Company Overview

May 2021

Leap Therapeutics | 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. 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. We assume no obligation to update any forward-looking statements, except as required by applicable law.

Leap Highlights

Oncology drug development company focused on DKN-01, anti-DKK1 antibody

STRATEGIC PARTNERSHIP & INVESTORS

BeiGene

Rights in Asia (excluding Japan), Australia, and New Zealand

$132 million in potential milestones plus royalties

Combinations with tislelizumab

STRONG CLINICAL DATA

Esophagogastric Cancer

Monotherapy, paclitaxel and PD-1 combination responses

PD-1 Combination: 50% ORR, 5.1 months PFS in DKK1-high 2L+ patients

Endometrial Cancer

Monotherapy CR

Monotherapy: 14% ORR, 3.0 months PFS in DKK1-high 2L+ patients

NEAR-TERM MILESTONES

Gastric/GEJ Cancer

DKN-01 + tislelizumab +/- chemo

- First Line Fully Enrolled
- Second Line DKK1-high Recruiting
- Initial Data Q3 2021

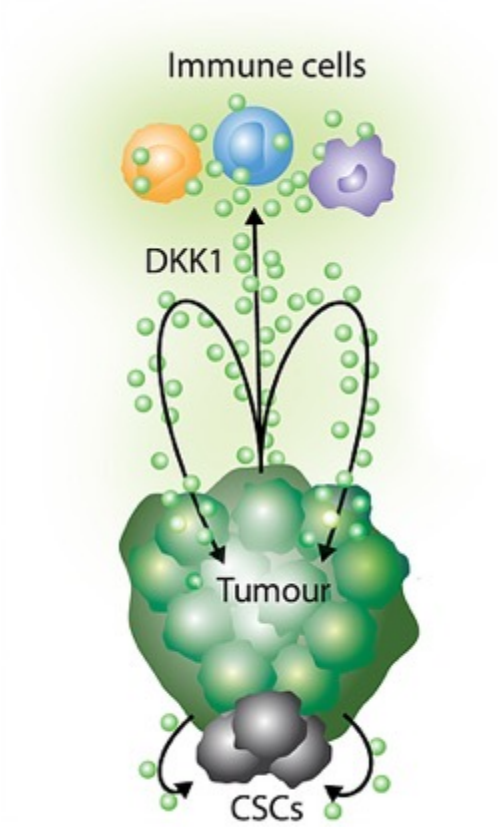
Prostate

NYU

DKN-01 +/- docetaxel

Investigator Sponsored Study Recruiting

DKK1 in Cancer



- Overexpression of DKK1 linked to poor prognosis
- Tumor cells secrete DKK1 promoting proliferation, metastasis and angiogenesis
- DKK1 suppresses anti-tumor immune responses
- Neutralizing DKK1 activates an innate immune response in oncology models

DKN-01

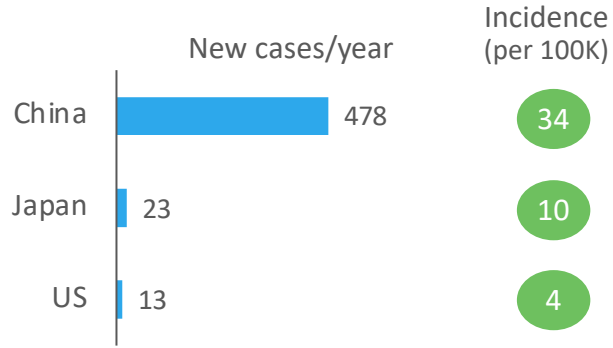
Esophagogastric Cancer Development

Esophagogastric Cancer is an Unmet Medical Need

Esophageal Cancer

477,900 New cases per year
375,000 Deaths per year

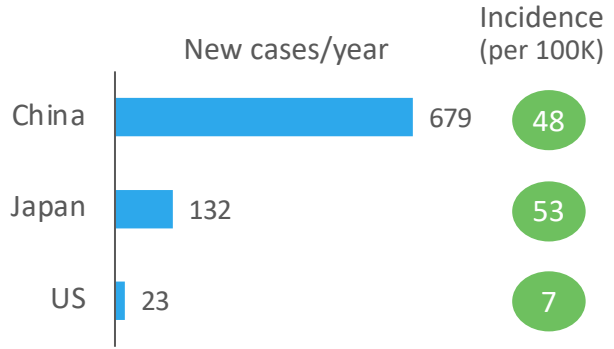
High incidence of esophageal cancer in China
Incidence of gastric cancer in China vs. US/Japan



Gastric Cancer

679,100 New cases per year
498,000 Deaths per year

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



Source: Cancer China statistics 2015, Cancer statistics in Japan 2013, American Cancer Society

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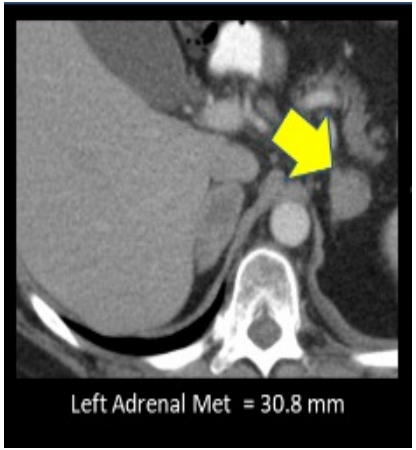
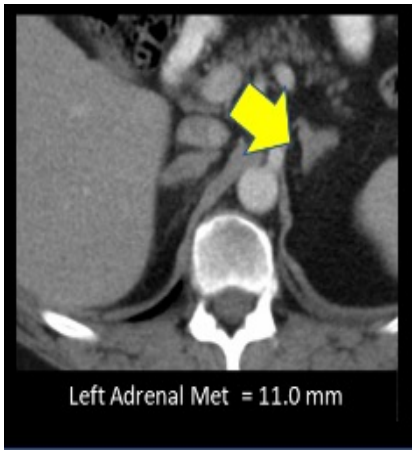
DKN-01 Single-Agent Activity in Heavily Pretreated Esophagogastric Cancer Patients

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

*By Blinded Independent Central Review

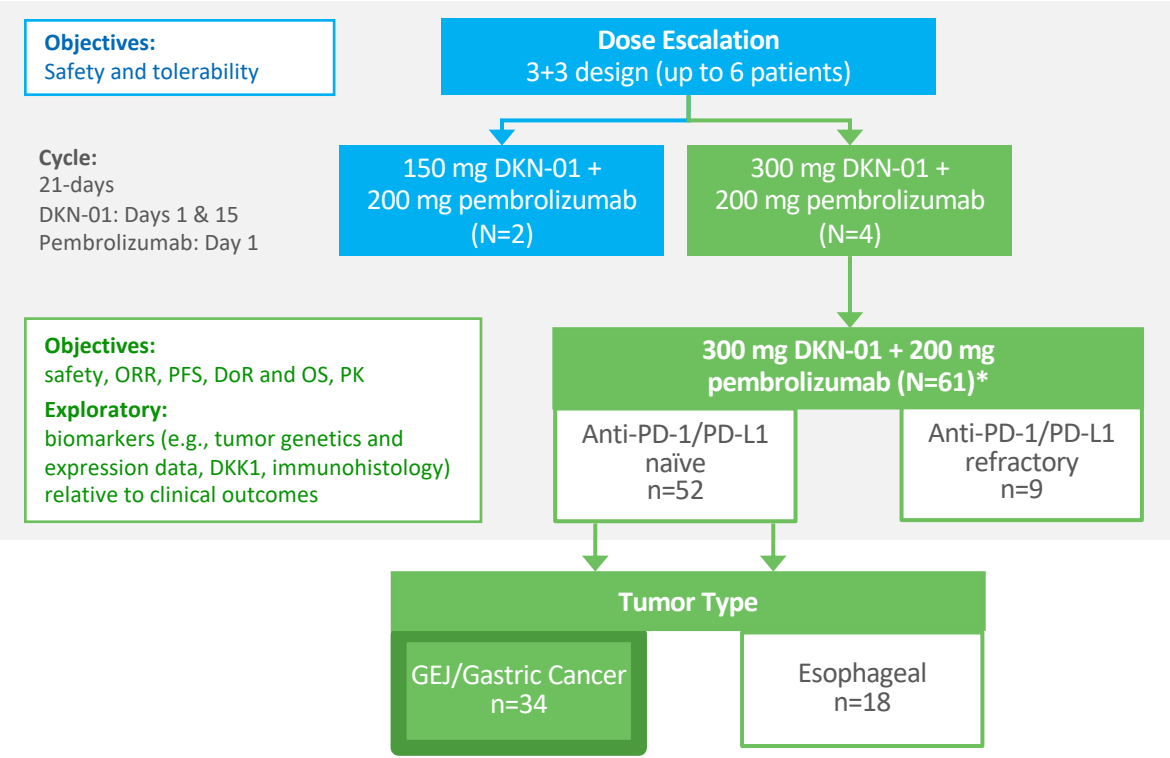
PD-1 Monotherapy in Esophagogastric Cancer Patients

	Second Line		Third Line +
	KN-181 Pembro mono (EA+ESCC)	KN-061 Pembro mono (GEJ/GC)	KN-059 Pembro mono (GEJ/GC)
N	314	296	259
ORR (%)	13.1	11.1	11.6
ORR in MSS Pts (%)	NR	9.3	9.0
PFS months (95% CI)	2.1 (2.1, 2.2)	1.5 (1.4, 1.6)	2.0 (2.0, 2.1)
OS months (95% CI)	7.1 (6.2, 8.1)	6.7 (5.4, 8.9)	5.6 (4.3, 6.9)

Response Rates and Median Progression-Free Survival Remain Low

KEYNOTE-731 Study Flow Diagram

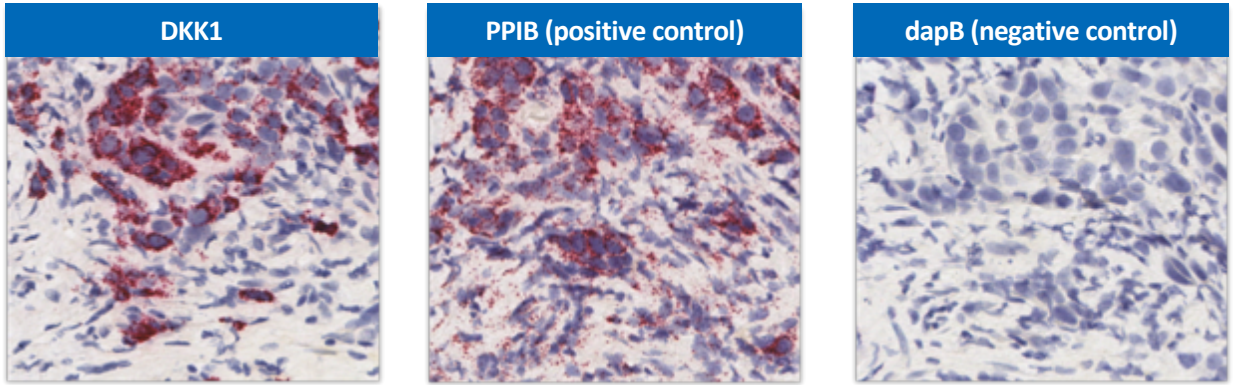
Esophagogastric Cancer – DKN-01 Plus Pembrolizumab



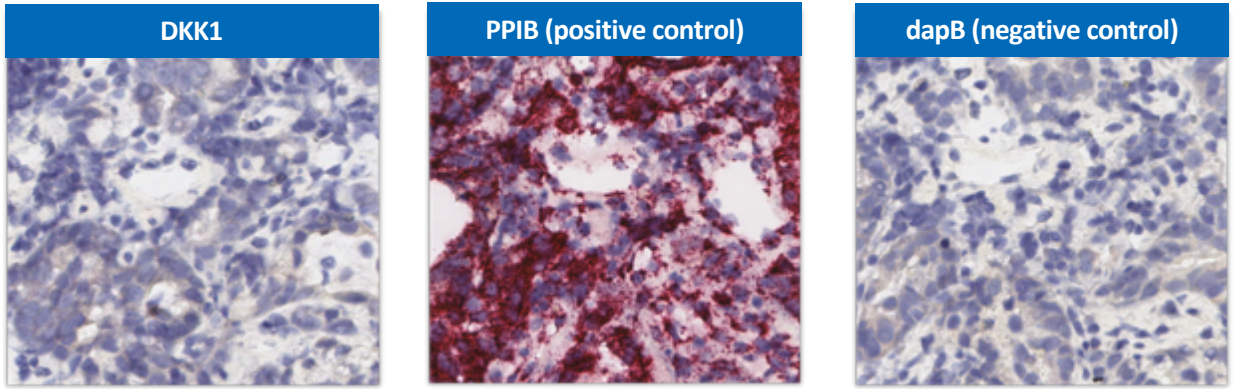
*Total N includes 4 patients from dose escalation

DKK1 RNAscope Tumor Biopsy Images

Patient with a partial response:
DKK1 H-score = 163



Patient with progressive disease:
DKK1 H-score = 7



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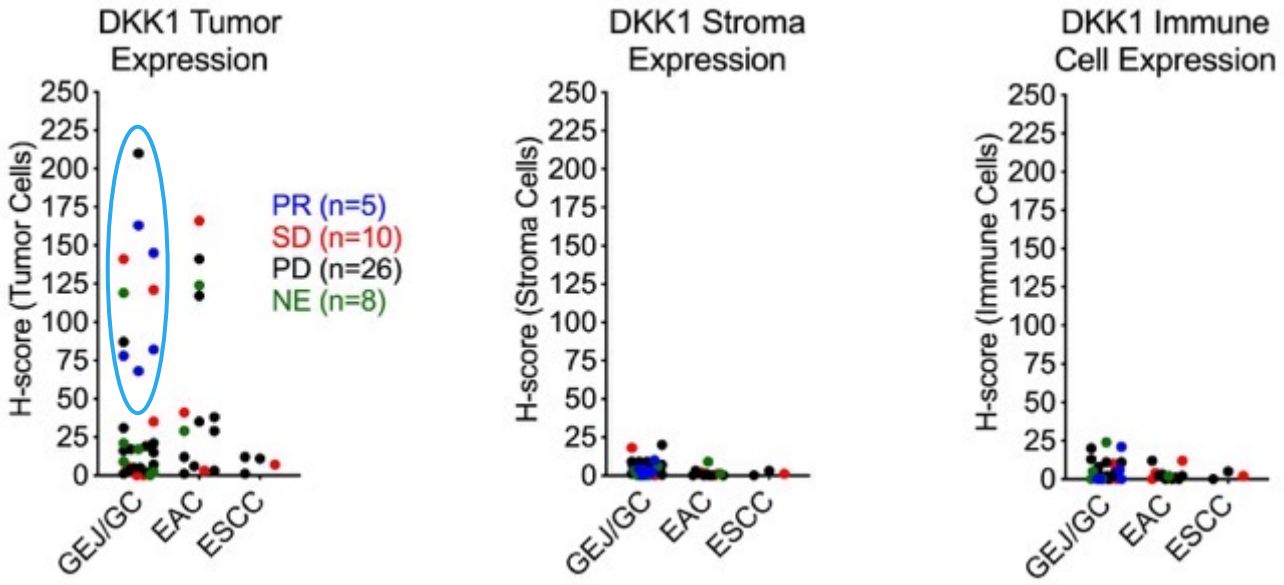
DKK1 Tumor Expression

Anti-PD-1/PD-L1 Naïve Esophagogastric Cancer

- Responding GEJ/GC patients have elevated levels of DKK1
- DKK1 is expressed in tumor cells



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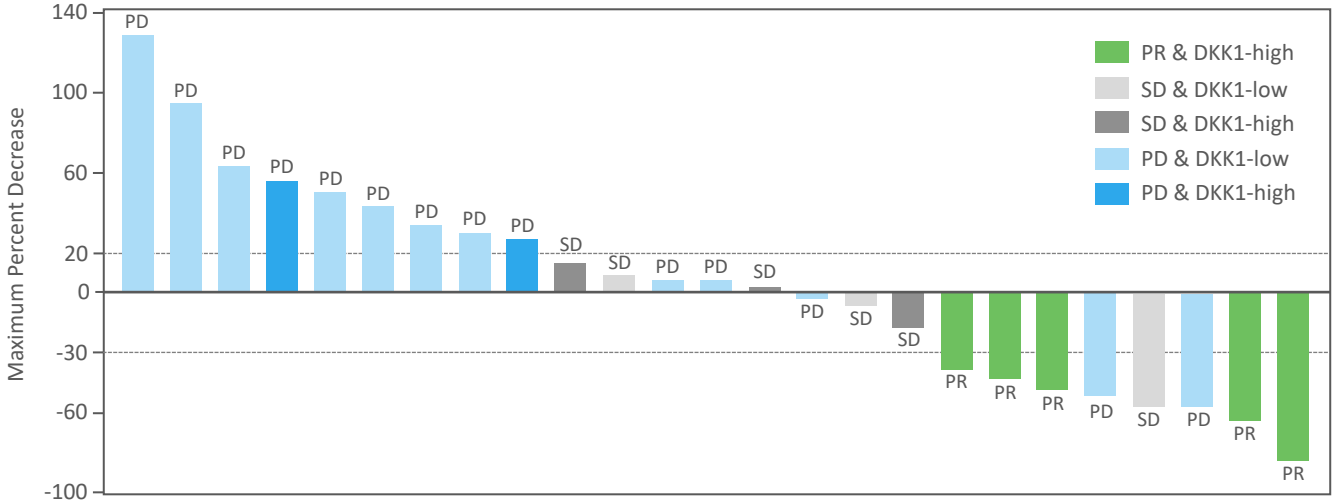
Better and More Durable Responses for DKK1-high Patients

Anti-PD-1/PD-L1 Naïve GEJ/GC Subgroup



Primary Location	Total (n)	RE* (n)	PR (n)	SD (n)	PD (n)	NE (n)	RE* ORR (n, %)	DCR (n,%)
DKK1 RNAscope*	31							
DKK1-high	11	10	5	3	2	1	5 (50)	8 (80)
DKK1-low	20	15	0	3	12	5	0 (0)	3 (20)

*DKK1-high ≥ upper tertile (35)

DKK1-high had an ORR of 50% (5 PR/10) and DCR of 80% (8/10)

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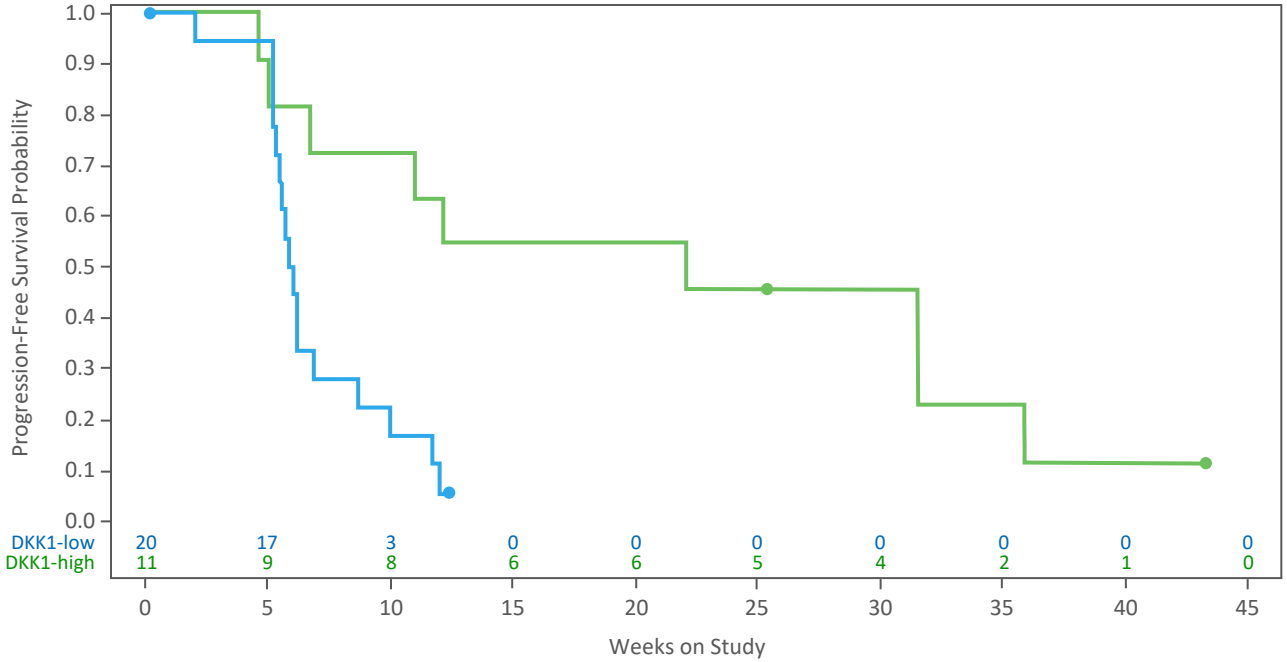
Longer PFS for DKK1-high Patients

Anti-PD-1/PD-L1 Naïve GEJ/GC Subgroup



	Median (95% CI)
DKK1-high	22.1 (5.0, 35.9)
DKK1-low	5.9 (5.3, 6.9)

*DKK1-high ≥ upper tertile 35

Median PFS longer in DKK1-high (22.1 weeks) vs. DKK1-low (5.9 weeks) patients

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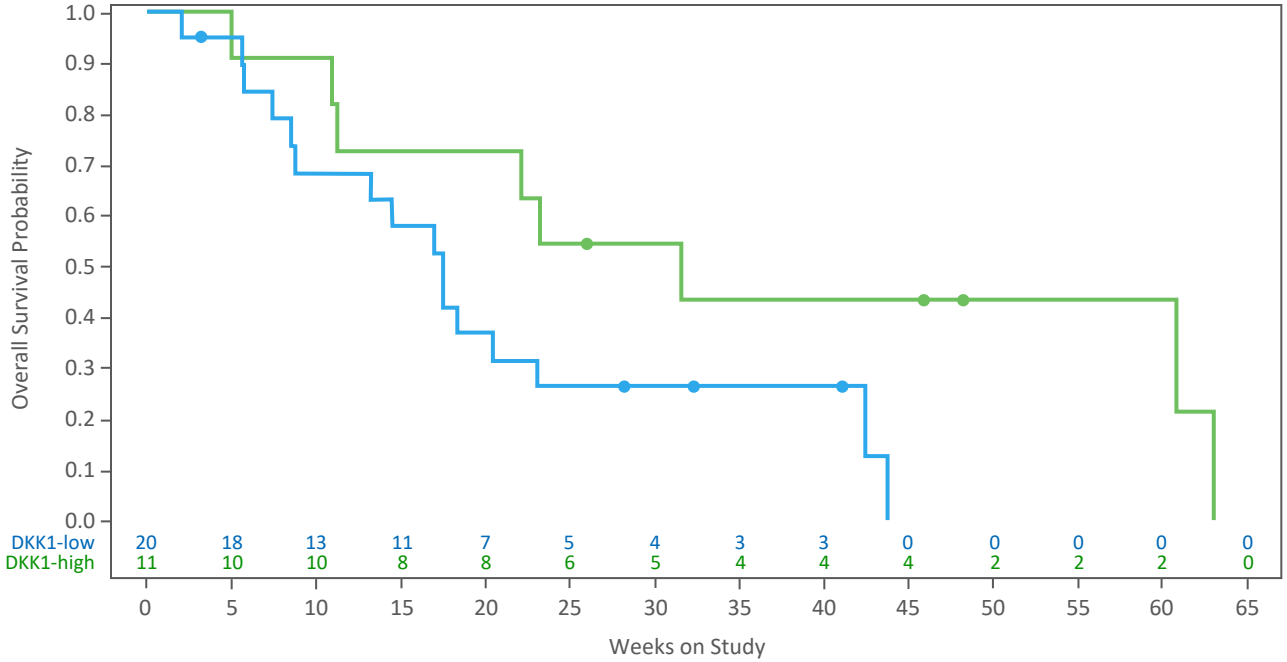
Longer OS for DKK1-high Patients

Anti-PD-1/PD-L1 Naïve GEJ/GC Subgroup



	Median (95% CI)
DKK1-high	31.6 (11.0, 63.0)
DKK1-low	17.4 (8.6, 23.1)

*DKK1-high ≥ upper tertile 35

Median OS longer in DKK1-high (31.6 weeks) vs. DKK1-low (17.4 weeks) patients

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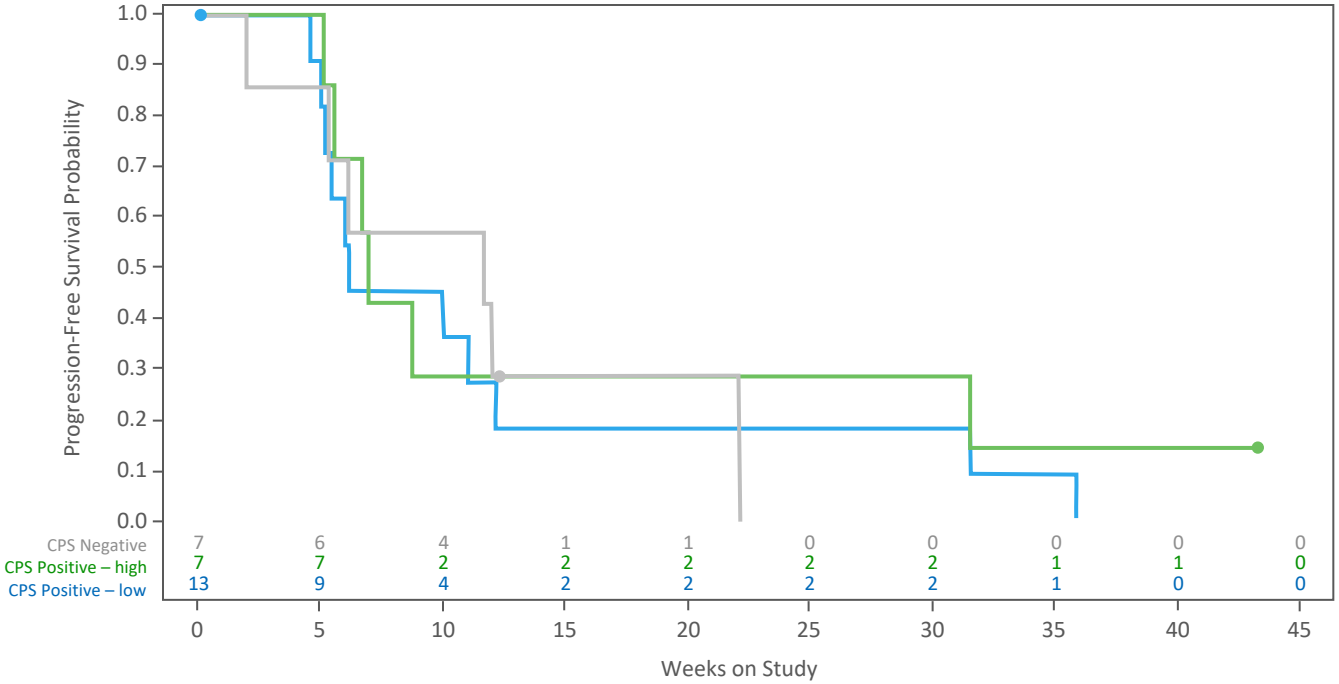
PD-L1 CPS Scores Not Associated with PFS



	Median (95% CI)
CPS Negative	11.7 (2.0, 22.1)
CPS Positive – low	6.1 (5.0, 12.1)
CPS Positive – high	6.9 (5.1, 31.6)

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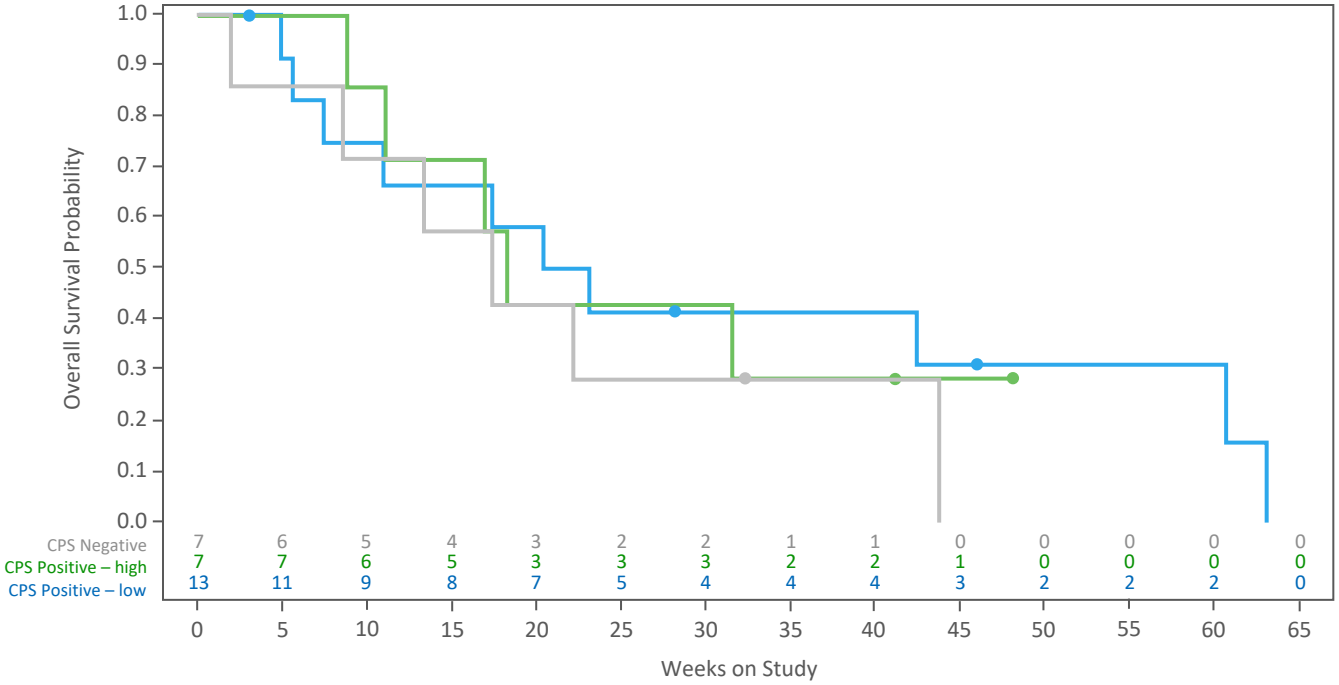
PD-L1 CPS Scores Not Associated with OS



	Median (95% CI)
CPS Negative	17.4 (2.0, 43.7)
CPS Positive – low	21.8 (5.6, 60.9)
CPS Positive – high	18.3 (8.7, NA)

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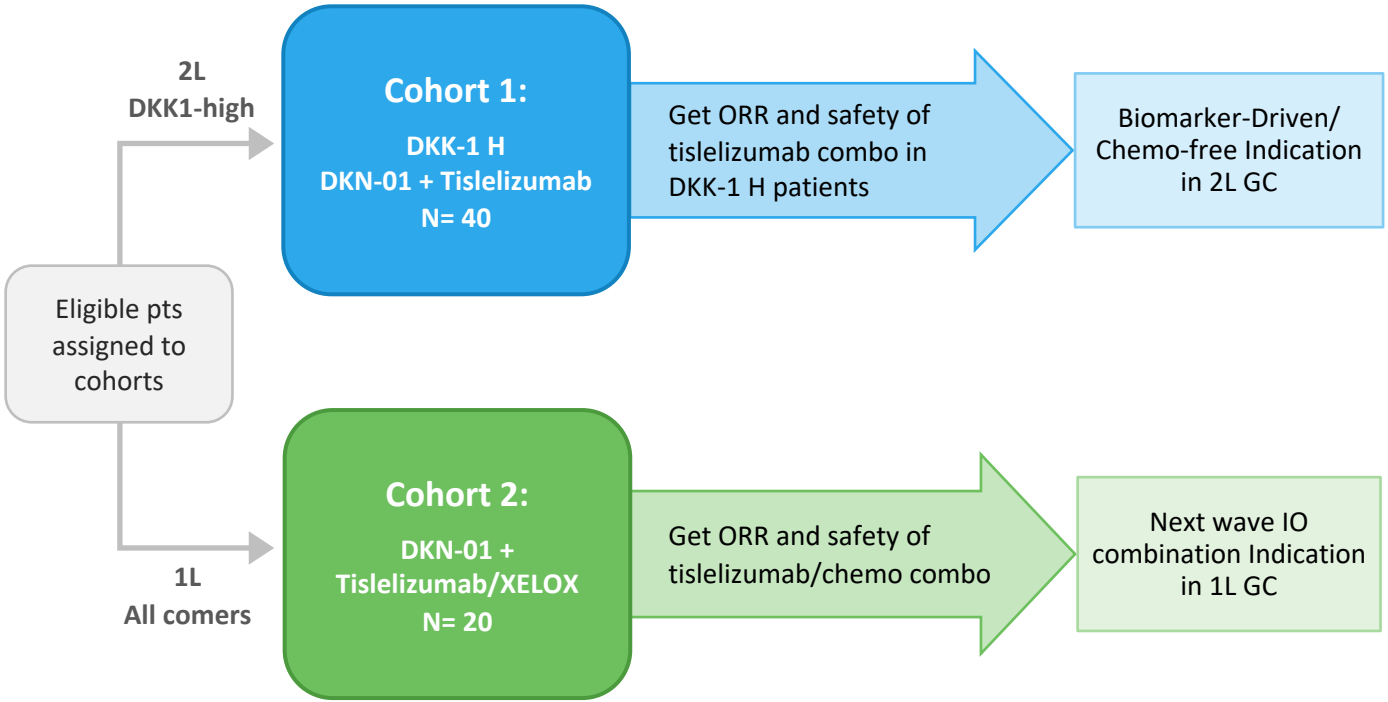
Study Design in Patients with Advanced Gastric/GEJ Adenocarcinoma

Assess the Safety and Anti-tumor Activity of DKN-01 in Combination with Tislelizumab +/- Chemo

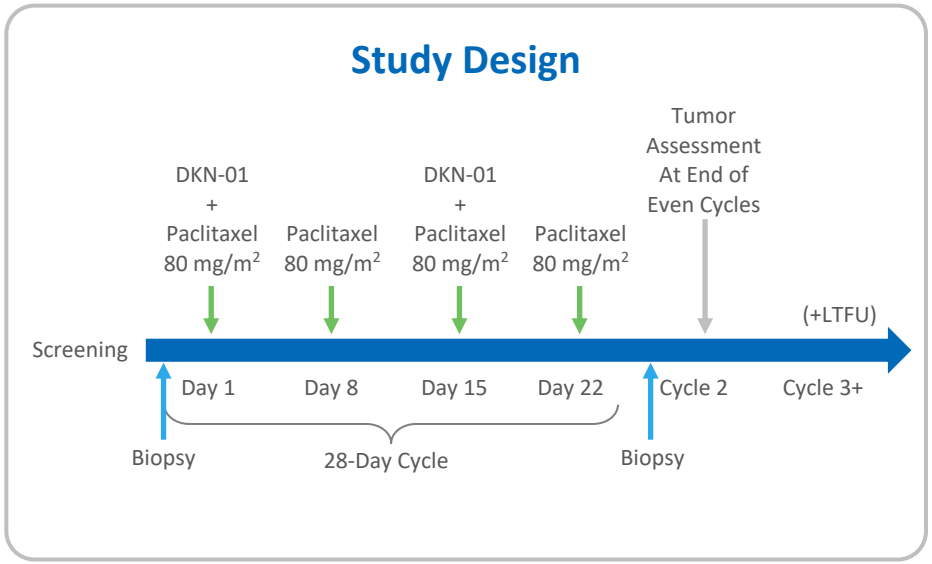


PD-1 Antibodies + Chemo in First-Line HER2- GEJ/Gastric Cancer Patients

	nivolumab		tislelizumab	pembrolizumab
	Checkmate-649 (All)	Checkmate-649 (CPS ≥ 5)	(All)	Keynote-062 (CPS ≥ 1)
N	789	473	15	257
ORR (%) (95% CI)	47 (43, 50)	50 (46, 55)	46.7 (21.3, 73.4)	48.6 (42.4, 54.9)
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)
OS months (95% CI)	13.8 (12.6, 14.6)	14.4 (13.1, 16.2)	NR	12.5 (10.8, 13.9)

ORR Benchmarks: 46.7% - 50%

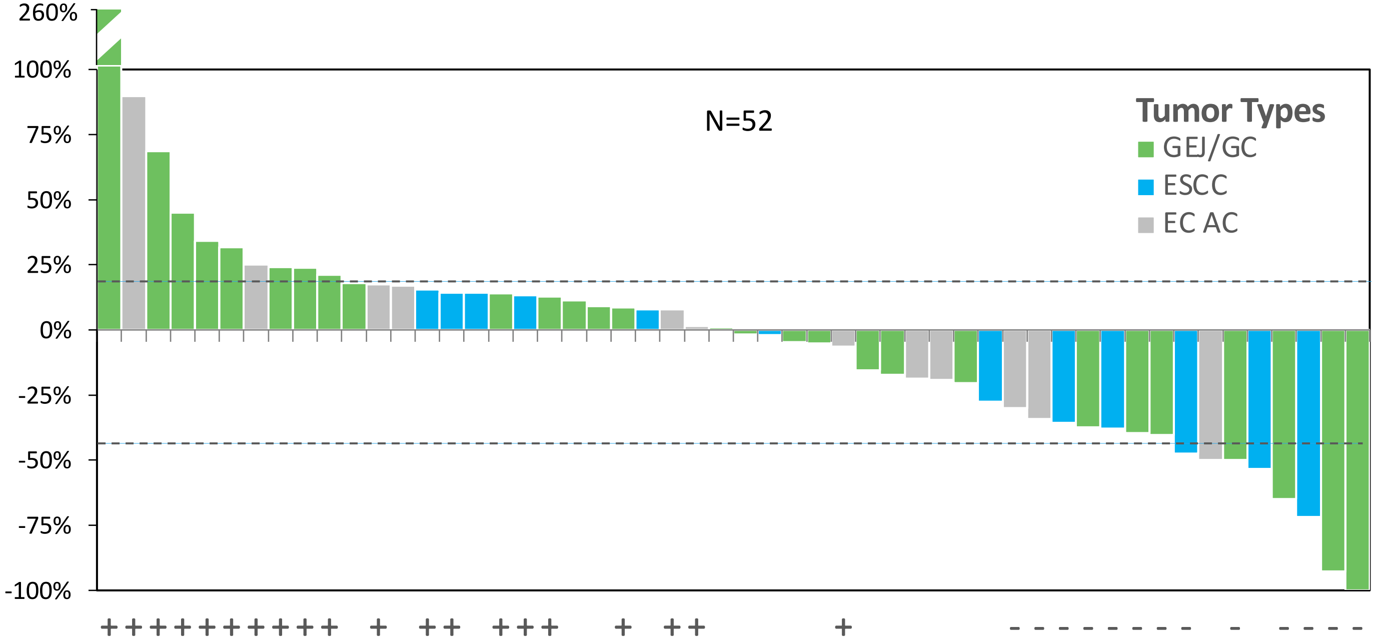
DKN-01 Plus Paclitaxel Esophagogastric Study Design



	DKN-01 150 mg + pac N=3	DKN-01 300 mg + pac N=56
Age (median, range)	56 (47, 73)	62.5 (34, 82)
Male (n, %)	3 (100)	43 (76.8)
White	3 (100)	48 (85.7)
Type of Cancer (n, %)		
Esophageal Squamous	-	13 (23.2)
Esophageal AC	1 (33.3)	12 (21.4)
GEJ AC	2 (66.7)	29 (51.8)
Gastric	-	2 (3.6)
Prior Therapy (median, range)	4 (2, 7)	2 (1, 6)
Taxane (n, %)	3 (100)	27 (48.2)
Ramucirumab (n, %)	1 (33.3)	7 (12.5)

Clinical Activity of DKN-01 Plus Paclitaxel

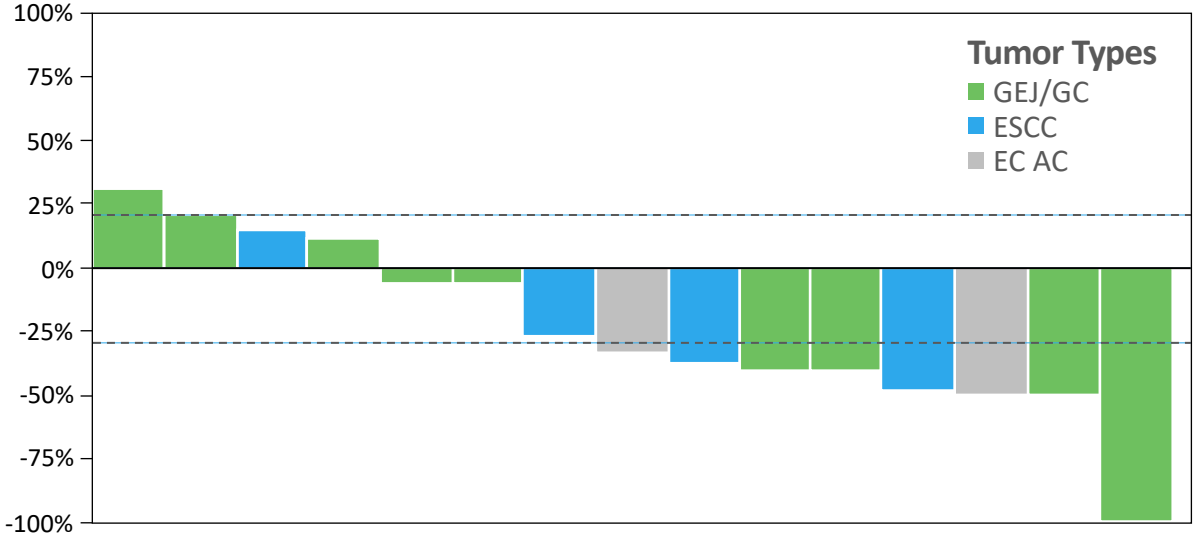
Evaluable Esophagogastric Patients by Tumor Location



Therapy	Patients Treated	Prior Therapies	Overall Response Rate	Stable Disease Rate	Disease Control Rate
DKN-01 + paclitaxel	52	1-7	**25%**	35%	60%

+ = PD, - = PR, no symbol = SD

DKN-01 Plus Paclitaxel Exceeds Benchmarks in Second-Line Esophagogastric Cancer



2nd Line	Study	n	ORR (%)	DCR (%)	PFS (months)	OS (months)
DKN-01 + pac		15	46.7%	73.3%	4.5	14.1
Ram + pac	RAINBOW	330	28%	80%	4.4	9.6
Pac	RAINBOW	335	16%	64%	2.9	7.4
Chemo	KN-181	314	6.7%	-	3.4	7.1

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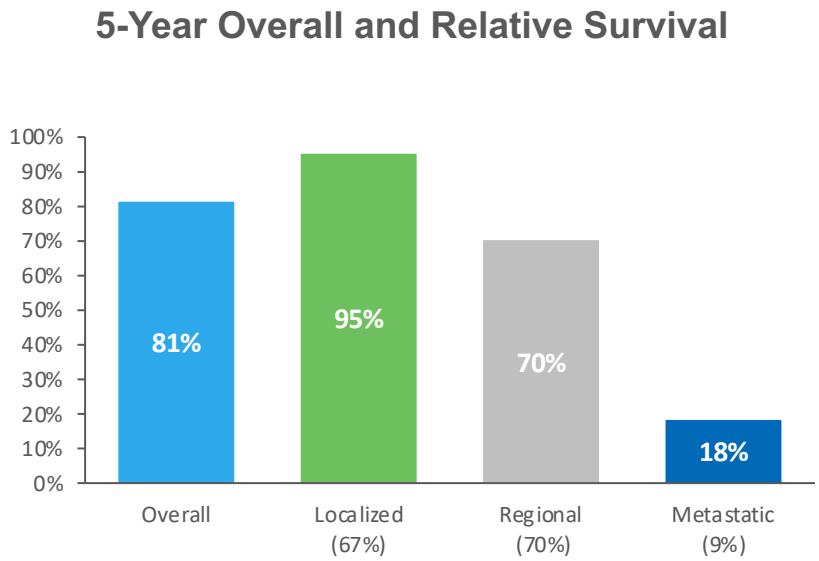
DKN-01

Gynecologic Cancer Development

Endometrial Cancer

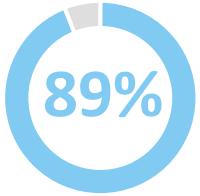
- Most common gynecological cancer in the western world
- ~62,000 annual cases in the United States and the incidence is increasing
- Fourth most common cancer in women in the United States
- Clinical risk factors include estrogen-only hormone replacement, obesity, chronic anovulation, tamoxifen therapy, nulliparity, early menarche, and late menopause



Single Agent Activity in Endometrial Cancer

Class	Drug name	ORR (%)	DCR (%)	mPFS (mos)
Anti-PD(L)-1: MSS/refractory PD-L1+	pembrolizumab	13	26	1.8
	dostarlimab	20	-	-
	durvalumab	6	-	-
	avelumab	3	-	-
Anti-angiogenic	bevacizumab	13.5	63.5	4.2
	lenvatinib	14.3	-	5.4
mTOR	everolimus	9	36	2.8

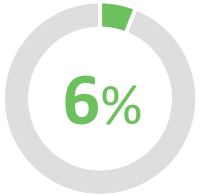
Pembrolizumab + Lenvatinib in Endometrial Cancer



Grade ≥3 Treatment-Emergent AEs[1]

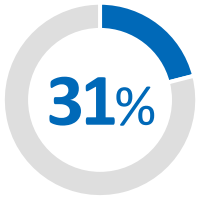
Any Grade Treatment-Emergent AEs[1]

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%) and urinary tract infection (25.6%).



FATAL ADVERSE REACTIONS[1]

Including gastrointestinal disorders: 1.2%, 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, pancreatitis, 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%), stomatitis (9%), abdominal pain, hemorrhages (7% each), renal impairment, decreased weight (6% each), rash, headache, increased lipase, and proteinuria (5% each).

AGENT	POPULATION	n	ORR	CR	PR	SD	mPFS
Len + Pembro 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*

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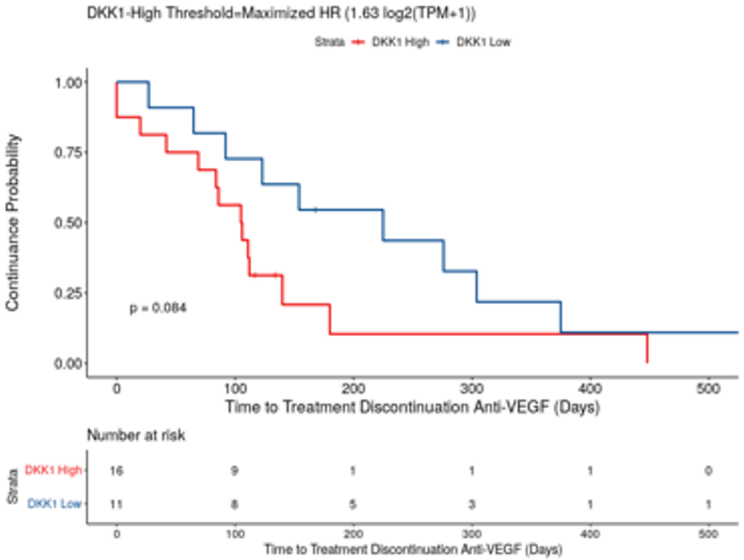
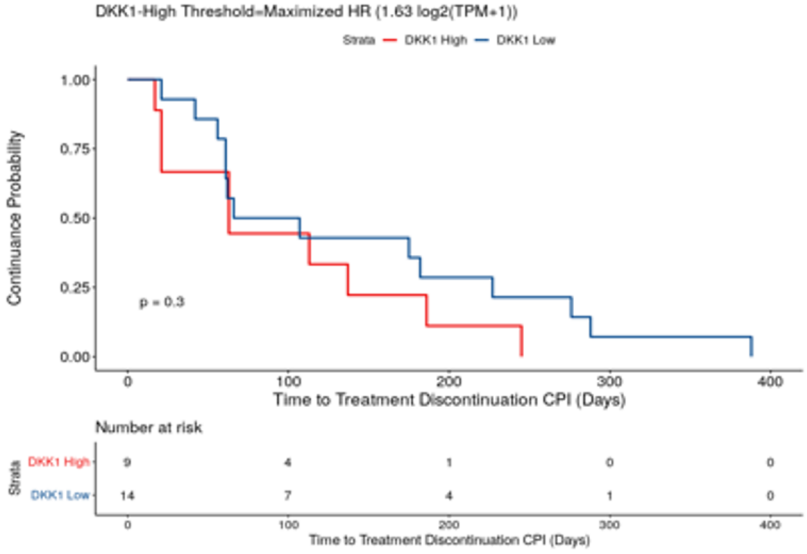
High DKK1 Is Associated with Poor Response to anti-VEGF and anti-PD-(L)1 in Endometrioid Endometrial Cancer Patients

Anti-VEGF treatment



PD-(L)1 treatment



TEMPUS

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DKN-01 Phase 2 Study Design

Primary objective:

Objective response rate (ORR)

Secondary objectives:

Exploring genetic mutations in the Wnt signaling pathway and tumoral DKK1 expression as predictive biomarkers

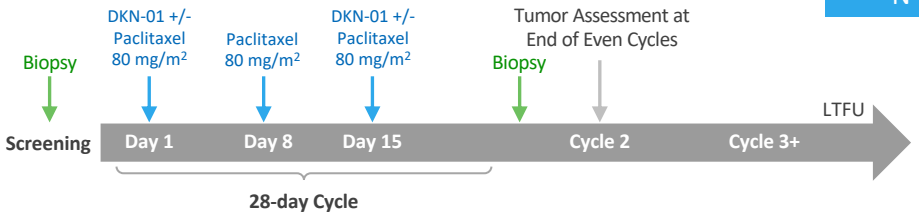
Eligible Patients

- Recurrent EEC
- Recurrent platinum-resistant/refractory EOC
- Recurrent MMMT
- ≥ 1 prior therapy
- Measurable disease
- 50% in each group with Wnt signaling alteration

DKN-01 300 mg Monotherapy N=52
- EEC N=29
- EOC N=14
- MMMT N=9

DKN-01 300 mg + Paclitaxel 80 mg N=59
- EEC N=24
- EOC N=19
- MMMT N=16

Data as of 28 Sep 2020. EEC: epithelial endometrial cancer; EOC: epithelial ovarian cancer; MMMT: carcinosarcoma (malignant mixed Mullerian tumor)



Basket study evaluating DKN-01 as monotherapy or in combination with paclitaxel in advanced gynecologic malignancies

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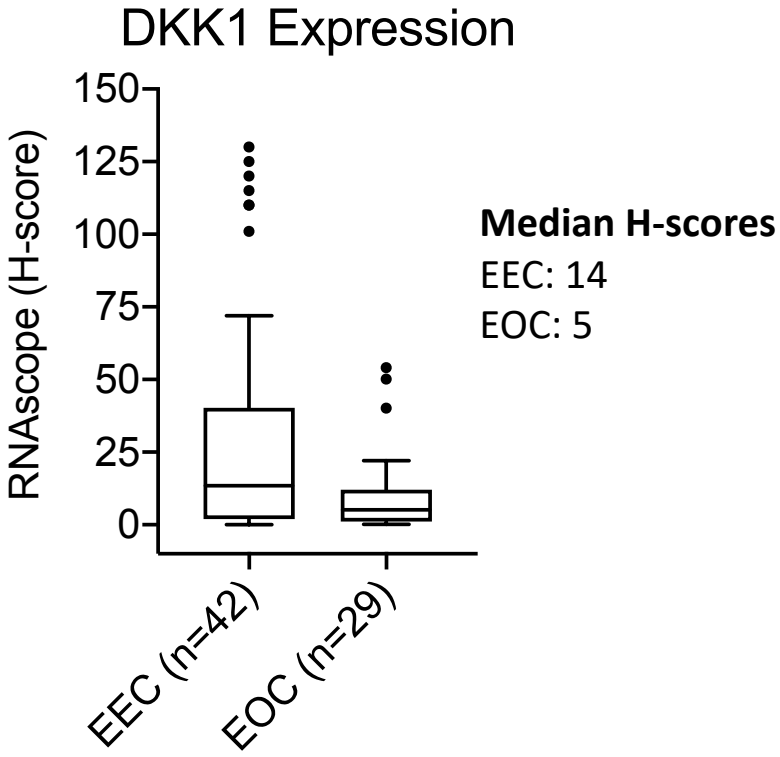
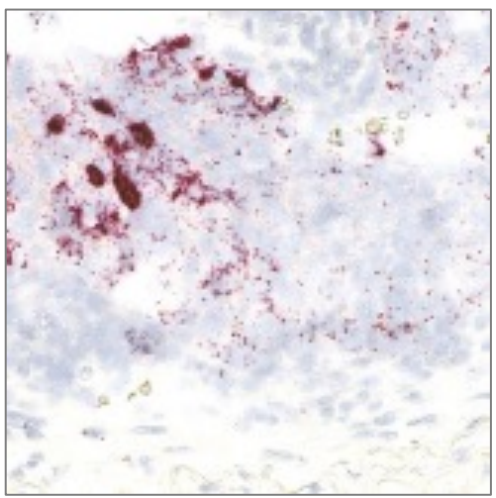
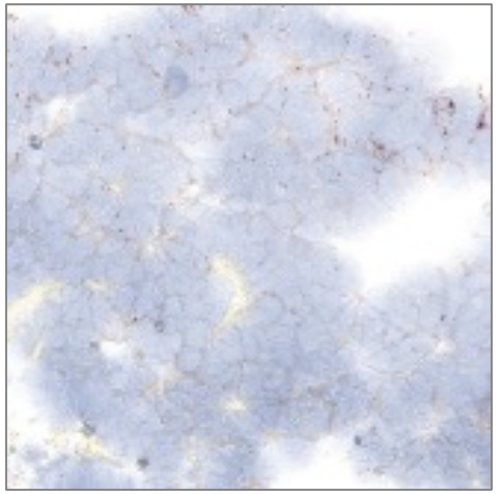
Endometrial Cancer Patients have Higher DKK1 Expression than Ovarian Cancer Patients



Median H-scores
EEC: 14
EOC: 5



H-score = 115
CTNNB1(S37F)

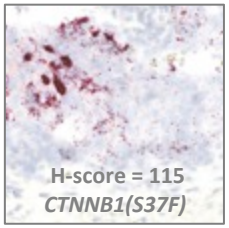


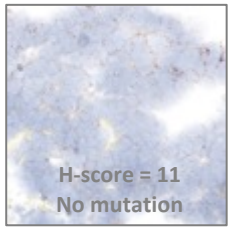
H-score = 11
No mutation

DKK1 High Expression Is Associated with Wnt Activating Mutations

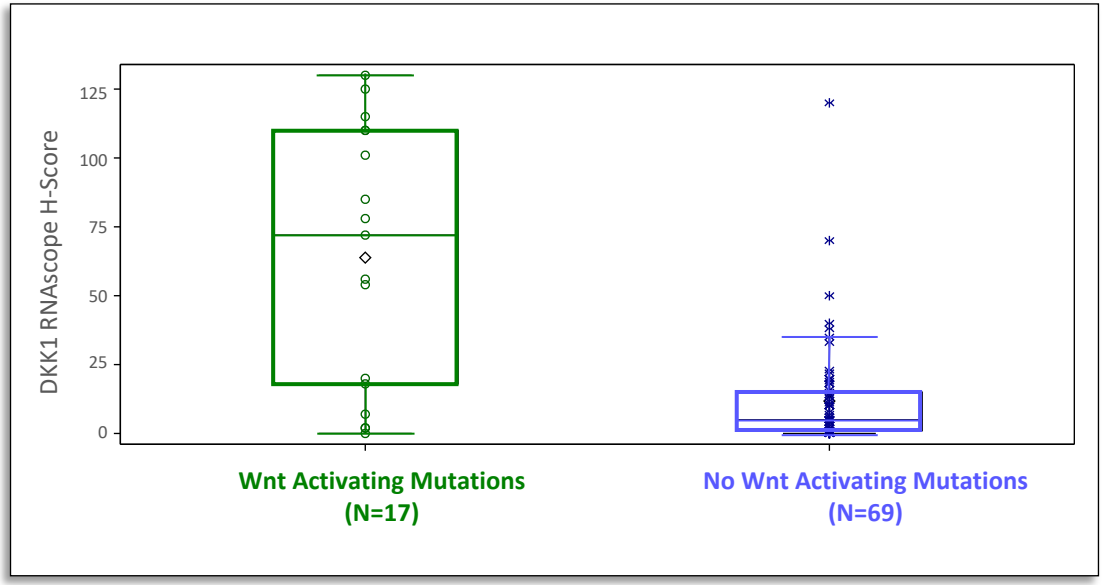
DKK1 RNAscope Evaluation
86 pts

Wnt Activating mutations	No Wnt Activating mutations
17 pts (20%)	69 pts (80%)
Median RNAscope H-score: 72	Median RNAscope H-score: 5





Distribution of DKK1 RNAscope H-Scores by Wnt Activating Mutation Status



Tumors with Wnt Activating Mutations have 14.4 times higher DKK1 expression

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DKN-01 Was Well Tolerated as Monotherapy and in Combination with Paclitaxel

- Related SAEs:
  - DKN-01 monotherapy: 5.8%
  - DKN-01 + paclitaxel combination: 6.8%
- No TEAEs which led to death

Most Common DKN-01 Related TEAEs

Monotherapy:
- Nausea (28.8%)
- Fatigue (26.7%)
- Constipation (11.5%)

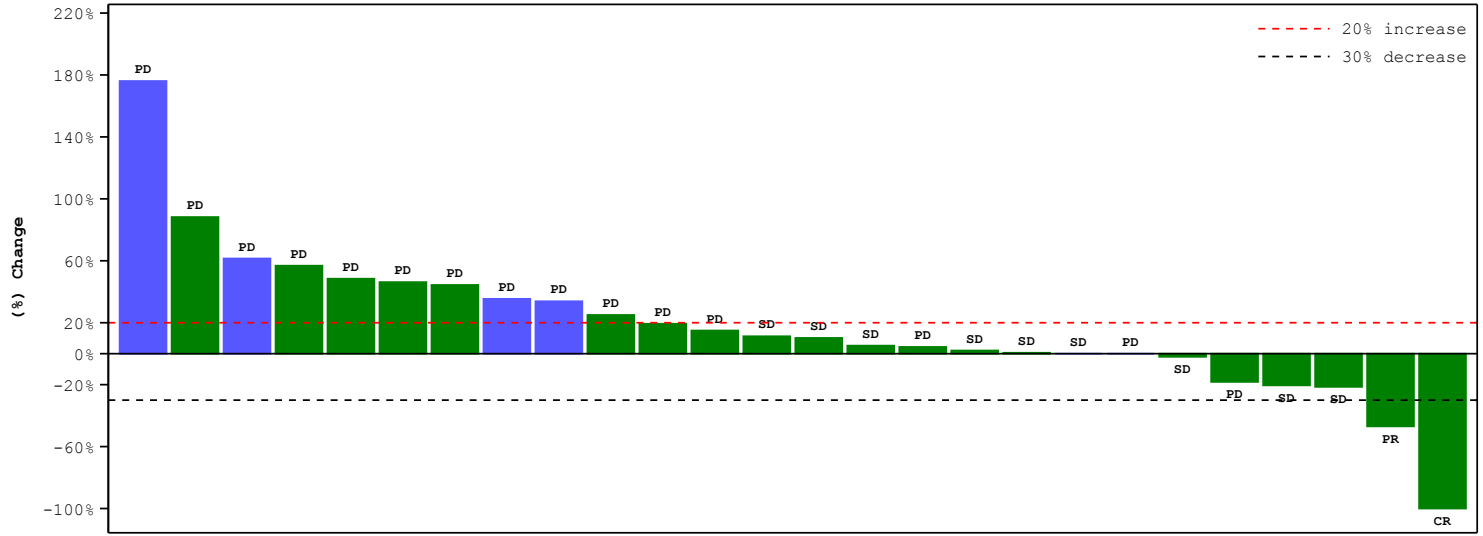
Combination therapy:
- Fatigue (30.5%)
- Anemia (27.1%)
- Diarrhoea (23.7%)
- Nausea (16.9%)
- Neutropenia (11.9%)

DKN-01 Related TESAEs

Monotherapy:
- Acute kidney injury (1.9%)
- Dyspnoea (1.9%)
- Nausea (1.9%)
- Oedema peripheral (1.9%)

Combination therapy:
- Anemia (1.7%)
- Colitis (1.7%)
- Hypokalemia (1.7%)
- Paresthesia (1.7%)

DKN-01 Monotherapy - Endometrial Cancer Overall Response



	Status	N	ORR	DCR	CR	PR	SD	PD	NE
EEC monotherapy	Wnt altered	21	10%	48%	1	1	8	10	1
	Non - Wnt altered	8	0%	13%	0	0	1	5	2

1 CR, 1 PR (ORR 10%) and 8 SD (50% DCR) vs. 1 SD (DCR 16.7%)

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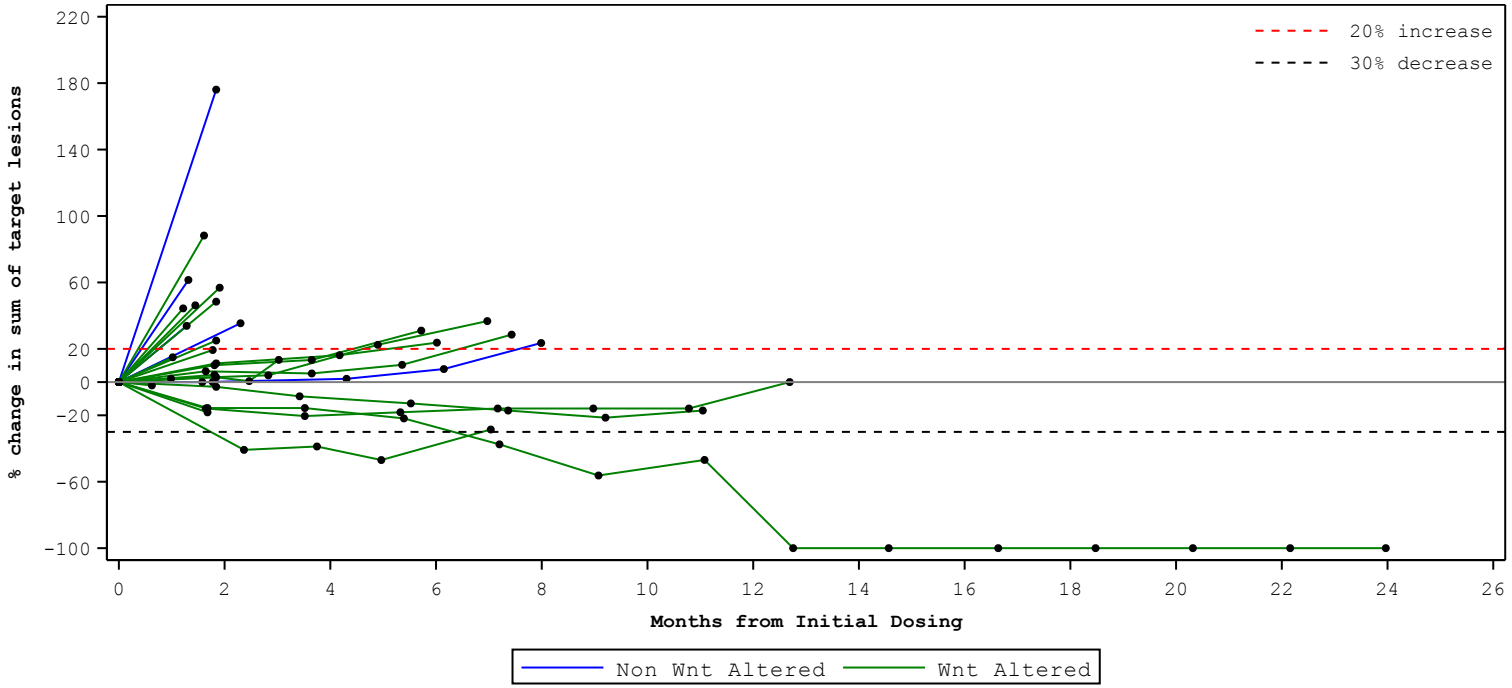
DKN-01 Monotherapy - Endometrial Cancer Durable Clinical Benefit



1 CR, 1 PR (ORR 10%) and 8 SD (50% DCR) vs. 1 SD (DCR 16.7%)

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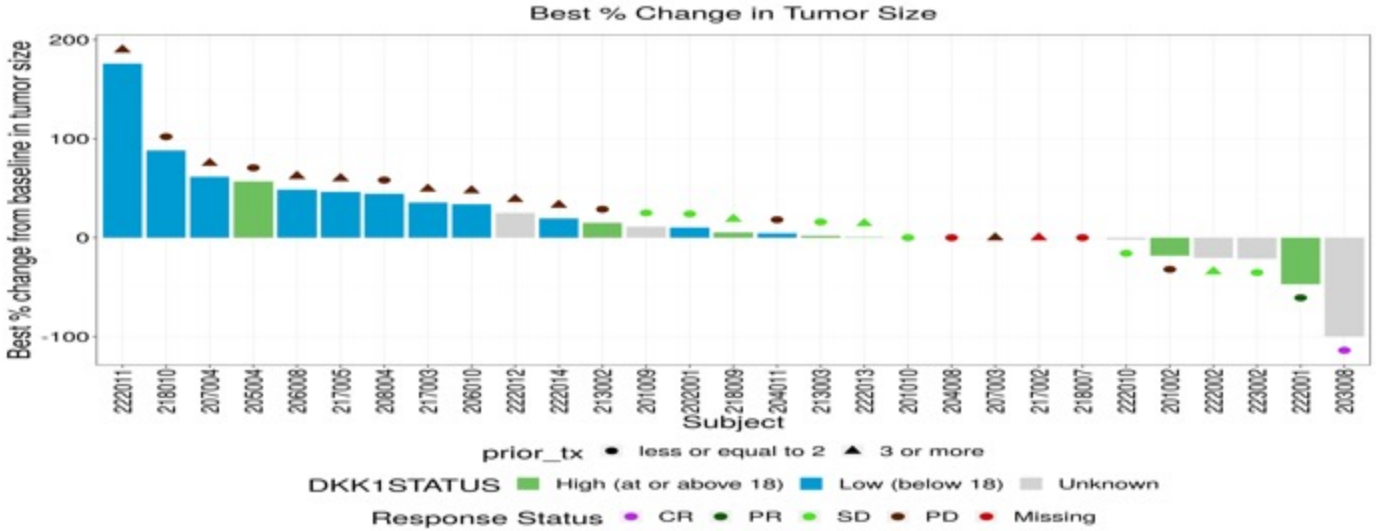
DKN-01 Monotherapy - Overall Response by DKK1 Tumoral Expression



	Status	N	ORR	DCR	CR	PR	SD	PD	NE
EEC monotherapy	DKK1-high (≥18)*	7	14%	57%	0	1	3	3	0
	DKK1-low (<18)	15	0%	7%	0	0	1	11	3
	Unknown	7	14%	86%	1	0	5	1	0

DKK1-high tumors have better ORR (14% vs. 0%) and clinical benefit (57% vs. 7%)

Patients with unknown DKK1 expression include CR, 86% DCR, and 3 patients with durable SD and Wnt activating mutations

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

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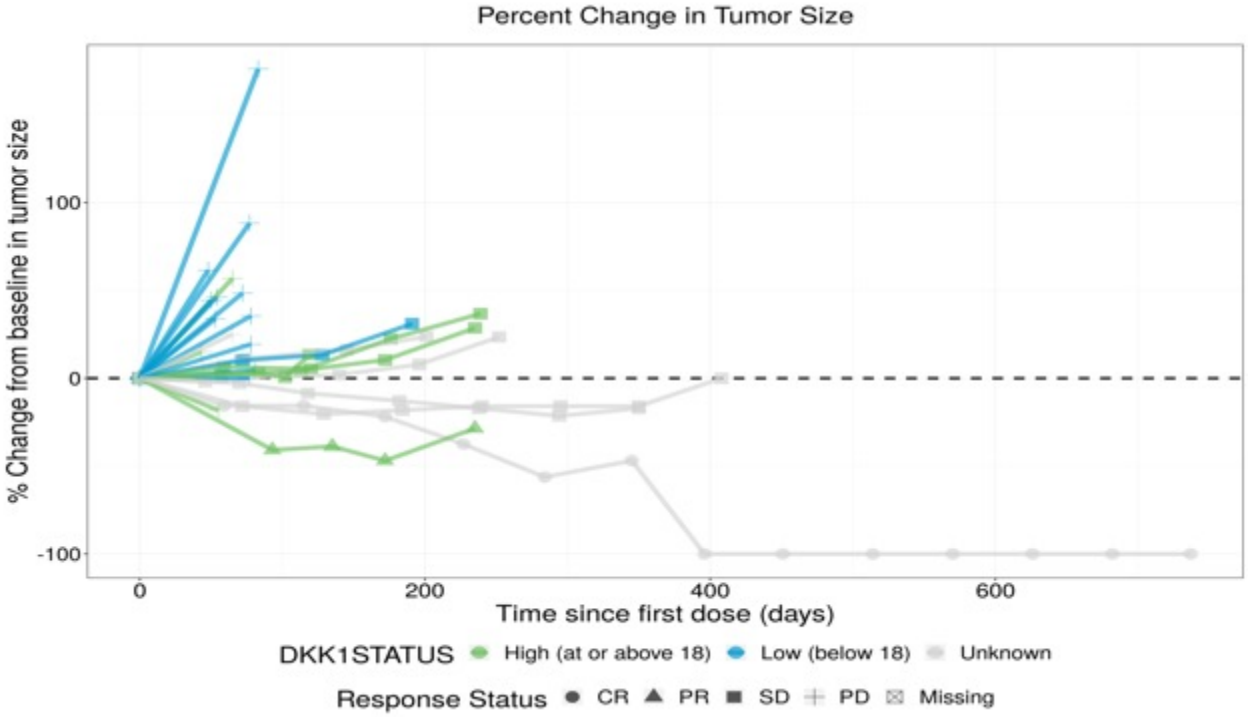
DKN-01 Monotherapy - Durable Clinical Benefit in DKK1-high Tumors



DKK1-high patients have more durable clinical benefit

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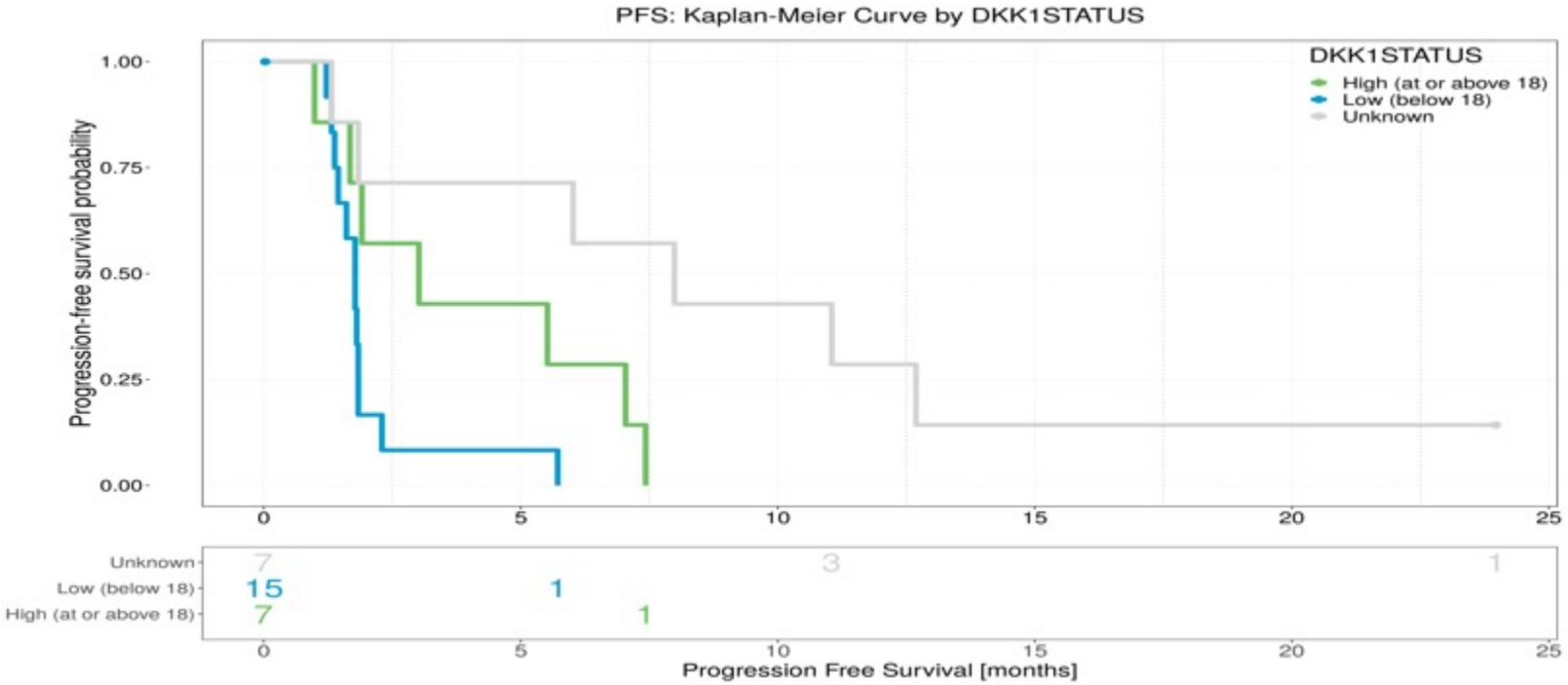
DKN-01 Monotherapy - Improved PFS with High Tumoral DKK1 Expression



DKK1-high patients have longer PFS (3.0 vs. 1.8 months [HR 0.39; 95 CI: 014, 1.1])

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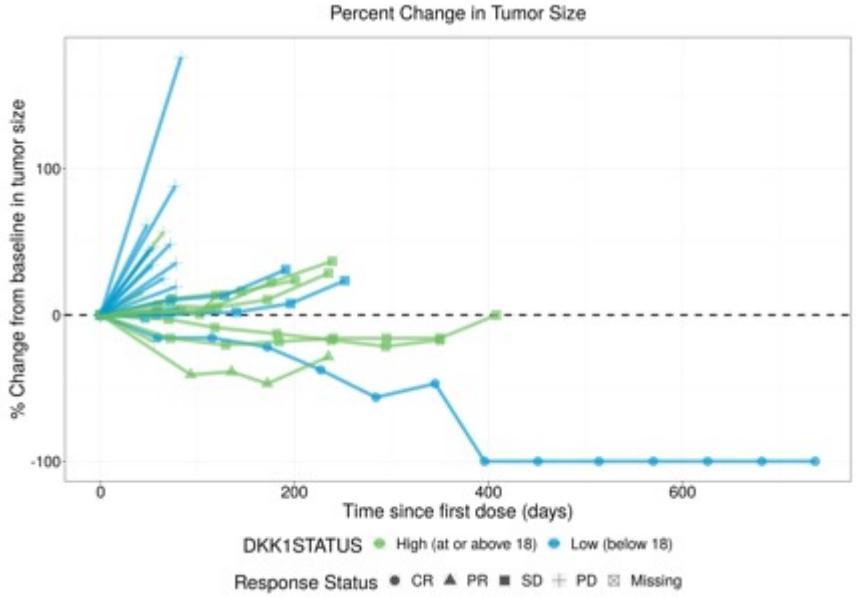
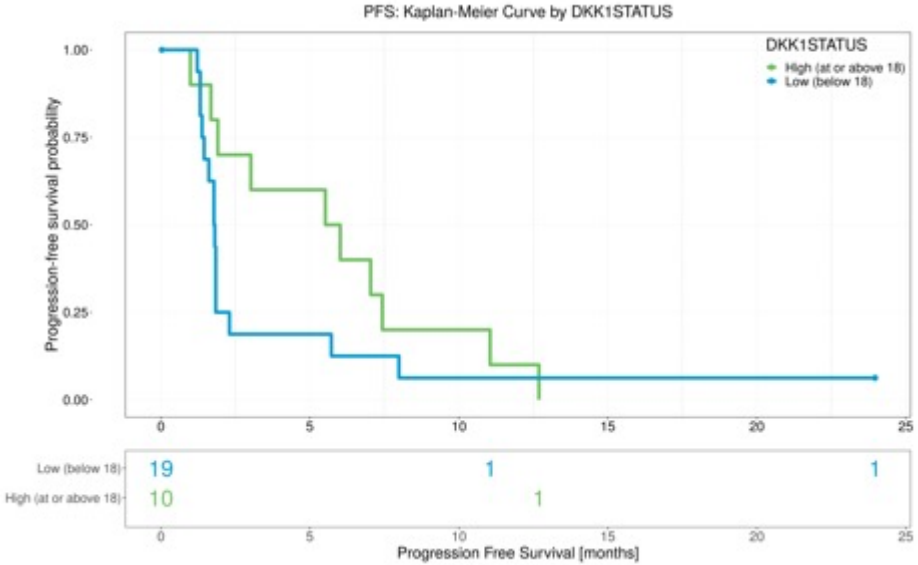
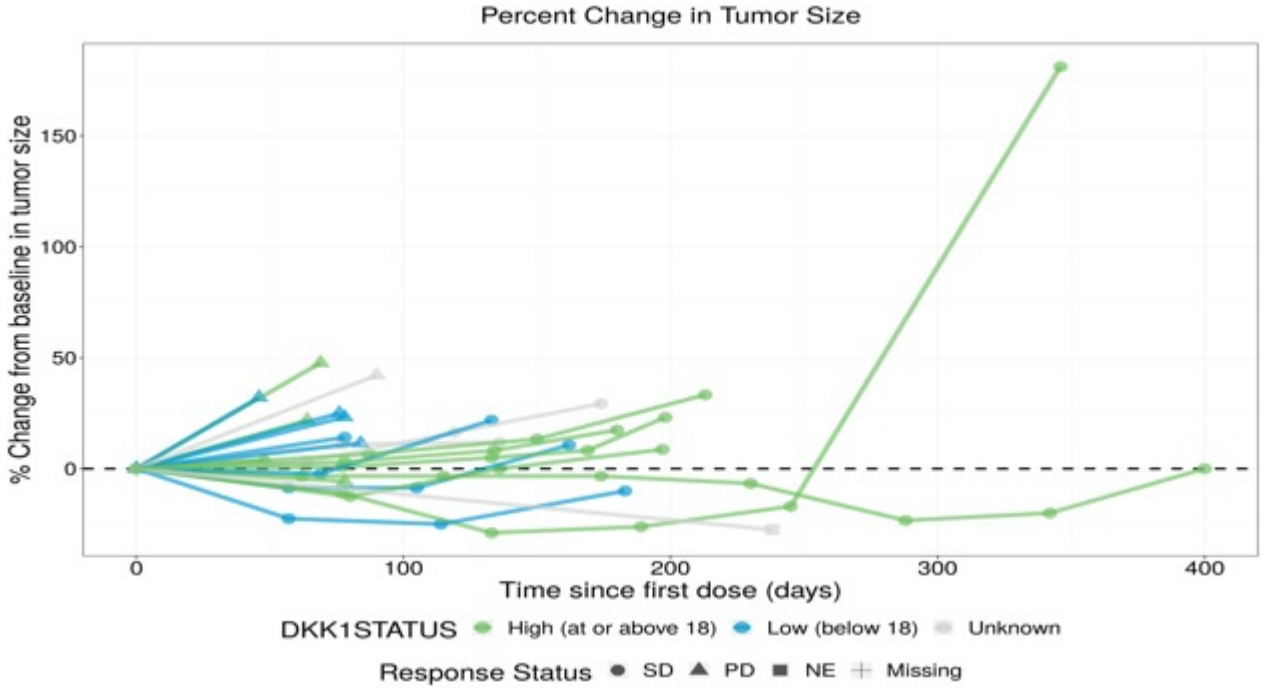
DKN-01 Monotherapy Sensitivity Analysis

- Sensitivity analysis reflecting 3 patients with known Wnt activating mutations considered to be DKK1-high
- Strengthens PFS compared to DKK1 low to 5.8 mos vs 1.8 mos (HR 0.565, 95% CI: 0.25, 1.28)





DKN-01 + Paclitaxel - Durable Clinical Benefit with High DKK1 Tumoral Expression



DKK1-high patients have more durable clinical benefit and longer PFS

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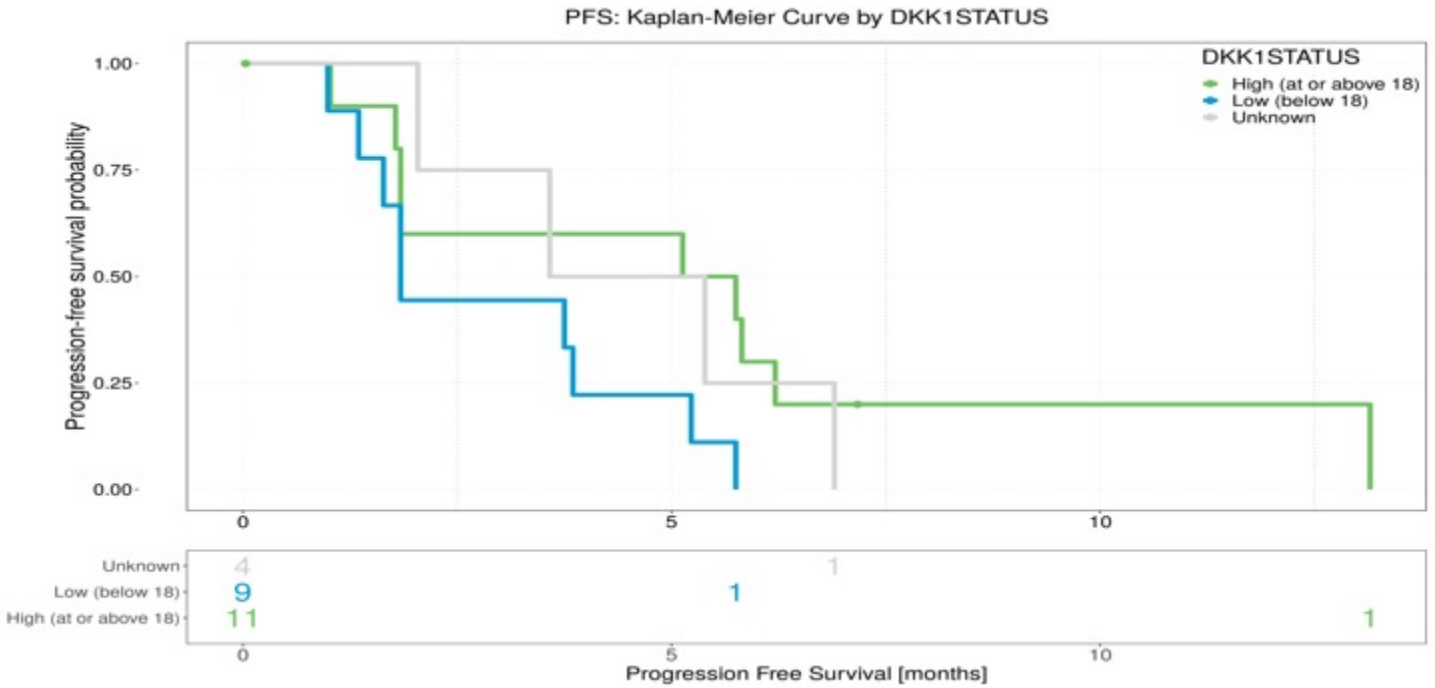
DKN-01 + Paclitaxel - Improved PFS with High Tumoral DKK1 Expression



DKK1-high patients have longer PFS (5.4 vs. 1.8 months [HR 0.34; 95 CI: 0.12, 0.97])

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Corporate Strategy

Leap-BeiGene Strategic Partnership

DKN-01 DEVELOPMENT

Option and License Agreement

Upfront Payment **$8M**

Option Fee **$3M**

Equity Investment **$5M**

> $10M

Option exercise fee

Based on data from DKN-01 plus tislelizumab combination studies in gastric cancer

Asia (excluding Japan), Australia, and New Zealand

$132M

Total Option Exercise, Clinical, Regulatory, and Commercial Milestones

Royalties

High-single digit to mid-teen double digits

Management Team

Christopher Mirabelli, PhD
Chairman of the Board

Douglas Onsi
President & Chief Executive Officer

Gus Lawlor
Chief Operating Officer

Cyndi Sirard, MD
Chief Medical Officer

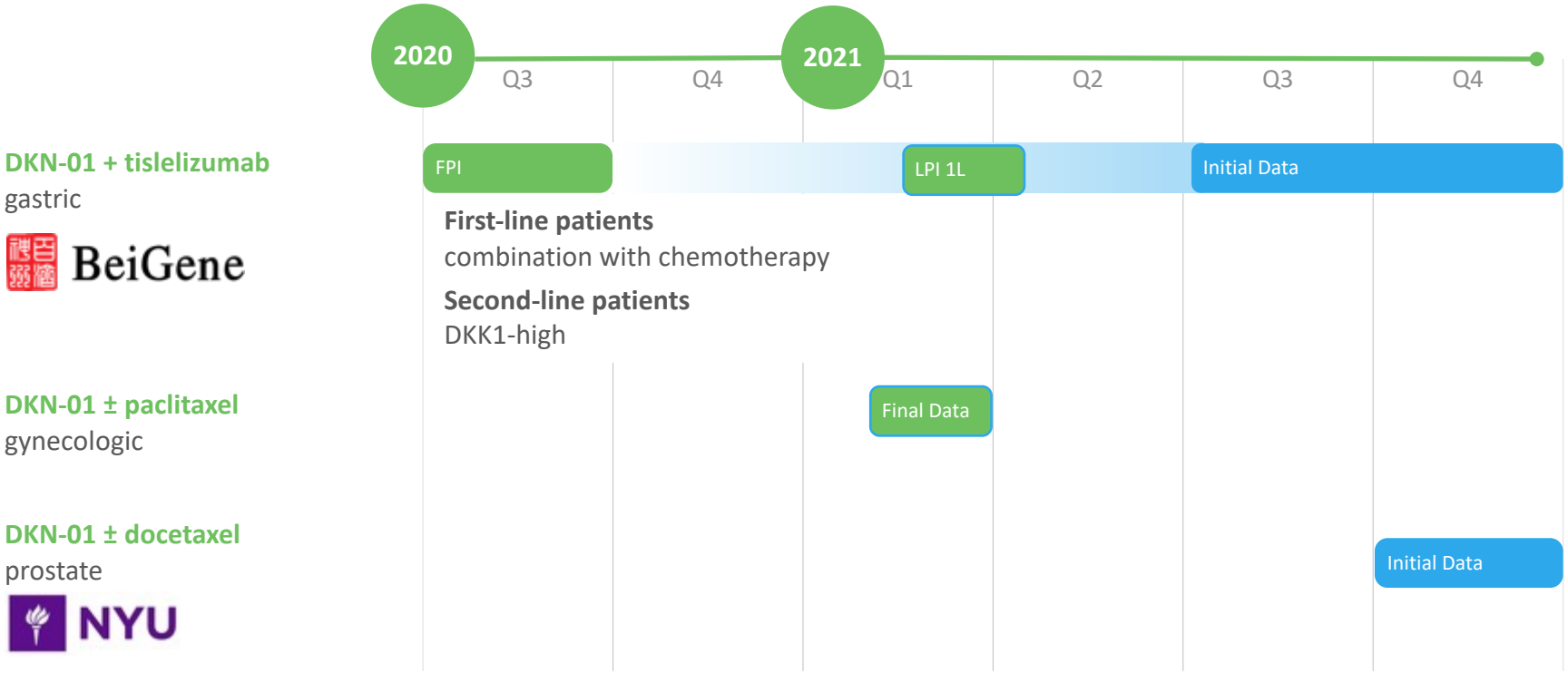
Mark O'Mahony
Chief Manufacturing Officer

Walter Newman, PhD
Senior Research Fellow

Jason Baum, PhD
Vice President, Head of Translational Medicine

Christine Granfield
Vice President, Head of Regulatory Affairs and Quality

Leap 2021 Objectives and Milestones



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