LEAP THERAPEUTICS

company presentation

40th Annual JPMorgan Healthcare Conference

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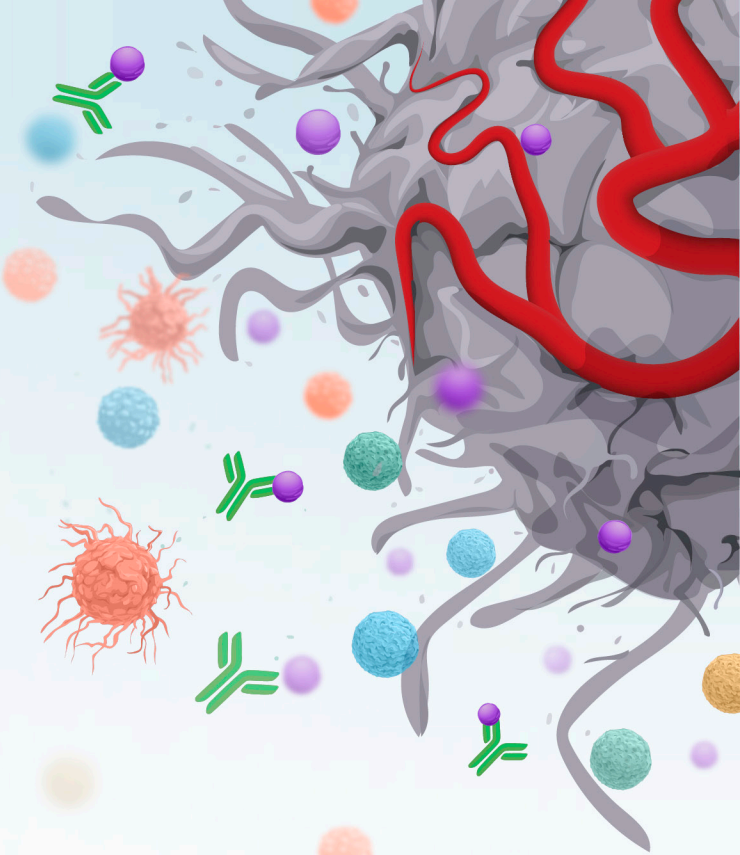
President and CEO

January 13, 2022



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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, 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.

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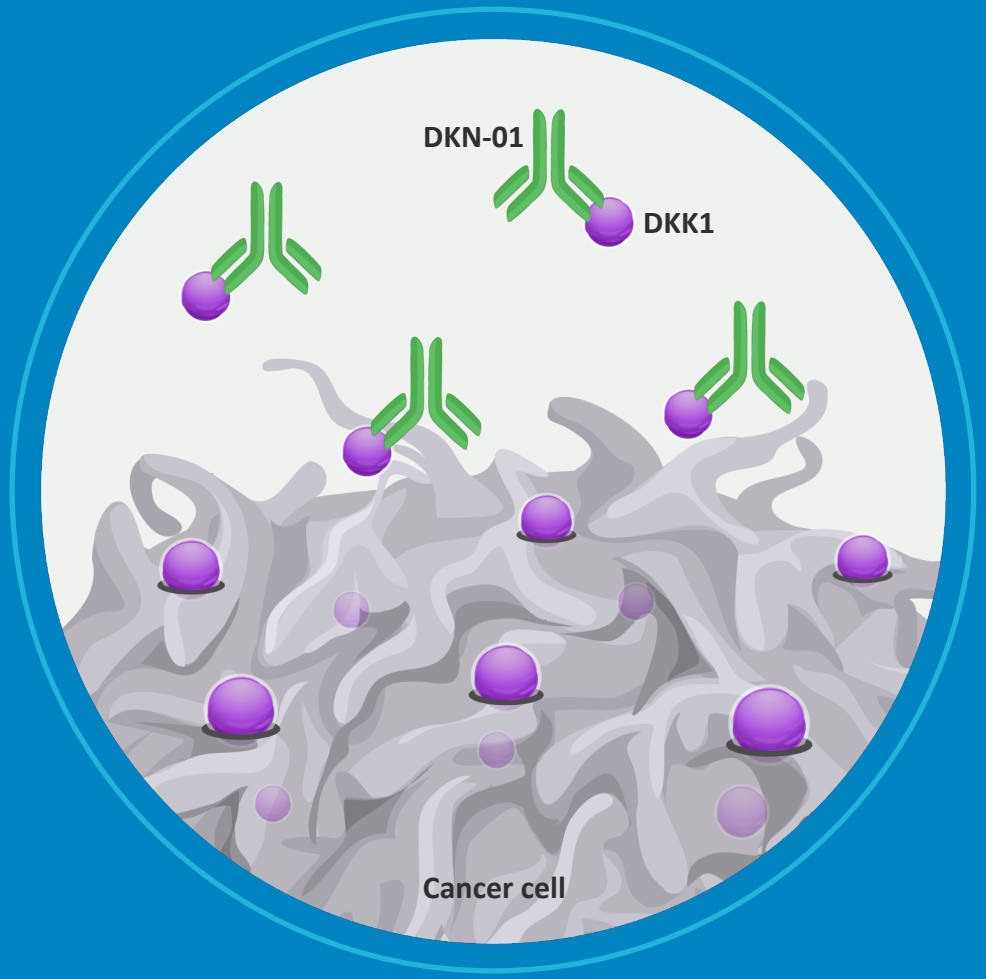
Investment highlights



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

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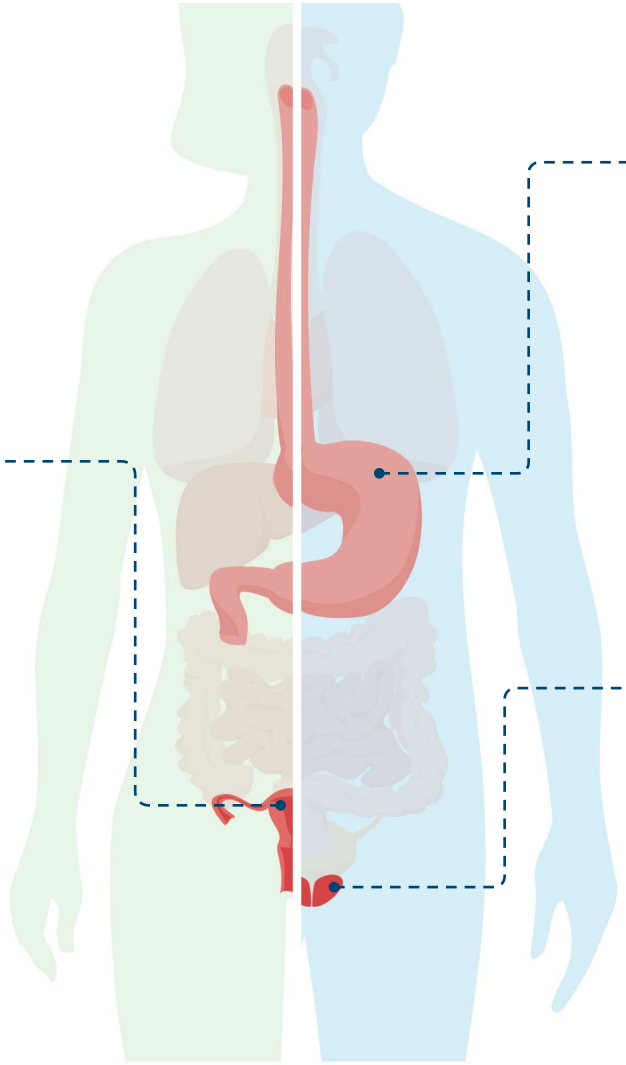
DKN-01: broad applications in oncology



Gastric cancer

DKN-01
+ anti-PD-1/PD-L1
+ chemotherapy

Endometrial cancer

DKN-01
+ paclitaxel

Prostate cancer

DKN-01
+ docetaxel

Leap Therapeutics -

clinical stage oncology company developing DKN-01, a monoclonal antibody which targets the DKK1 protein

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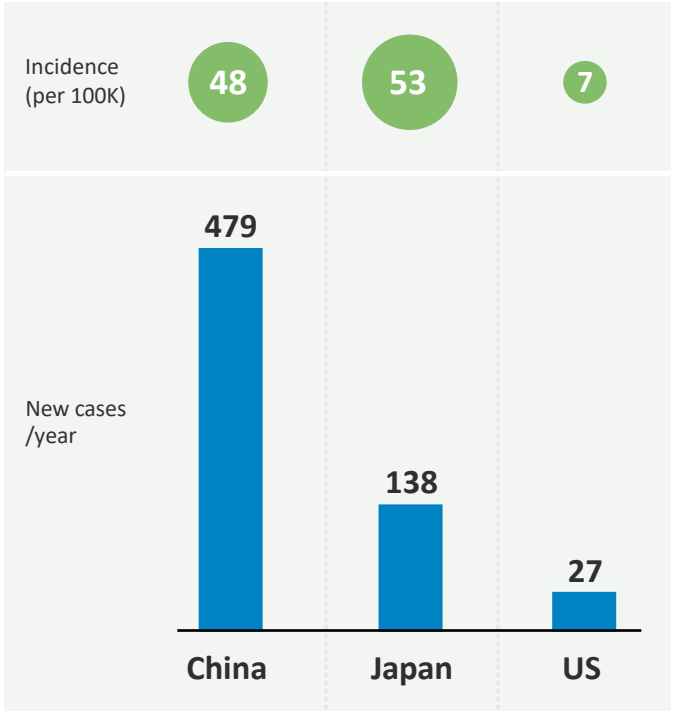
Strategic partnership with BeiGene

Leap offers novel therapy to large unmet need in Asia in gastric cancer

Gastric cancer:



1,089,103
New cases 2020

768,793
Deaths 2020

High incidence of gastric cancer in Asia
Incidence of gastric cancer in China/Japan/US

BeiGene offers expertise in clinical development and commercialization in Asia

> $10M
Option exercise fee based on data from DKN-01 plus tislelizumab combination studies in gastric cancer

$132M
Total option exercise, clinical, regulatory, and commercial milestones

$15.25M
Total payments to date:

$3M Option fee
$12.25M Equity Investment

Royalties
High single digits to mid-teen double digits

Source: WHO Globocan 2020, American Cancer Society

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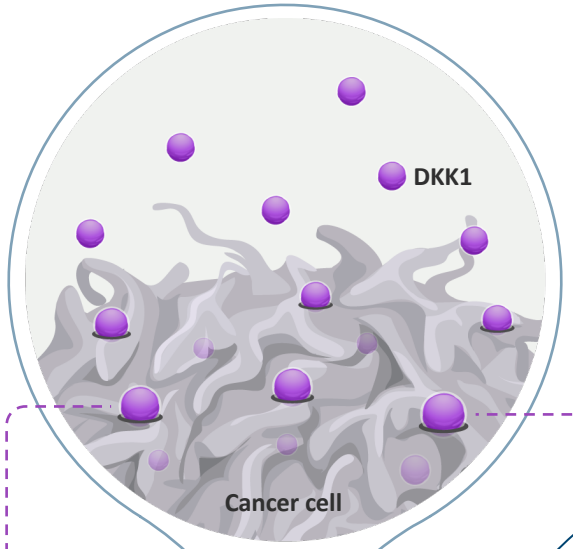
The role of DKK1 in cancer



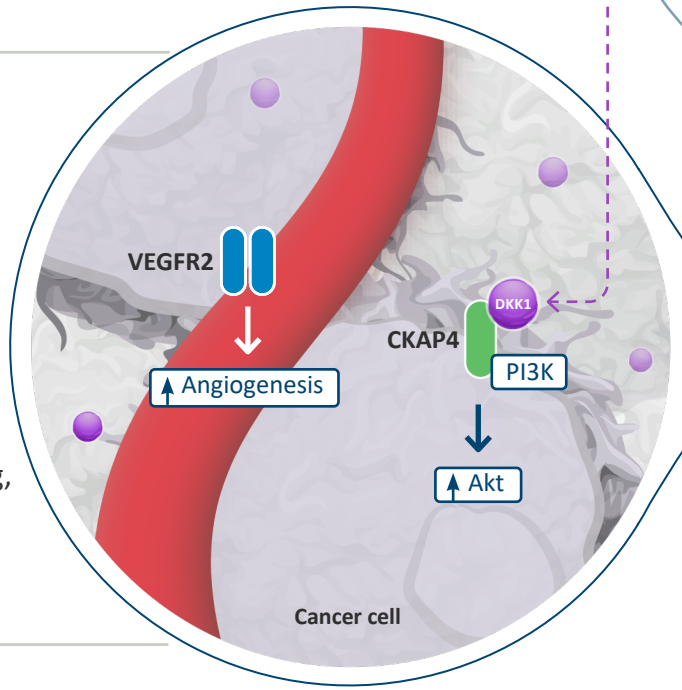
DKK1 is produced and secreted by cancer cells, functions on several tumor pathways and nearby immune cells

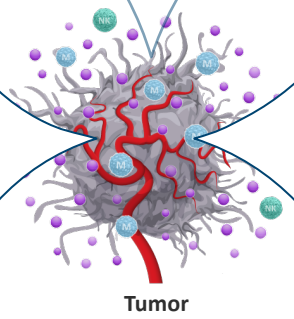
Angiogenesis

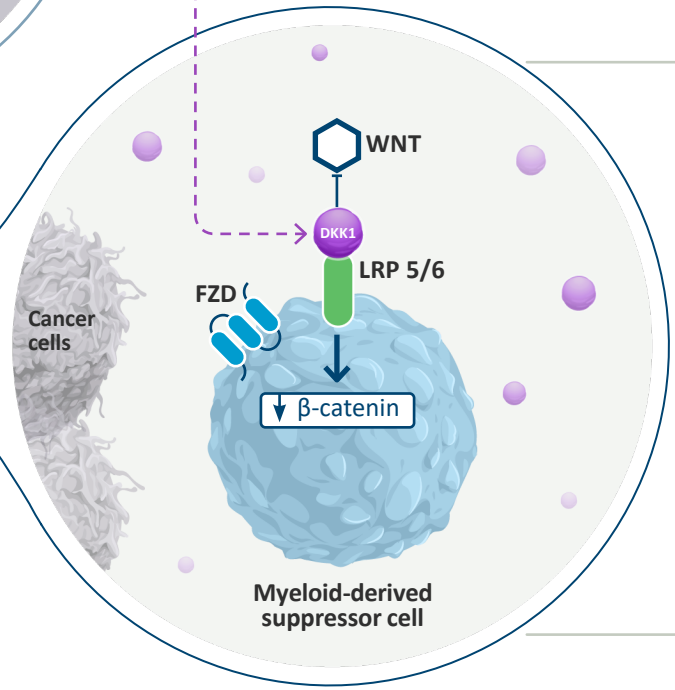
Upregulates VEGFR2, increases formation of tumor blood vessels

Cell proliferation

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







Enhances MDSC cells

Inhibits B-catenin dependent Wnt signaling to enhance suppressive activity

Suppresses NK cells

Helps tumor cells escape NK cells

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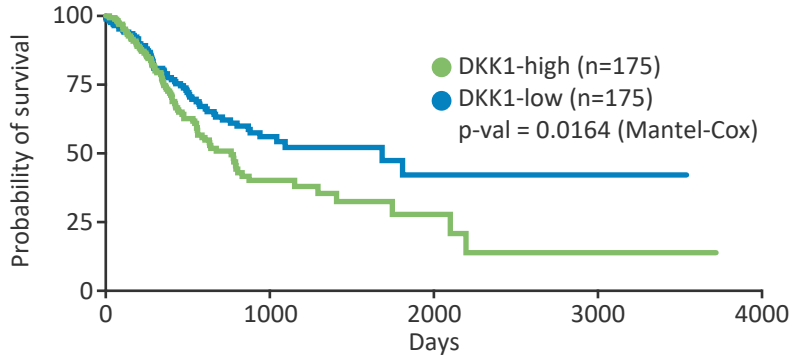
DKK1-high levels are associated with poor survival

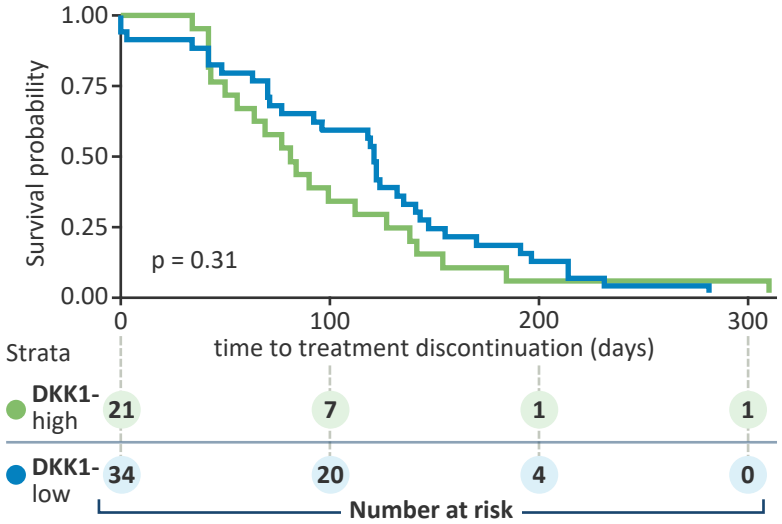
High levels of DKK1 correlate with shorter overall survival In gastric cancer

TCGA STAD dataset

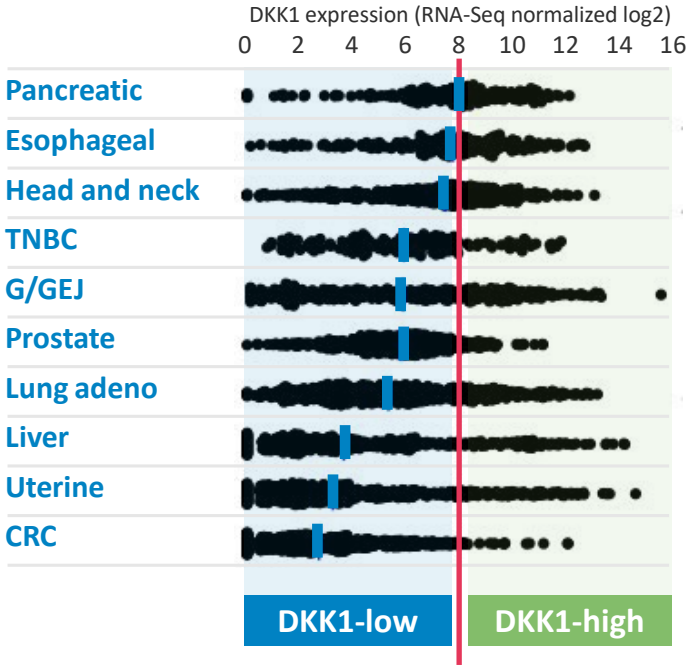


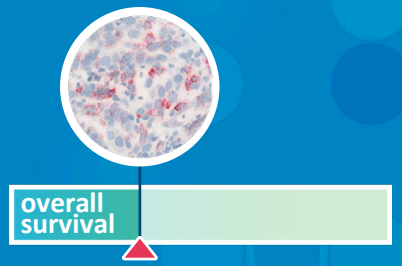
DKK1-high is associated with poor response to first-line platinum + fluoropyrimidine based therapies in GEJ/gastric cancer patients

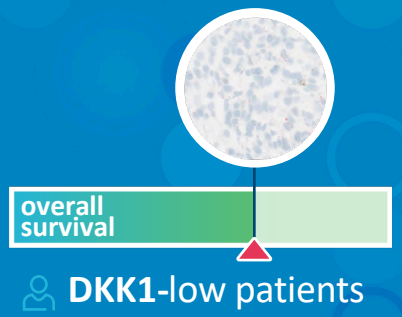
Collaboration with Tempus



DKK1 expression data (TCGA):







~2.5 years shorter OS in DKK1-high patients

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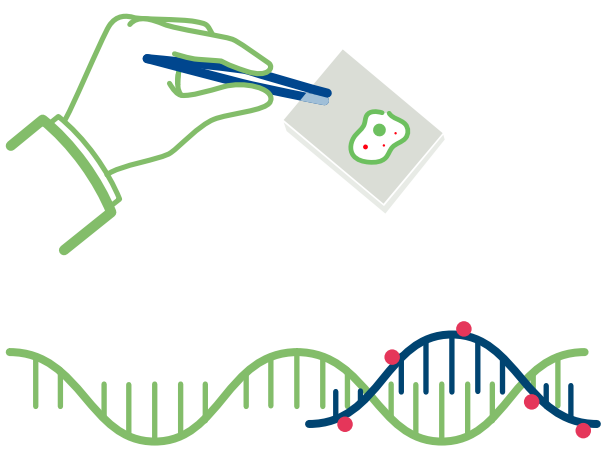
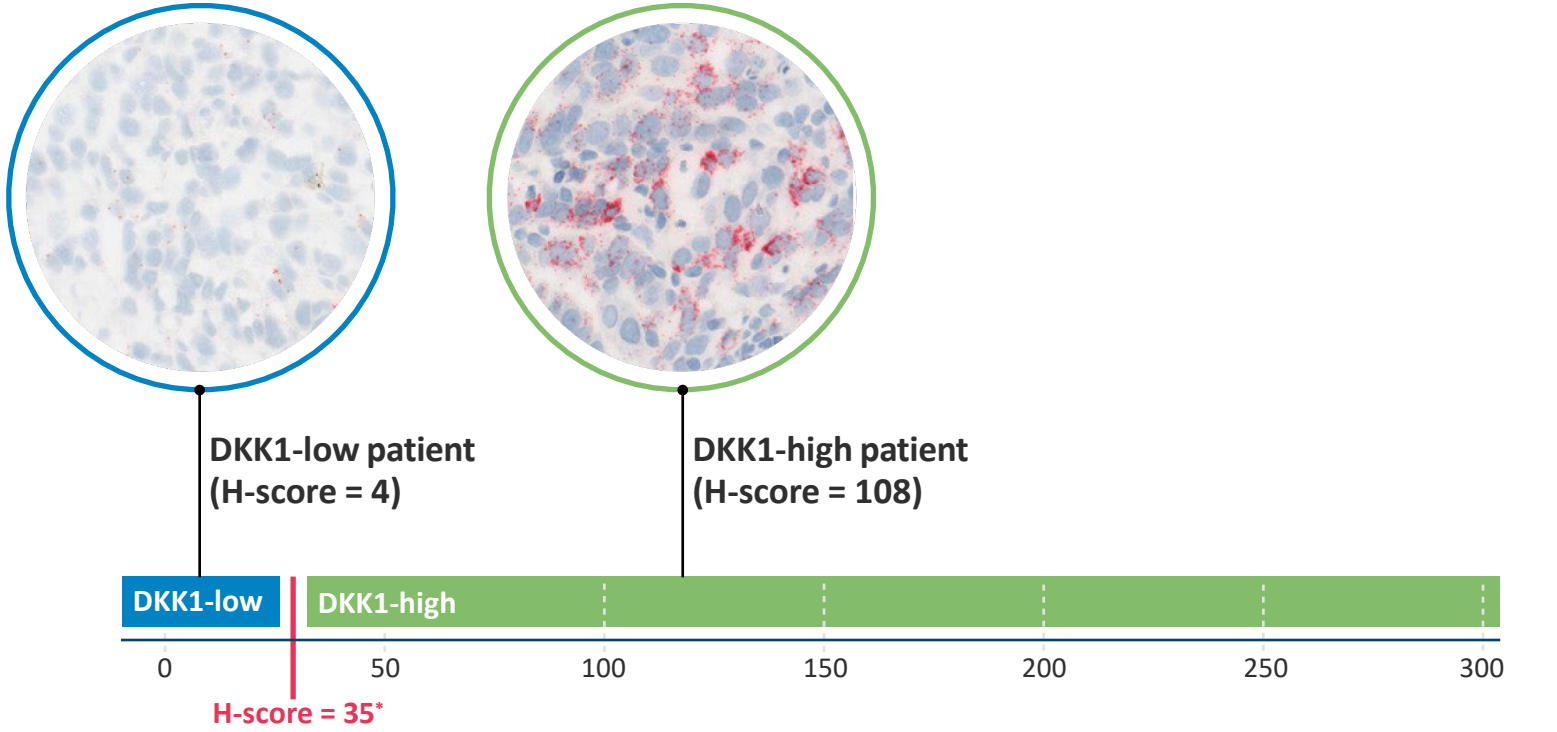
DKK1 expression determined using RNAscope





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 was identified for gastric cancer from our study of DKN-01 + pembrolizumab

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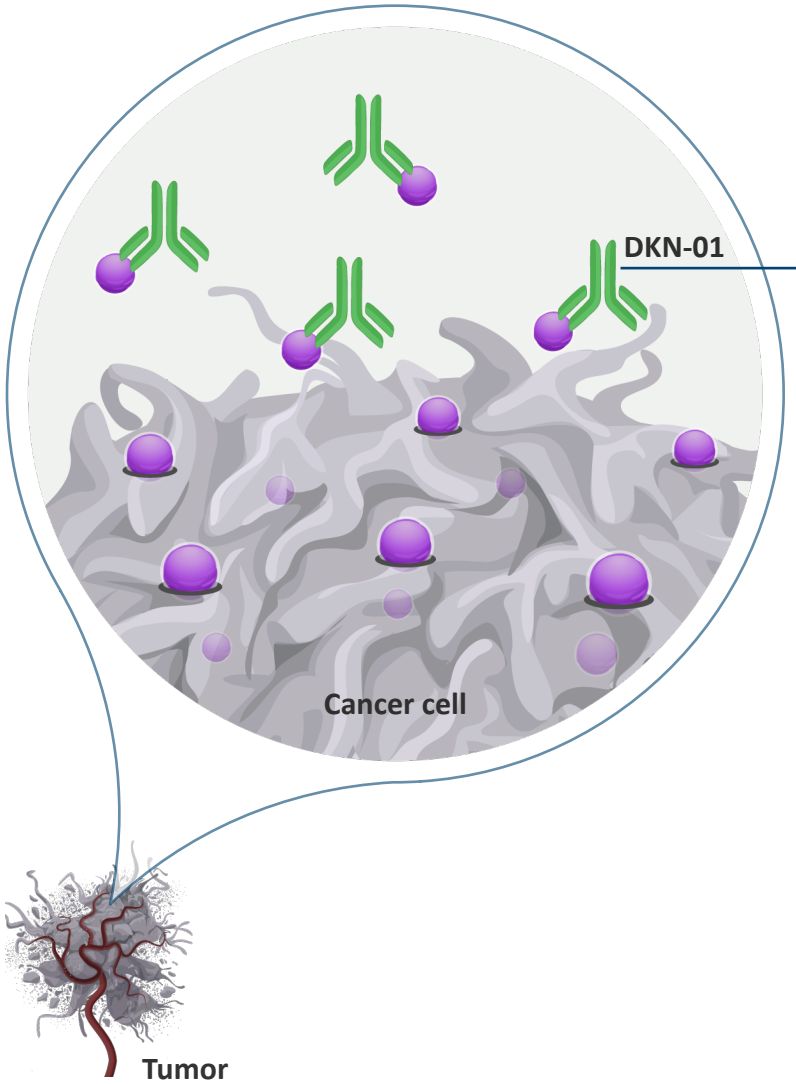
DKN-01 - an anti-DKK1 antibody



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.

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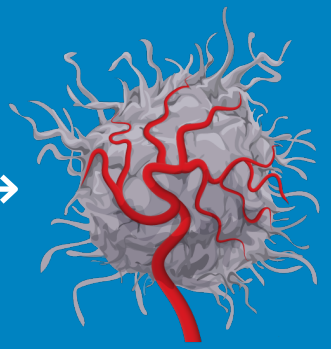
DKN-01 + anti-PD-1 combination

DKN-01 stimulates innate immune system:

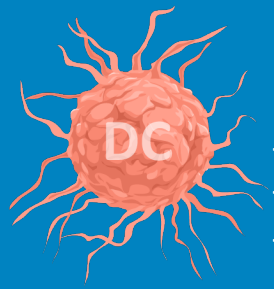
Stimulates activity of NK cells

Induces pro-inflammatory tumor microenvironment

Upregulates PD-L1 (the target for 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

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Pipeline

Gastric cancer

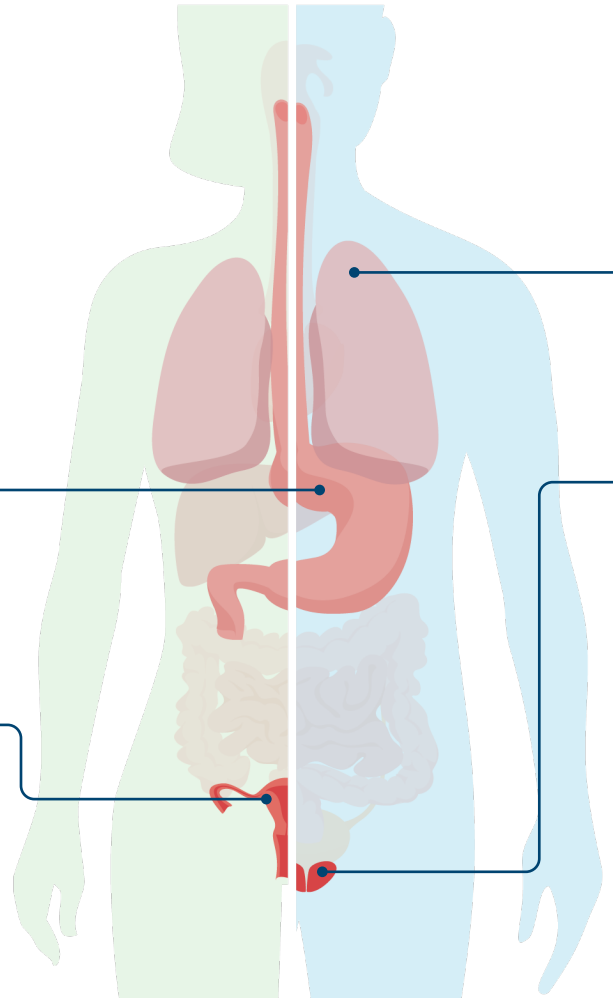
DKN-01 new data
+ anti-PD-1 tislelizumab
+ chemotherapy (1L)

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

- Phase 2
- 1L PFS Data, 2L initial data Q1 2022
- Final 1L data expected in Q3 2022

Endometrial cancer

DKN-01
+ paclitaxel



Lung cancer

DKN-01

Prostate cancer

DKN-01
+ docetaxel

- Investigator sponsored study
- Initial data expected mid-2022

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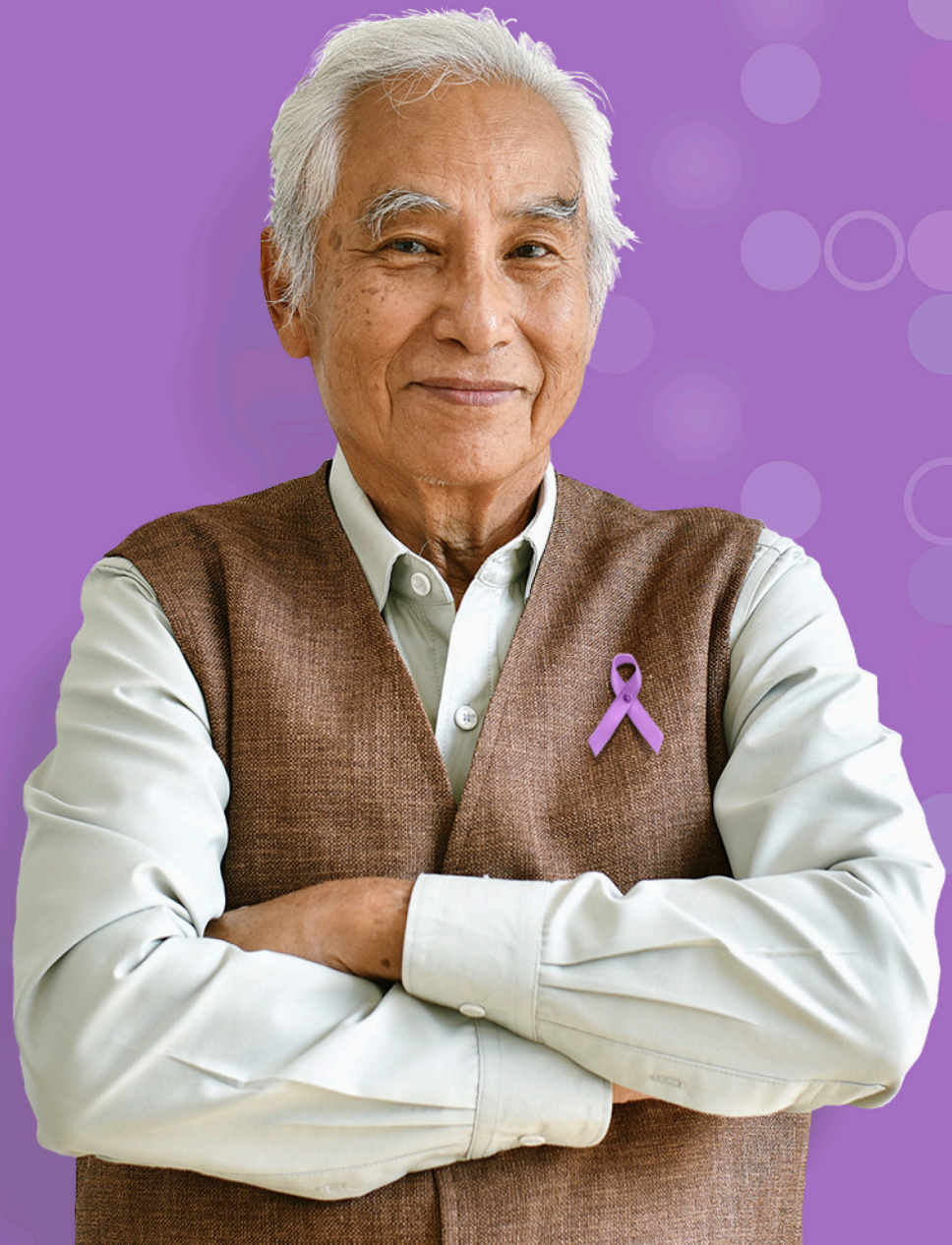
DKN-01

Gastric cancer development

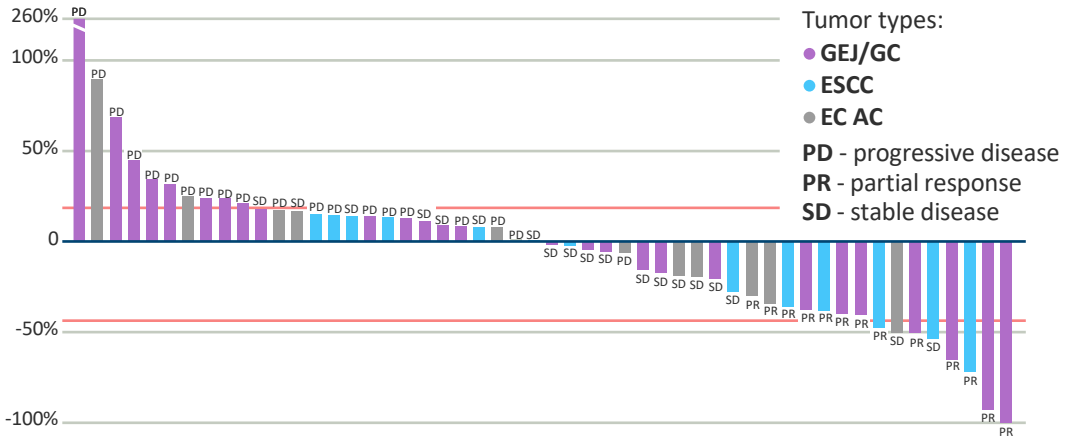


Clinical activity of DKN-01 plus paclitaxel or anti-PD-1 antibody

GEJ/GC
Historical data

DKN-01
+ paclitaxel

N=52
2L-7L esophagogastric pts



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

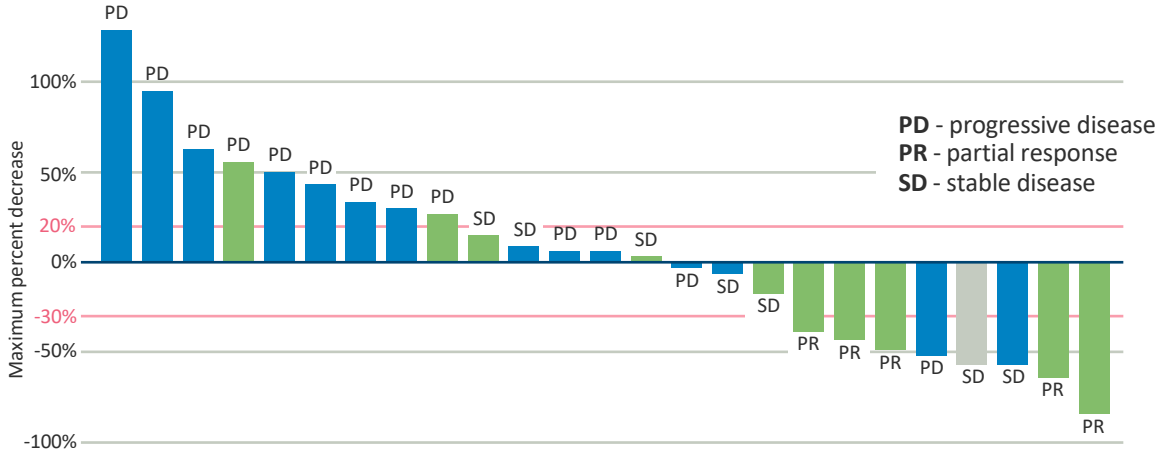
Strong broad activity in esophagogastric cancer in heavily pretreated patients

	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

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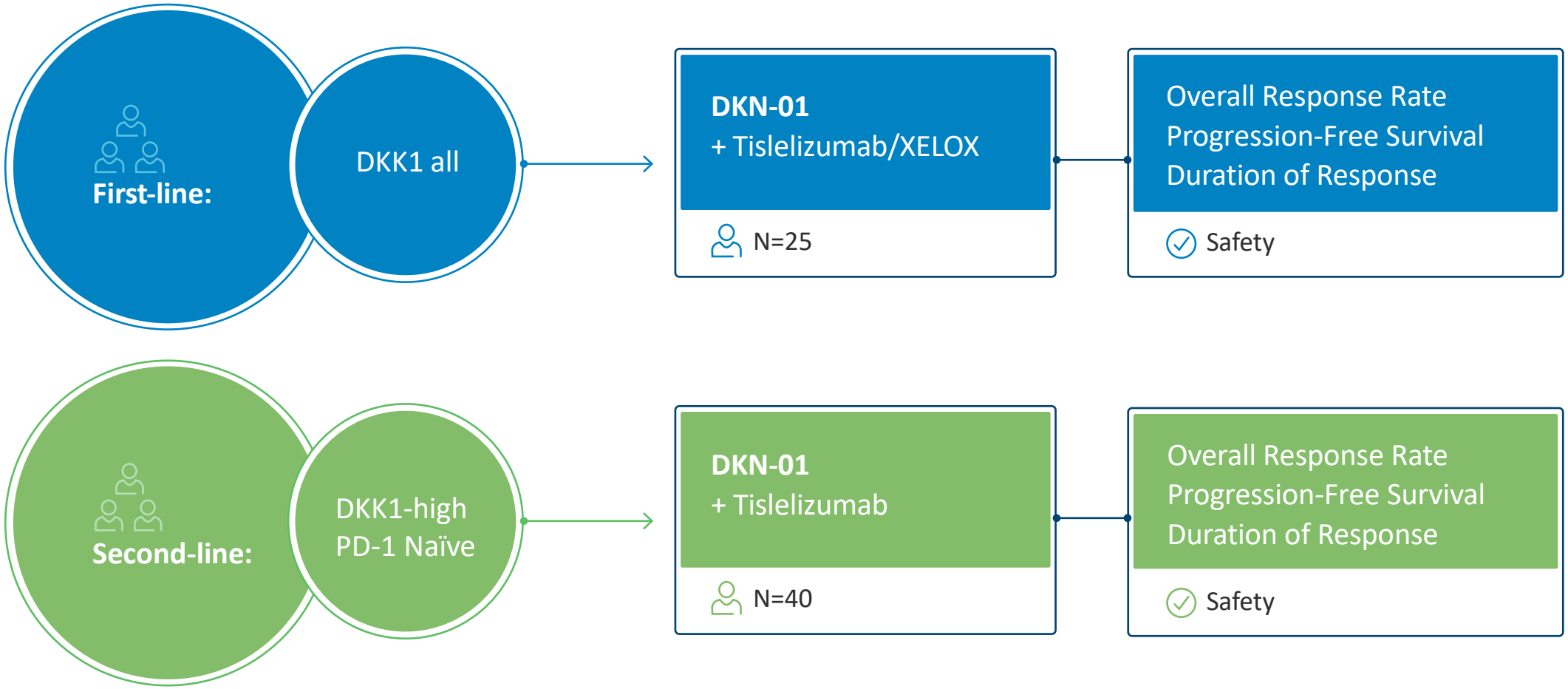
DisTinGuish study design: advanced GEJ/Gastric cancer

GEJ/GC
DKN-01
+ Tislelizumab
+ chemotherapy

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

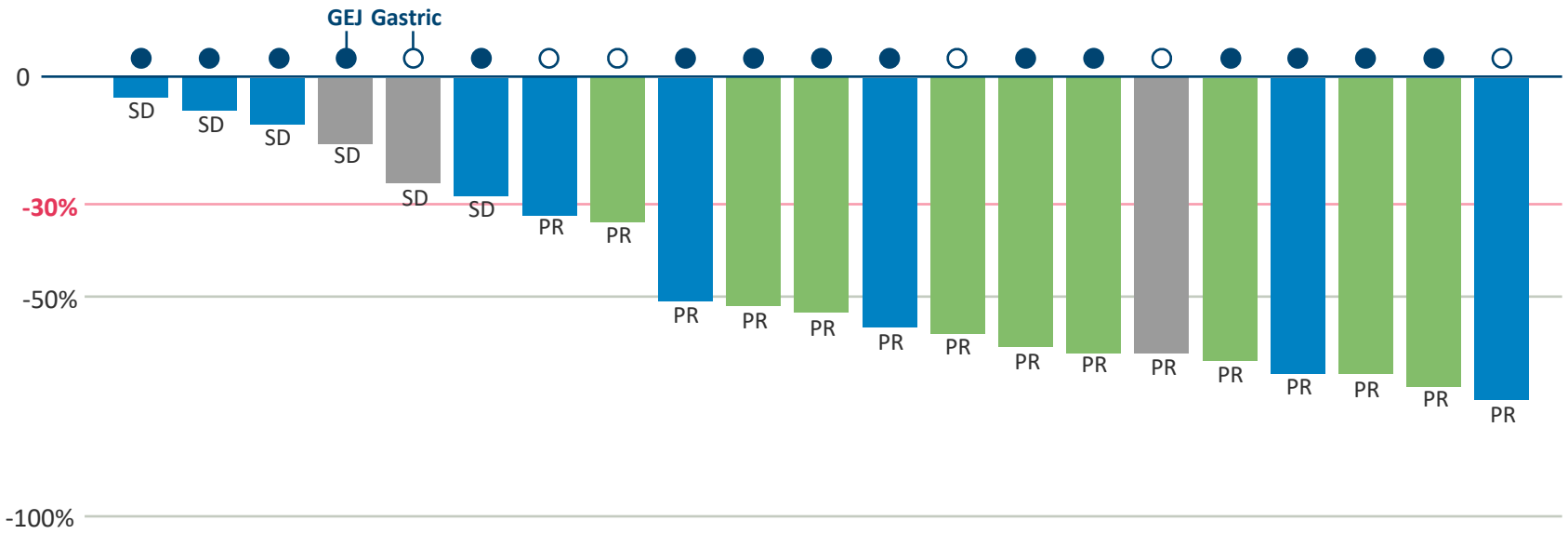


BeiGene | leaptherapeutics

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
PR - partial response	15 (68.2%)	9 (90.0%)	5 (55.6%)	1 (33.3%)
SD - stable disease	6 (27.3%)	0	4 (44.4%)	2 (66.7%)
PD - progressive disease	0	0	0	0
Non-evaluable	1 (4.5%)	1 (10.0%)	0	0

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

68.2%
ORR in the mITT population

*mITT population includes all patients who received > 1 dose of DKN-01

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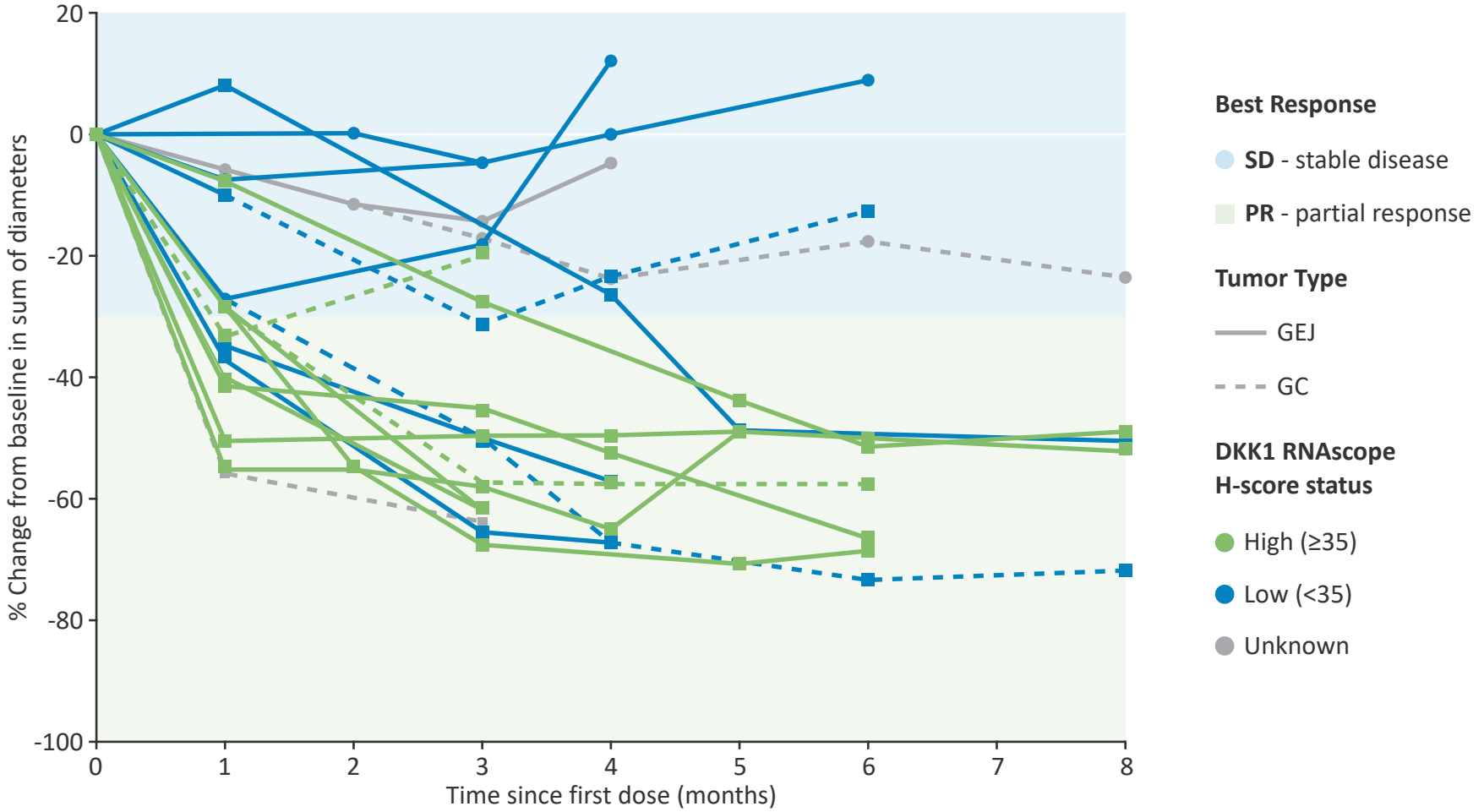
Durable response by DKK1 expression

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

Best % change in sum of diameters



90%
ORR in DKK1-high patients

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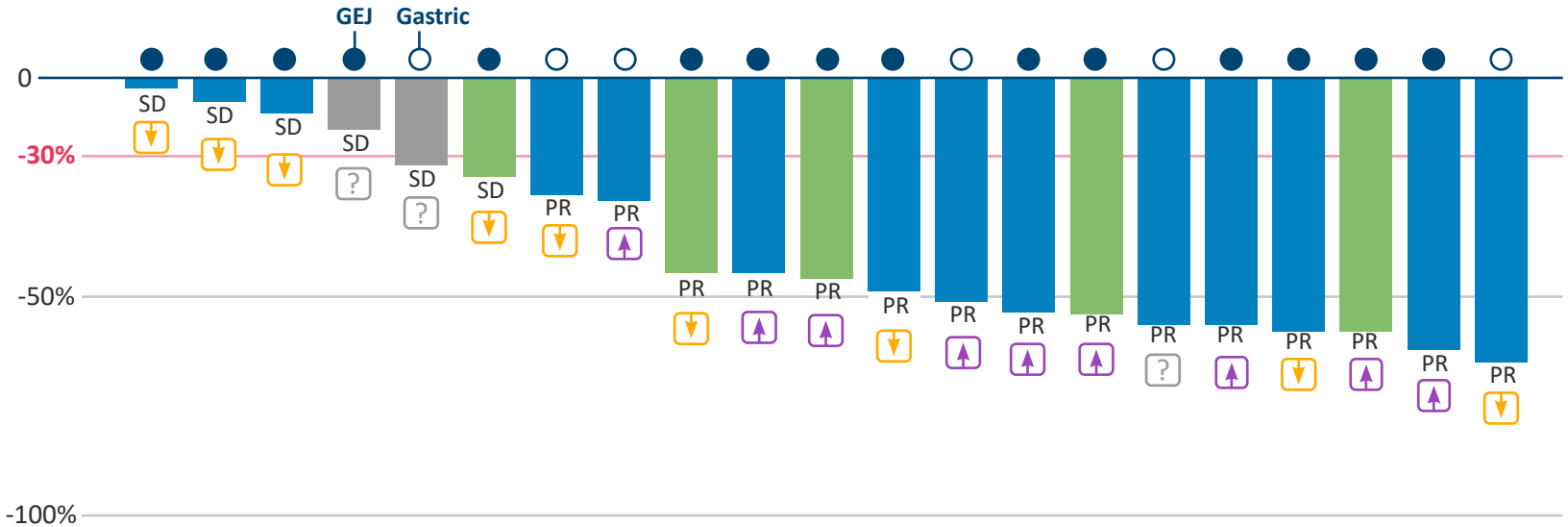
Best overall response by PD-L1 expression

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
PR - partial response	3 (75%)	1 (50%)	6 (100%)	4 (57%)	1 (100%)
SD - stable disease	0	1 (50%)	0	3 (43%)	0
PD - progressive disease	0	0	0	0	0
Non-evaluable	1 (25%)	0	0	0	0
	N=6 **67% ORR**		N=14 **79% ORR**		

79%
ORR in PD-L1 low patients

vCPS: visually-estimated combined positive score; PD-L1: programmed death-ligand 1

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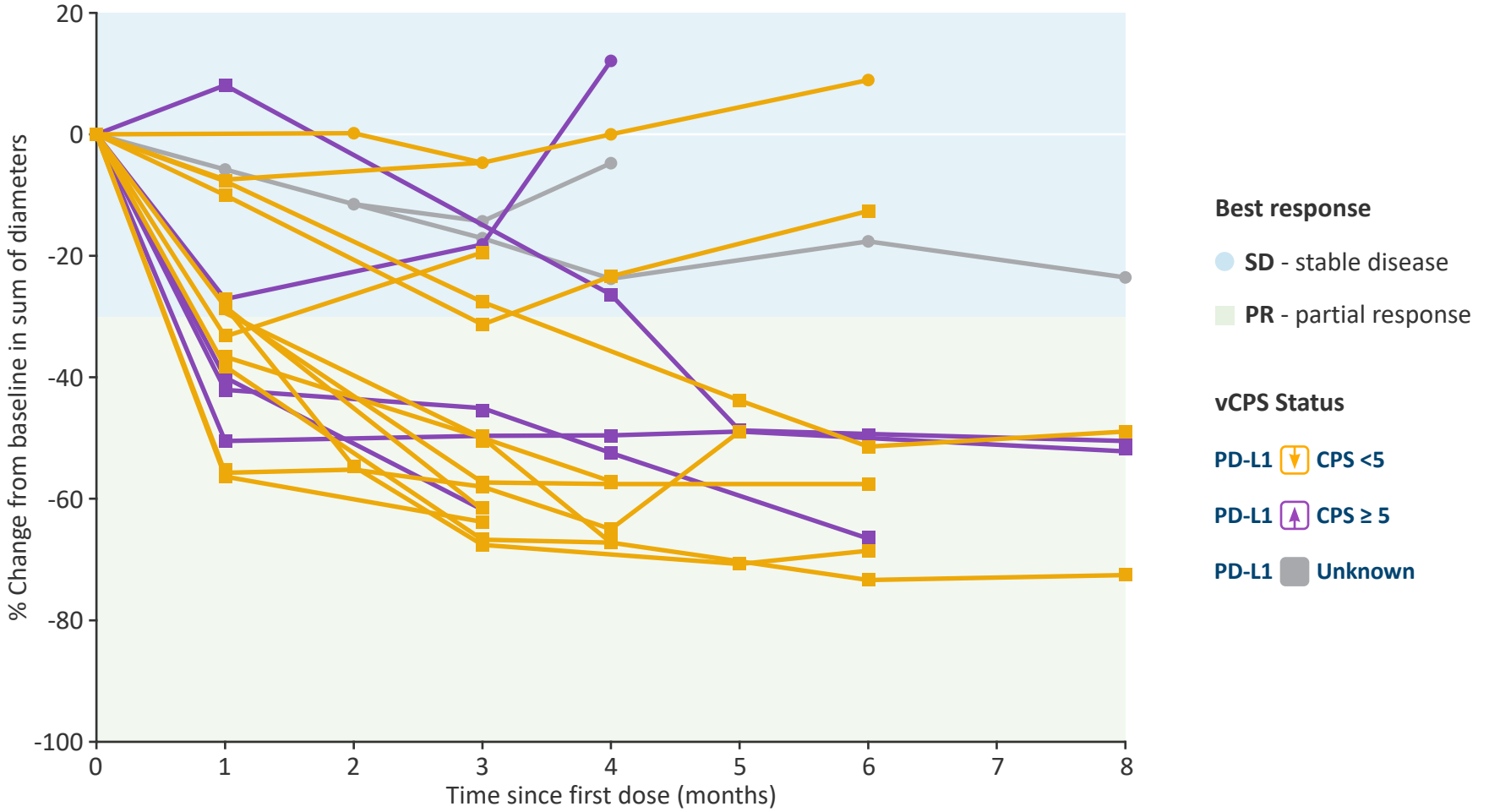
Durable responses independent of PD-L1 expression

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

Best % change in sum of diameters



100% ORR in DKK1-high/ PD-L1-low patients

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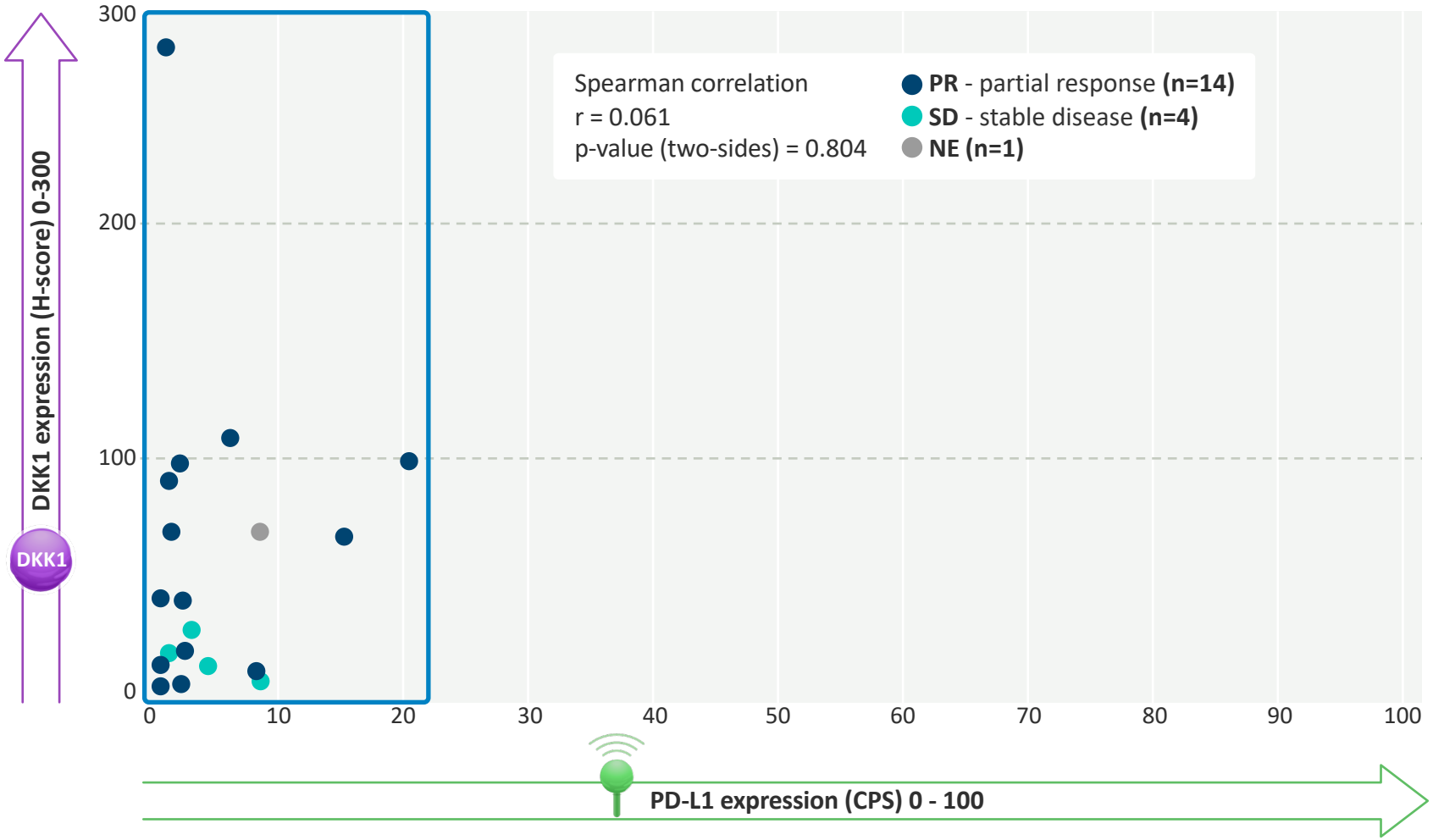
DKK1 and PD-L1 expression are not correlated

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



This population had low overall PD-L1 expression

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Competitive benchmarks for PD-1 + chemotherapy in 1L GEJ/GC patients

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

PD-1 antibodies plus chemotherapy

	Nivolumab		Tislelizumab	Pembrolizumab
	Checkmate-649 (All) N=789	Checkmate-649 PD-L1 CPS ≥ 5 N=473	(All) N=15	Keynote-062 PD-L1 CPS ≥ 1 N=251
OS months (95% CI)	13.8 (12.6, 14.6)	14.4 (13.1, 16.2)	NR	12.5 (10.8, 13.9)
DOR months (95% CI)	8.5 (7.2, 9.9)	9.5 (8.1, 11.9)	NR	6.8 (5.5, 8.3)
PFS months (95% CI)	7.7 (7.1, 8.5)	7.7 (7.0, 9.2)	6.11 (3.8, NE)	6.9 (5.7, 7.3)
ORR (%) (95% CI)	**47%** (43%, 50%)	**50%** (46%, 55%)	**46.7%** (21.3%, 73.4%)	**48.6%** (42.4%, 54.9%)

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DKN-01 highlights in gastric cancer

DKK1 is an important new therapeutic target in esophagogastric 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

DKK1-high
90% ORR

DKK1-low
56% ORR

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

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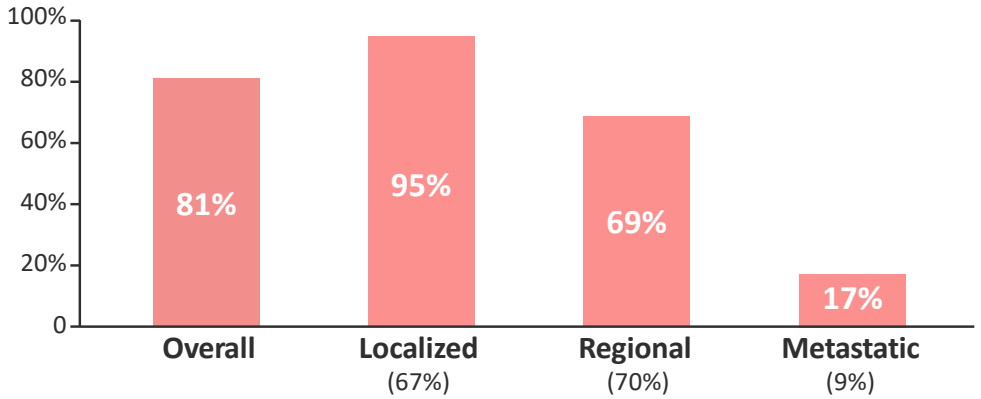
DKN-01

Endometrial cancer development

Endometrial Cancer

5-Year overall and relative survival:



Most common gynecological cancer in the western world

~66,500

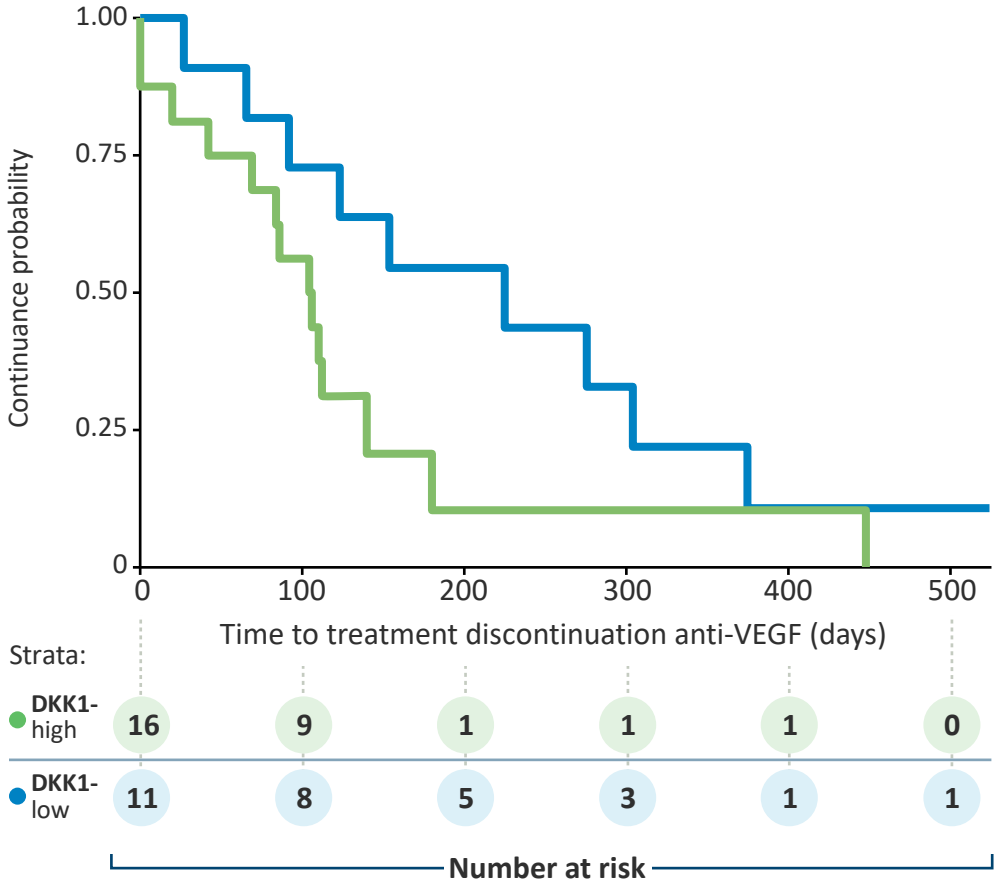
~66,500 annual cases in the United States and the incidence is increasing

Fourth most common cancer in women in the United States

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

High DKK1 is associated with poor response to anti-VEGF and anti-PD-L1 in endometrioid endometrial cancer patients

Anti-VEGF treatment:



Source: American Cancer Society

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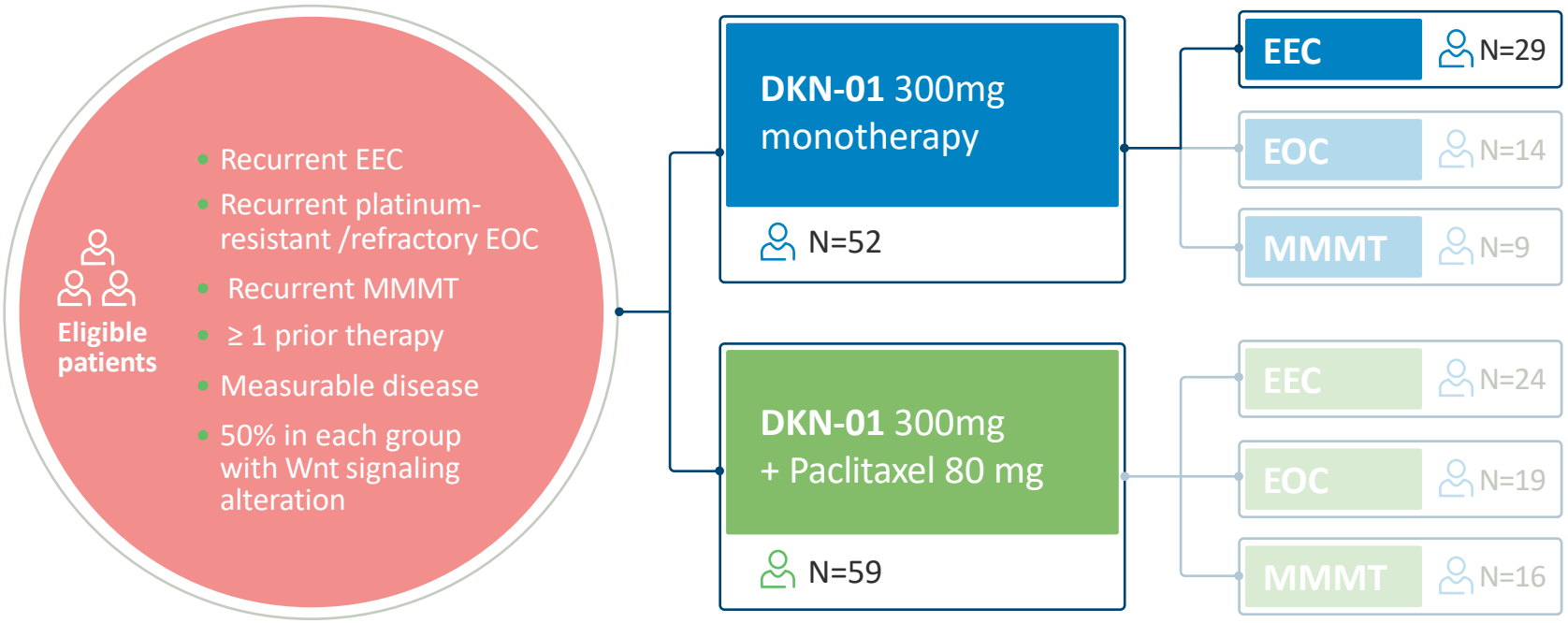
Phase 2 study design evaluating DKN-01 monotherapy and in combination in advanced gynecologic malignancies



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

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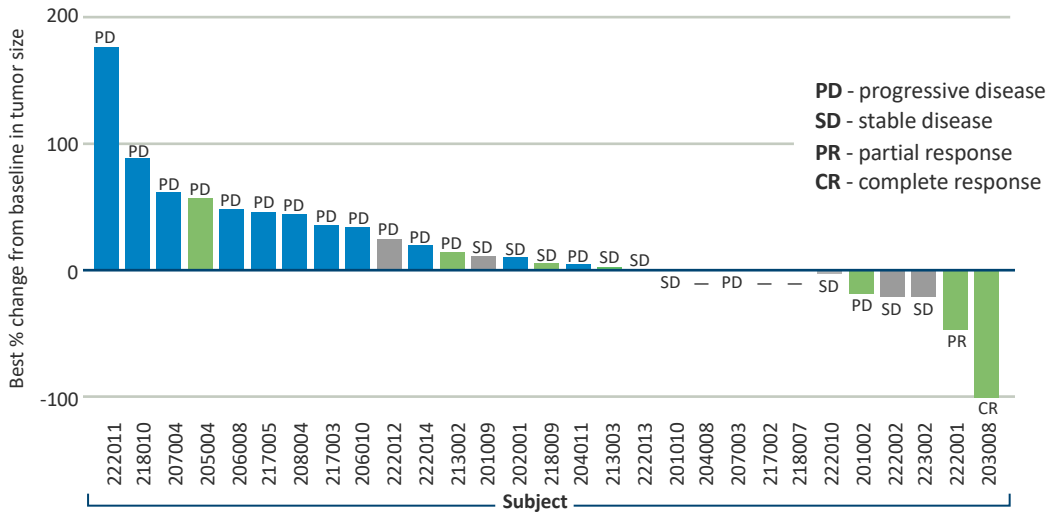
DKN-01 monotherapy - overall response by DKK1 tumoral expression

Overall response by DKK1 tumoral expression



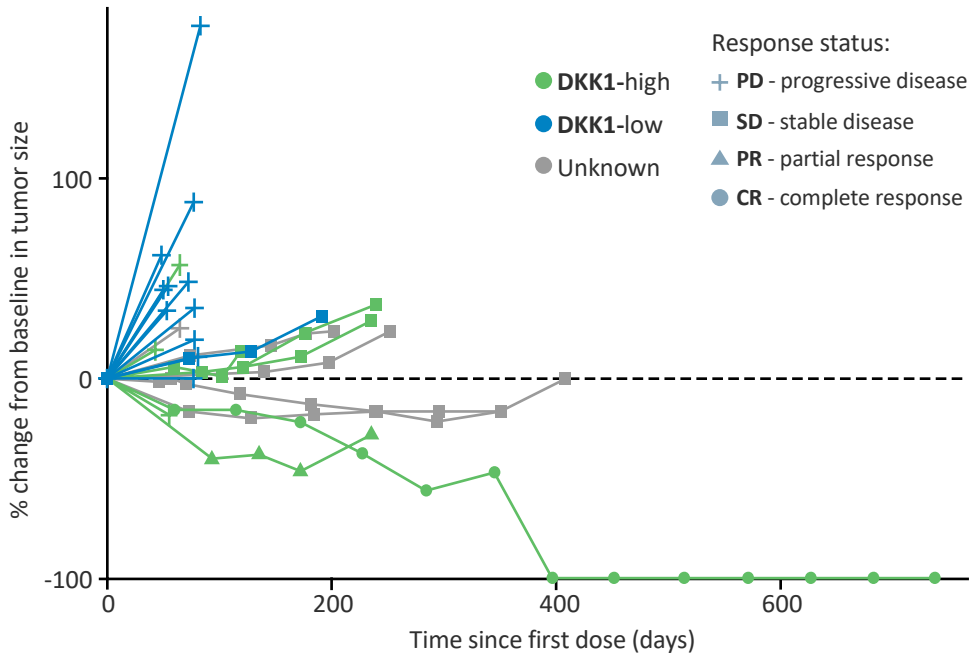
Status	Total	CR	PR	SD	PD	NE	ORR	DCR
DKK1-high (≥18)*	n=8	1	1	3	3	0	25%	63%
DKK1-low (<18)	n=15	0	0	1	11	3	0%	7%
Unknown	n=6	0	0	5	1	0	0%	83%

*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])

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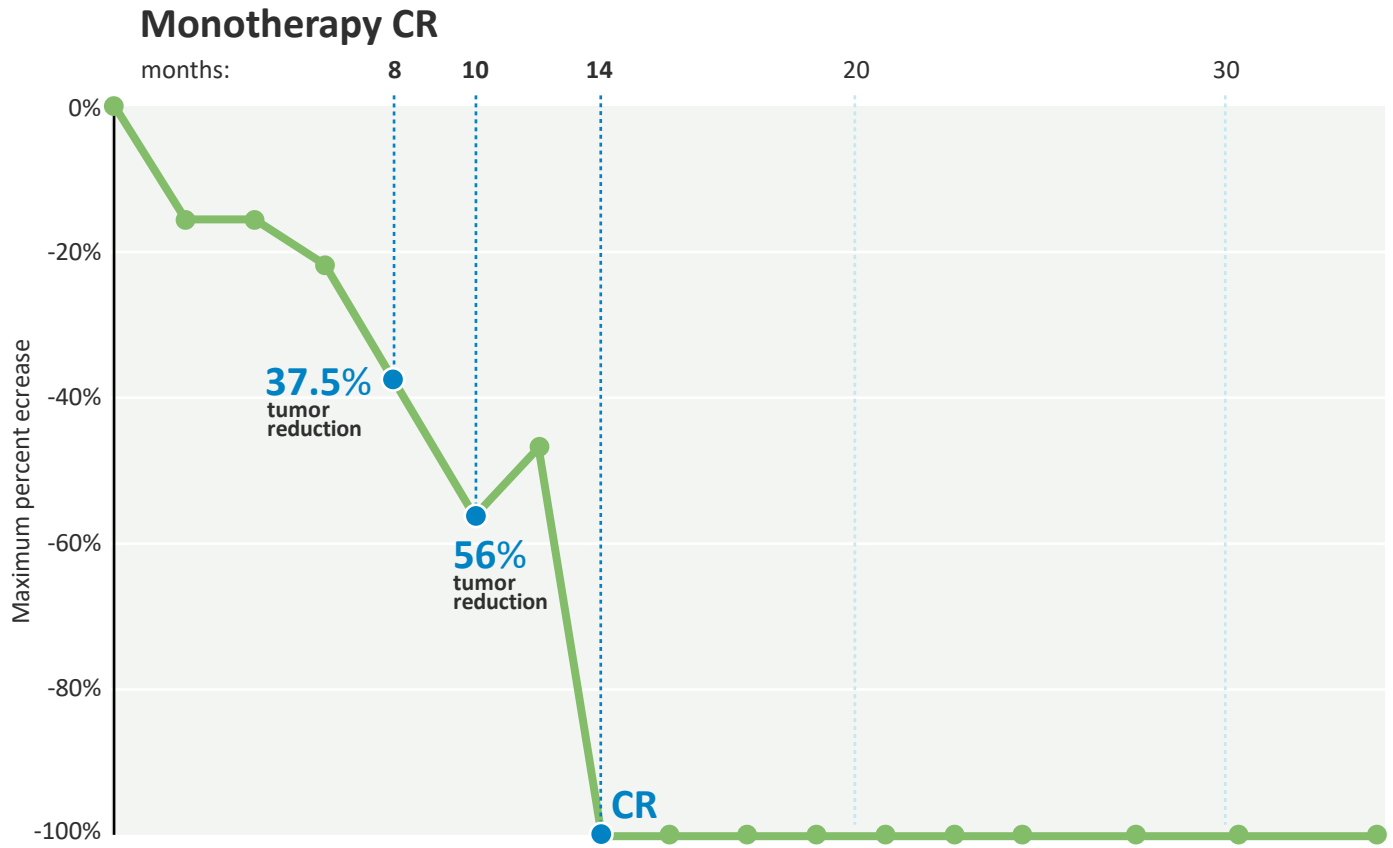
Complete response in endometrial cancer patient on DKN-01 monotherapy

- **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



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Leap 2022 clinical milestones

Gastric cancer

DKN-01
+ tislelizumab

BeiGene

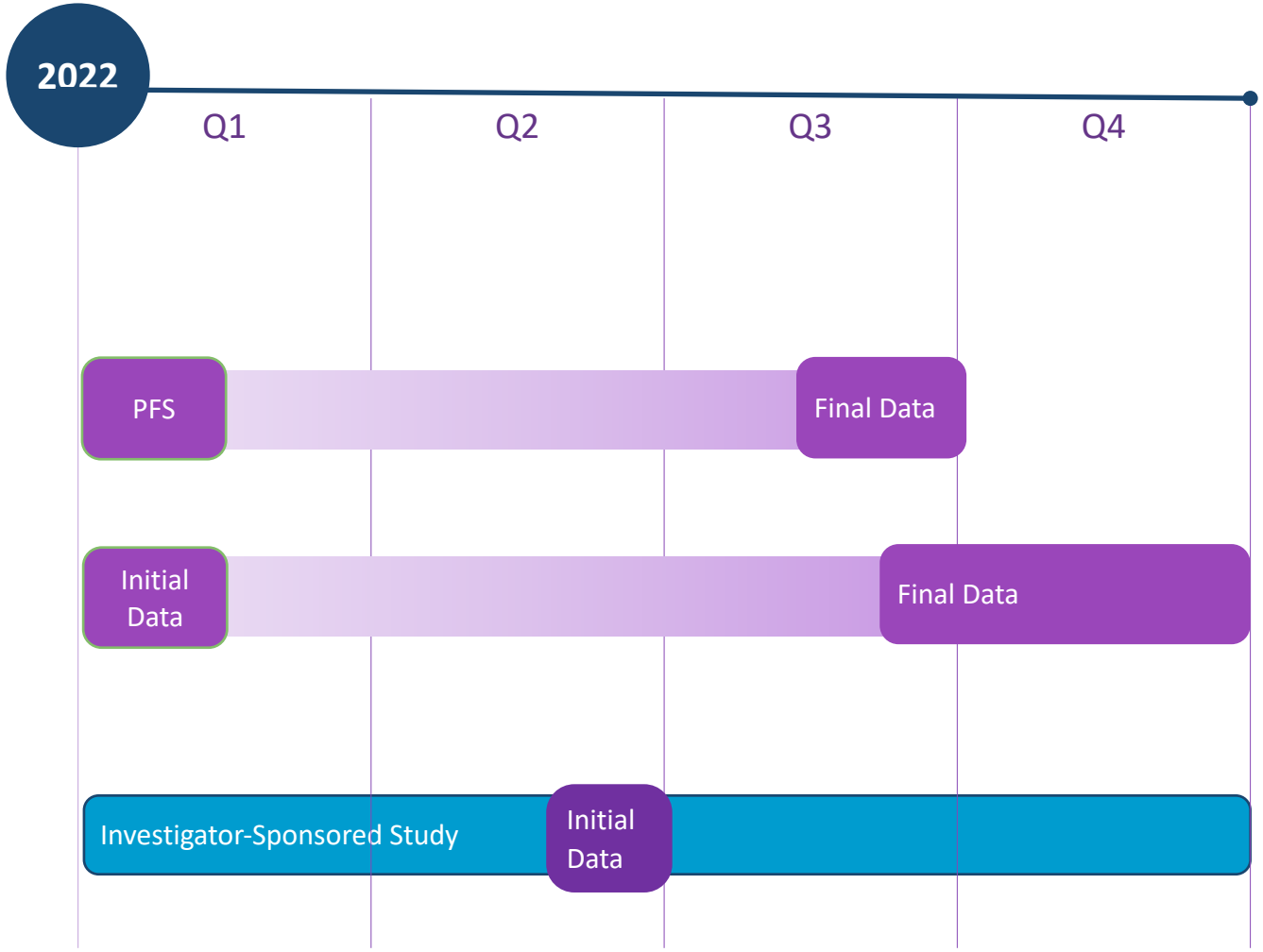
First-line patients
combination with chemotherapy

Second-line patients
DKK1-high

Prostate cancer

DKN-01
+ docetaxel

NYU



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