-01 + pembrolizumab

leaptherapeutics

DKN-01 single agent activity in heavily pretreated esophagogastric cancer patients

2L+ EGC
DKN-01

On study 1 year, reduction -33.9%
failed prior anti-PD-L1 + IDOi



Baseline

4-month scan

Best overall response of 20 evaluable patients*	
Partial response	2
Stable disease	6
Progressive disease	12

2 monotherapy PRs

Clinical benefit rate 40%

*By Blinded Independent Central Review

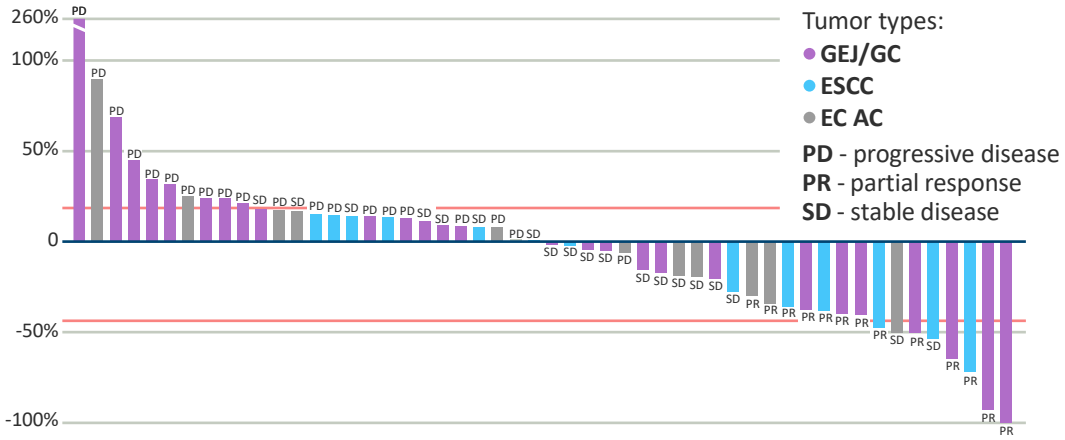
leaptherapeutics

Clinical activity of DKN-01 plus paclitaxel or anti-PD-1 antibody

GEJ/GC
Historical data

DKN-01
+ paclitaxel

N=52
2L-8L esophagogastric pts



	Patients treated	Prior therapies	Overall response rate (ORR)	Disease control rate (DCR)
DKN-01 + paclitaxel	N=52	1-7	**25%**	**60%**

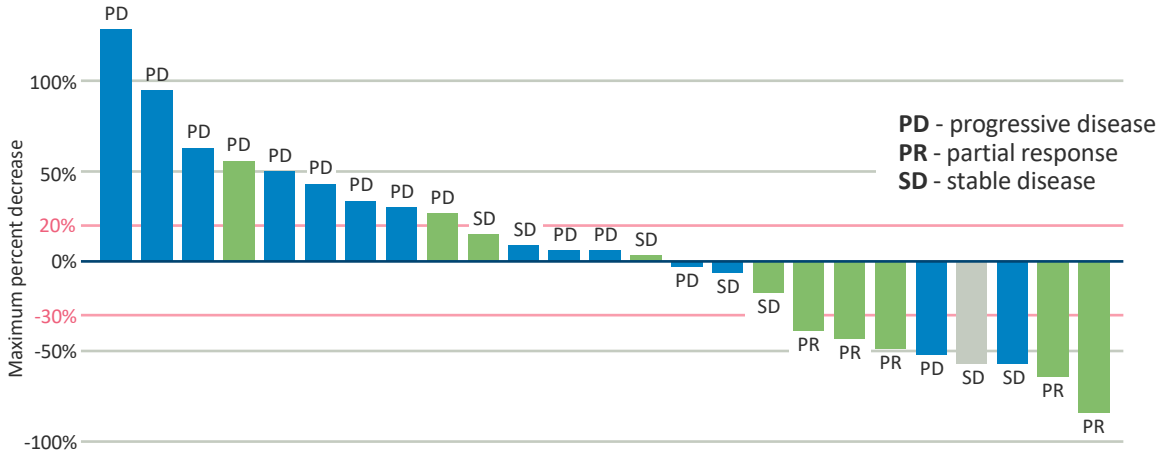
Strong broad activity in esophagogastric cancer in heavily pretreated patients

	Patients treated	PFS (months)	OS (months)	Overall response rate (ORR)	Disease control rate (DCR)
DKN-01 + paclitaxel	N=15	4.5	12.7	**46.7%**	**73.3%**

ORR in 2L patients is ~47%

DKN-01
+ pembro

N=31
2L+ GEJ/GC pts



location	Total (n)	PFS (mo)	OS (mo)	RE (n)	PR (n)	SD (n)	PD (n)	NE (n)	Overall response rate (ORR)	Disease control rate (DCR)
DKK1-high	n=11	5.1	7.3	10	5	3	2	1	**5 (50%)**	**8 (80%)**
DKK1-low	n=20	1.4	4	15	0	3	12	5	**0 (0%)**	**3 (20%)**

*DKK1-high ≥ upper tertile (35)

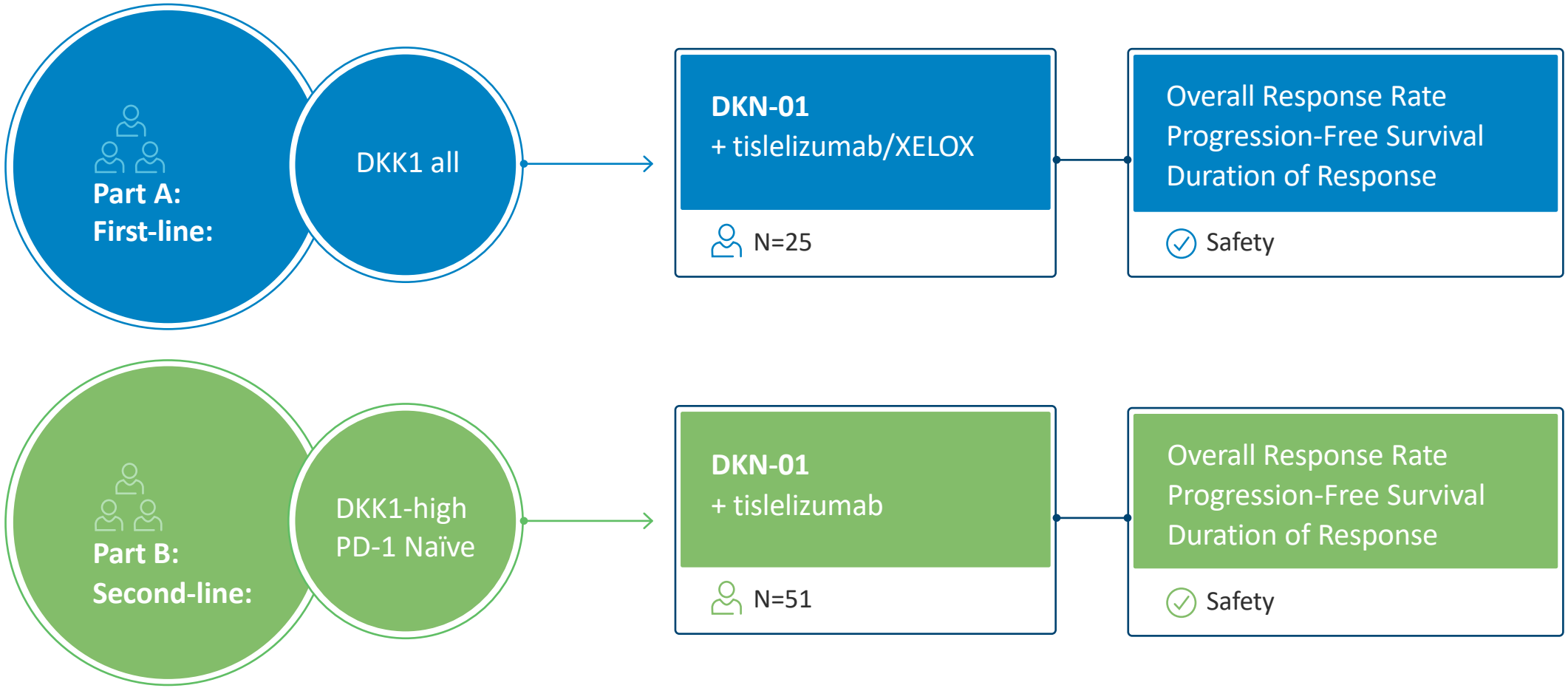
Achieved improved ORR, PFS, and OS in DKK1-high patients
Identified H-score threshold for DKK1 high/low expression

leaptherapeutics

DisTinGuish study design: advanced GEJ/Gastric cancer

1L GEJ/GC
DKN-01
+ tislelizumab
+ chemotherapy

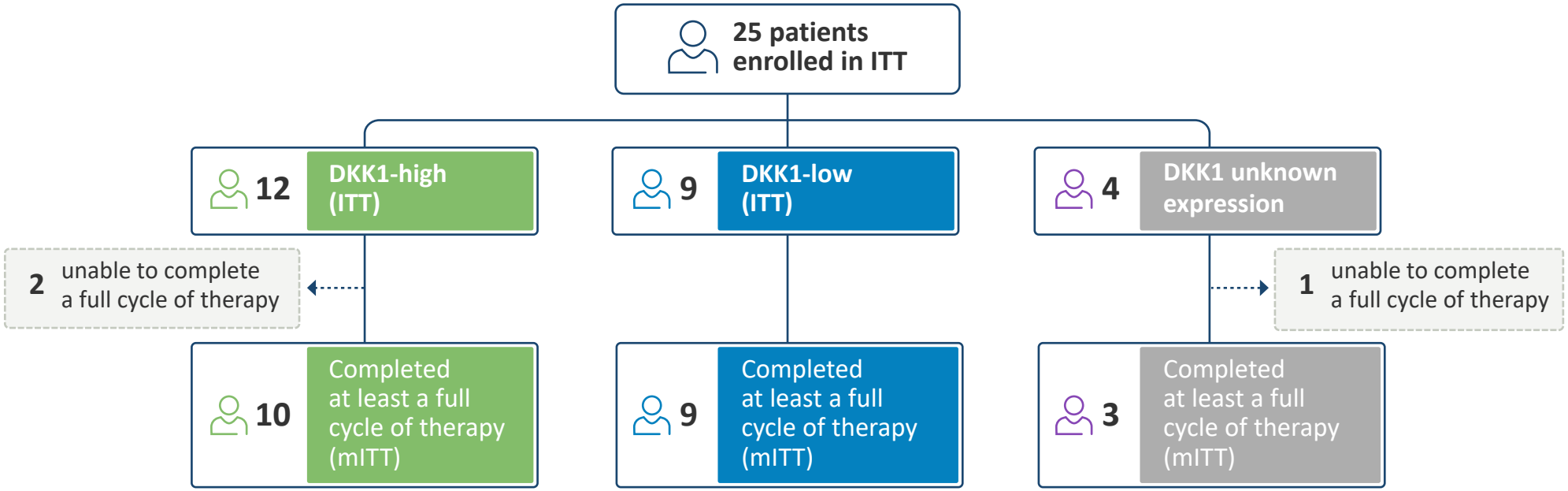
Assess the safety and anti-tumor activity of DKN-01 in combination with tislelizumab +/- chemotherapy

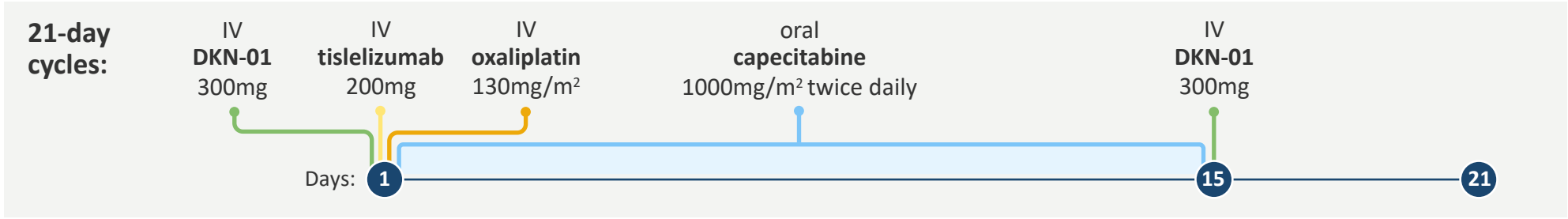


BeiGene | leaptherapeutics

DisTinGuish Part A consort diagram

1L GEJ/GC
DKN-01
+ tislelizumab
+ chemotherapy





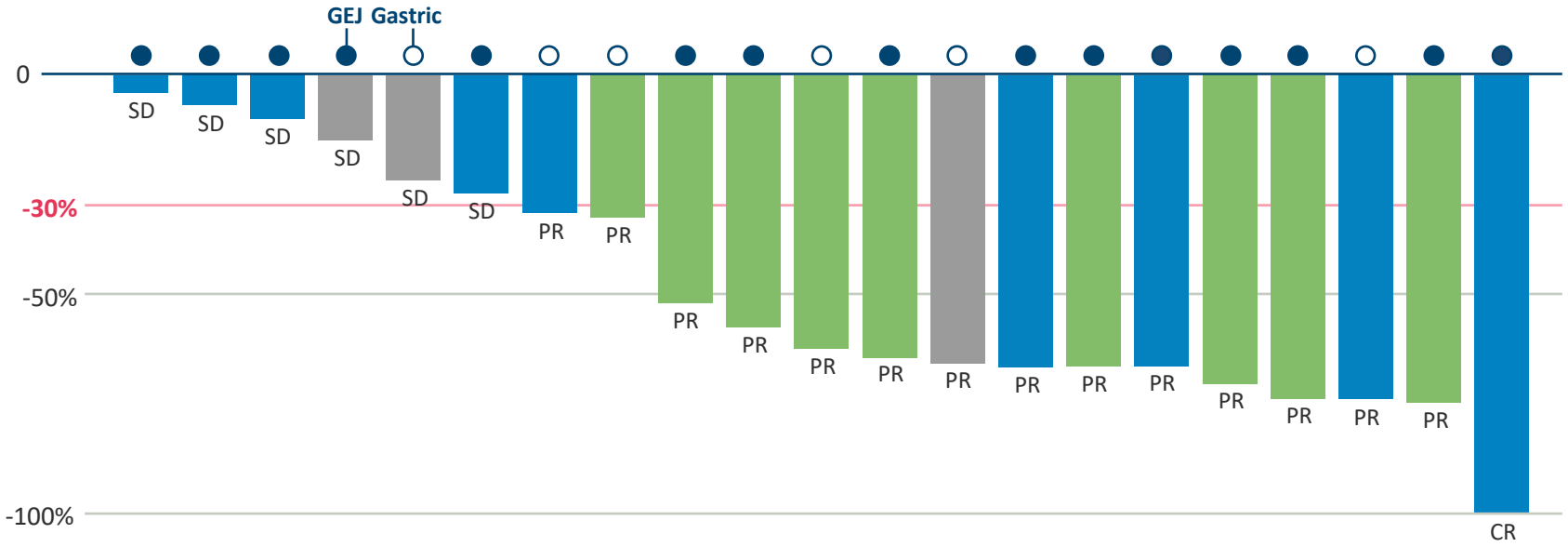
DKK1-high: H-score ≥35; DKK1-low: H-score <35

leaptherapeutics

Best overall response by DKK1 expression

1L GEJ/GC
DKN-01
+ tislelizumab
+ chemotherapy

Best % change in sum of diameters



	mITT* population N=22	**DKK1**-high N=10	**DKK1**-low N=9	**DKK1**-unknown N=3
CR - complete response	1 (4.5%)	0	1 (11.1%)	0
PR - partial response	14 (63.6%)	9 (90.0%)	4 (44.4%)	1 (33.3%)
SD - stable disease	6 (27.3%)	0	4 (44.4%)	2 (66.7%)
PD - progressive disease	0	0	0	0
NE - non-evaluable	1 (4.5%)	1 (10.0%)	0	0

All 9 of the evaluable DKK1-high patients had a partial response

1 PR went to curative surgery with pathological CR

68.2%
ORR in the mITT population

(1 CR; 14 PR)

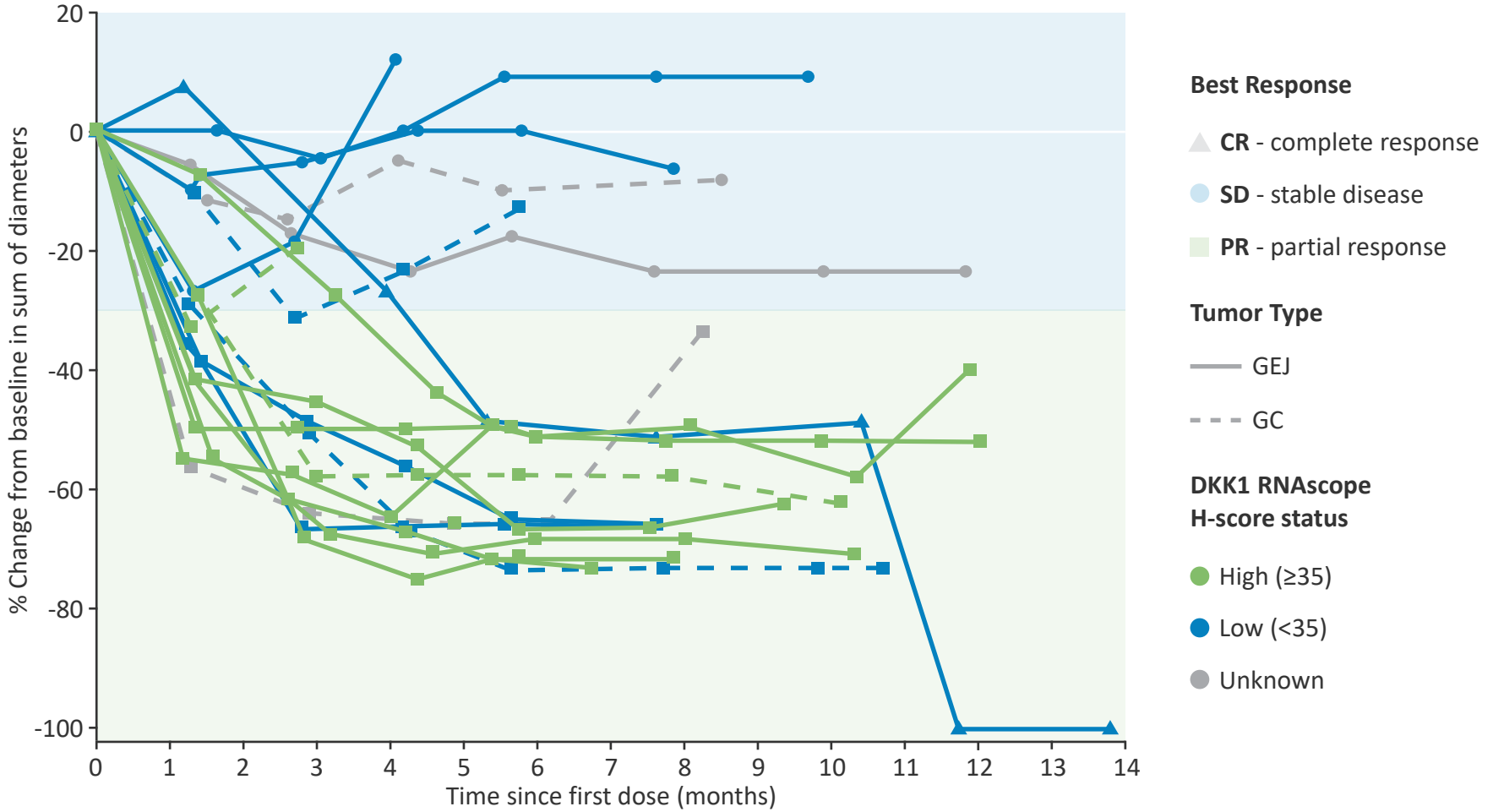
*mITT population includes all patients who received > 1 dose of DKN-01
As presented at ASCO GI 2022

leaptherapeutics

Durable response by DKK1 expression

1L GEJ/GC
DKN-01
+ tislelizumab
+ chemotherapy

Best % change in sum of diameters



90%
ORR in DKK1-high patients

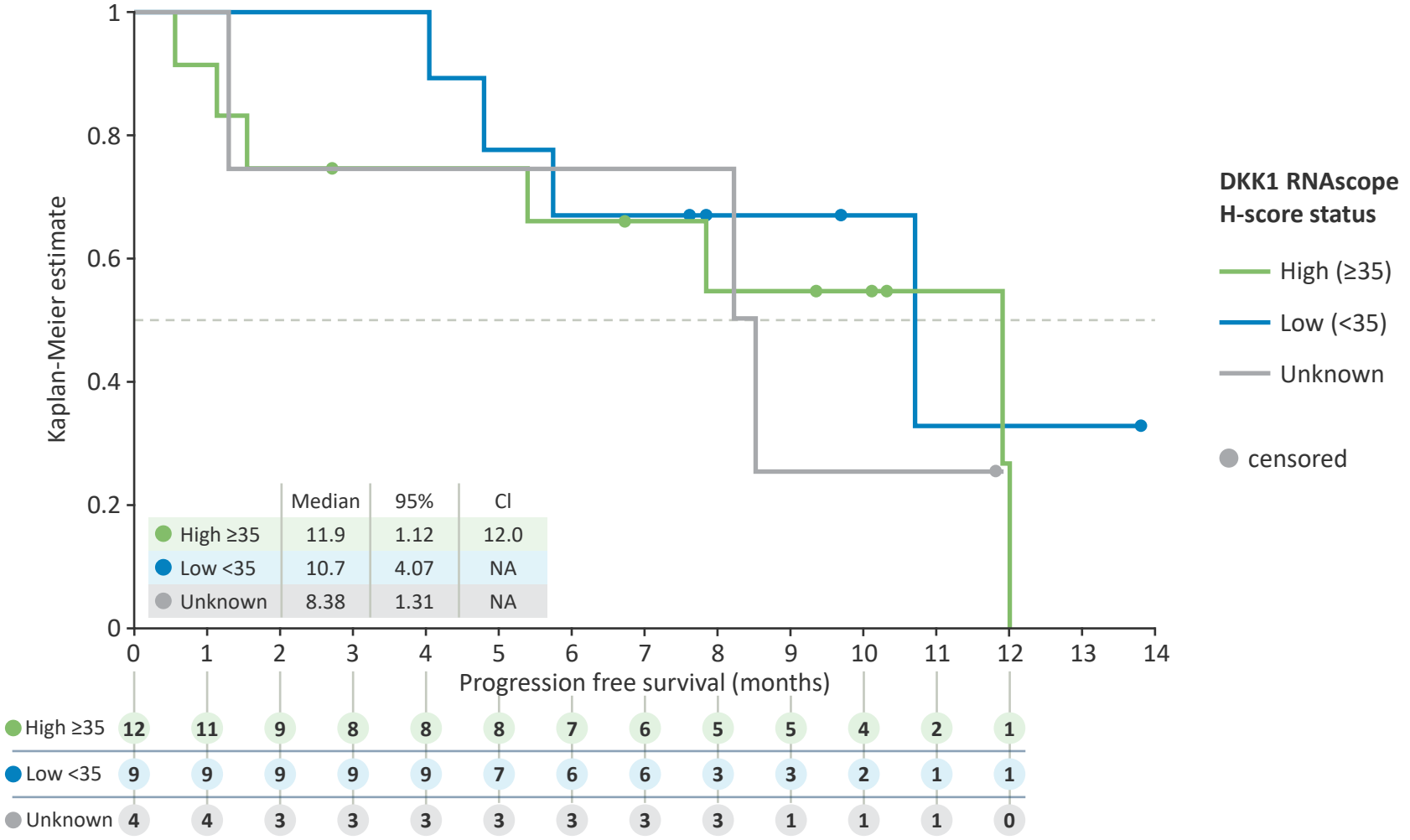
As presented at ASCO GI 2022

leaptherapeutics

PFS longer in DKK1-high patients

1L GEJ/GC
DKN-01
+ tislelizumab
+ chemotherapy

Progression-free survival by DKK1 status (N=25)



Median PFS all: 10.7 mo

Median PFS for DKK1-high: 11.9 mo

Median PFS from Checkmate-649 (nivolumab + chemo): 7.7 months

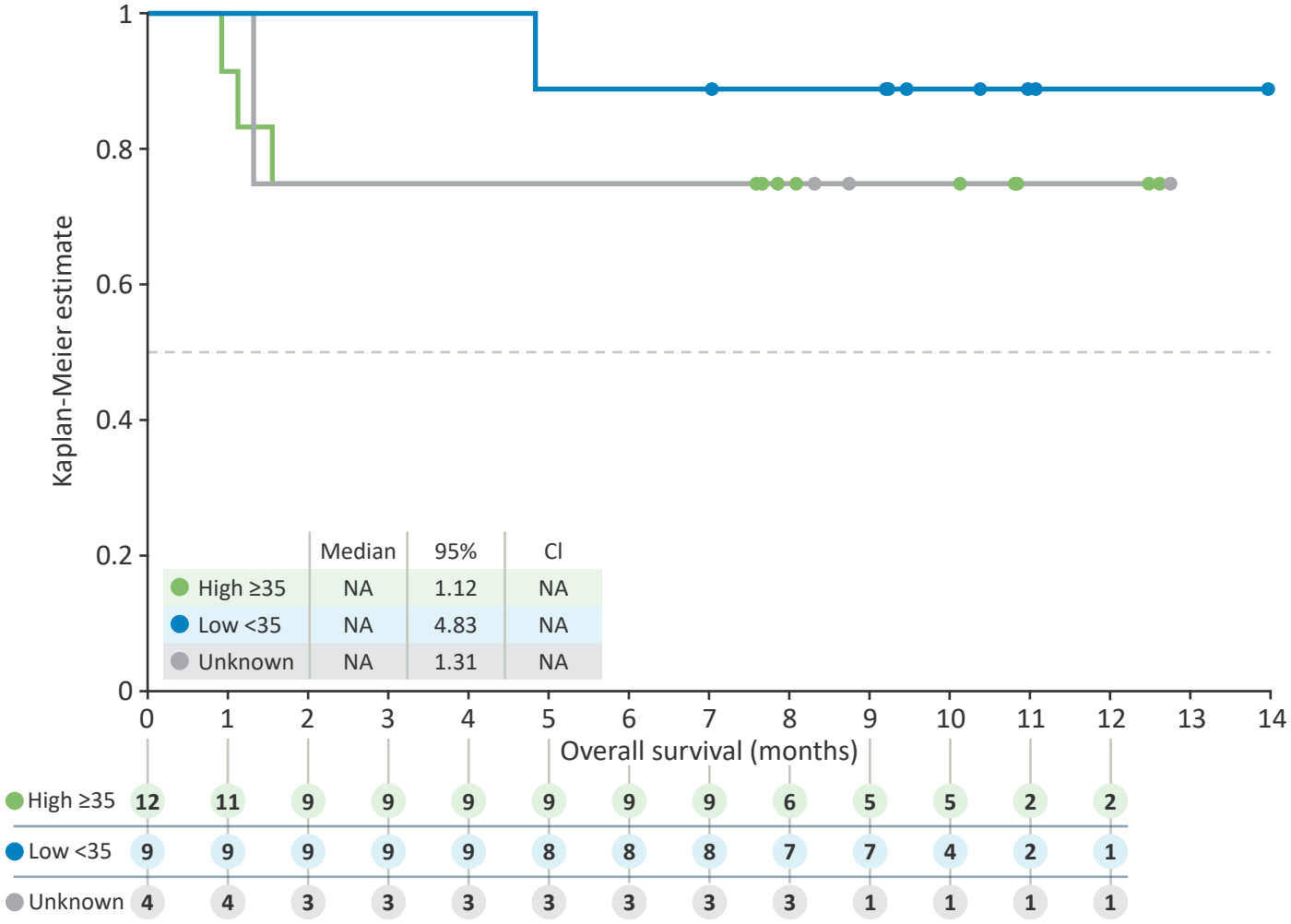
As presented at ASCO GI 2022

leaptherapeutics

Overall survival not reached

1L GEJ/GC
DKN-01
+ tislelizumab
+ chemotherapy

Overall survival by DKK1 status (N=25)



DKK1 RNAscope H-score status

- High (≥35)
- Low (<35)
- Unknown
- censored

Median OS from Checkmate-649 (nivolumab + chemo): 13.8 months

As presented at ASCO GI 2022

leaptherapeutics

Best overall response by PD-L1 expression

1L GEJ/GC
DKN-01
+ tislelizumab
+ chemotherapy

Best % change in sum of diameters

	PD-L1 CPS ≥5		PD-L1 CPS <5		
	DKK1-high N=4	**DKK1**-low N=2	**DKK1**-high N=6	**DKK1**-low N=7	**DKK1**-unknown N=1
CR - complete response		1 (50%)			
PR - partial response	3 (75%)	0	6 (100%)	4 (57%)*	1 (100%)
SD - stable disease	0	1 (50%)	0	3 (43%)	0
PD - progressive disease	0	0	0	0	0
NE - non-evaluable	1 (25%)	0	0	0	0
	N=6 **67% ORR**		N=14 **79% ORR**		

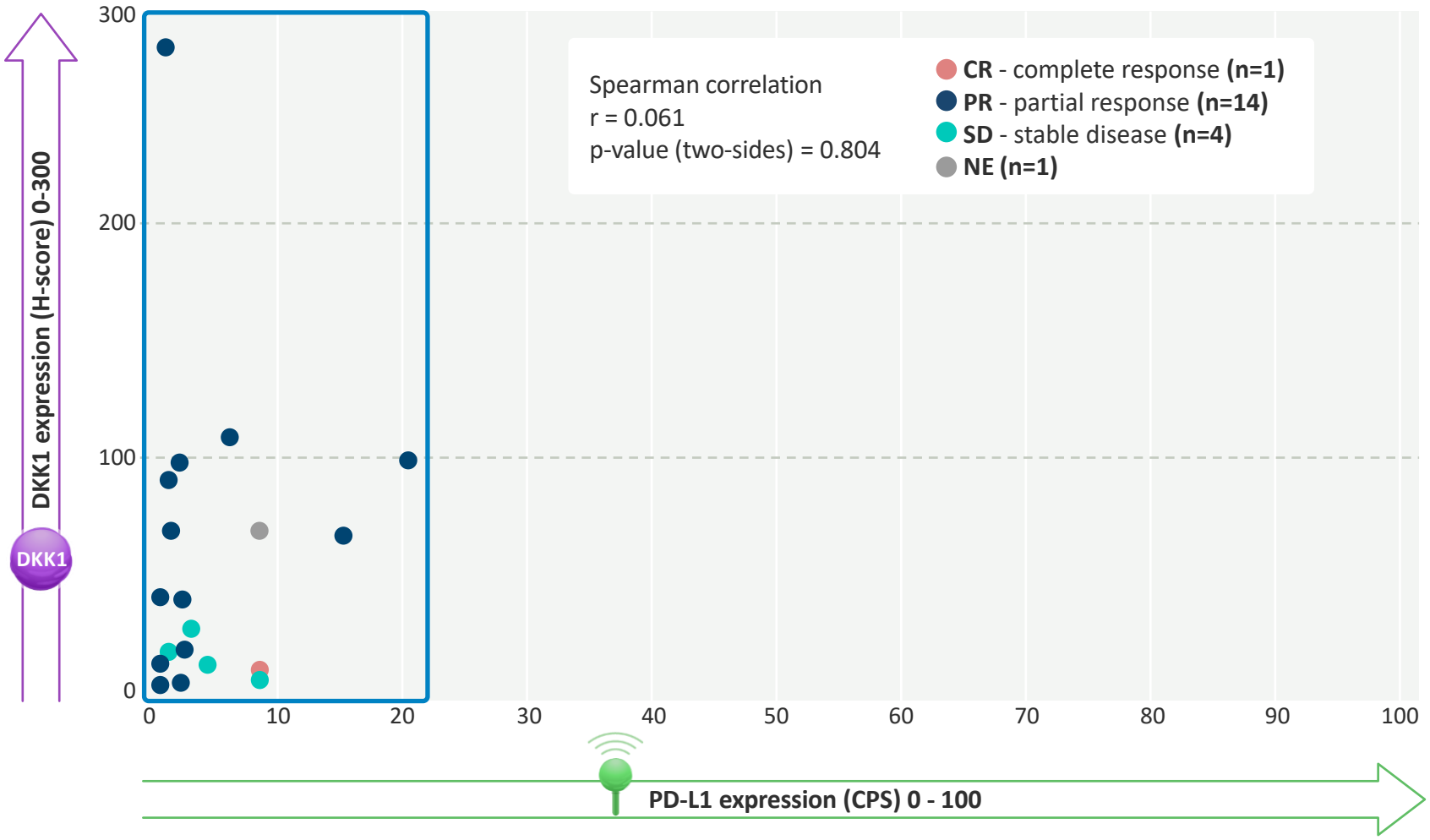
vCPS: visually-estimated combined positive score; PD-L1: programmed death-ligand 1
*Includes one pathologic CR
As presented at ASCO GI 2022

79%
ORR in PD-L1 low patients

leaptherapeutics

DKK1 and PD-L1 expression are not correlated

1L GEJ/GC
DKN-01
+ tislelizumab
+ chemotherapy



This population had low overall PD-L1 expression

As presented at ASCO GI 2022

leaptherapeutics

DKN-01 plus tislelizumab and chemotherapy safety profile

1L GEJ/GC
DKN-01
+ tislelizumab
+ chemotherapy

Combination DKN-01+ tislelizumab + capox was well tolerated with manageable toxicity

Most common DKN-01-related adverse events were low grade (G1/2):

Fatigue, nausea, diarrhoea, neutrophil count decreased, platelet count decreased

5 patients experienced six Grade ≥3 DKN-01-related adverse events:

Diarrhoea (1), neutrophil count decreased (1), blood phosphorus decreased (2), pulmonary embolism (2)

No Grade 4 events

TEAEs leading to death (Grade 5) within 30 days of last dose

- Pulmonary embolism (1) assessed by the investigator as related to regimen
- Aspiration pneumonia (1) and hepatic failure (1) both assessed as possibly related to disease progression

Preferred terms:	Part A (N=25) No. Patients (%)
TEAEs leading to death within 30 days of last dose	3 (12%)
Any adverse event	25 (100%)
Grade ≥ 3 events	14 (56%)
DKN-01-related	5 (20%)
Serious adverse events	10 (40%)
DKN-01-related	2 (8%)
Events leading to DKN-01 discontinuation	3 (12%)
DKN-01-related	1 (4%)
Events leading to DKN-01 dose reduction	1 (4%)
Drug-related adverse events	
DKN-01-related	14 (56%)
Tislelizumab-related	17 (68%)
Capecitabine-related	24 (96%)
Oxaliplatin-related	25 (100%)
Regimen-related	25 (100%)

leaptherapeutics

DisTinGuish Part C randomized study

1L GEJ/GC
DKN-01
+ tislelizumab
+ chemotherapy

Key eligibility criteria:

- No prior therapy for unresectable locally advanced or metastatic gastric/GEJ adenocarcinoma
- RECIST v1.1 measurable disease
- Her2 negative

Stratification factors:

- DKK1 expression (TPS ≥ 20% vs < 20%)
- PD-L1 (CPS ≥5 vs < 5)

N=160
1:1

DKN-01
+ tislelizumab
+ SOC chemotherapy
(XELOX or mFOLFOX6)

N=80

Tislelizumab
+ SOC chemotherapy
(XELOX or mFOLFOX6)

N=80

Primary objective:
PFS DKK1-high

Secondary objectives:
– PFS all patients
– OS, DKK1-high and all
– ORR, DKK1-high and all

leaptherapeutics

DKN-01 highlights in gastric cancer

DKK1 is an important new therapeutic target in gastric cancer

DKK1-high is associated with aggressive biology, poor response to standard 5-FU therapy, and shorter survival

DKN-01
+ anti-PD-1 tislelizumab
+ chemotherapy (1L)

Overall
68% ORR
10.7m PFS

DKK1-high
90% ORR
11.9m PFS

DKK1-low
56% ORR
10.7m PFS

PD-L1 ↓ CPS <5
79% ORR

DKK1-high
PD-L1 ↓ CPS <5
100% ORR

Response is correlated with DKK1 expression and independent of PD-L1 expression

leaptherapeutics

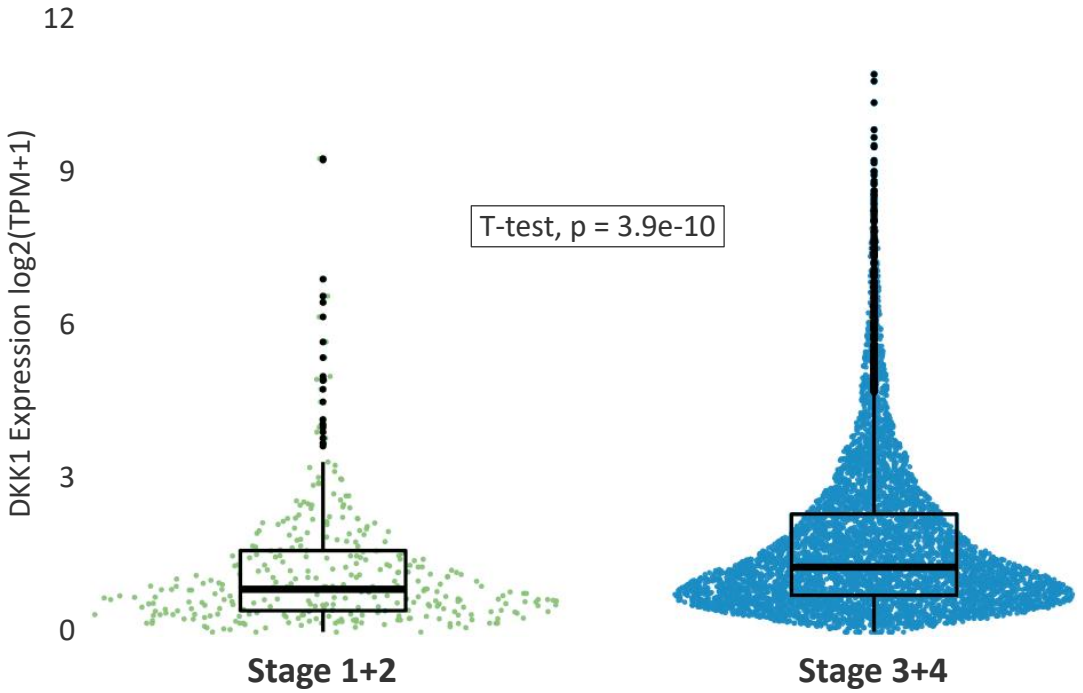
DKN-01

Colorectal cancer development

Rationale for targeting colorectal cancer

- CRC is characterized by hyperactivation of the Wnt pathway, often believed to be the initiating and driving event
- DKK1 drives resistance to 5FU; DKN-01 has demonstrated prior synergy with 5FU-based regimen in GEA
- Preclinically DKN-01 treatment:
  - Shows additive activity with 5FU and is able to overcome 5FU-resistance in xenograft models
  - Has activity alone and with anti-PD-1 in syngeneic models
  - Has activity in wild type and PIK3CA mutant models alone and with a PIK3CA inhibitor

DKK1 elevated in advanced CRC (Tempus)

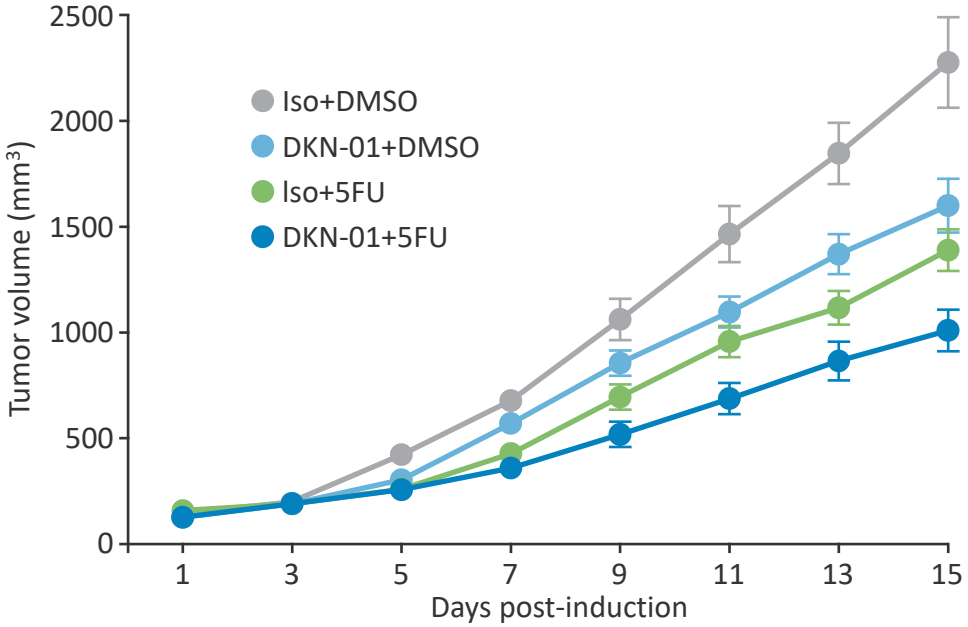


leaptherapeutics

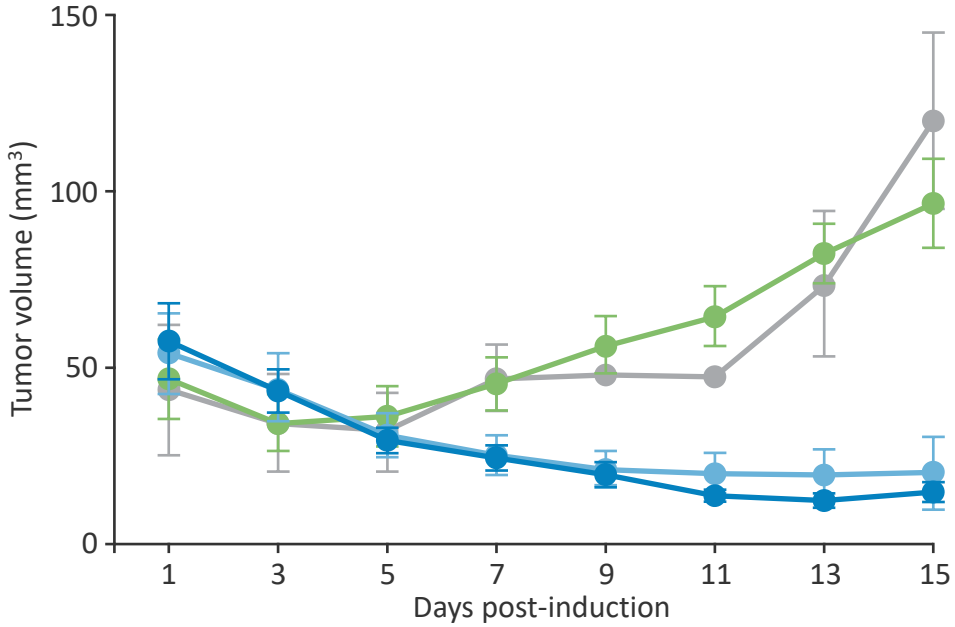
DKN-01 activity in combination with 5-FU chemotherapy in colorectal cancer models

- DKN-01 has efficacy in CRC syngeneic models including HCT116
- Additive activity was seen with 5FU chemotherapy
- In a 5FU chemotherapy-resistant model, DKN-01 demonstrates significant inhibition of tumor growth

HCT116 parental



HCT116 5FU-resistant



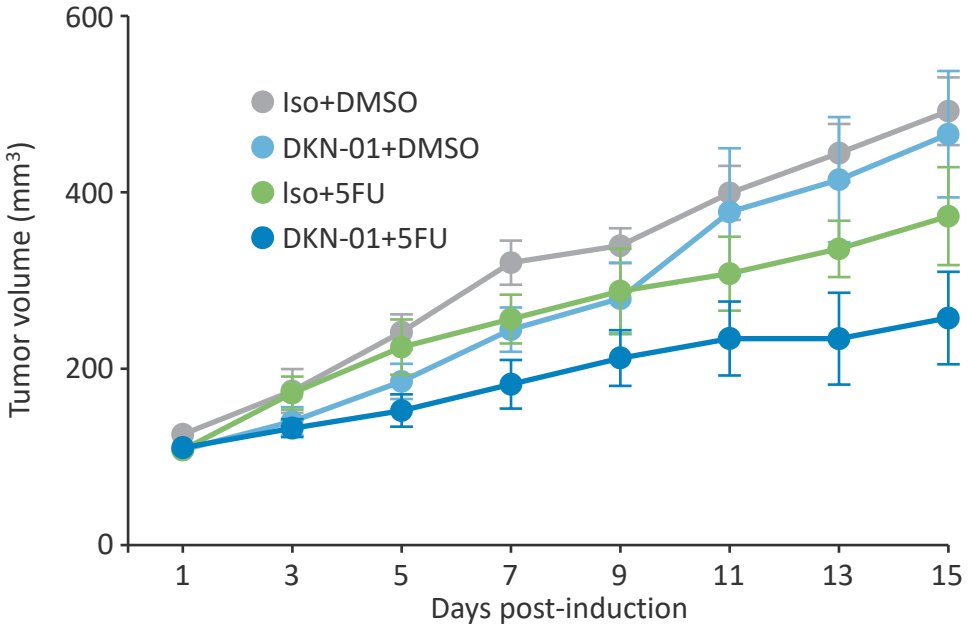
Data courtesy of Goel Lab at City of Hope Cancer Center

leaptherapeutics

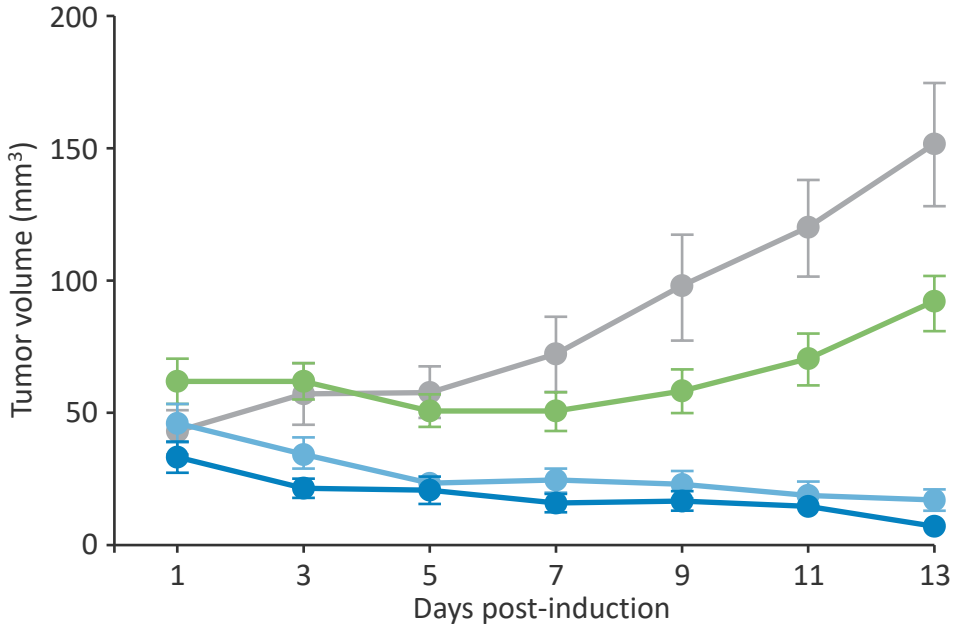
DKN-01 activity in combination with 5-FU chemotherapy in colorectal cancer models

- DKN-01 has efficacy in CRC syngeneic models including SW480
- Additive activity was seen with 5FU chemotherapy
- In a 5FU chemotherapy-resistant model, DKN-01 demonstrates significant inhibition of tumor growth

SW480 parental



SW480 5FU-resistant

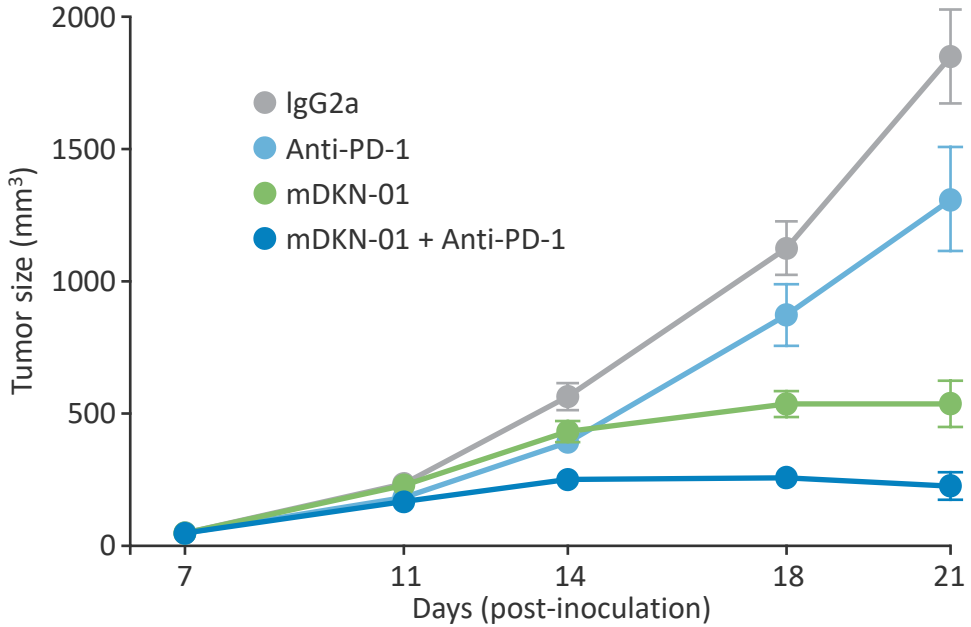


Data courtesy of Goel Lab at City of Hope Cancer Center

leaptherapeutics

DKN-01 activity in combination with PD-1 antibody in colorectal cancer model

- DKN-01 has efficacy in CRC syngeneic models including CT26
- Additive activity was seen with an anti-PD-1 antibody



Single Agent Activity

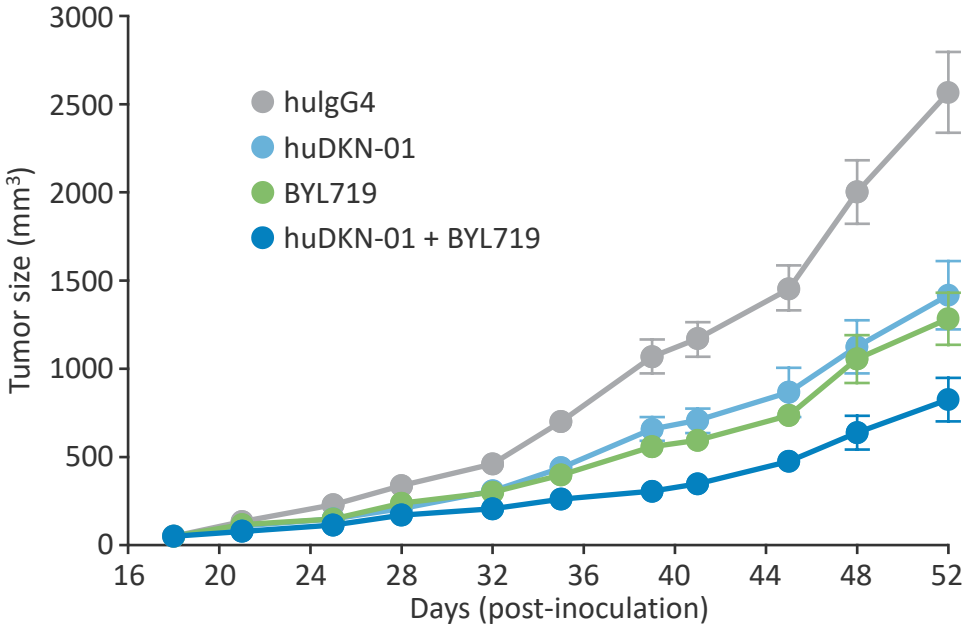
Additive Activity with Anti-PD-1 Antibody

leaptherapeutics

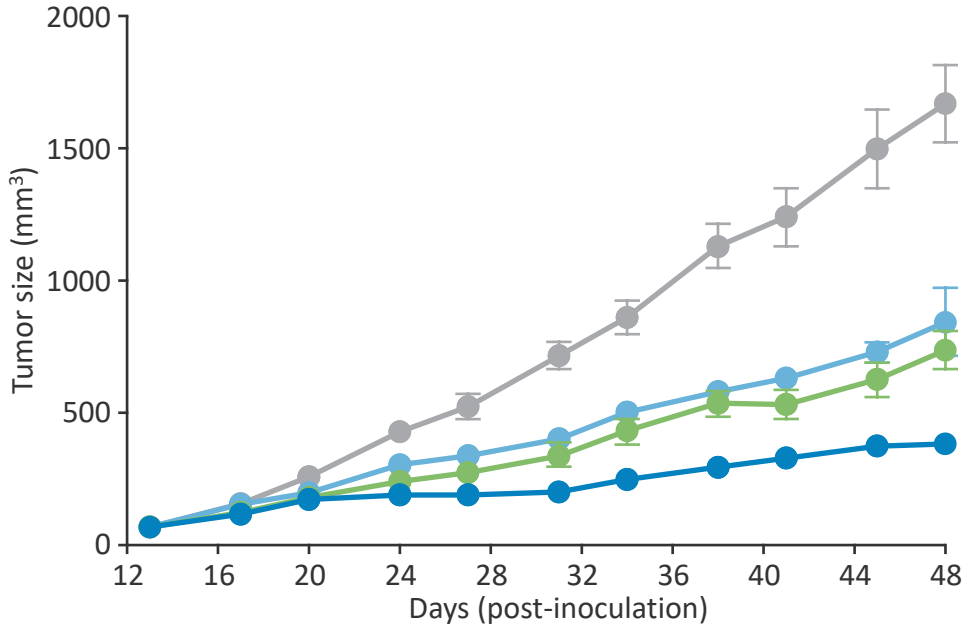
DKN-01 activity in combination with PI3 kinase inhibitor in colorectal cancer models

- DKN-01 has efficacy in CRC xenograft models, including with PIK3CA mutation
- Additive activity was seen with an PI3 kinase inhibitor

HCT116 parental



HCT116 + PIK3CA H1047R mutation

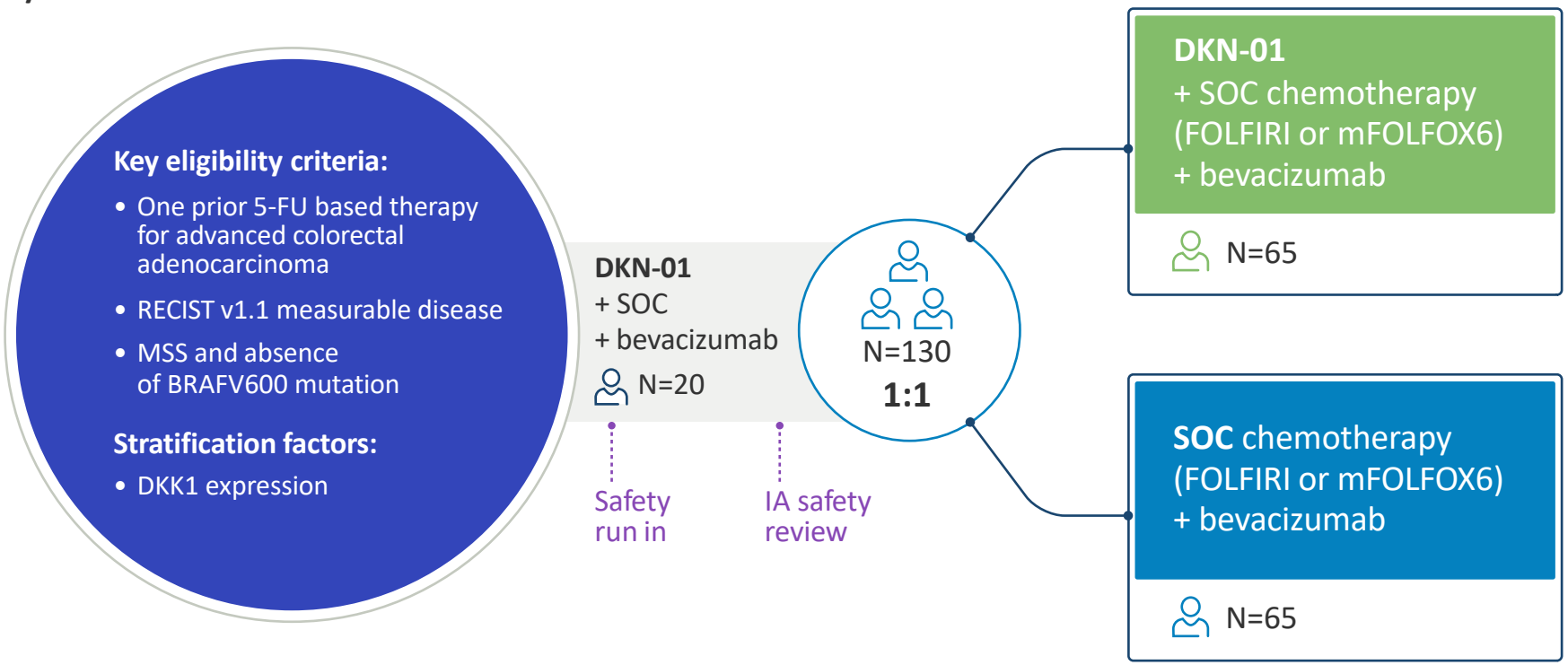


leaptherapeutics

DKN-01 colorectal cancer study

2L CRC
DKN-01
+ bevacizumab
+ chemotherapy

Randomized phase 2 study of FOLFIRI/FOLFOX and bevacizumab +/- DKN-01 as second-line treatment of advanced colorectal cancer



- **Primary objective:**
  PFS (SOC: mPFS 5.7 mos)
- **Secondary objectives:**
  – ORR (SOC: ORR 5%)
  – DoR
  – OS

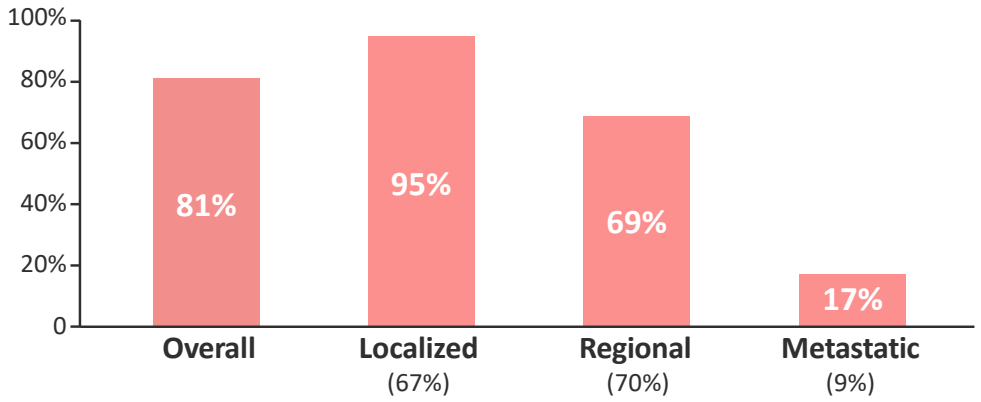
leaptherapeutics

DKN-01

Endometrial cancer development

Endometrial Cancer

5-Year overall and relative survival:



Most common gynecological cancer in the western world

~66,500

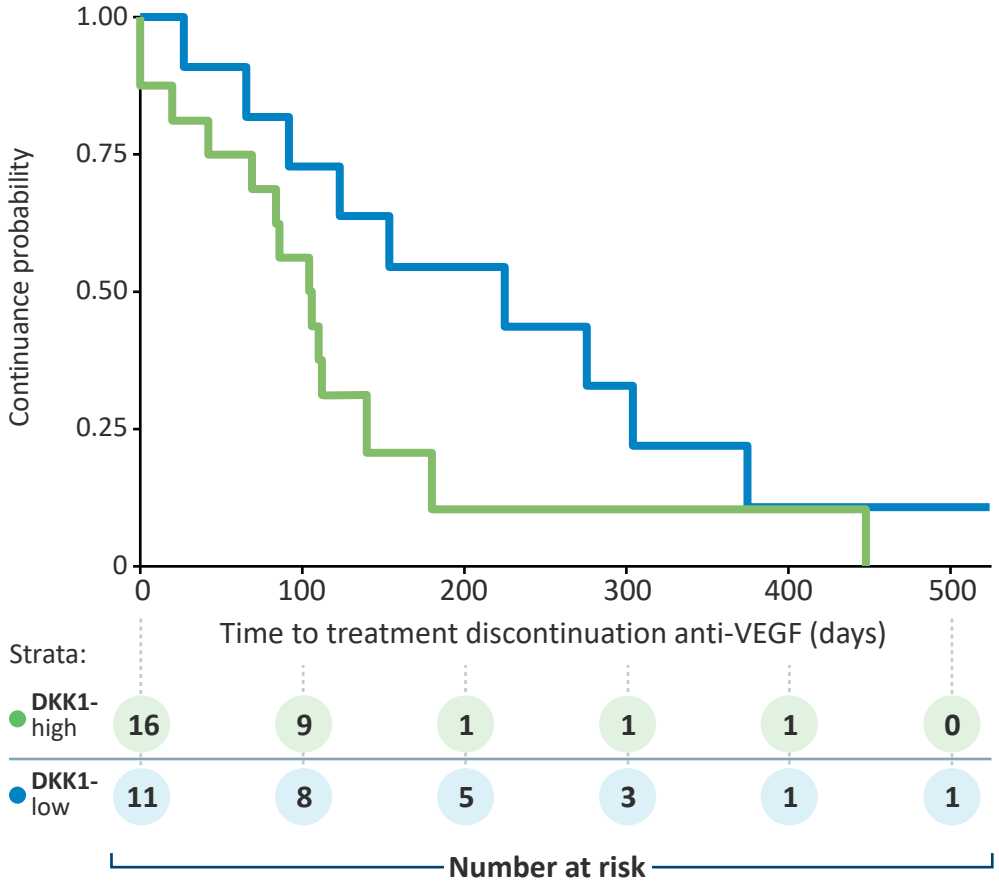
~66,500 annual cases in the United States and the incidence is increasing

Fourth most common cancer in women in the United States

Clinical risk factors include estrogen-only hormone replacement, obesity, chronic anovulation, tamoxifen therapy, nulliparity, early menarche, and late menopause

High DKK1 is associated with poor response to anti-VEGF therapy in endometrioid endometrial cancer patients

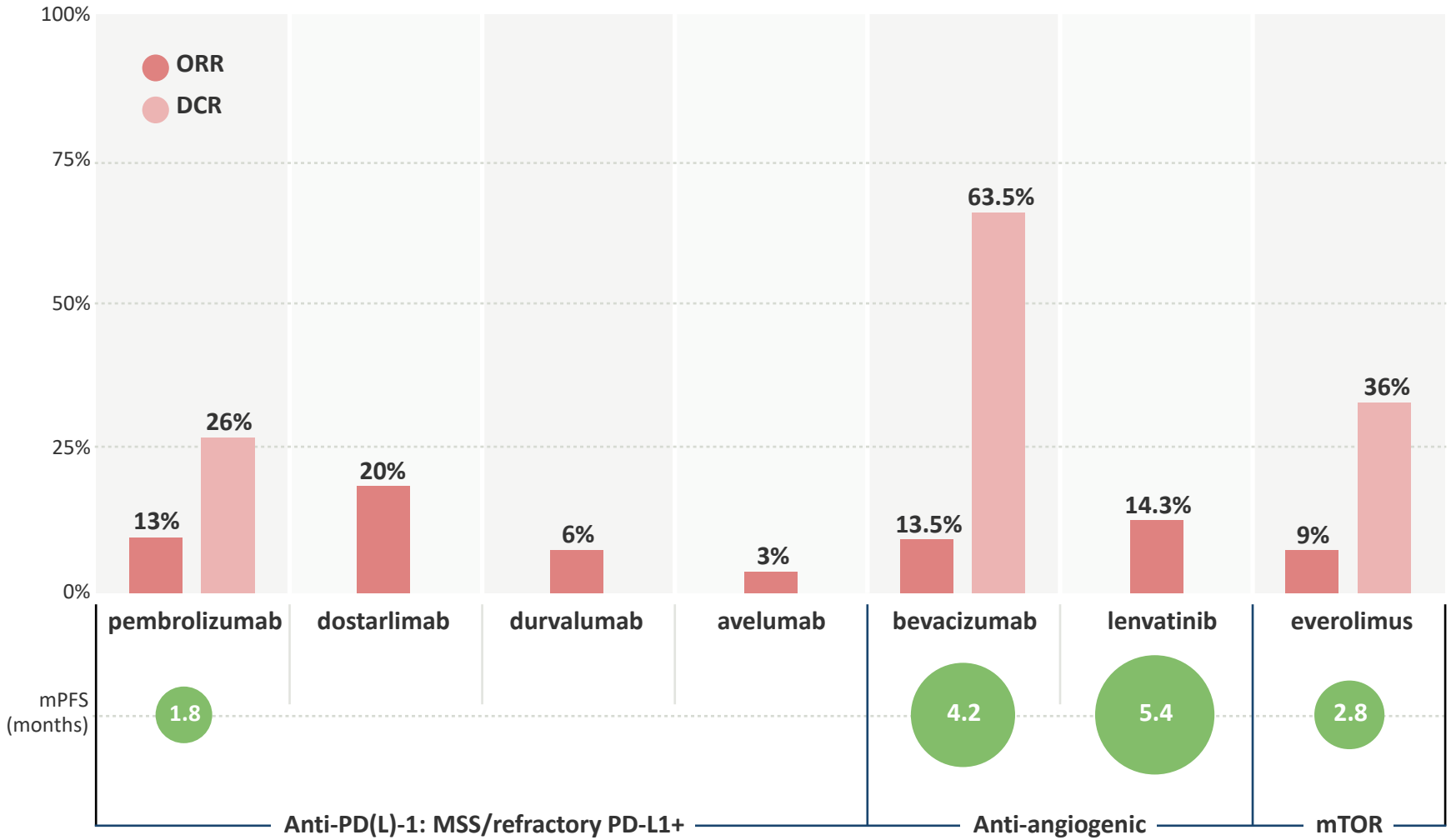
Anti-VEGF treatment:



Source: American Cancer Society, Tempus real world evidence

leaptherapeutics

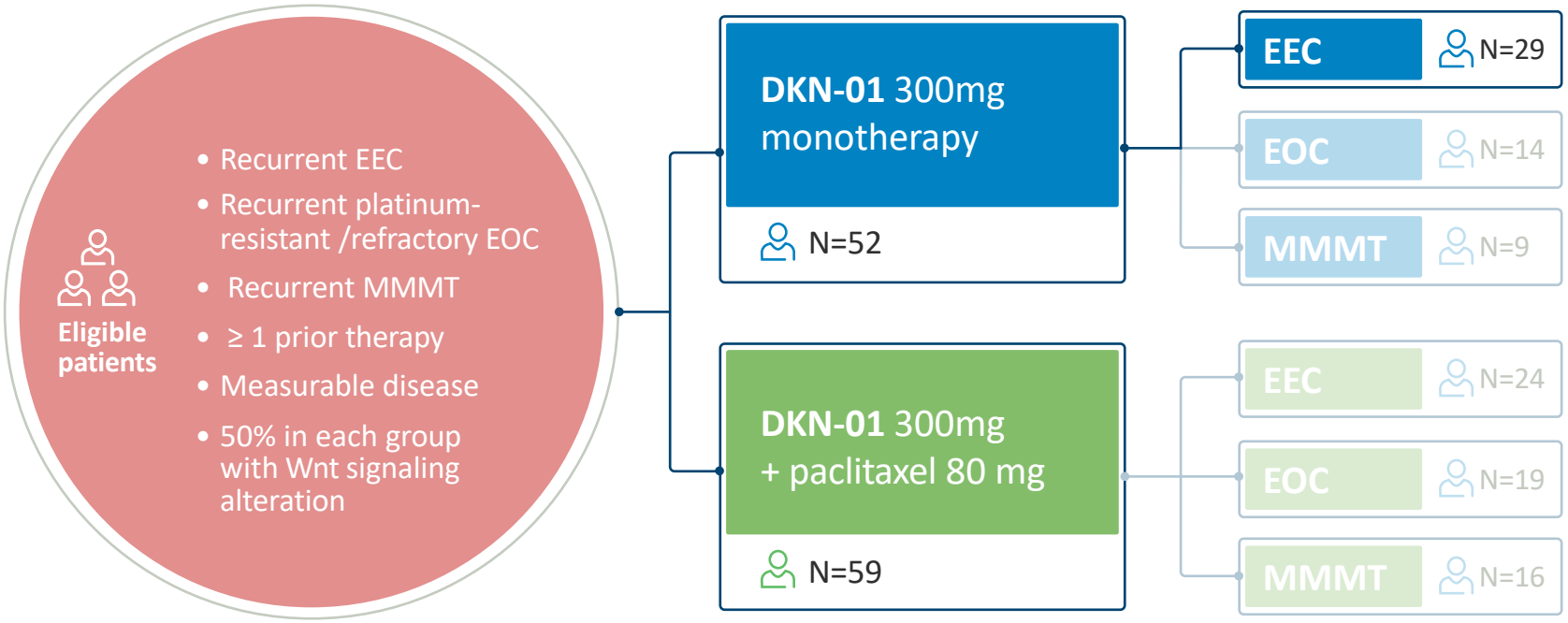
Single agent activity in endometrial cancer



Single agent activity is very low, ranging from 3 - 20%

leaptherapeutics

Phase 2 study design evaluating DKN-01 monotherapy and in combination in advanced gynecologic malignancies



- **Primary objective:** Overall response rate (ORR)
- **Secondary objectives:** Exploring genetic mutations in the Wnt signaling pathway and tumoral DKK1 expression as predictive biomarkers

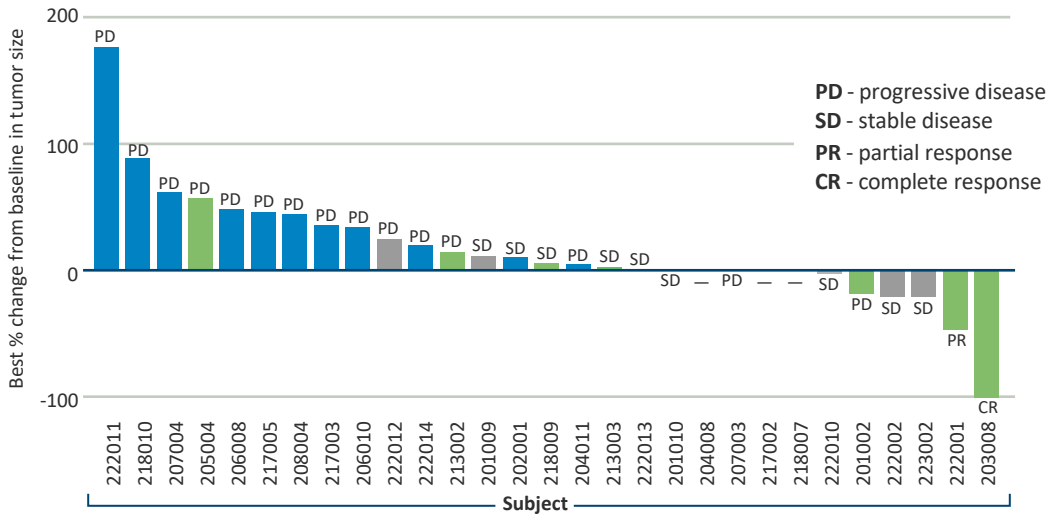
EEC - epithelial endometrial cancer
EOC - epithelial ovarian cancer
MMMT - malignant mixed Müllerian cancer

leaptherapeutics

DKN-01 monotherapy - overall response by DKK1 tumoral expression

2L+ EEC
DKN-01
+ monotherapy

Overall response by DKK1 tumoral expression



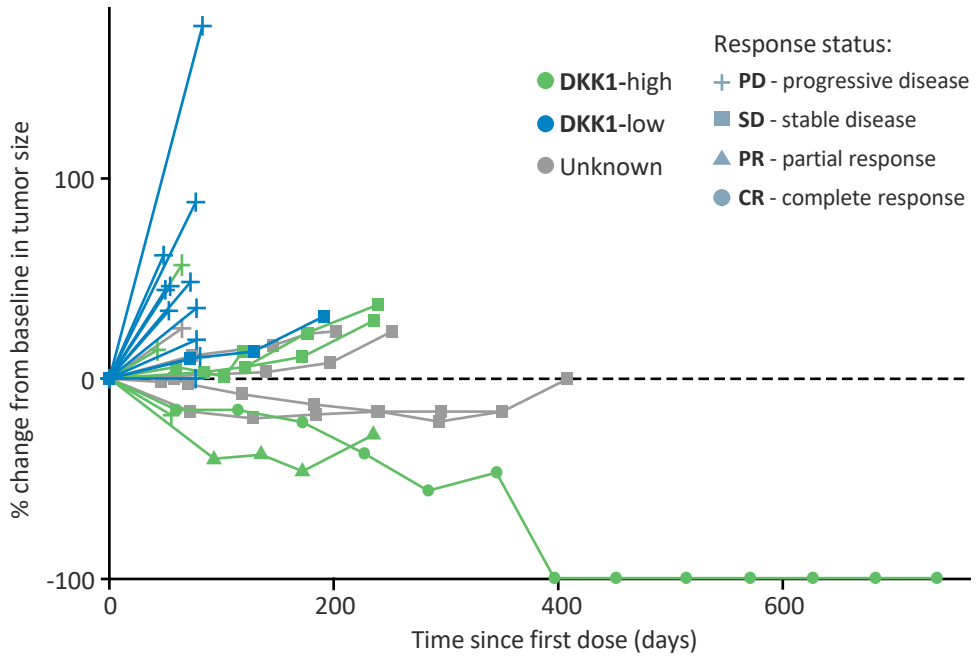
Status	Total	CR	PR	SD	PD	NE	ORR	DCR
DKK1-high (≥18)*	n=8	1	1	3	3	0	25%	63%
DKK1-low (<18)	n=15	0	0	1	11	3	0%	7%
Unknown	n=6	0	0	5	1	0	0%	83%

*H-score ≥ 18, upper tertile of overall study population

DKK1-high tumors have better ORR (25% vs. 0%) and clinical benefit (63% vs. 7%)

Patients with unknown DKK1 expression include 3 patients with durable SD and Wnt activating mutations

Durable clinical benefit in DKK1-high tumors



DKK1-high patients have longer progression-free survival (4.3 vs. 1.8 months [HR 0.26; 95 CI: 0.09, 0.75])

leaptherapeutics

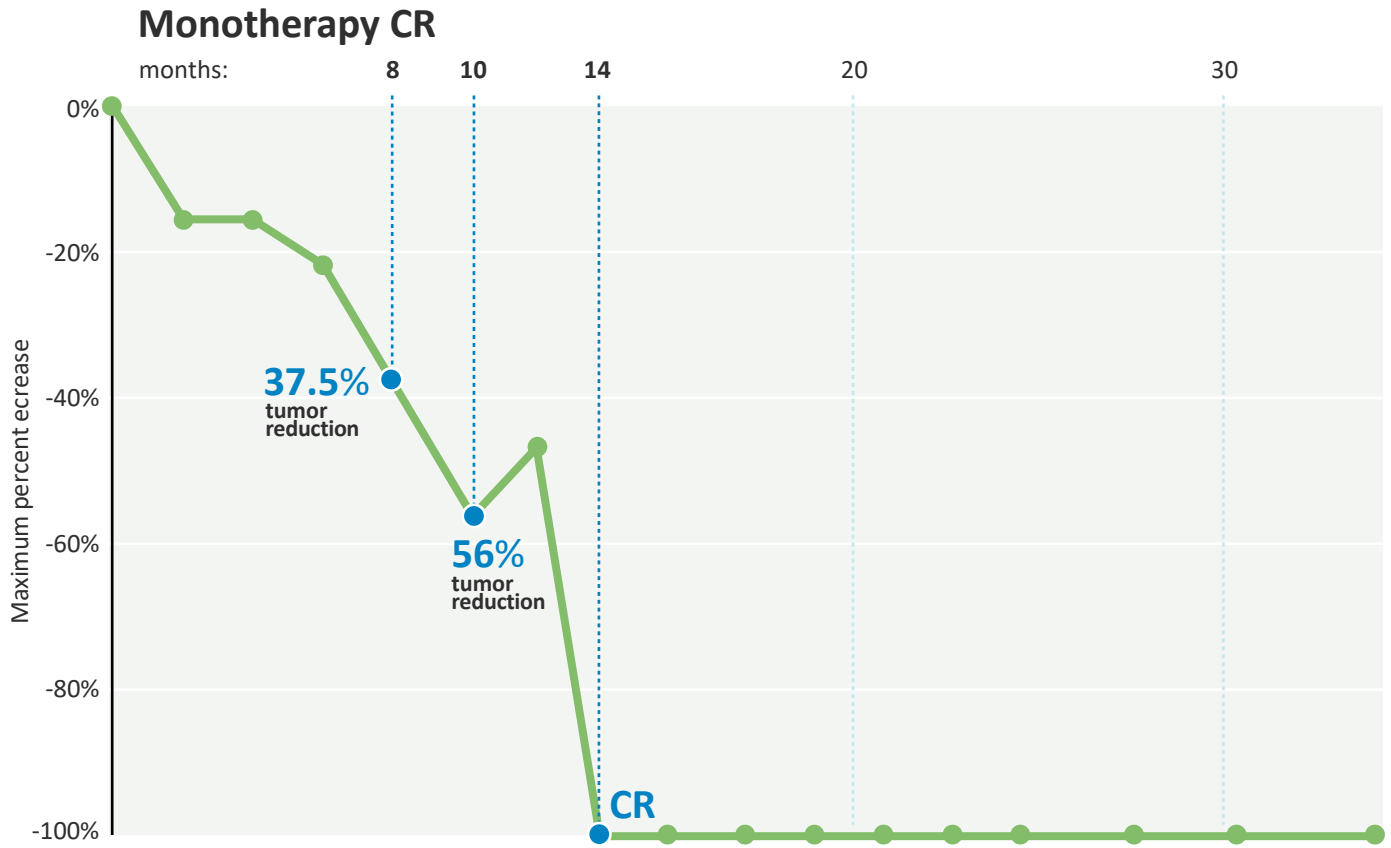
Complete response in endometrial cancer patient on DKN-01 monotherapy

2L+ EEC
DKN-01
+ monotherapy

- **Patient:** 60 yo female with recurrent endometrial cancer
- **Prior treatment:** radiation and chemotherapy poorly tolerated (neuropathy and thrombocytopenia)
- **Baseline disease characteristics:** MSI-H, TMB: 46.65
- **Genetics:** ARID1A, PIK3CA; DKK1-high

Treatment:
DKN-01 monotherapy

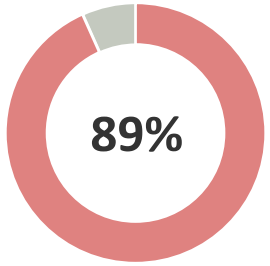
Enrolled in July 2018



leaptherapeutics

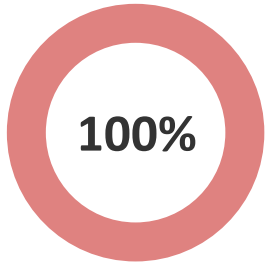
Pembrolizumab + lenvatinib in second-line endometrial cancer

Grade ≥3 treatment-emergent AEs[1]

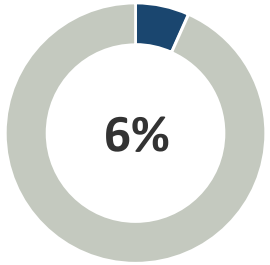


most common AE's with Lenvima + Keytruda treated patients:
hypertension (64.0%), hypothyroidism (57.4%), diarrhea (54.2%), nausea (49.5%), decreased appetite (44.8%), vomiting (36.7%), weight decrease (34.0%), fatigue (33.0%), arthralgia (30.5%), proteinuria (28.8%), anemia (26.1%), constipation (25.9%), urinary tract infection (25.6%).

Any grade treatment-emergent AEs[1]

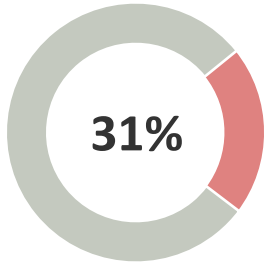


Fatal adverse reactions[1]



Including gastrointestinal disorders: cardiac disorders: 0.5%, general disorders: 1.5%, infections: 0.7%, decreased appetite: 0.2%, neoplasms, nervous system, psychiatric, renal, reproductive, or respiratory disorders: 0.2% each.

Lenvima discontinuation[1]



Keytruda discontinuation 19%[1,2]:
Most common AE's leading to discontinuation of Keytruda: adrenal insufficiency, colitis, pancreatitis and muscular weakness (2% each).

AE's leading to interruption of Keytruda (49%)[2]:
fatigue (14%), diarrhea, and decreased appetite (6% each), rash (5%), renal impairment, vomiting, increased lipase, decreased weight (4% each), nausea, increased blood alkaline phosphatase, and skin ulcer (3% each), adrenal insufficiency, increased, amylase, hypocalcemia,hypomagnesemia, hyponatremia, peripheral edema, musculoskeletal pain, and syncope (2% each).

AE's leading to reduction or interruption of Lenvima (88%)[2]:
fatigue (32%), hypertension (26%), diarrhea (18%), nausea, palmar-plantar erythrodysesthesia, vomiting (13% each), decreased appetite (12%), musculoskeletal pain (11%), stomatisis (9%), abdominal pain, herorrhades (7% each), renal impairment, decreased weight (6% each), rash, headache, increased lipase, and proteinuria (5% each).

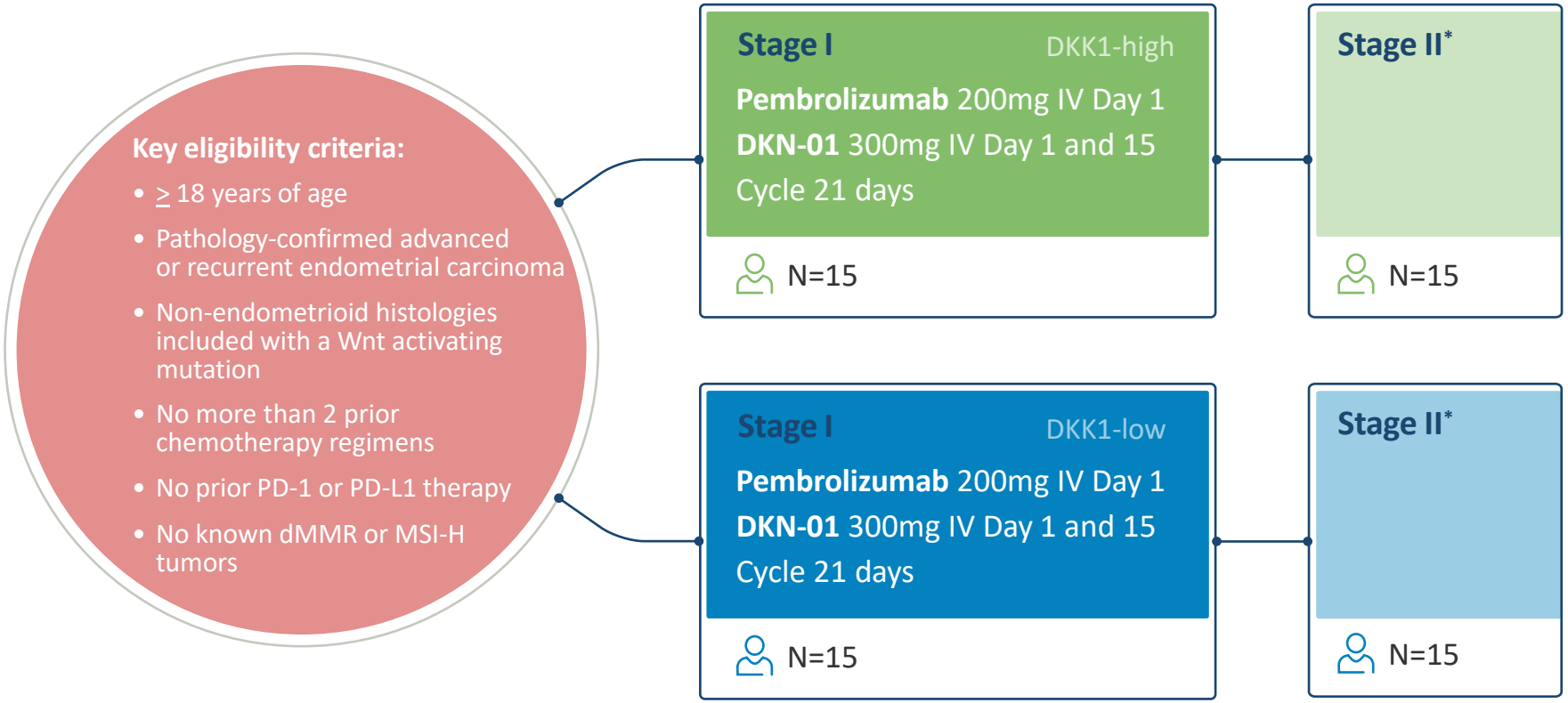
	Population:	n	ORR	CR	PR	SD	mPFS
Lenvima + Keytruda KN-775	**Post platinum-based therapy, all-comers (dMMR + pMMR)**	**411**	**31.9%**	**6.6%**	**25.3%**	**47.0%**	**7.2 months**
	Post platinum-based therapy pMMR	**346**	**30.3%**	**5.2%**	**25.1%**	**48.6%**	**6.6 months**

[1]KEYNOTE-775 data presented at SGO 2021
[2]FDA Approves LENVIMA® (lenvatinib) plus KEYTRUDA® (pembrolizumab) Combination Treatment for Patients with Certain Types of Endometrial Carcinoma. *https://www.eisai.com/news/2019/news201967.html*

leaptherapeutics

DKN-01 plus pembrolizumab endometrial cancer study

2-3L EEC
DKN-01
+ pembrolizumab



Open-label, phase 2 trial,
Bayesian optimal phase II design,
Investigator-initiated study with pembrolizumab supplied by Merck.

Primary objective:
Objective response rate (ORR)

Secondary objectives:
Clinical benefit,
PFS, OS, DOR

* Move to Stage II based on ORR in Stage I

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

UAB

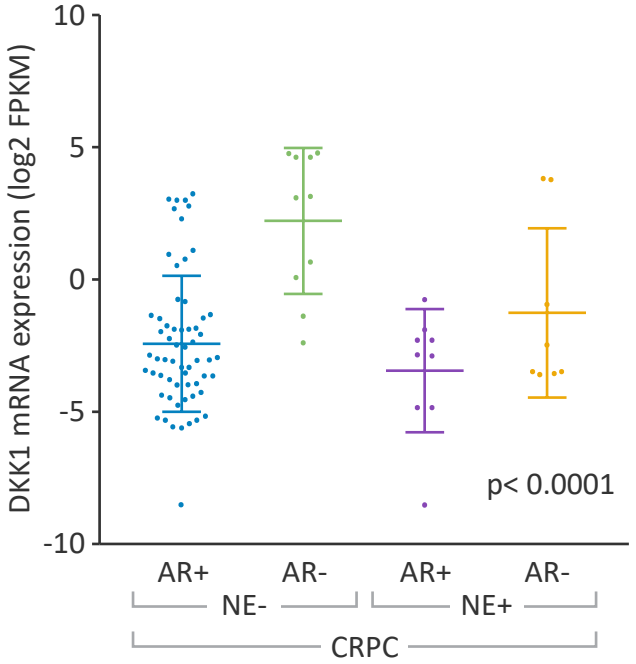
leaptherapeutics

DKN-01

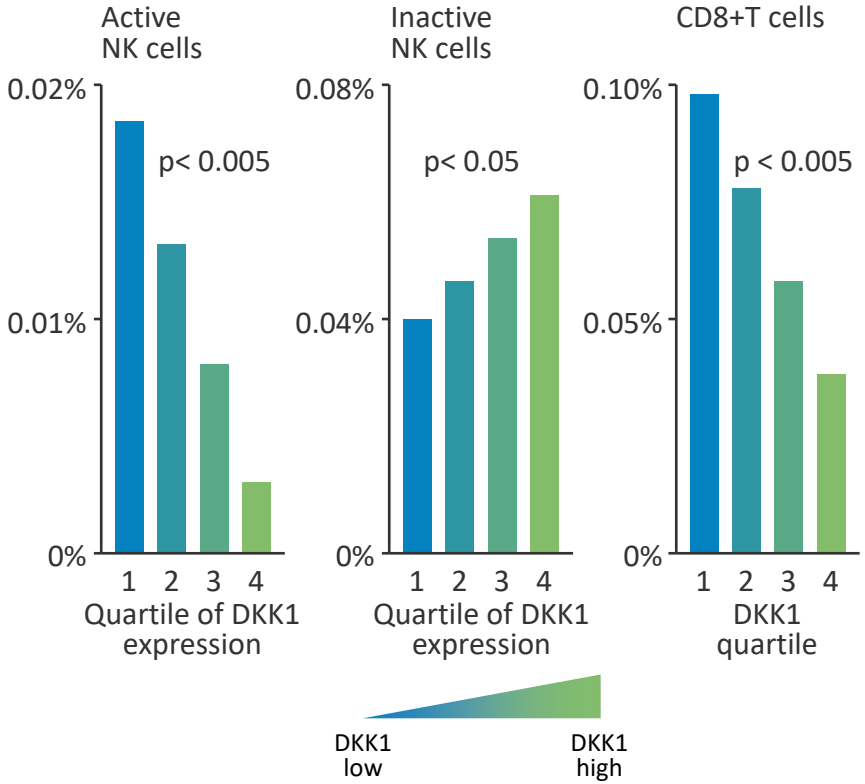
Prostate cancer development

DKK1 and DKN-01 in prostate cancer

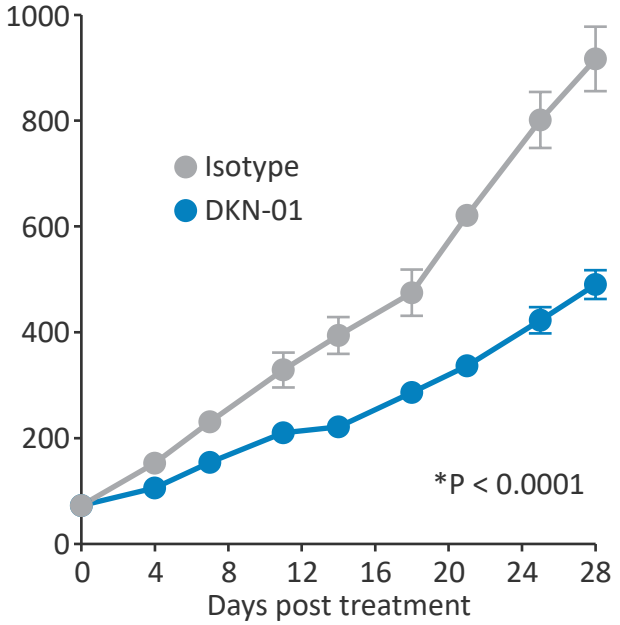
DKK1 expression is regulated by AR in CRPC tumor biopsies



CIBERSORT analysis shows DKK1 expression associated with reduced inflammatory infiltrate



DKN-01 has efficacy in a PC3 SCID xenograft



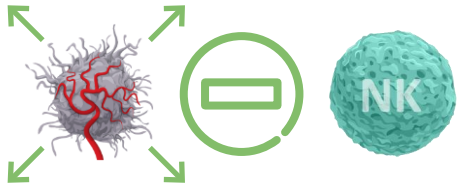
David Wise ASCO 2017

leaptherapeutics

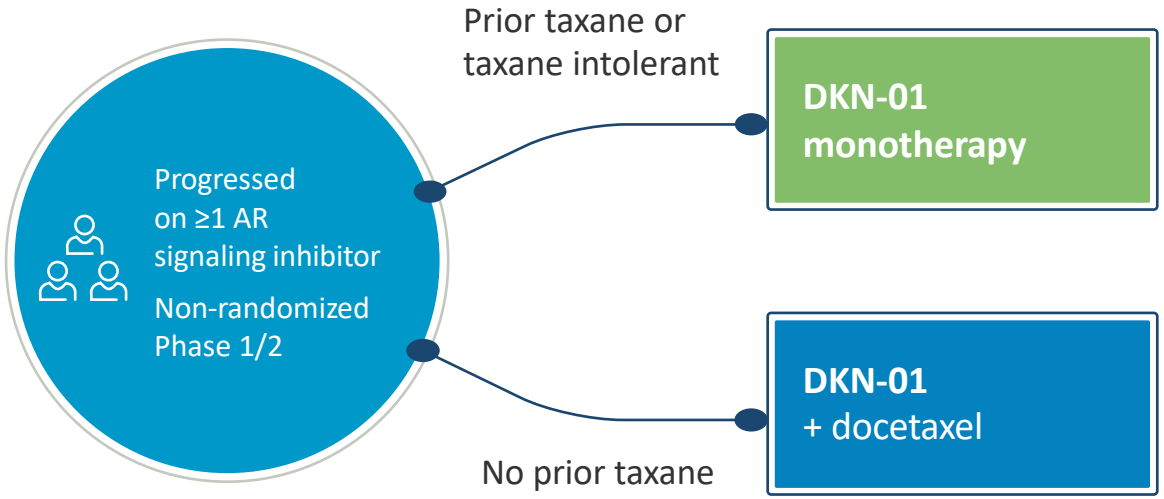
Investigator-initiated study in advanced metastatic castration-resistant prostate cancer (mCRPC)

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.



leaptherapeutics

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 N=4	600mg N/A N=3	300mg 75mg/m² N=3	600mg 75mg/m² 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).

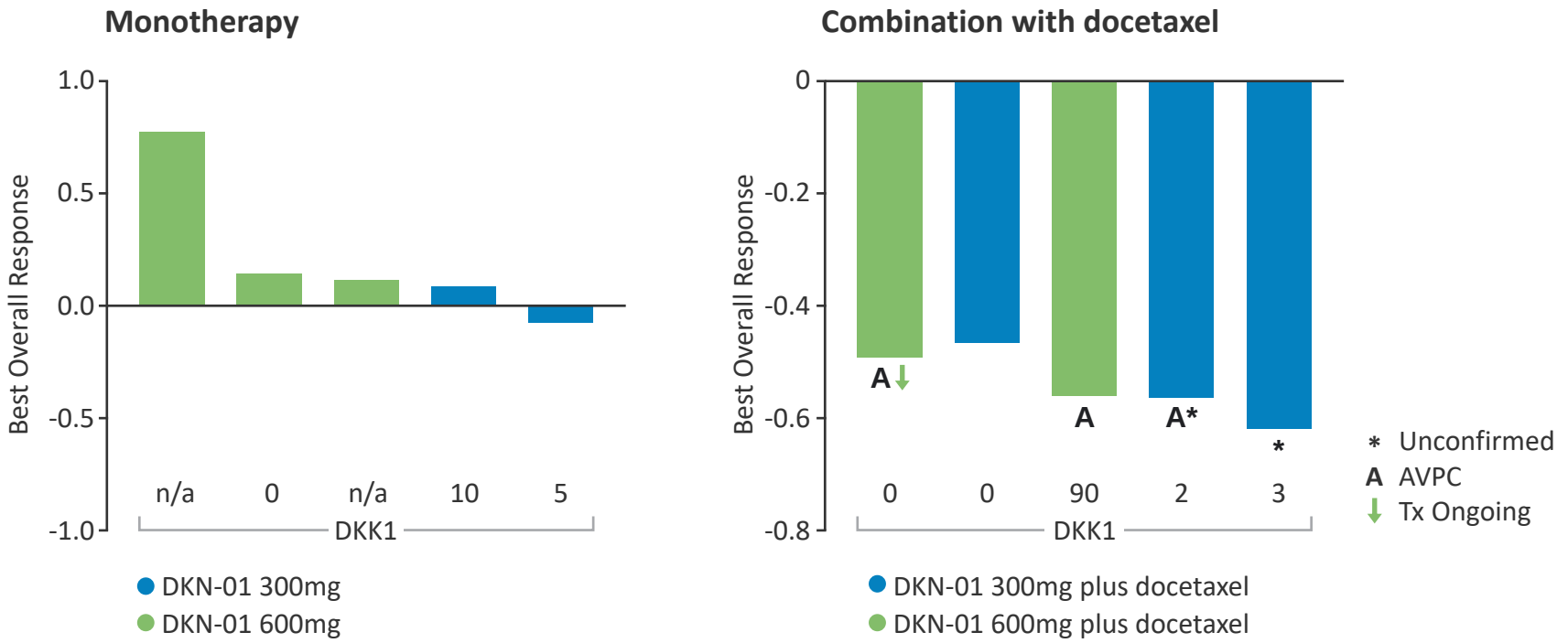
Secondary endpoints: of the study was to correlate anti-tumor activity, DKK1 expression (cutoff H-score ≥ 1), and clinical evidence of aggressive variant prostate cancer (AVPC).

leaptherapeutics

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

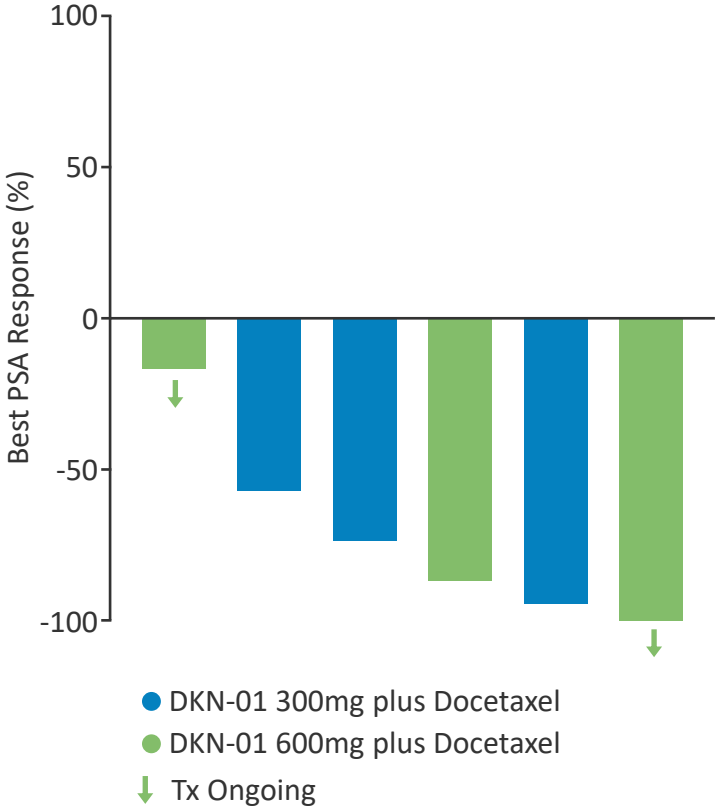
leaptherapeutics

DKN-01 activity in combination with docetaxel

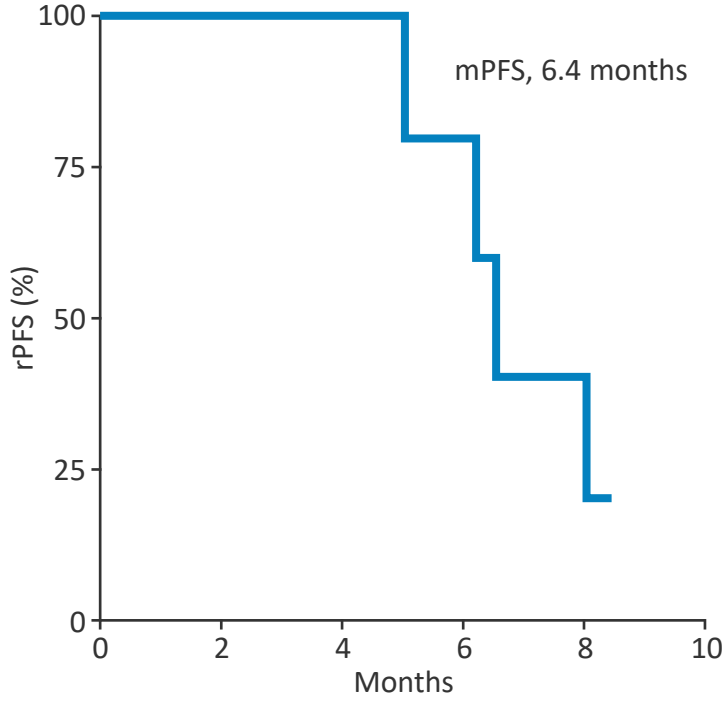
2L+ mCRPC
DKN-01
+ docetaxel

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

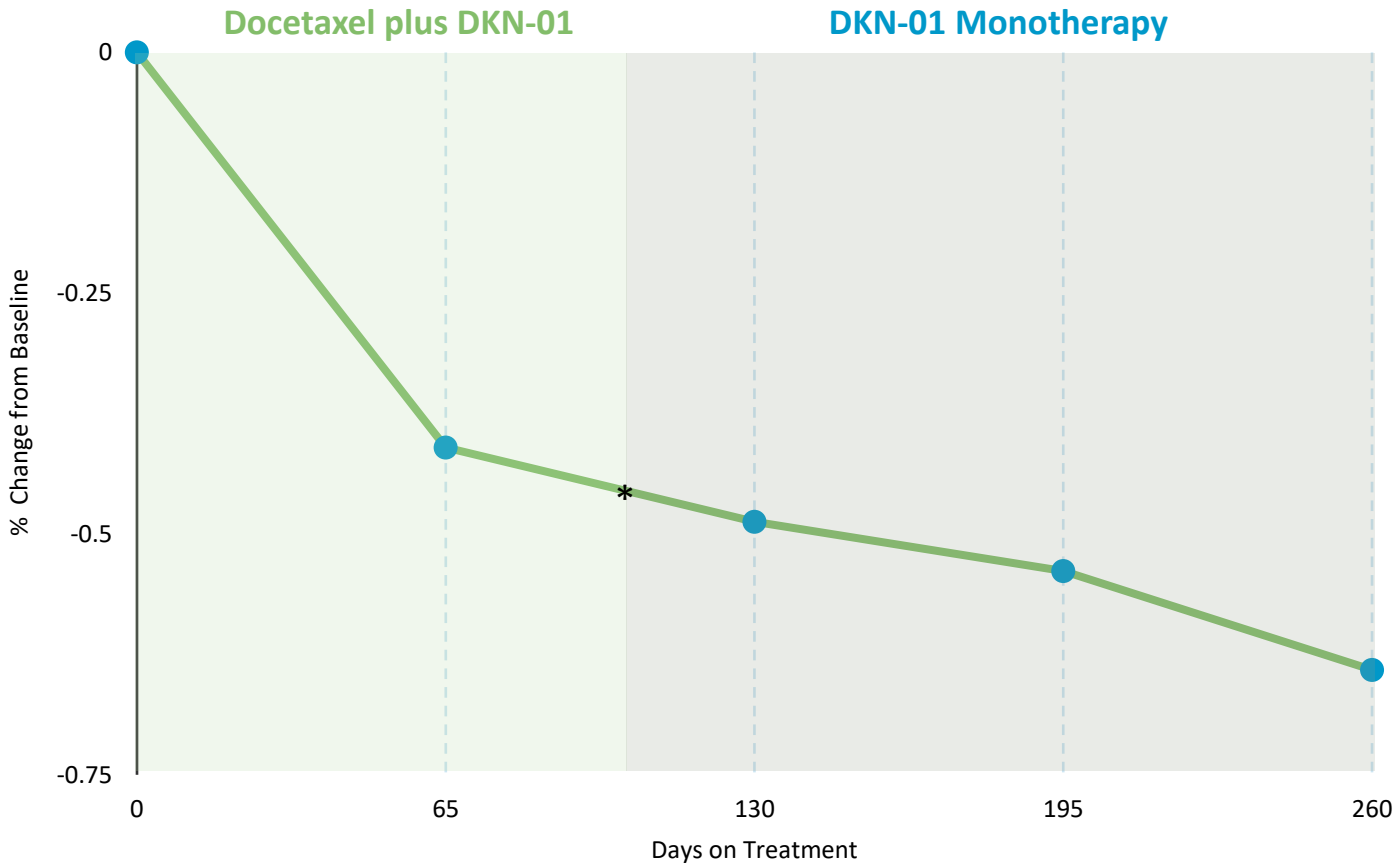
leaptherapeutics

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

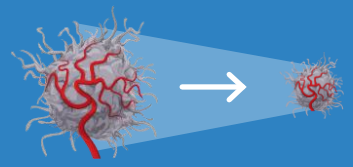
* Docetaxel discontinued due to toxicity

leaptherapeutics

DKN-01 highlights in prostate cancer

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

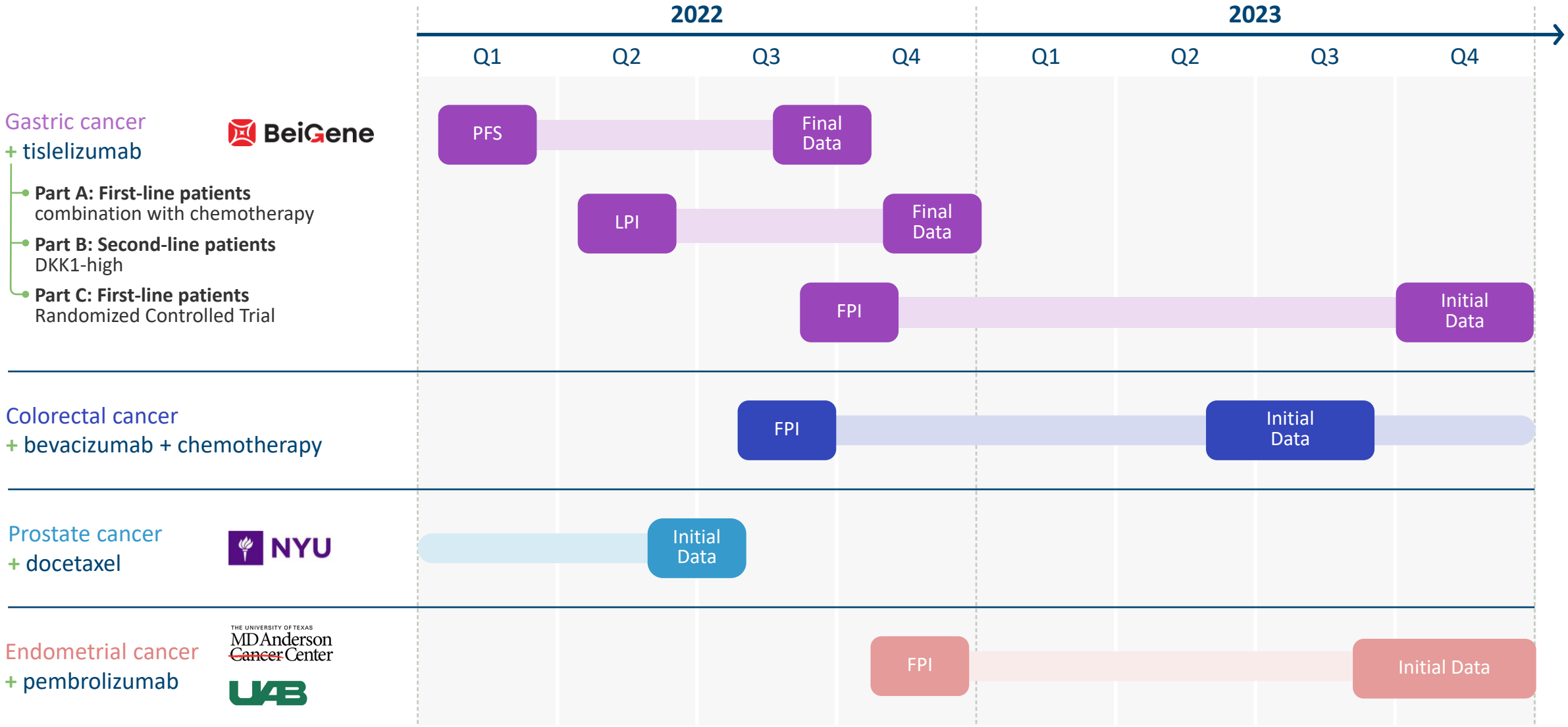
leaptherapeutics

DKN-01 DEVELOPMENT STRATEGY

2022-2023 Milestones

leaptherapeutics

Leap 2022-2023 clinical milestones



leaptherapeutics

QUESTIONS & ANSWERS

leaptherapeutics