1차 치료 / Combi

KEYNOTE 189

KR-KEY-00389 12/2022

Selected Safety Information (SSI)

MSD's promotional materials are mandated to present Selected Safety Information aiming for balanced delivery of product advantages and limitations.

Here you can find **the latest version of KEYTRUDA's Selected Safety Information.**

Please read before entering.

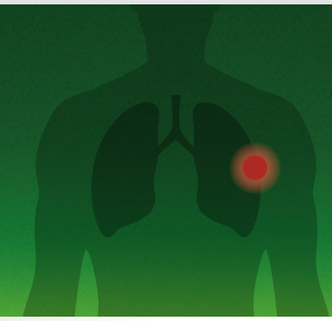
SSI 바로가기

KR-KEY-00229

KR-KEY-00389 12/2022

Updated Analysis of KEYNOTE-189 Study Design

PD-L1 발현율에 관계없이 전이성 비편평 비소세포폐암의 1차 치료로서 병용요법 연구[1,a]



KEYNOTE-189

전이성 비편평 비소세포폐암에 대한 무작위, 이중 눈가림, 다기관 3상 임상연구

▶ **Primary endpoint :** 전체 생존기간(OS), 무진행 생존기간(PFS) ▶ **Secondary endpoint :** 객관적 반응률(ORR), 반응 지속기간(DOR), 안전성

전이성 비편평 비소세포폐암 환자 (n=616)

- PD-L1 발현율에 관계없이
- 이전에 전신 치료 경험이 없는 환자
- EGFR, ALK 변이가 없는 환자
- ECOG PS 0 또는 1

→ **2:1로 환자 무작위 배정**

키트루다 병용요법 (n=410)

키트루다 200 mg + Pemetrexed 500 mg/m^2 + Cisplatin 75 mg/m^2 또는 Carboplatin AUC 5 mg/mL/min (Q3W, 4회)

→ **키트루다** 200 mg + Pemetrexed 500 mg/m^2 (Q3W)

→ 총합 35회까지 투여 (질환이 진행되거나 허용 불가능한 독성이 발생하지 않은 경우)

Placebo 병용요법 (n=206)

Placebo (saline) 200 mg + Pemetrexed 500 mg/m^2 + Cisplatin 75 mg/m^2 또는 Carboplatin AUC 5 mg/mL/min (Q3W, 4회)

→ Placebo (saline) 200 mg + Pemetrexed 500 mg/m^2 (Q3W)

→ 총합 35회까지 투여 (질환이 진행된 경우 키트루다 단독요법으로 crossover 허용)

- **Exploratory endpoint:**
  - 뇌전이 또는 간전이를 동반한 전이성 비편평 비소세포폐암 환자의 OS, PFS 분석
  - 1차에서 키트루다 투여군에 배정된 환자들의 2차 치료에서의 무진행 생존기간(PFS-2)
- **Stratification factors:**
  - PD-L1 (TPS <1% vs. ≥1%)
  - 백금요법 (Cisplatin vs. Carboplatin)
  - 흡연 이력 (없음 vs. 있음)

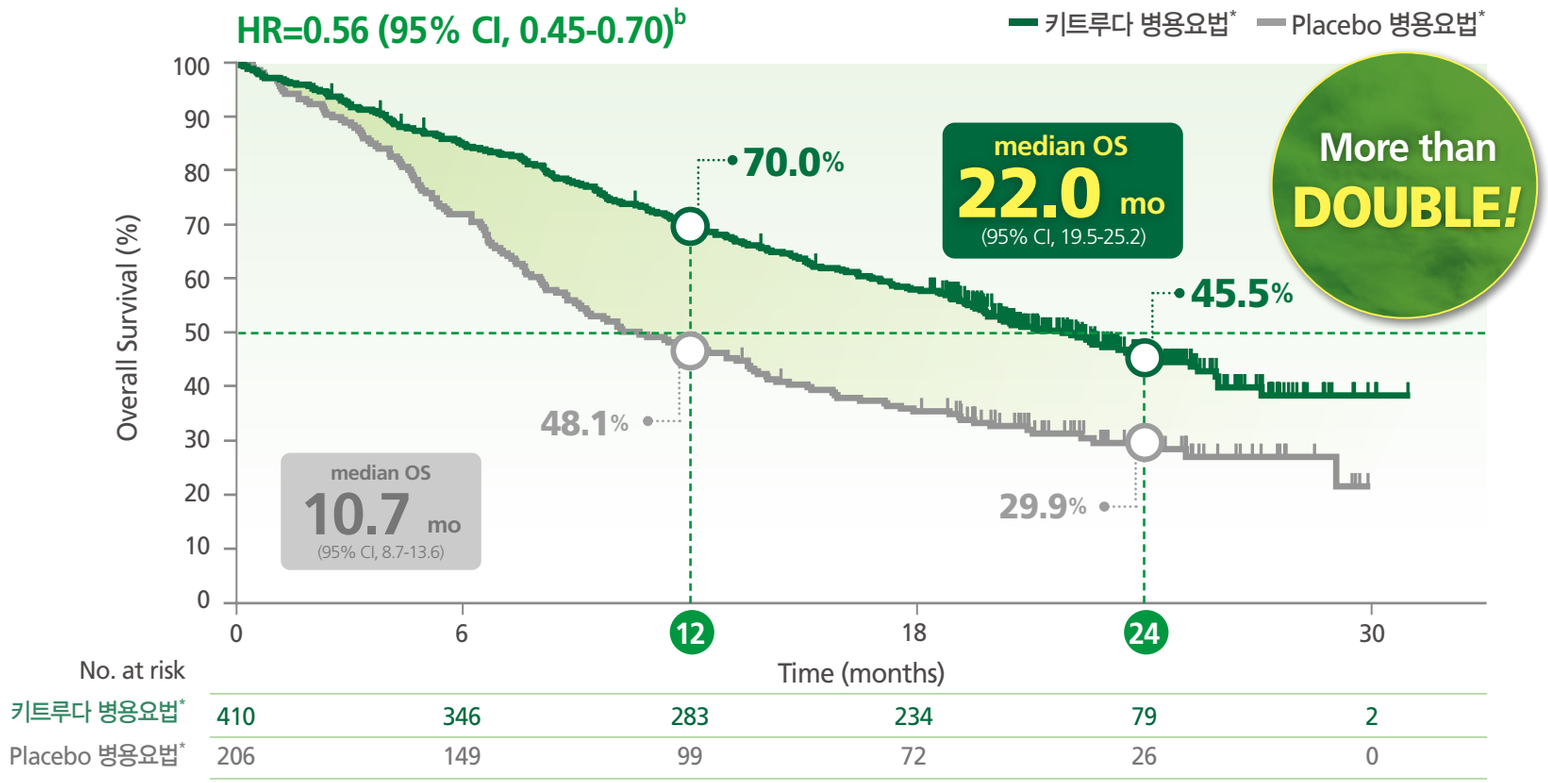
a. Median(range) study follow-up(time from randomization to database cutoff) was 23.1(18.6-30.9) months. Data cutoff : Sep. 21, 2018.
PD-L1 : Programmed death ligand 1, **OS :** Overall survival, **PFS :** Progression-free survival, **ORR :** Objective response rate, **DOR :** Duration of response, **EGFR :** Epidermal growth factor receptor, **ALK :** Anaplastic lymphoma kinase, **ECOG PS :** Eastern Cooperative Oncology Group performance status, **Q3W :** Every 3 weeks, **AUC :** Area under the curve, **TPS :** Tumor proportion score

Reference & Study design

KR-KEY-00389 12/2022

전체 생존기간 (OS) - Total Population

Kaplan-Meier Estimates of OS in KEYNOTE-189[1,a]



- 전체 생존기간 중앙값은 키트루다 병용요법* 투여군에서 22.0개월(95% CI, 19.5-25.2), Placebo 병용요법* 투여군에서 10.7개월(95% CI, 8.7-13.6)이었습니다.
- Placebo 병용요법* 투여군 중 84명(40.8%)의 환자가 질병 진행 후 키트루다 단독요법으로 cross-over하였습니다.

Adapted from Gadgeel S, *et al.*[1]

키트루다 병용요법* 투여군은, Placebo 병용요법* 투여군 대비

사망 위험 44% 감소 & mOS 2배 이상 연장

* pemetrexed 500 mg/m^2 + platinum(cisplatin 75 mg/m^2 or carboplatin AUC 5 mg/mL/min)
a. Median(range) study follow-up(time from randomization to database cutoff) was 23.1(18.6-30.9) months. Data cutoff : Sep. 21, 2018.
b. A stratified Cox proportional hazards model with Efron's method of tie handling was used to determine HRs and 95% CIs.
OS : Overall survival, **mOS :** Median overall survival, **HR :** Hazard ratio, **CI :** Confidence interval, **mo :** Months

Reference & Study design

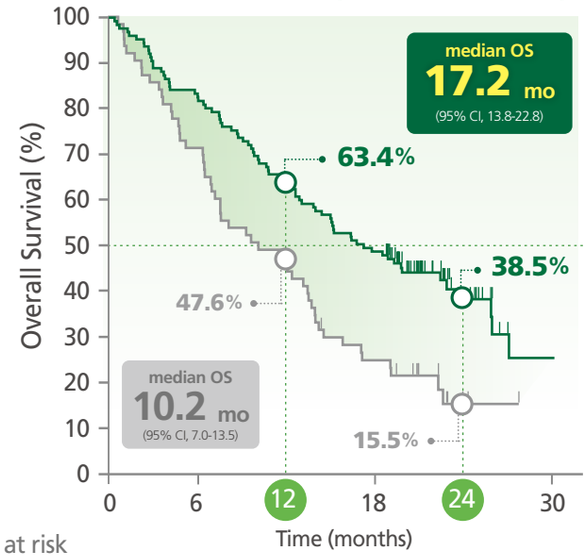
전체 생존기간 (OS) - According to PD-L1 TPS

Kaplan-Meier Estimates of OS in KEYNOTE-189[1,a]

키트루다 병용요법* Placebo 병용요법*

PD-L1 TPS <1%

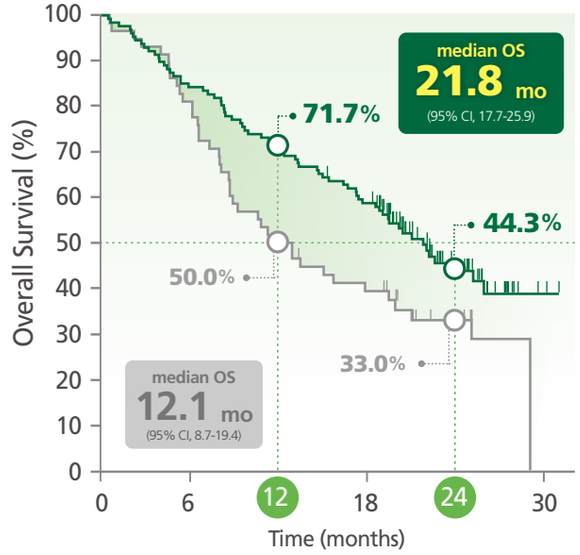
HR=0.52 (95% CI, 0.36-0.74)[b]



No. at risk						
키트루다 병용요법*	127	104	79	61	17	0
Placebo 병용요법*	63	45	30	15	2	0

PD-L1 TPS 1-49%

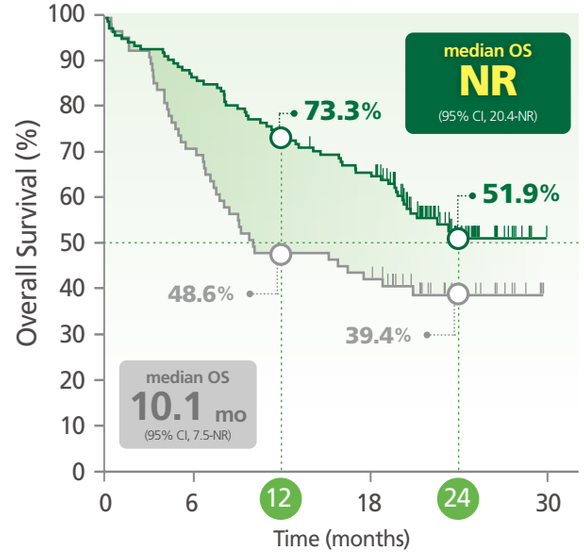
HR=0.62 (95% CI, 0.42-0.92)[b]



키트루다 병용요법*	128	107	91	74	26	2
Placebo 병용요법*	58	47	29	22	11	0

PD-L1 TPS ≥50%

HR=0.59 (95% CI, 0.39-0.88)[b]



키트루다 병용요법*	132	114	95	85	29	0
Placebo 병용요법*	70	50	34	30	11	0

Adapted from Gadgeel S, *et al.*[1]

키트루다 병용요법* 투여군은, Placebo 병용요법* 투여군 대비

PD-L1 발현율에 관계없이 사망 위험 감소 & mOS 연장

* pemetrexed 500 mg/m^2 + platinum(cisplatin 75 mg/m^2 or carboplatin AUC 5 mg/mL/min)

a. Median(range) study follow-up(time from randomization to database cutoff) was 23.1(18.6-30.9) months. Data cutoff : Sep. 21, 2018.

b. A stratified Cox proportional hazards model with Efron's method of tie handling was used to determine HRs and 95% CIs.

OS : Overall survival, **mOS :** Median overall survival, **TPS :** Tumor proportion score, **PD-L1 :** Programmed death ligand 1, **NR :** Not reached, **HR :** Hazard ratio, **CI :** Confidence interval, **mo :** Months

Reference & Study design

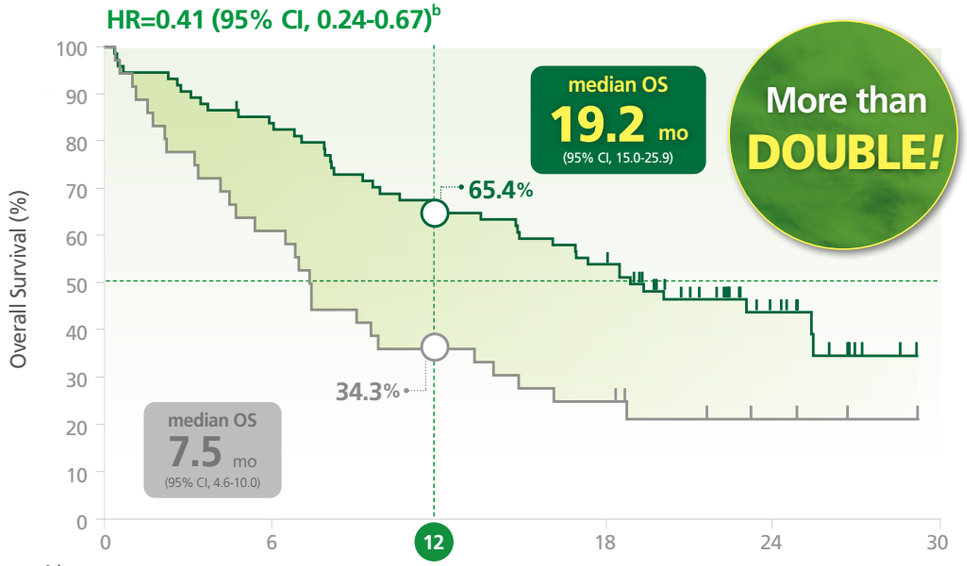
전체 생존기간 (OS) - Brain Metastasis

Kaplan-Meier Estimates of OS in KEYNOTE-189[1,a]

키트루다 병용요법* Placebo 병용요법*

With Brain Metastases

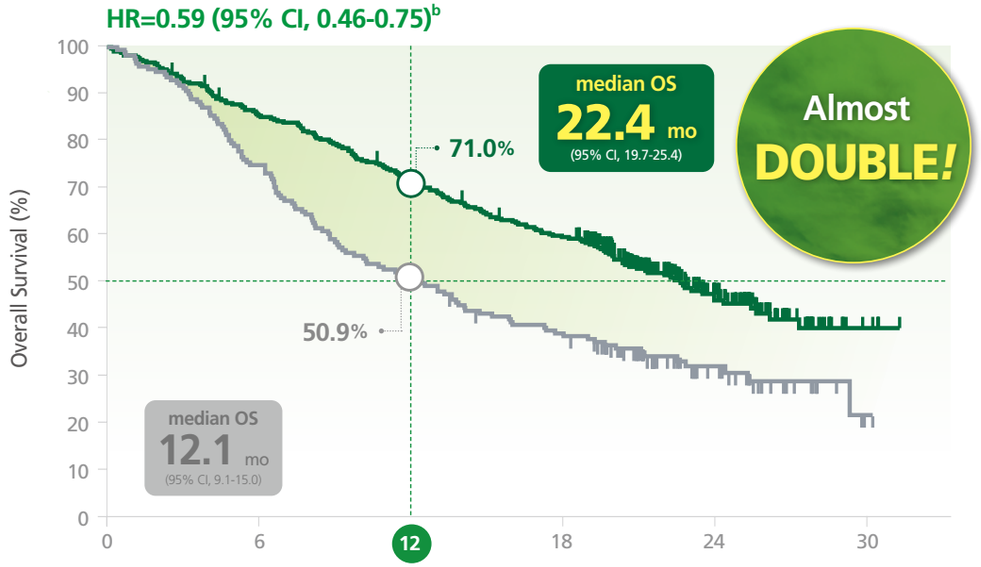
HR=0.41 (95% CI, 0.24-0.67)[b]



No. at risk						
키트루다 병용요법*	73	61	47	38	14	0
Placebo 병용요법*	35	21	12	8	3	0

Without Brain Metastases

HR=0.59 (95% CI, 0.46-0.75)[b]



키트루다 병용요법*	337	285	236	196	65	2
Placebo 병용요법*	171	128	87	64	23	0

Adapted from Gadgeel S, *et al.*[1]

키트루다 병용요법* 투여군은, Placebo 병용요법* 투여군 대비

뇌전이 동반 여부와 관계없이 사망 위험 감소 및 mOS 약 2배 연장

* pemetrexed 500 mg/m^2 + platinum(cisplatin 75 mg/m^2 or carboplatin AUC 5 mg/mL/min)
a. Median(range) study follow-up(time from randomization to database cutoff) was 23.1(18.6-30.9) months. Data cutoff : Sep. 21, 2018.
b. A stratified Cox proportional hazards model with Efron's method of tie handling was used to determine HRs and 95% CIs.
OS : Overall survival, **mOS :** Median overall survival, **HR :** Hazard ratio, **CI :** Confidence interval, **mo :** Months

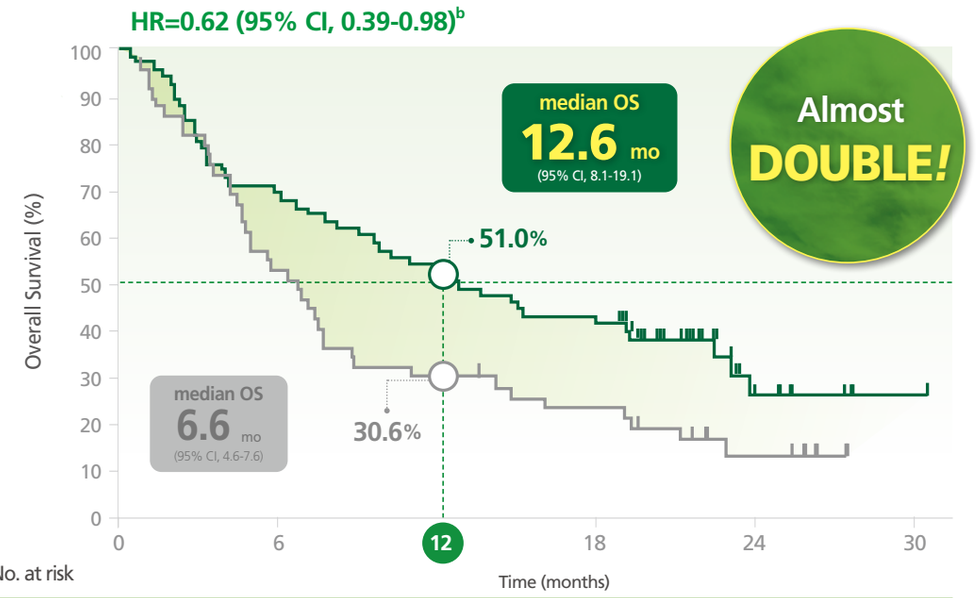
Reference & Study design

전체 생존기간 (OS) - Liver Metastasis

Kaplan-Meier Estimates of OS in KEYNOTE-189[1,a]

키트루다 병용요법* Placebo 병용요법*

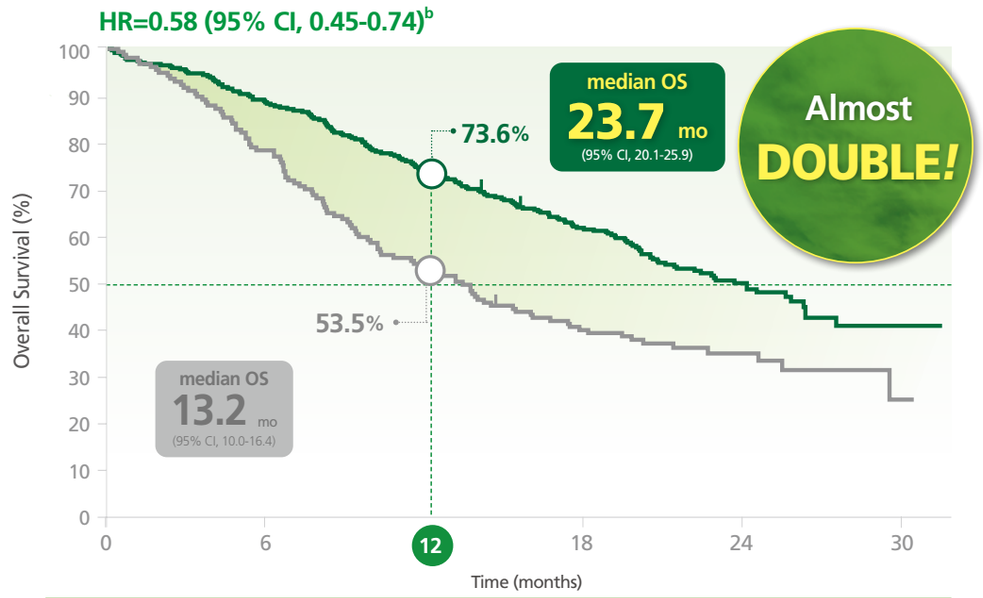
With Liver Metastases



No. at risk

키트루다 병용요법*	66	45	33	27	5	1
Placebo 병용요법*	49	26	15	11	4	0

Without Liver Metastases



키트루다 병용요법*	344	301	250	207	74	1
Placebo 병용요법*	157	123	84	61	22	0

Adapted from Gadgeel S, *et al.*[1]

키트루다 병용요법* 투여군은, Placebo 병용요법* 투여군 대비

간전이 동반 여부와 관계없이 사망 위험 감소 및 mOS 약 2배 연장

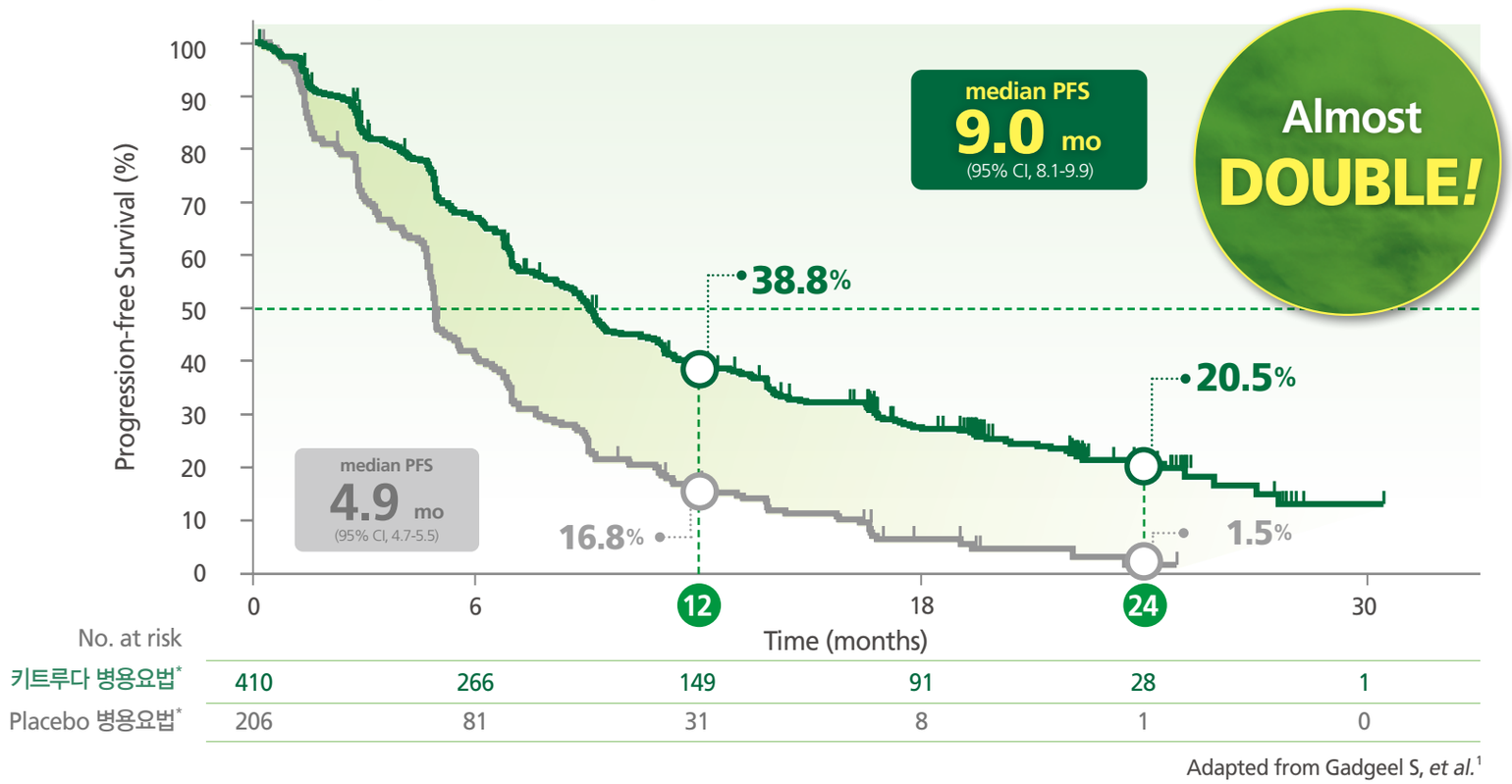
* pemetrexed 500 mg/m^2 + platinum(cisplatin 75 mg/m^2 or carboplatin AUC 5 mg/mL/min)
a. Median(range) study follow-up(time from randomization to database cutoff) was 23.1(18.6-30.9) months. Data cutoff : Sep. 21, 2018.
b. A stratified Cox proportional hazards model with Efron's method of tie handling was used to determine HRs and 95% CIs.
OS : Overall survival, **mOS :** Median overall survival, **HR :** Hazard ratio, **CI :** Confidence interval, **mo :** Months

Reference & Study design

무진행 생존기간 (PFS) - Total Population

Kaplan-Meier Estimates of PFS in KEYNOTE-189[1,a]

HR=0.48 (95% CI, 0.40-0.58)[b]



No. at risk						
키트루다 병용요법*	410	266	149	91	28	1
Placebo 병용요법*	206	81	31	8	1	0

Adapted from Gadgeel S, *et al.*[1]

- 무진행 생존기간 중앙값은 키트루다 병용요법* 투여군에서 9.0개월(95% CI, 8.1-9.9), Placebo 병용요법* 투여군에서 4.9개월(95% CI, 4.7-5.5)이었습니다.

키트루다 병용요법* 투여군은, Placebo 병용요법* 투여군 대비

질병 진행 또는 사망 위험 52% 감소 & mPFS 약 2배 연장

* pemetrexed 500 mg/m^2 + platinum(cisplatin 75 mg/m^2 or carboplatin AUC 5 mg/mL/min)
a. Median(range) study follow-up(time from randomization to database cutoff) was 23.1(18.6-30.9) months. Data cutoff : Sep. 21, 2018.
b. A stratified Cox proportional hazards model with Efron's method of tie handling was used to determine HRs and 95% CIs.
PFS : Progression-free survival, **mPFS :** Median progression-free survival, **HR :** Hazard ratio, **CI :** Confidence interval, **mo :** Months

Reference & Study design

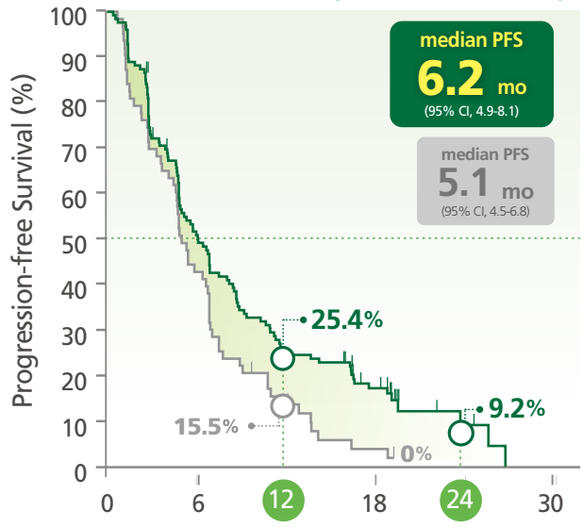
무진행 생존기간 (PFS) - According to PD-L1 TPS

Kaplan-Meier Estimates of PFS in KEYNOTE-189[1,a]

키트루다 병용요법* Placebo 병용요법*

PD-L1 TPS <1%

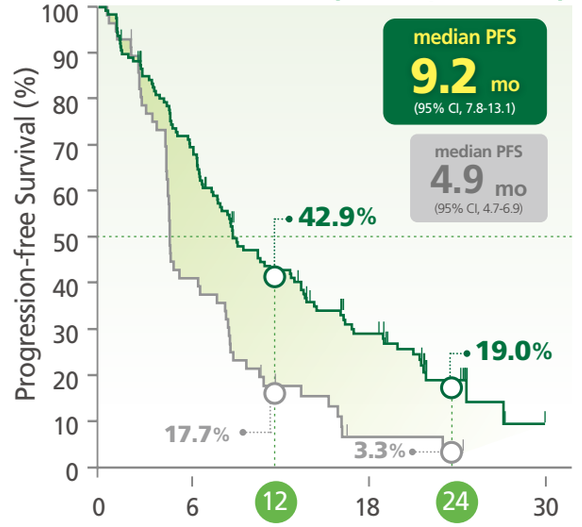
HR=0.64 (95% CI, 0.47-0.89)[b]



No. at risk						
키트루다 병용요법*	127	63	31	17	3	0
Placebo 병용요법*	63	27	9	2	0	0

PD-L1 TPS 1-49%

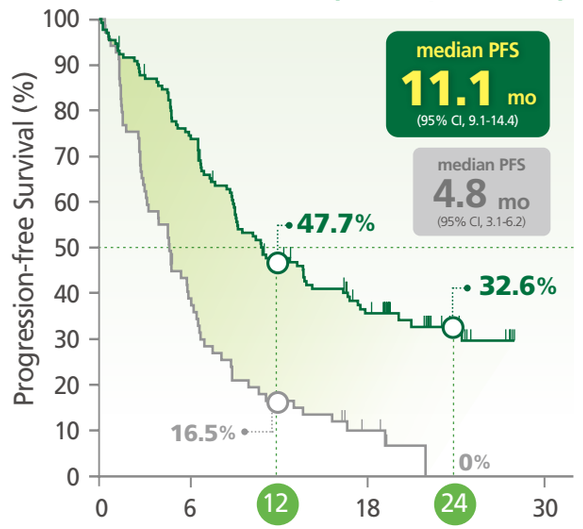
HR=0.51 (95% CI, 0.36-0.73)[b]



128	89	50	29	11	1
58	23	8	2	1	0

PD-L1 TPS ≥50%

HR=0.36 (95% CI, 0.26-0.51)[b]



132	97	59	40	12	0
70	27	11	4	0	0

Adapted from Gadgeel S, *et al.*[1]

키트루다 병용요법* 투여군은, Placebo 병용요법* 투여군 대비

PD-L1 발현율에 관계없이 mPFS 연장

* pemetrexed 500 mg/m^2 + platinum(cisplatin 75 mg/m^2 or carboplatin AUC 5 mg/mL/min)

a. Median(range) study follow-up(time from randomization to database cutoff) was 23.1(18.6-30.9) months. Data cutoff : Sep. 21, 2018.

b. A stratified Cox proportional hazards model with Efron's method of tie handling was used to determine HRs and 95% CIs.

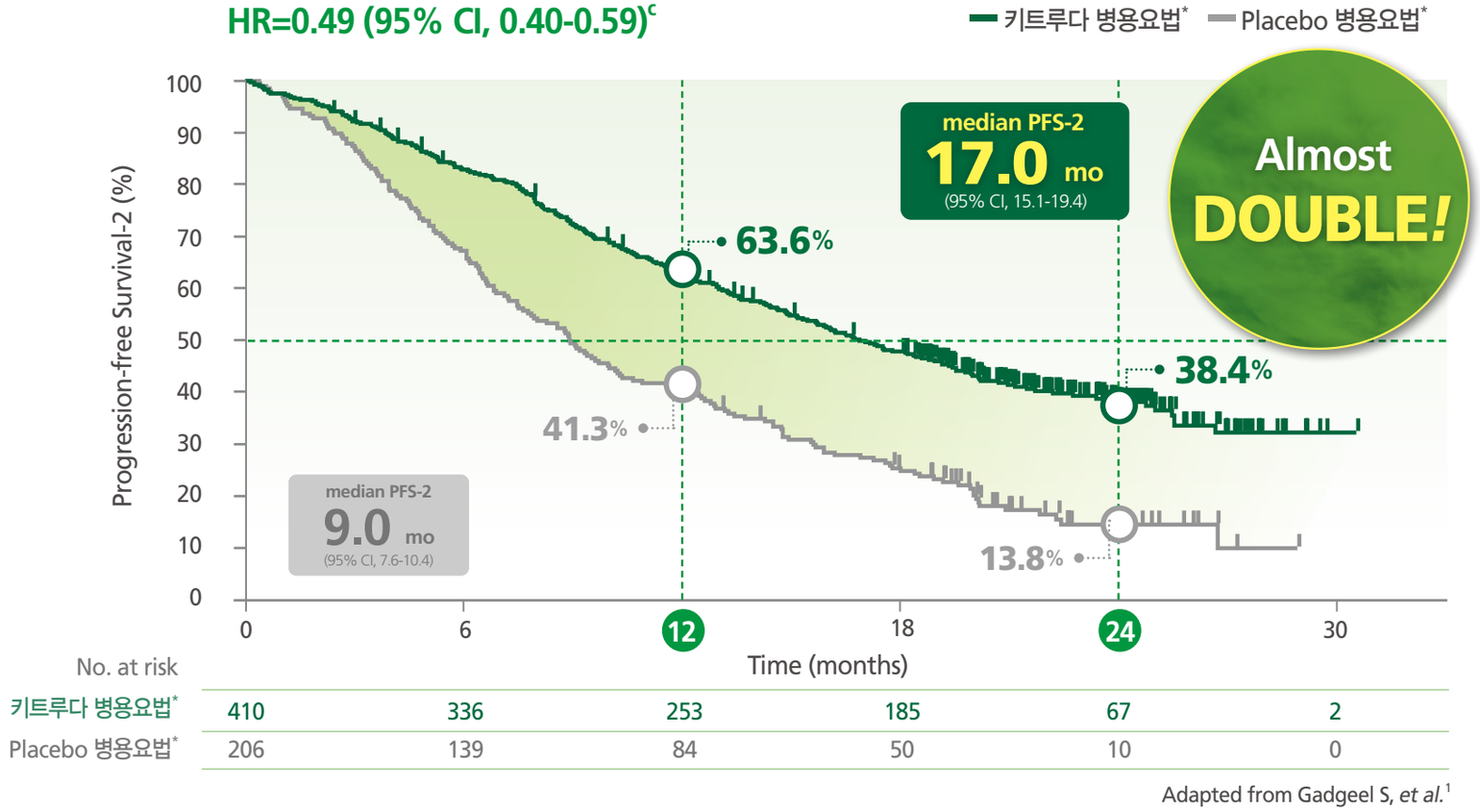
PFS : Progression-free survival, **mPFS :** Median progression-free survival, **TPS :** Tumor proportion score, **PD-L1 :** Programmed death ligand 1, **HR :** Hazard ratio, **CI :** Confidence interval, **mo :** Months

Reference & Study design

무진행 생존기간-2 (PFS-2)[a] - Total Population

Kaplan-Meier Estimates of PFS-2 in KEYNOTE-189[1,b]

HR=0.49 (95% CI, 0.40-0.59)[c]



Almost DOUBLE!

No. at risk						
키트루다 병용요법*	410	336	253	185	67	2
Placebo 병용요법*	206	139	84	50	10	0

Adapted from Gadgeel S, *et al.*[1]

- PFS-2 중앙값은 키트루다 병용요법* 투여군에서 17.0개월(95% CI, 15.1-19.4), Placebo 병용요법* 투여군에서 9.0개월(95% CI, 7.6-10.4)이었습니다.
- **1차부터 키트루다 병용요법*으로 시작**하는 것은 **다음 차수의 치료 효과**에도 **긍정적 영향**을 줍니다.

키트루다 병용요법* 투여군은, Placebo 병용요법* 투여군 대비

다음 차수 치료 중 질병 진행 또는 사망 위험 51% 감소 & mPFS-2 약 2배 연장

* pemetrexed 500 mg/m^2 + platinum(cisplatin 75 mg/m^2 or carboplatin AUC 5 mg/mL/min)
a. PFS-2 was defined as the time from randomization to objective tumor progression on next-line treatment (including subsequent anti-PD-[L]1 therapy) or death from any cause, whichever occurred first.
b. Median(range) study follow-up(time from randomization to database cutoff) was 23.1(18.6-30.9) months. Data cutoff : Sep. 21, 2018.
c. A stratified Cox proportional hazards model with Efron's method of tie handling was used to determine HRs and 95% CIs.
PFS-2 : Progression-free survival-2, **mPFS-2 :** Median progression-free survival-2, **HR :** Hazard ratio, **CI :** Confidence interval, **mo :** Months

Reference & Study design

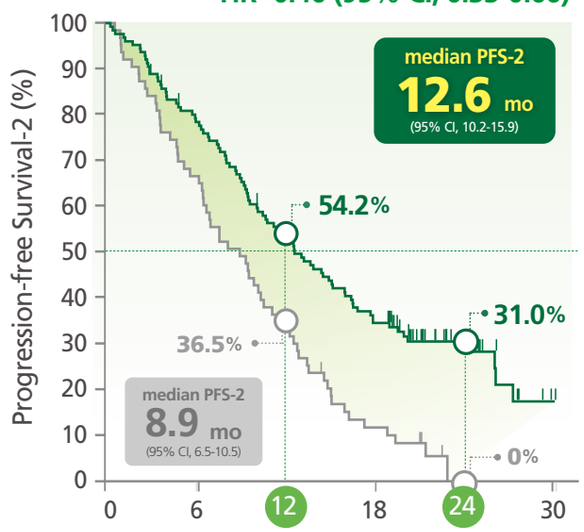
무진행 생존기간-2 (PFS-2)[a] - According to PD-L1 TPS

Kaplan-Meier Estimates of PFS-2 in KEYNOTE-189[1,b]

키트루다 병용요법* Placebo 병용요법*

PD-L1 TPS <1%

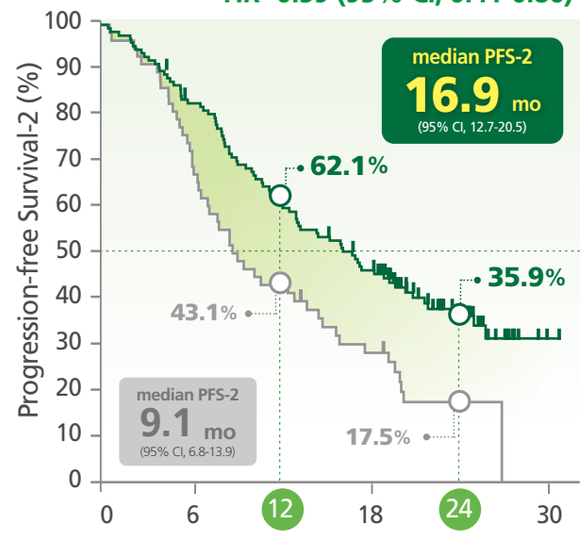
HR=0.46 (95% CI, 0.33-0.66)[c]



No. at risk						
키트루다 병용요법*	127	99	65	42	14	0
Placebo 병용요법*	63	42	23	7	0	0

PD-L1 TPS 1-49%

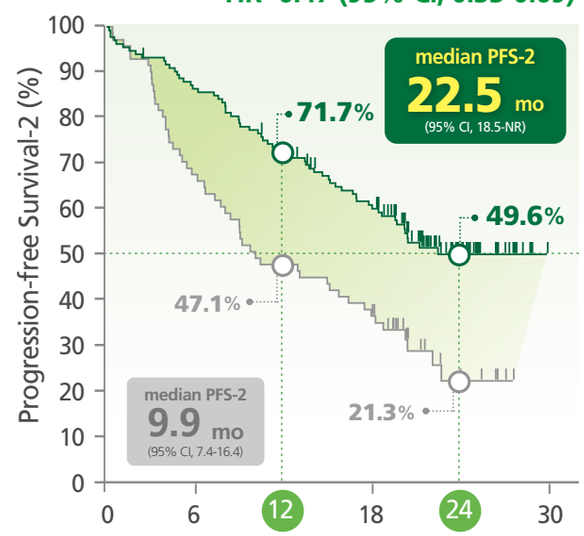
HR=0.59 (95% CI, 0.41-0.86)[c]



128	104	78	56	23	2
58	43	24	15	4	0

PD-L1 TPS ≥50%

HR=0.47 (95% CI, 0.33-0.69)[c]



132	113	93	75	26	0
70	47	33	25	5	0

Adapted from Gadgeel S, *et al.*[1]

키트루다 병용요법* 투여군은, Placebo 병용요법* 투여군 대비

PD-L1 발현율에 관계없이 다음 차수 치료 중 질병 진행 또는 사망 위험 감소 & mPFS-2 연장

* pemetrexed 500 mg/m^2 + platinum(cisplatin 75 mg/m^2 or carboplatin AUC 5 mg/mL/min)

a. PFS-2 was defined as the time from randomization to objective tumor progression on next-line treatment (including subsequent anti-PD-[L]1 therapy) or death from any cause, whichever occurred first.

b. Median(range) study follow-up(time from randomization to database cutoff) was 23.1(18.6-30.9) months. Data cutoff : Sep. 21, 2018.

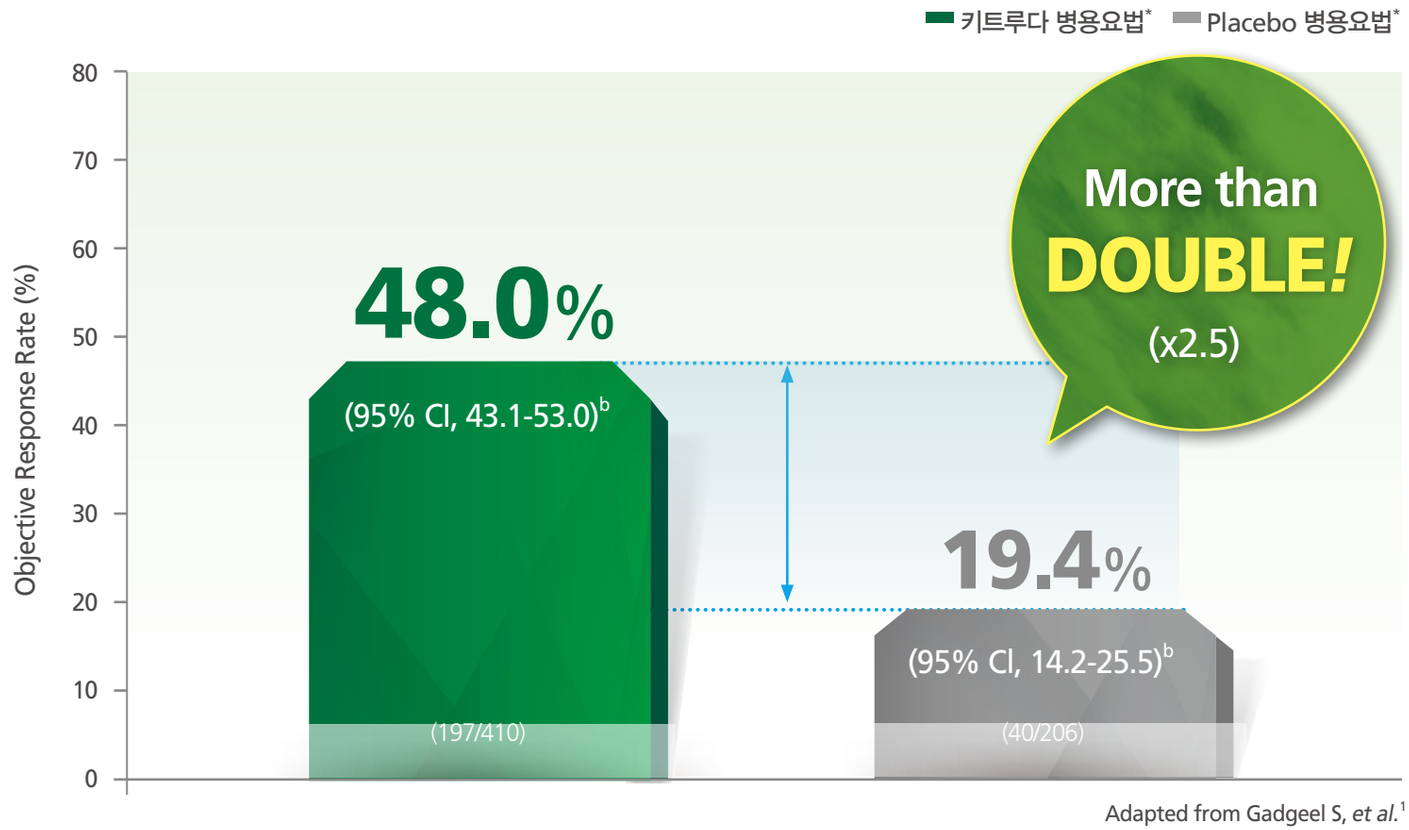
c. A stratified Cox proportional hazards model with Efron's method of tie handling was used to determine HRs and 95% CIs.

PFS-2 : Progression-free survival-2, **mPFS-2 :** Median progression-free survival-2, **TPS :** Tumor proportion score, **PD-L1 :** Programmed death ligand 1, **NR :** Not reached, **HR :** Hazard ratio, **CI :** Confidence interval, **mo :** Months

Reference & Study design

객관적 반응률 (ORR) - Total Population

ORR in KEYNOTE-189[1,a]



Adapted from Gadgeel S, *et al.*[1]

- **반응기간 중앙값(median DOR)**[c]은 키트루다 병용요법* 투여군에서 12.4개월(Range, 1.1+ to 29.0+),[d] Placebo 병용요법* 투여군에서 7.1개월(Range, 2.4 to 22.0+)[d]이었습니다.

키트루다 병용요법* 투여군은, Placebo 병용요법* 투여군 대비
객관적 반응률(ORR) 2배 이상 증가

* pemetrexed 500 mg/m^2 + platinum(cisplatin 75 mg/m^2 or carboplatin AUC 5 mg/mL/min)
a. Median(range) study follow-up(time from randomization to database cutoff) was 23.1(18.6-30.9) months. Data cutoff : Sep. 21, 2018.
b. A stratified Cox proportional hazards model with Efron's method of tie handling was used to determine 95% CIs.
c. Kaplan-Meier estimate.
d. + indicates no progressive disease by the time of last disease assessment.
ORR : Objective response rate, **DOR :** Duration of response, **CI :** Confidence interval

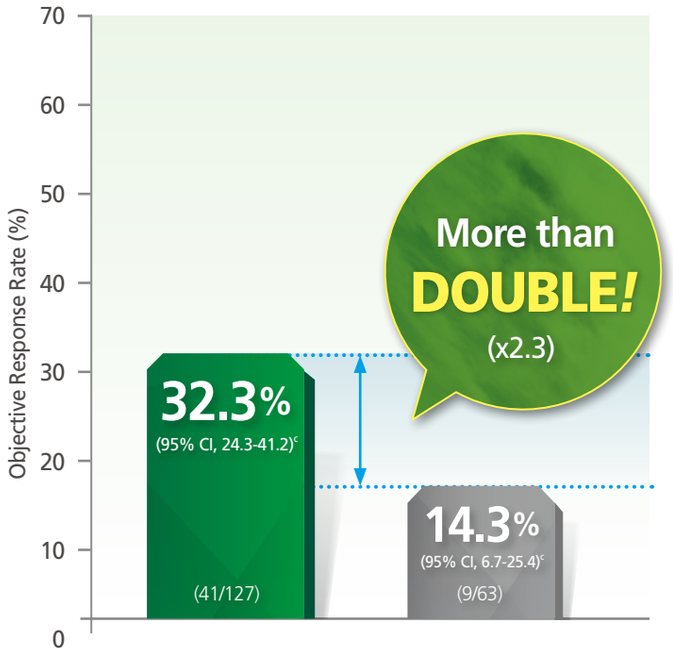
Reference & Study design

객관적 반응률 (ORR) - According to PD-L1 TPS

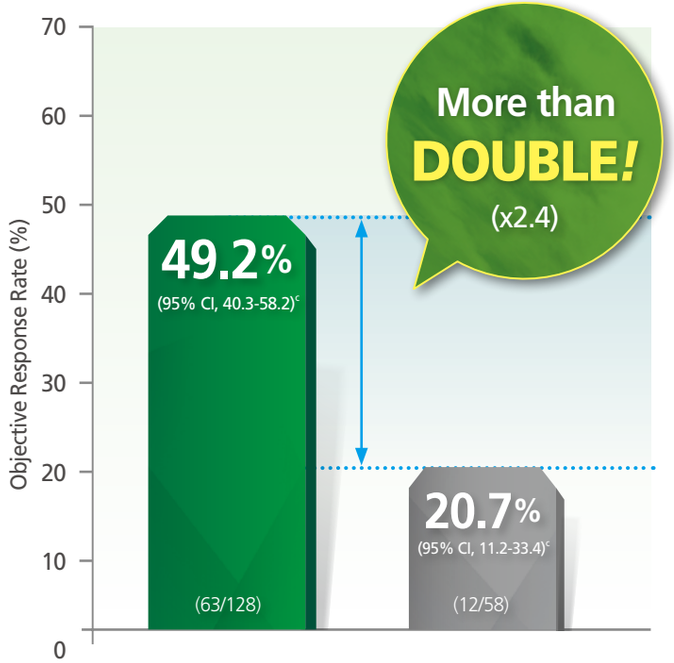
ORR in KEYNOTE-189[1,a]

키트루다 병용요법* Placebo 병용요법*

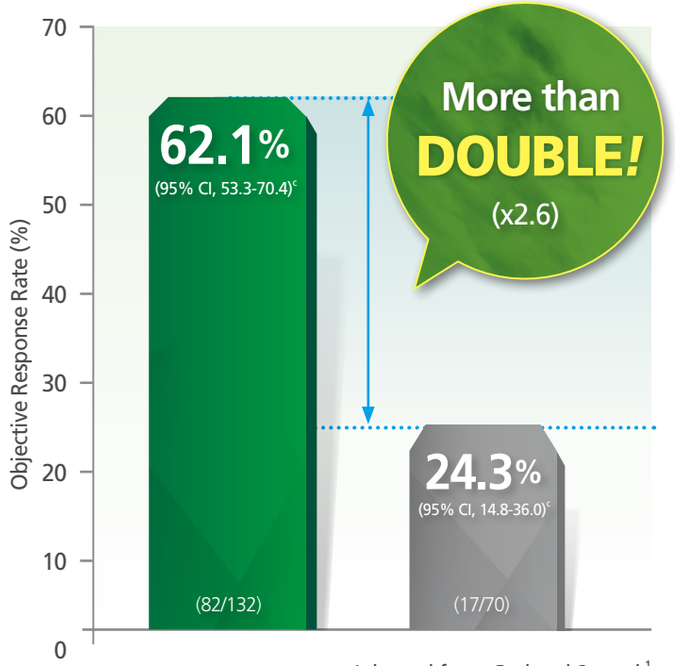
PD-L1 TPS <1%[b]



PD-L1 TPS 1-49%[b]



PD-L1 TPS ≥50%[b]



Adapted from Gadgeel S, *et al.*[1]

키트루다 병용요법* 투여군은, Placebo 병용요법* 투여군 대비

PD-L1 발현율에 관계없이 ORR 2배 이상 증가

[median DOR(months)] **TPS <1%:** 10.8(range, 1.1+ to 22.6) vs. 7.8(range, 4.1 to 18.1+), **TPS 1-49%:** 12.9(range, 2.1+ to 29.0+) vs. 7.6(range, 2.4 to 22.0+), **TPS ≥50%:** 15.1(range, 1.2+ to 26.8+) vs. 7.1(range, 3.4 to 19.4) in the KEYTRUDA combination group and placebo combination group, respectively. (+ indicates no progressive disease by the time of last disease assessment.)

* pemetrexed 500 mg/m^2 + platinum(cisplatin 75 mg/m^2 or carboplatin AUC 5 mg/mL/min)

a. Median(range) study follow-up(time from randomization to database cutoff) was 23.1(18.6-30.9) months. Data cutoff : Sep. 21, 2018.

b. Excludes 38 patients for whom PD-L1 expression could not be evaluated.

c. A stratified Cox proportional hazards model with Efron's method of tie handling was used to determine 95% CIs.

ORR : Objective response rate, **TPS :** Tumor proportion score, **PD-L1 :** Programmed death ligand 1, **CI :** Confidence interval

Reference & Study design

안전성 프로파일[a,b]

Event	키트루다 병용요법* (N = 405)	Placebo 병용요법* (N = 202)
	Number of patients (%)	
1회 이상 발생한 이상반응	404 (99.8)	200 (99.0)
3등급 이상	291 (71.9)	135 (66.8)
치료관련 이상반응으로 인한 중단	136 (33.6)	33 (16.3)
이상반응으로 인한 사망[c]	29 (7.2)	14 (6.9)
면역-매개 이상반응[d]	107 (26.4)	26 (12.9)
3등급 이상	44 (10.9)	9 (4.5)

- 가장 흔한 이상반응은 키트루다 병용요법* 투여군과 Placebo 병용요법* 투여군에서 각각 오심 56.8%(230명) vs. 53.0%(107명), 빈혈 47.4%(192명) vs. 48.5%(98명), 피로 42.5%(172명) vs. 38.6%(78명) 이었습니다.

- 가장 흔한 면역매개 이상반응은 키트루다 병용요법* 투여군과 Placebo 병용요법* 투여군에서 각각 갑상선 저하증 7.9%(32명) vs. 2.5%(5명), 갑상선기능항진증 4.9%(20명) vs. 3.0%(6명), 폐렴 4.9%(20명) vs. 3.0%(6명) 이었습니다.

키트루다 병용요법* 투여군의 이상반응 중
3등급 이상의 발생 빈도는 Placebo 병용요법* 투여군과 유사

* pemetrexed 500 mg/m^2 + platinum(cisplatin 75 mg/m^2 or carboplatin AUC 5 mg/mL/min)
a. Median(range) study follow-up(time from randomization to database cutoff) was 23.1(18.6-30.9) months. Data cutoff : Sep. 21, 2018.
b. Reported in all patients who received ≥1 dose of study treatment.
c. 8 patients(2.0%) in the pembrolizumab-combination group and 2 patients in the placebo-combination group died of adverse events attributed by the investigator to study treatment.
d. Events were based on a list from the sponsor and considered regardless of attribution to treatment or immune relatedness by the investigator.

Reference & Study design

Updated Analysis of KEYNOTE-189 Summary

PD-L1 발현율에 관계없이 전이성 비편평 비소세포폐암의 1차 치료로서 키트루다 병용요법* 연구[1]

키트루다 병용요법* 투여군은, Placebo 병용요법* 투여군 대비

전체 생존기간 중앙값(mOS) 연장

More than **DOUBLE!**

객관적 반응률(ORR) 증가

More than **DOUBLE!** (x2.5)

PD-L1 발현이 음성이거나, **PD-L1 검사 결과가 없는 환자**를 포함한 **모든 Nonsquamous mNSCLC 환자**에게

"키트루다 1차 병용요법*으로 More TOMORROWs의 가능성을 열어주세요!"

* pemetrexed 500 mg/m^2 + platinum(cisplatin 75 mg/m^2 or carboplatin AUC 5 mg/mL/min)

PD-L1 : Programmed death ligand 1, **mOS :** Median overall survival, **ORR :** Objective response rate, **mNSCLC :** Metastatic non-small-cell lung cancer

Reference & Study design

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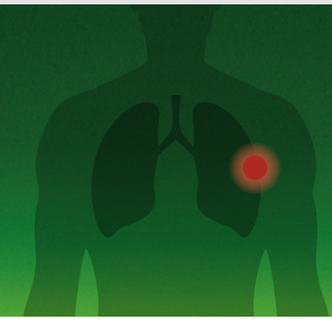
KEYNOTE-189 용법·용량

키트루다®와 Pemetrexed 및 백금 화학요법(Carboplatin 또는 Cisplatin)과의 병용요법



치료 용량[2-4,a-d]

KEYTRUDA®
200 mg IV over 30 minutes (매 3주마다)

P — Pemetrexed
500 mg/m^2 IV over 10 minutes (매 3주마다)

C — Carboplatin
AUC 5 mg/mL/min IV over 15-60 minutes (매 3주마다)

or

C — Cisplatin
75mg/m^2 IV (매 3주마다) beginning cisplatin 30 minutes after pemetrexed is completed.

※ 이 약을 화학요법제와 병용하여 투여하는 경우 이 약이 먼저 투여되어야 합니다. 병용하여 투여하는 화학요법제의 허가사항을 함께 참고합니다.
1. 초기 4 cycles은 KEYTRUDA + Pemetrexed + Platinum 요법으로 투여합니다.
2. 이후엔 KEYTRUDA + Pemetrexed 유지 요법으로 투여하며, 초기 4 cycles를 포함하여 총 35 cycles까지 투여 가능합니다.

전처치 용법·용량[5]

FA — Folic Acid
350-1000 µg PO daily (Pemetrexed 초회 투여 전 7일 동안 최소한 5회 엽산을 복용해야 하며, 치료 전체 기간과 이 약 최종 투여 후 21일 동안 복용을 지속해야 합니다.)

D/D — Dexamethasone(or equivalent)
4 mg PO BID (Pemetrexed 투여 전일, 당일, 다음 날 투여)

B12 — Vitamin B12
1000 µg IM (Pemetrexed 초회 투여 전 1주 이내에 1회, 그 후로는 매 3주기마다 1회씩 투여)

a. KEYTRUDA + carboplatin or cisplatin and pemetrexed Q3W for 4 cycles.
b. KEYTRUDA was given Q3W for up to a total of 35 cycles with pemetrexed maintenance therapy.
c. Patients in the placebo-pemetrexed-platinum group who had disease progression verified by BICR were eligible to cross over.
d. Treatment with KEYTRUDA continued until disease progression, unacceptable toxicity, or up to a total of 35 cycles. Pemetrexed is mandatory in maintenance therapy.
AUC : Area under the curve, **IV :** Intravenous, **IM :** Intramuscular, **PO :** By mouth, **BID :** Twice a day

Reference

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KEYNOTE-189 투여 스케줄

투여 스케줄[2-5]

KEYTRUDA® over 30 minutes*
→ **P** Pemetrexed over 10 minutes
→ **C** Carboplatin over 15-60 minutes
or
→ INTERVAL for 30 minutes
→ **C** Cisplatin†
→ Hydration procedures†

* 기관마다 infusion pump의 다양성을 고려하여 30분 투여 시간에서 -5 mins ~ +10 mins window는 허용되었습니다.
† Cisplatin의 투여 시간 및 투여 전/후 수화 절차는 각 나라의 허가사항 또는 practice를 따르도록 되어 있습니다.

	day -7	day -6	day -5	day -4	day -3	day -2	day -1
Premedication regimen	B12	ONCE EVERY THIRD CYCLE					
	FA	AT LEAST 5 DAILY DOSES THIS WEEK					D/D
Cycle 1~4	day 1	day 2	day 3	day 4	day 5	day 6	day 7
	KEYTRUDA + P + C or C; FA, D/D	FA, D/D	FA	FA	FA	FA	FA
	day 8	day 9	day 10	day 11	day 12	day 13	day 14
	FA	FA	FA	FA	FA	FA	FA
	day 15	day 16	day 17	day 18	day 19	day 20	day 21

a. Treatment with KEYTRUDA continued until disease progression, unacceptable toxicity, or up to a total of 35 cycles. Pemetrexed is mandatory in maintenance therapy.
B_{12} : Vitamin B_{12}, **FA :** Folic acid, **D/D :** Dexamethasone

Reference

KR-KEY-00389 12/2022

KEYNOTE-189 투여 스케줄

투여 스케줄[2-5]

Premedication regimen

day -7	day -6	day -5	day -4	day -3	day -2	day -1
B_{12}	ONCE EVERY THIRD CYCLE					
FA	AT LEAST 5 DAILY DOSES THIS WEEK					D/D

Cycle 1~4

day 1	day 2	day 3	day 4	day 5	day 6	day 7
P + C or C						
FA D/D	FA D/D	FA	FA	FA	FA	FA
day 8	day 9	day 10	day 11	day 12	day 13	day 14
FA	FA	FA	FA	FA	FA	FA
day 15	day 16	day 17	day 18	day 19	day 20	day 21
FA	FA	FA	FA	FA	FA	FA D/D

Maintenance therapy

day 1	day 2	day 3	day 4	day 5	day 6	21 -day cycle continues
Maintenance therapy up to a total of 35 cycles[a]						
P						
FA D/D	FA D/D	FA	FA	FA	FA	FA

a. Treatment with KEYTRUDA continued until disease progression, unacceptable toxicity, or up to a total of 35 cycles. Pemetrexed is mandatory in maintenance therapy.
B_{12} : Vitamin B_{12}, **FA :** Folic acid, **D/D :** Dexamethasone

Reference

Reference

1. Gadgeel S, *et al.* Updated analysis from KEYNOTE-189: Pembrolizumab or placebo plus pemetrexed and platinum for previously untreated metastatic nonsquamous non–small-cell lung cancer. *J Clin Oncol*. 2020;38(14):1505-1517.

2. Gandhi L, *et al.* Pembrolizumab plus chemotherapy in metastatic non–small-cell lung cancer. *N Engl J Med*. 2018;378:2078-2092.

3. Gandhi L, *et al.* Pembrolizumab plus chemotherapy in metastatic non–small-cell lung cancer(protocol). *N Engl J Med*. DOI: 10.1056/NEJMoa1801005.

4. 키트루다 제품 허가사항. 식품의약품안전처.

5. Pemetrexed 제품 허가사항. 식품의약품안전처.

Study design

This study was conducted to evaluate the longest efficacy and safety outcomes of KEYNOTE-189 study. In global, double-blind, placebo-controlled, phase 3 KEYNOTE-189 trial, combination of pemetrexed and a platinum-based drug + either pembrolizumab or placebo in patients with nonsquamous NSCLC with any level of PD-L1 expression were compared. 616 patients were at least 18 years of age and had pathologically confirmed metastatic nonsquamous NSCLC without sensitising EGFR or ALK mutations. Patients were randomly assigned (2:1) to receive pemetrexed (500 mg/m^2) and a platinum-based drug (cisplatin 75 mg/m^2 vs. carboplatin AUC 5 mg/ml/min), plus either 200 mg of pembrolizumab (n=410) or placebo (n=206) every 3 weeks for 4 cycles, followed by pembrolizumab or placebo for up to a total of 35 cycles plus pemetrexed maintenance therapy. At data cutoff (September 21, 2018), median (range) study follow-up (time from randomization to database cutoff) was 23.1 (18.6 to 30.9) months. Randomization was stratified according to PD-L1 tumour proportion score (≥1 vs. <1%), choice of platinum-based drug (cisplatin vs. carboplatin), and smoking history (never vs. former or current). The two primary endpoints were overall survival and progression free survival.[1,2]

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