# THE EFFICIENCY OF CHEMOTHERPY PLUS PEMBROLIZUMAB REGIMEN IN PATIENTS WITH STAGE IV NON-SMALL CELL LUNG CANCER REAL-WORLD DATA OF THONG NHAT HOSPITAL

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# OPENING

Unresectable or metastatic non-small cell lung cancer

- High incidence and death rates
- Targeted drugs such as EGFR, ALK, ROS1 TKIs… induce high ORRs 60-80%, require specific sensitive gene mutation
- Chemotherapy offered low ORRs 30-40% associated with high degree of toxicity.
- Immune checkpoint inhibitors (monotherapy or combination with chemotherapy) become new era in cancer treatment, whose toxicity are under investigation.

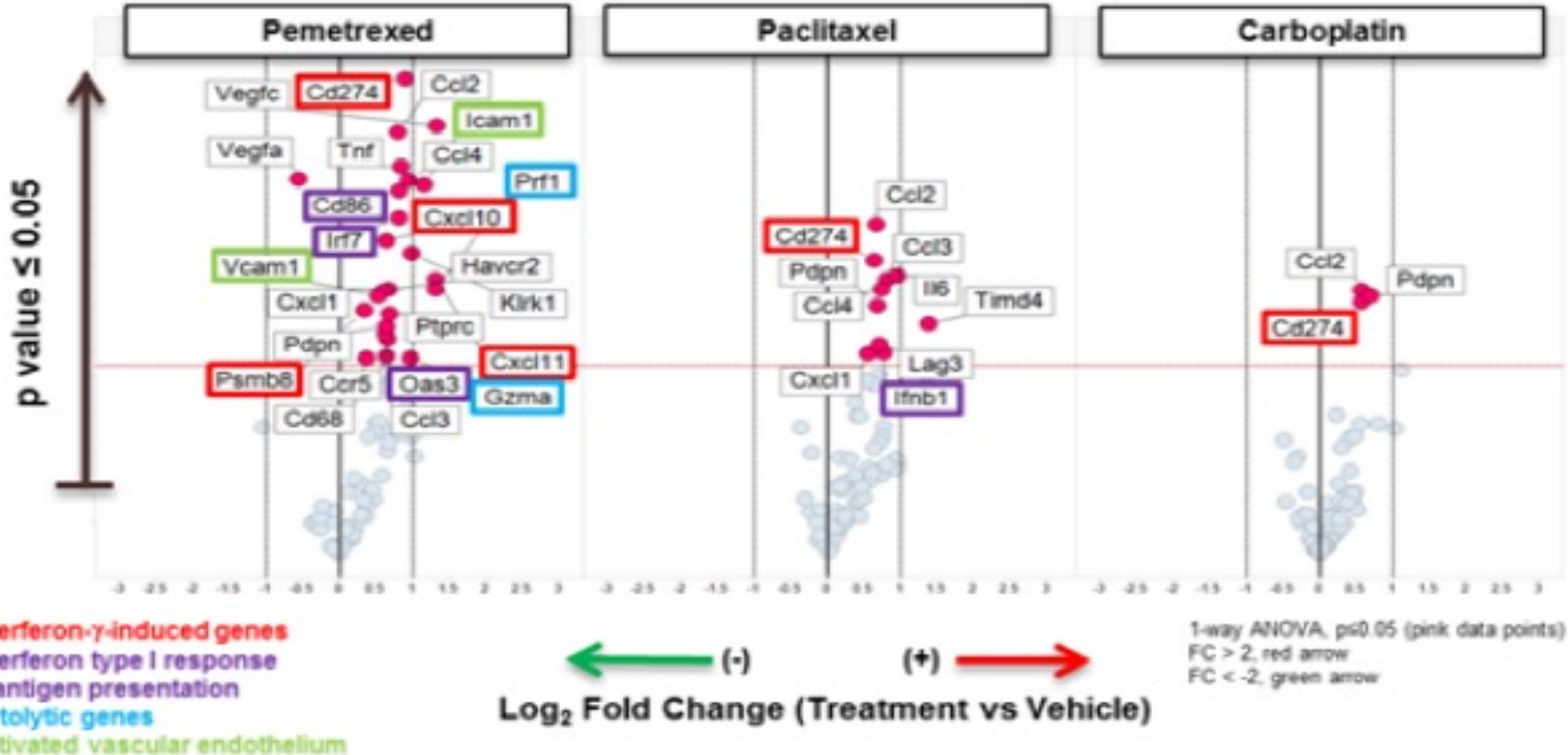
# IMMUNOTHERAPY IN THE FIRST-LINE TREATMENT OF ADVANCED NON-SMALL-CELL LUNG CANCER (NSCLC)


ipilimumab
nivolumab
pembrolizumab
atezolizumab
durvalumab…

**100M Race**

# MECHANISM OF COMBINATION IMMUNOTHERAPY WITH CHEMOTHERAPY

- **Pemetrexed & Paclitaxel induce immunogenic form biomarkers**



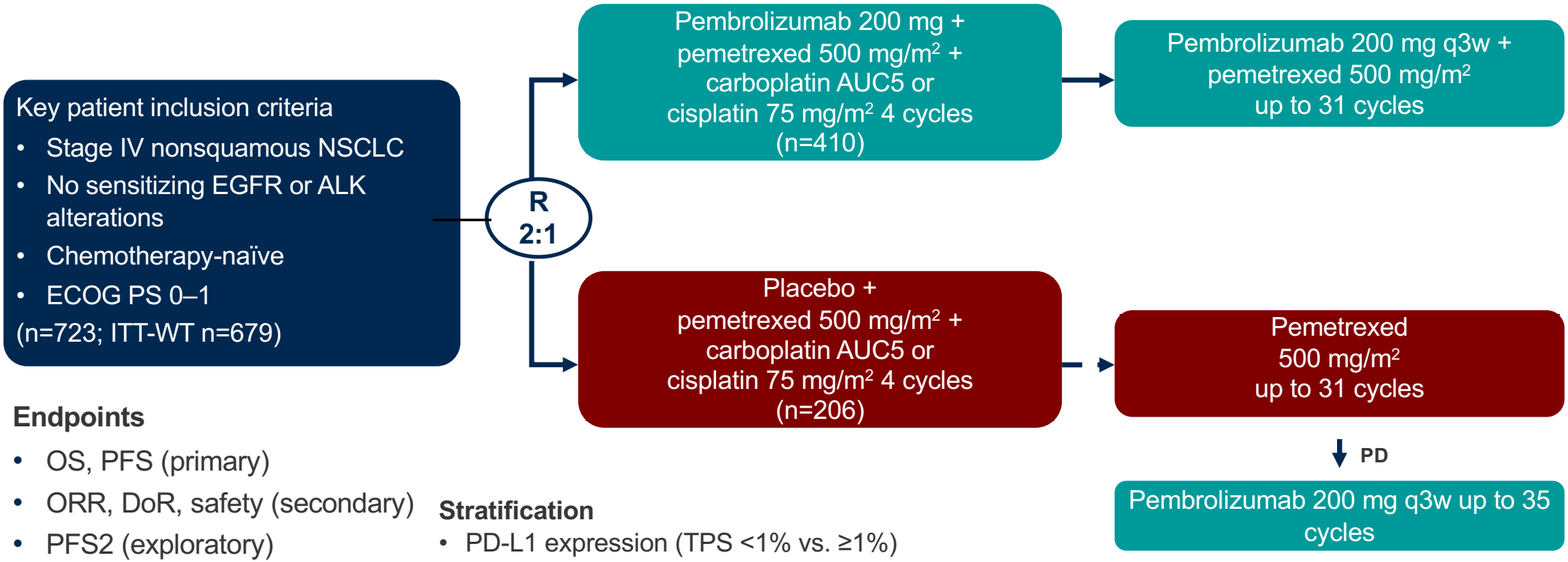

*Novosiadly, AACR 2017*

# MECHANISM OF COMBINATION IMMUNOTHERAPY WITH CHEMOTHERAPY

- IO likewise affects chemotherapy-sensitive tumors
- Chemotherapy eliminate Myeloid-derived suppressor cells (MDSC)
- Increasing neoantigen presentation
- Activate immune cells
- Immunomodulatory effects

*Destafano, Early Phase Cancer Immunotherapy 2018*

# KEYNOTE-189:
# Pembrolizumab plus Chemotherapy in 1L for Metastatic NSCLC




**Endpoints**

- OS, PFS (primary)
- ORR, DoR, safety (secondary)
- PFS2 (exploratory)

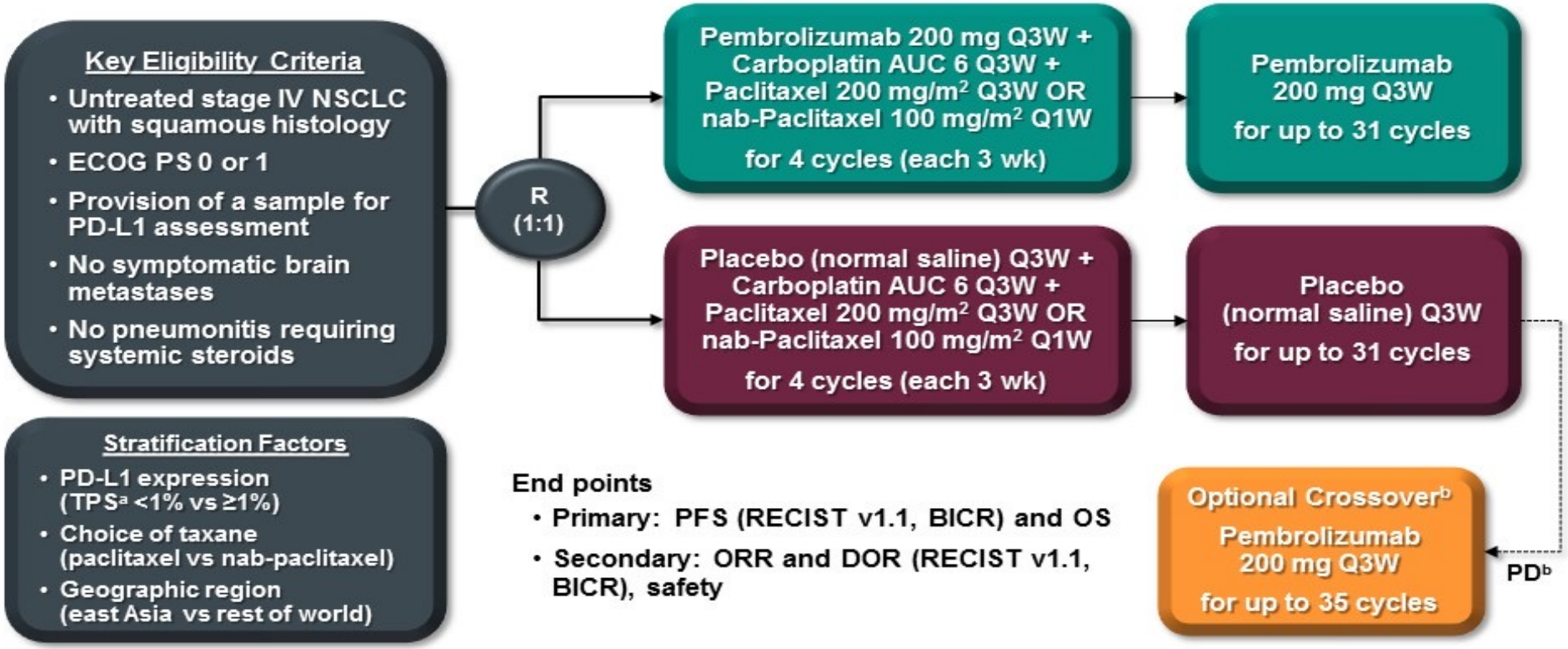
**Stratification**

- PD-L1 expression (TPS <1% vs. ≥1%)
- Platinum (cisplatin vs. carboplatin)
- Smoking history (never vs. former/current)

Gadgeel SM, et al. J Clin Oncol 2019;37(suppl):Abstr 9013

Paz-Ares KN407 ASCO 2018

# KEYNOTE-407 Study Design (NCT02775435)

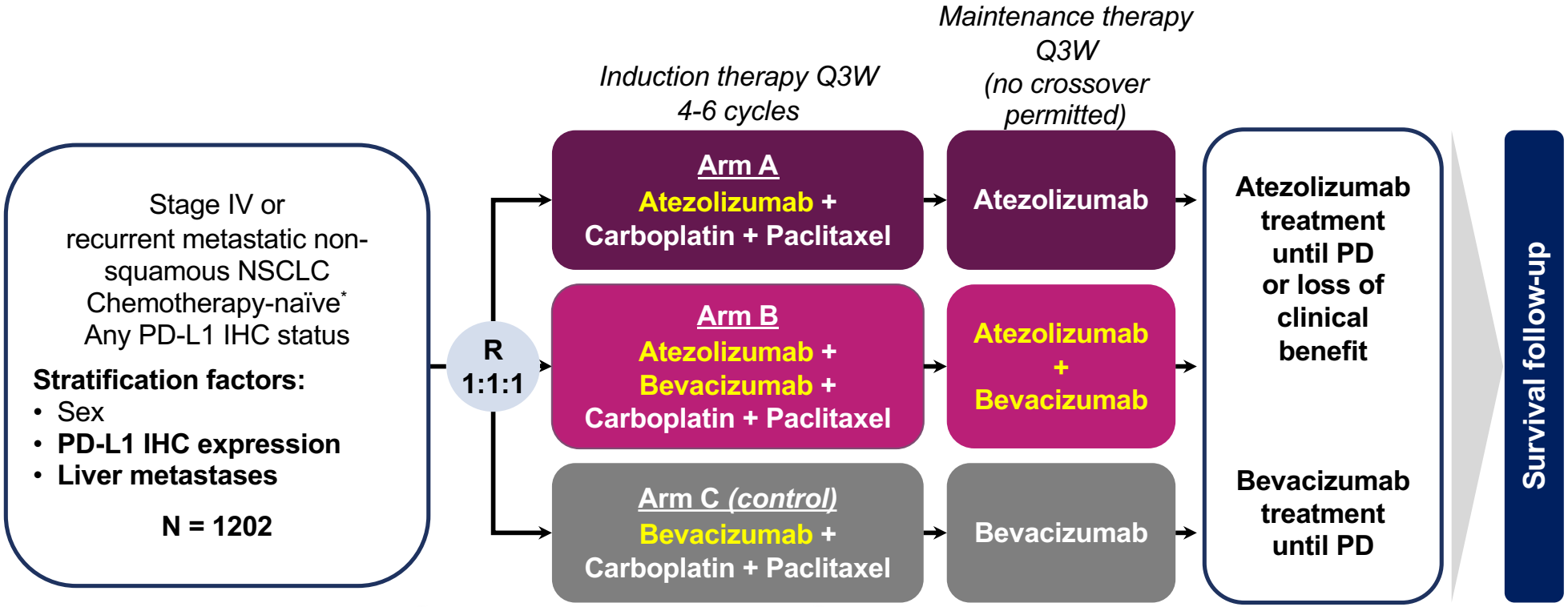



BICR, blinded independent central radiologic review. [a]Percentage of tumor cells with membranous PD-L1 staining assessed using the PD-L1 IHC 22C3 pharmDx assay. [b]Patients could crossover during combination therapy or monotherapy. To be eligible for crossover, PD must have been verified by BICR and all safety criteria had to be met.

N Engl J Med 2018; 379:2040-2051

# IMPOWER 150 Study design

Phase 3, multicenter, international, randomized, open label, mNSCLC non-squamous Chemotherapy-naïve




*Patients with a sensitising *EGFR* mutation or *ALK* translocation must have disease progression or intolerance to treatment with one or more approved targeted therapies Socinski, et al. N Engl J Med 2018

# Toxicities Associated With Immune Checkpoint Inhibitors

| | Chemotherapy | Immunotherapy |
|---|---|---|
| Incidence (moderate/severe AEs) | Almost all patients | Majority without |
| AE profile | Well described | Variable |
| Affected systems/organs | Few organs affected | Any organ |
| Time course | Well established | Variable (even after end of Tx) |
| | Predictable | Relatively unpredictable |

Slide credit: clinicaloptions.com

# OBJECTIVE

Evaluate efficacy and safety of pembrolizumab in combination with chemotherapy regimen in patients with stage IV NSCLC in Oncology Department of Thong Nhat Hospital

- **Method:** Retrospective descriptive case series in 1/2019 and cut-off data on 1/6/2023.
- **Study subjects:** All patients with stage IV NSCLC treated with pembrolizumab in combination with chemotherapy in Oncology Department of Thong Nhat Hospital from 1/2019 met the selection criteria.
- **Selection criteria:** Stage IV NSCLC patients treated with at least 3 cycles of chemotherapy plus pembrolizumab.
- **Exclusive criteria:** only 2 cycles received, treated with pembrolizumab as single agent, secondary cancer, threshold severity of internal and surgical disease, sensitive EGFR mutation, incomplete archival records.
- **Objectives:** Evaluation of efficacy and safety of chemotherapy in combination with pembrolizumab regimen in patients with stage IV NSCLC without driver mutations.

# RESULT: PATIENTS CHARACTERISTICS

- Screened on total 46 patients with stage IV NSCLC treated with pembrolizumab
- 33 patients who met the following criteria were included in our retrospective study

| Age | Male:female(%) | ex-smoker or current smokers |
|---|---|---|
| 69 (42-86) | 78.8:21.2 | 34.9% |

| Adenocarcioma:Squamous (%) | First line | Majority metastasis organs | Brain/liver metastasis rate | %PS 0:1:2 |
|---|---|---|---|---|
| 81.8:18.2 | 75.8% (25/33) | Bone, pleural effusion | 15.2% | 15:58:27 |

# RESULT: PATIENTS CHARACTERISTICS

- 33 patients stage IV NSCLC

| %PD-L1 | PD-L1≥50 | 50>PD-L1≥1 | PD-L1<1 |
|---|---|---|---|
| Number of patietns (%) | 6(18.2) | 15(45.5) | 12(36.3) |

- Mean number of cycles: 8.4. Median number of cycles: 6.
- Minimum number of cycles received by patient: 3. There was 1 patient who completed 35 cycles. 10/33(30%) patients stopped treatment due to unaffordability
- 17/33(51.2%) patients experienced failure to comply with treatment regimen
- 28/33 patients received pembrolizumab 200mg, 5 patients received 100mg were post-first-line

# DISCUSSION: PATIENT CHARACTERISTICS

- Common mean age seen in lung cancer studies were typically between the ages of 50 and 70
- In study of Vũ Văn Vũ, patients who has better PS demonstrated longer OS

  (Log-rank 6,88 p=0,03)
- The incidence ratio of male:female = 3-4:1, particularly 8:1
- Recently, the incidence of lung cancer in women has been increasing:
  - Women are more engaged with business
  - Women are more likely exposed to smoking habits.


1. Vũ Văn Vũ, Đặng Thanh Hồng, Nguyễn Thị Minh Khang, Trần Quang Thuận, Nguyễn Mạnh Quốc, Trần Thị Ngọc Mai (2004). "Hóa liệu pháp ung thư phổi không tế bào nhỏ giai đoạn tiến xa tại Bệnh viện Ung bướu TPHCM 2001-2002". Y Học TP.Hồ Chí Minh, 8 (Phụ bản số 2), tr 154-169.
2. Nguyễn Việt Quang, Huỳnh Quyết Thắng, Tăng Kim Sơn & Huỳnh Thảo Luật (2015). "Đánh giá hiệu quả hóa trị ung thư phổi không tế bào nhỏ giai đoạn IIIB-IV bằng phác đồ Paclitaxel-Carboplatin tại Bệnh viện Ung bướu Cần Thơ". Tạp chí Ung thư học Việt Nam, 4, tr 141-147.
3. Đặng Thanh Hồng & Vũ Văn Vũ (2000). "Ghi nhận bước đầu điều trị ung thư phổi không phải tế bào nhỏ giai đoạn tiến xa với Gemzar-Carboplatin". Tạp chí thông tin Y Dược, 8, tr 146-149.
4. Gandhi L et al. N Engl J Med 2018;378:2078–2092;
5. Garassino MC et al. Presented at the 2019 American Association for Cancer Research (AACR) Annual Meeting, 29 March–18 April, 2019, Atlanta, USA; 3\
6. Gadgeel S et al. Presented at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting, 31 May – 4 June, 2019, Chicago, USA.
7. L. Paz-Ares et al; Pembrolizumab plus Chemotherapy for Squamous Non–Small-Cell Lung Cancer; DOI: 10.1056/NEJMoa1810865.
8. Lê Tuấn Anh & Nguyễn Ngọc Bảo Hoàng. Đặc điểm lâm sàng và điều trị của 1158 bệnh nhân ung thư phổi tại Trung tâm Ung bướu Chợ Rẫy, tạp chí Y học thực hành. 2013;8(878):20-22.

# BASELINE CHARACTERISTICS & RESPONSE EVALUATION

- Adenocarcinoma: squamous #4:1, recently, adenocarcinoma increase in prevalence
- 25/33(75.8%) of patients received pembrolizumab plus chemotherapy as 1st-line treatment
- 5 cases had brain-liver metastasis, others had bone- 2 lungs metastasis or pericardial effusion …
- PS=0-2
- 6/33(18.2%) patients had high PD-L1 expression
- 100% patients have been received chemotherapy in combination with pembrolizumab
- Minimum number of cycles: 3

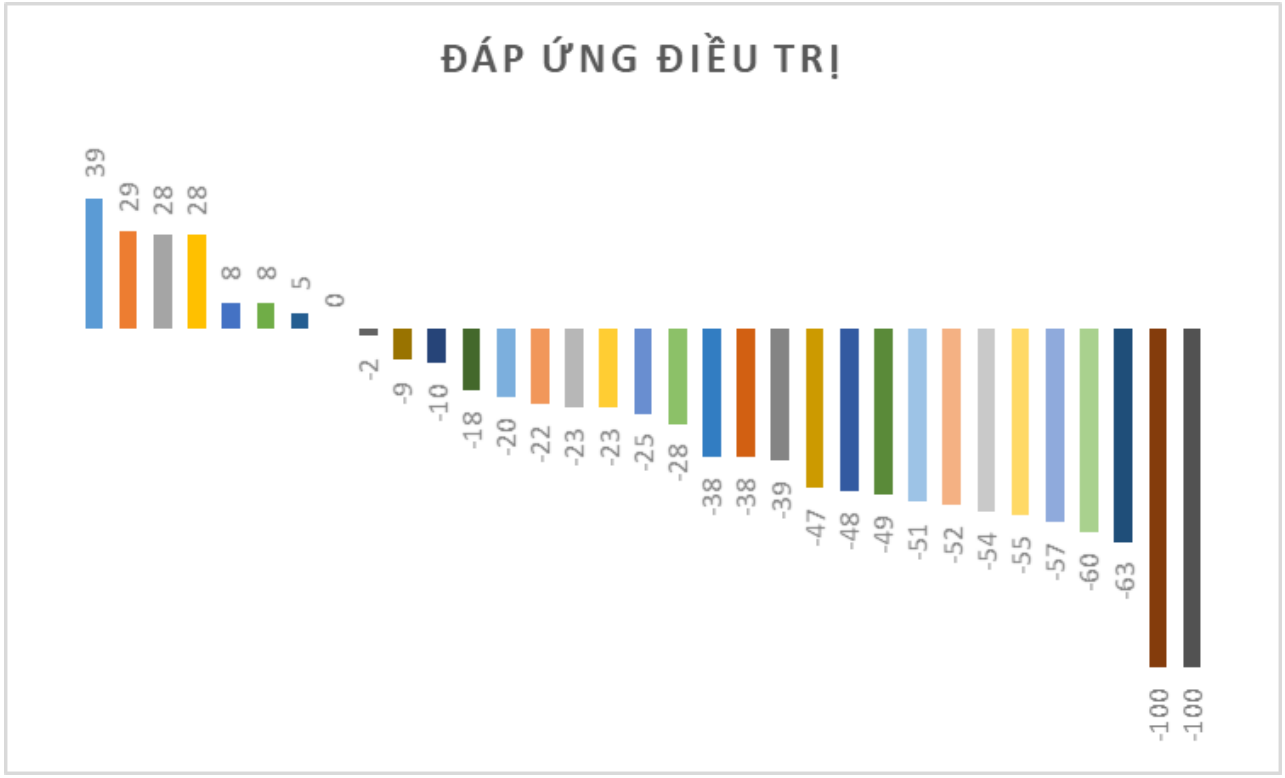
# RESULT: SUBJECTIVE RESPONSE ASSESSMENT

- 25/33(75.8%) patients demonstrated relief of symptoms such as bone pain, back pain, cough and dyspnea
- Vũ Văn Vũ, Nguyễn Thị Phương Hồng(2017) EGFR TKIs 1-2 generations reduced 100% symptoms.
- Trương Vương Vũ, Trần Đình Thanh… chemotherapy reduced 50-70% symptoms
- Nguyễn Thị Thu Hà: pembrolizumab monotherapy for patients with high PD-L1 expression in 1st line and 2nd line treatment resulted in 76% subjective response
- Nguyễn Tiến Sơn(2023) more than 50% of patients received subjective response (chest pain, dyspnea) after 1-2-4 weeks, symptoms such as cough, fatigue, or shortness of breath are significantly reduced.

1. Vũ Văn Vũ, Nguyễn Thị Phương Hồng (2017). "Đánh giá kết quả TKIs điều trị ung thư phổi không tế bào nhỏ giai đoạn tiến xa, di căn; tạp chí Ung thư học Việt Nam", luận văn chuyên khoa 2 trường ĐHYD Tp.HCM. 2. Trương Vương Vũ (2018). "Kết quả hóa trị ung thư phổi không tế bào nhỏ giai đoạn tiến xa tại bệnh viện đa khoa tỉnh Khánh Hòa". Luận án chuyên khoa cấp II, Đại học Y Dược thành phố Hồ Chí Minh. 3. Nguyễn Thị Thu Hà (2020). "Đánh giá kết quả điều trị ung thư phổi không tế bào nhỏ giai đoạn tiến xa bằng phác đồ pembrolizumab". *Tạp chí y học 4-2020*, *Luận văn thạc sĩ y học,* Trường Đại học Y Hà Nội 4. Nguyễn Tiến Sơn, "Đánh giá hiệu quả và an toàn phác đồ có Pembrolizumab trong điều trị bước 1 ung thư phổi không tế bào nhỏ di căn".2023; Luận văn chuyên khoa 2, trường ĐHYD TPHCM.

# RESULT: OBJECTIVE RESPONSE

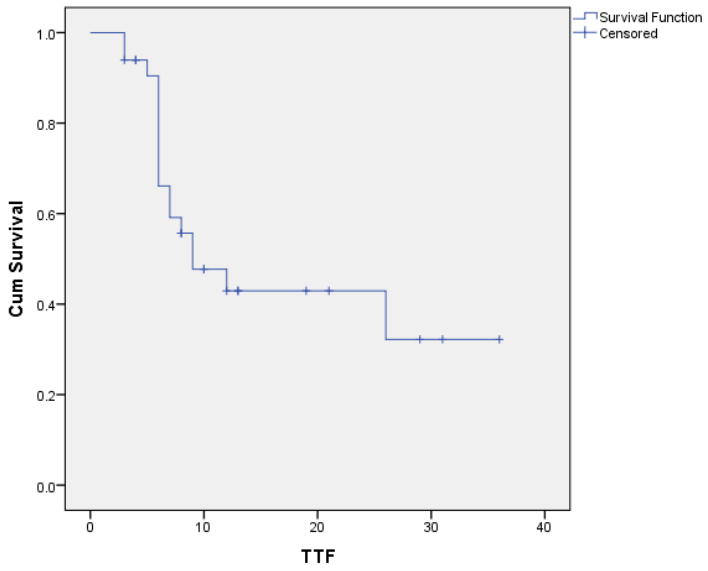
- ORR 45.5% CR 6%
- SD 42.4%
- PD 12.1%
- %ORR 1st line:2nd line=52:0
- %ORR adenocarcinoma: squamous= 48:33.3

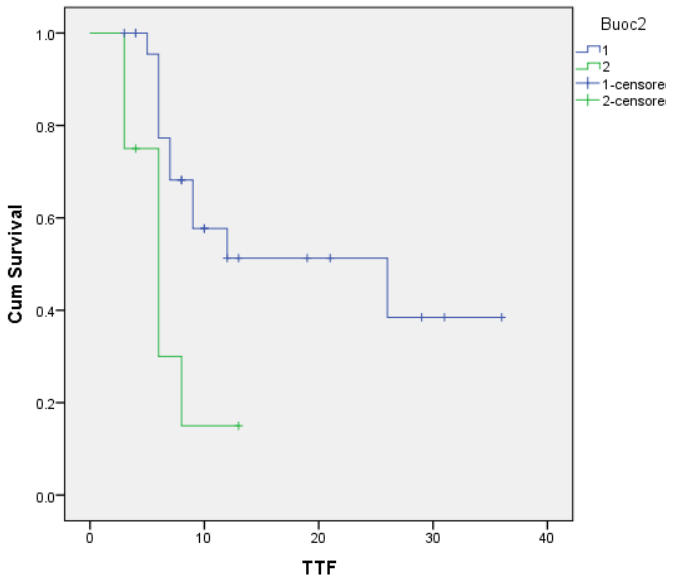


# RESULT: RESPONSE RATE BY PD-L1 STRATIFICATION AND TREATMENT LINE

| | %CR | %PR | %SD | %PD |
|---|---|---|---|---|
| **PD-L1<1%** | | 42 | 58 | |
| **PD-L1[1:49]%** | 7 | 47 | 33 | 13 |
| **PD-L1≥50%** | 17 | 17 | 33 | 33 |
| **1st line** | 8 | 52 | 40 | |
| **Post 1st line** | | | 50 | 50 |

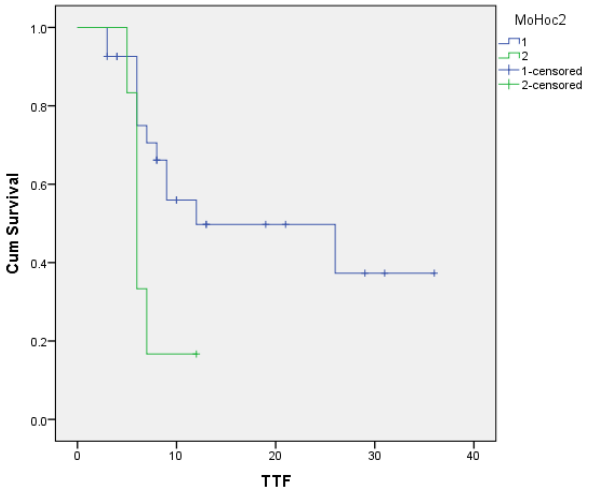
# MEDIAN TTF



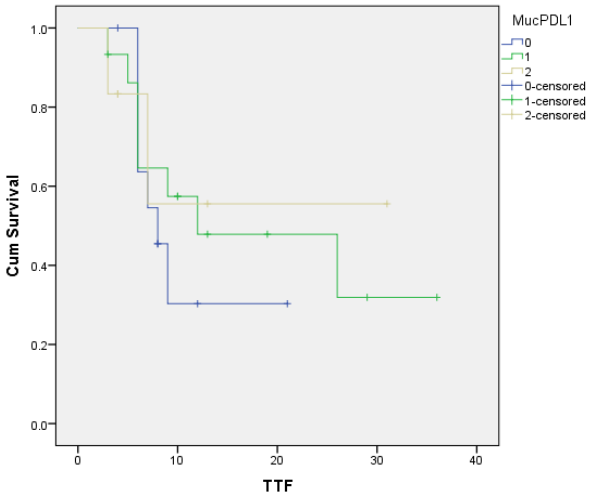




- mTTF 9 months (3.17:14.83) 95% CI; mTTF 1st line:post-1st-line=26:6 months, Chi-square Log-Rank p=0.012

# MEDIAN TTF



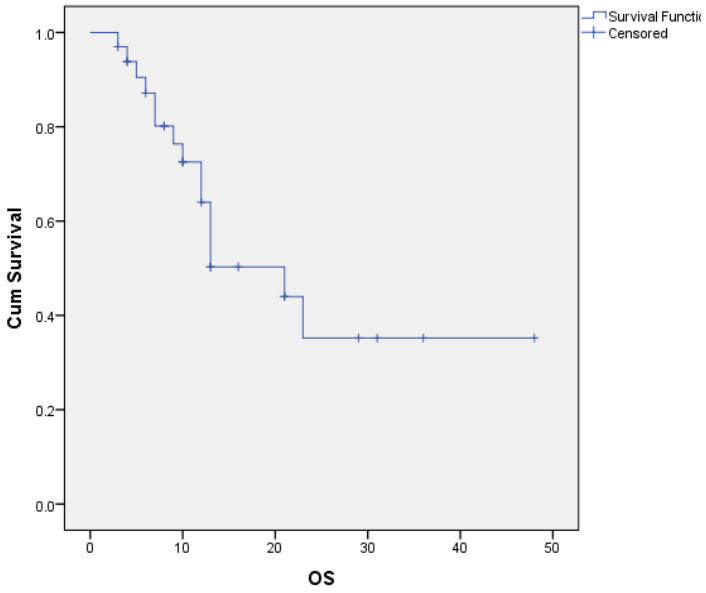

1: tuyến 2: gai

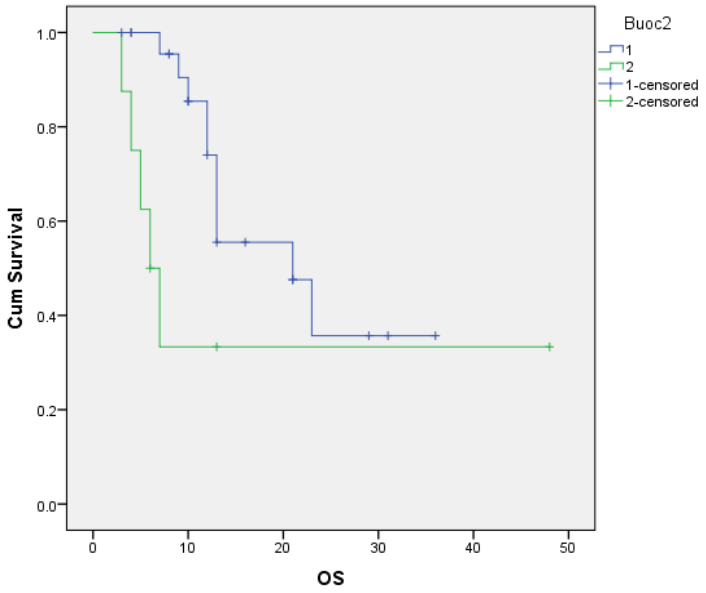



0:<1% 1: 1-49% 2: ≥50%

- mTTF adenocarcinoma:squamous=12:6 months Log Rank p=0.052; mTTF PD-L1 expression: <1%:1-49% :≥50%=8:12:NR (NR: not reach)

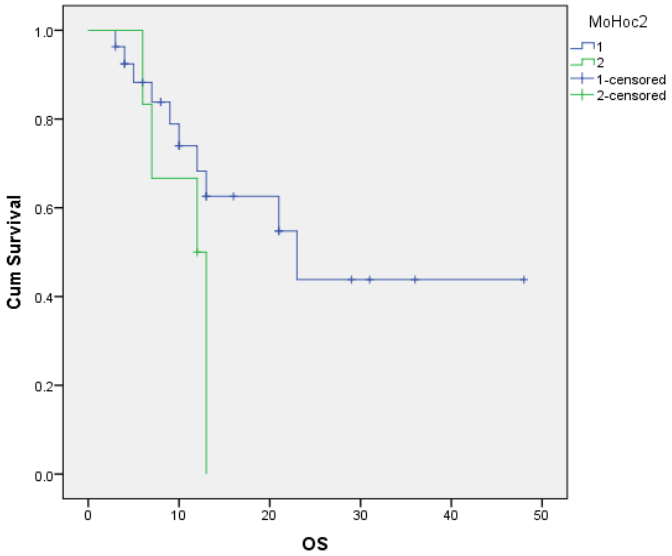
# MEDIAN OS



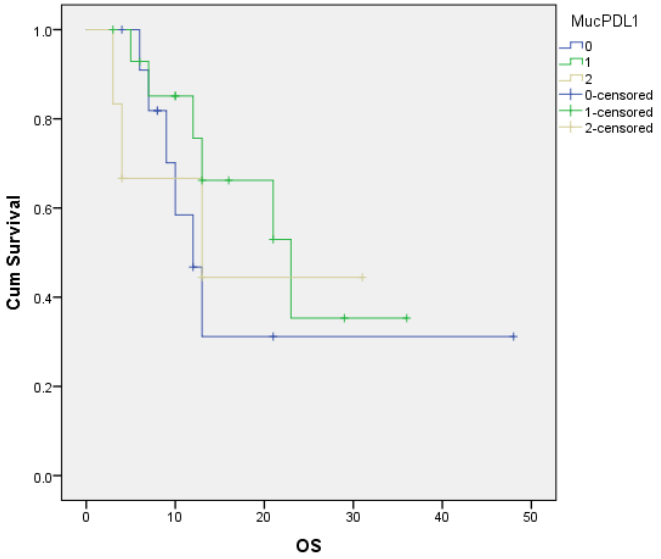




- mOS 21 months 95% CI, mOS 1st line:post-1st-line =21:6 months, Chi-Square Log-Rank p=0.045

# MEDIAN OS




1: tuyến  2: gai




0:<1%  1: 1-49%  2: ≥50%

- mOS adenocarcinoma:squamous=23:12 months  Log Rank p=0.071; mOS  PD-L1 expression <1%:1-49% :≥50% =12:23:13 months p=0.593

# DISCUSSION

- Nguyễn Đặng Thuận An(2022) retrospective study of 29 patients who had NSCLC stage IV treated first-line with chemotherapy combine pembrolizumab stratified by PD-L1 expression (therein 8/29 patients(27.6%) had PD-L1 ≥50%)
- ORR 10.2% (CR 3.4%) mPFS 9 months, mOS 12.5 months
- Majority of toxicity occurrence were grade 1-2: hepatitis accounted for 20.8%, 2/29 patients (6.9%) caught interstitial pneumonia, 2/29 patients (6.9%) had renal failure, 1 patients had adrenal insufficiency and well-controlled with supportive care

1. Nguyễn Đặng Thuận An (2022). "Efficacy And Safety Of Pembrolizumab In The Treatment Of Metastatic Non Small Cell Lung Cancer" báo cáo tại Hội nghị khoa học thường niên BV Chợ Rẫy 2023, 18 April 2023, TPHCM

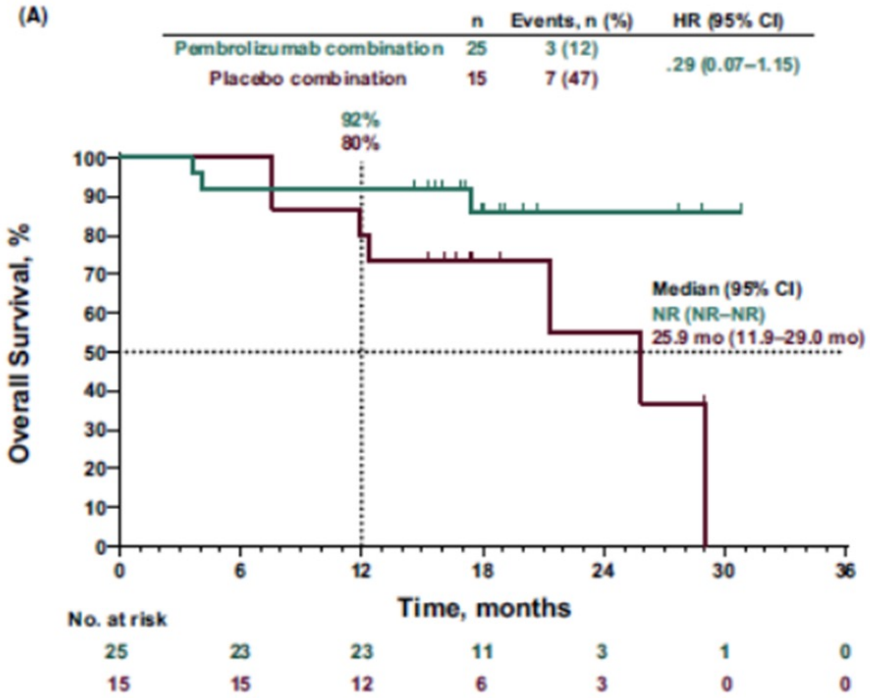
# DISCUSSION

- Nguyễn Tiến Sơn(2023) retrospective study of 40 patients who has NSCLC stage IV, including 28/40 patients (70%) treated by chemotherapy combined pembrolizumab in first-line with different PD-L1 expression (5/28 patients (17,9%) had PD-L1≥50%)
- ORR 60,7% (CR 10,7%), mTTF 8,6 months, mOS not reach
- Majority of toxicity occurrence were grade 1-2: hepatitis accounted for 15%, 3/28 patients (10,7%) caught interstitial pneumonia grade 2, 1 patient had hyperthyroidism then well-controlled with antithyroid therapeutics, 1 patient had hypothyroidism with no treatment required, 1 patients occurs tuberculosis reactivation

1. Nguyễn Tiến Sơn, "Đánh giá hiệu quả và an toàn phác đồ có Pembrolizumab trong điều trị bước 1 ung thư phổi không tế bào nhỏ di căn".2023; Luận văn chuyên khoa 2, trường ĐHYD TPHCM.

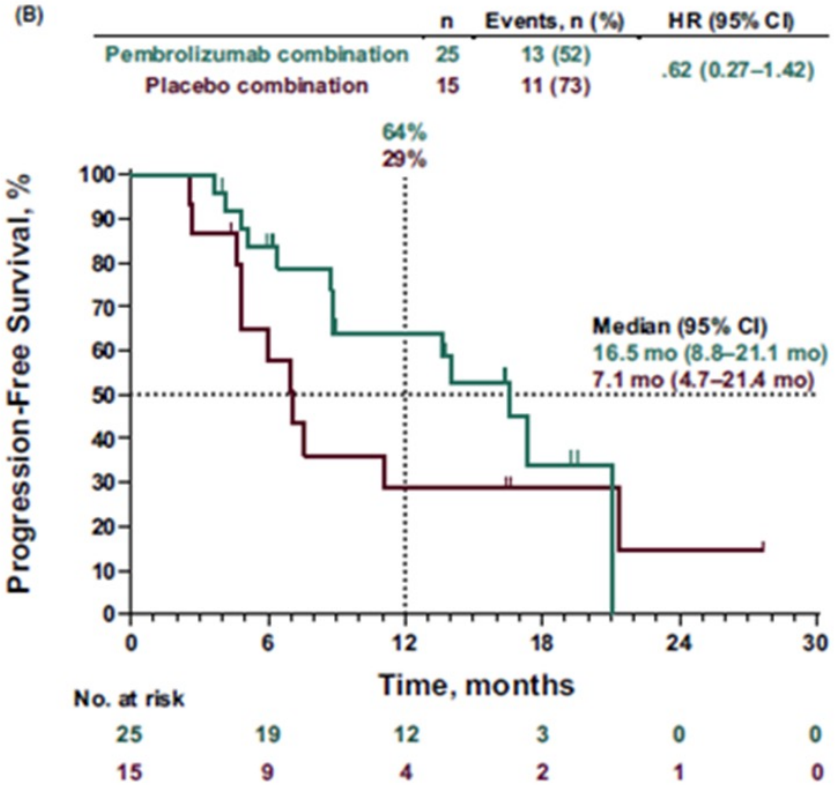
- Hidehito et al(2021)(KEYNOTE-189) study of 40 Japanese patients who received first line treatment of stage IV NSCLC adenocarcinoma histology (chemotherapy+ pembrolizumab n=25, chemotherapy+placebo n=15)

- Efficacy and safety equivalent to the general population.
- Combination chemotherapy and pembrolizumab regimen prolonged OS, PFS, PFS-2 versus chemotherapy only
- At cut off timepoint, median following up time was 18.7 months
  - ✓ mOS of combination chemotherapy and pembrolizumab group was NR vs 25.9 months of chemotherapy group




1.L. Gandhi et al; Pembrolizumab plus Chemotherapy in Metastatic Non–Small-Cell Lung Cancer; DOI: 10.1056/NEJMoa1801005
2.Hidehito et al; Pembrolizumab plus pemetrexed-platinum for metastatic nonsquamous non–small-cell lung cancer: KEYNOTE-189 Japan Study. Cancer Science. 2021;112:3255–3265

- ✓ mPFS 16.5 months of combination arm vs 7.1 months chemotherapy arm
- ✓OS rate và PFS 12-month rate was similar to ITT population
- ✓ There were no grade 5 AE. The incidence rate of grade 3-4 AE were 72% vs 60%. Immune-related AEs: 40% vs 20%, 4%  vs 0% infusion related AE



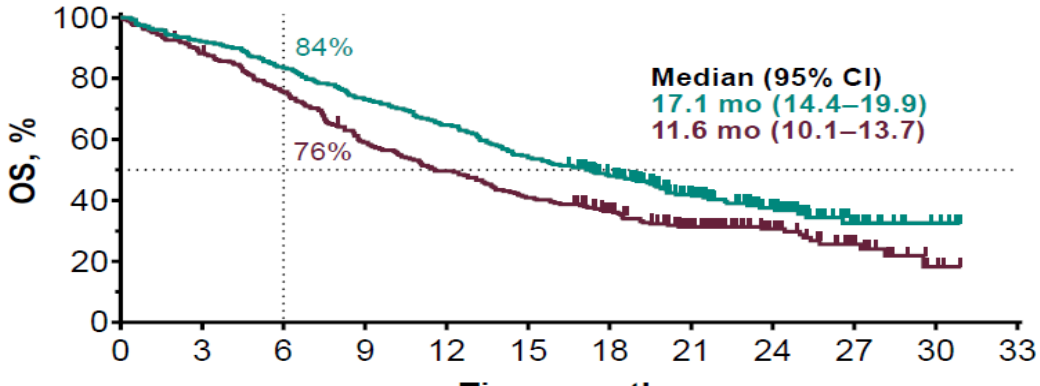

1.L. Gandhi et al; Pembrolizumab plus Chemotherapy in Metastatic Non–Small-Cell Lung Cancer; DOI: 10.1056/NEJMoa1801005
2.Hidehito et al; Pembrolizumab plus pemetrexed-platinum for metastatic nonsquamous non–small-cell lung cancer: KEYNOTE-189 Japan Study. Cancer Science. 2021;112:3255–3265

- Y Cheng et al(2021)(Keynote 407) study of 125 Chinese patients who had stage IV NSCLC squamous cell histology treated first-line (chemotherapy+pembrolizumab n=65, chemotherapy+placebo n=60)
- Data analyzed in this population were consistent with data in ITT population examined previously
  - mOS of combination chemotherapy and pembrolizumab was 15.9 vs 11.3 months (HR=0,44; 95% CI; 0,24-0,81) (improving in all subgroup by ages, gender, PS and PD-L1 expression)
  - Improve PFS (HR, 0.32; 95% CI, 0.21-0.49). ORR 78,5% vs 41,7% advantages on combination arm

1.L. Paz-Ares et al; Pembrolizumab plus Chemotherapy for Squamous Non–Small-Cell Lung Cancer; DOI: 10.1056/NEJMoa1810865
2.Y Cheng et al; Keynote-407 China Extension study: Pembrolizumab (pembro) plus chemotherapy in Chinese patients with metastatic squamous NSCLC; https://doi.org/10.1093/annonc/mdz446.019

# Overall Survival

## KEYNOTE-407 Global Study[1]

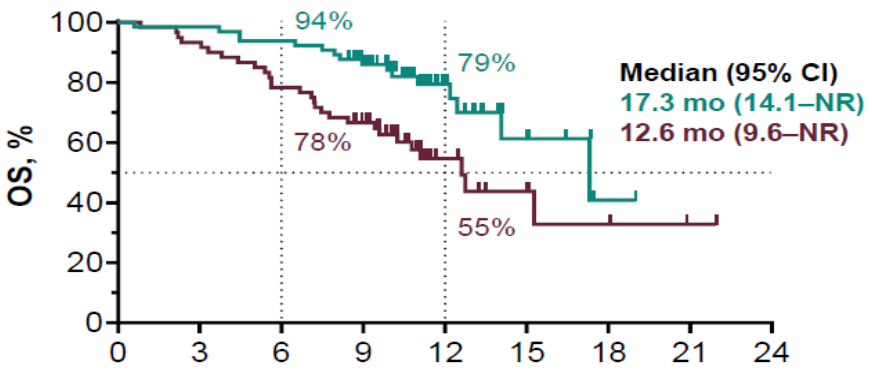



No. at risk

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 278 | 256 | 232 | 203 | 180 | 150 | 119 | 80 | 46 | 14 | 4 | 0 |
| 281 | 245 | 210 | 163 | 137 | 113 | 91 | 61 | 36 | 16 | 3 | 0 |

| | Events, n (%) | HR (95% CI) |
|---|---|---|
| Pembro + Chemo | 168 (60.4) | 0.71 (0.58–0.88) |
| Control | 197 (70.1) | |

## KEYNOTE-407 China Extension Study




| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 65 | 64 | 61 | 49 | 17 | 5 | 1 | 0 | 0 |
| 60 | 56 | 47 | 37 | 11 | 4 | 3 | 1 | 0 |

| | Events, n (%) | HR (95% CI) |
|---|---|---|
| | 16 (24.6) | 0.44 (0.24–0.81) |
| | 28 (46.7) | |

NR, not reached.

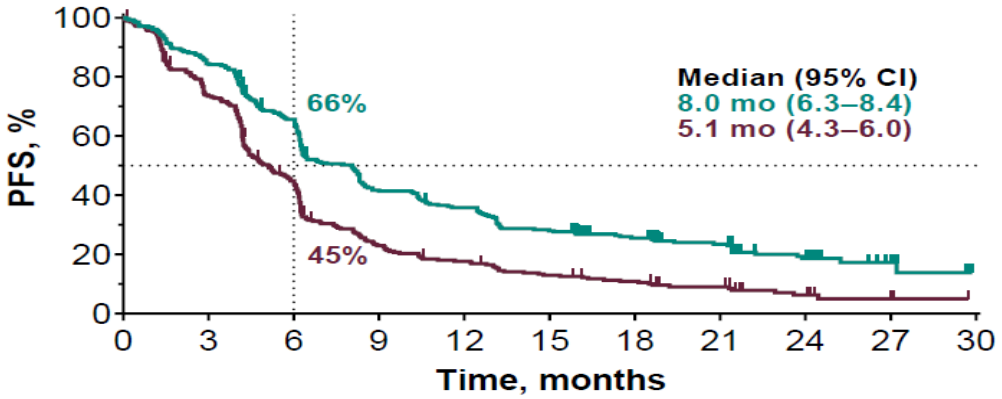
1. Paz-Ares L, et al. ESMO 2019, September 27–October 1, 2019, Barcelona, Spain (LBA852).

Data cutoff date: May 9, 2019 (both global and extension study).


1.L. Paz-Ares et al; Pembrolizumab plus Chemotherapy for Squamous Non–Small-Cell Lung Cancer; DOI: 10.1056/NEJMoa1810865 2.Y Cheng et al; Keynote-407 China Extension study: Pembrolizumab (pembro) plus chemotherapy in Chinese patients with metastatic squamous NSCLC https://doi.org/10.1093/annonc/mdz446.019

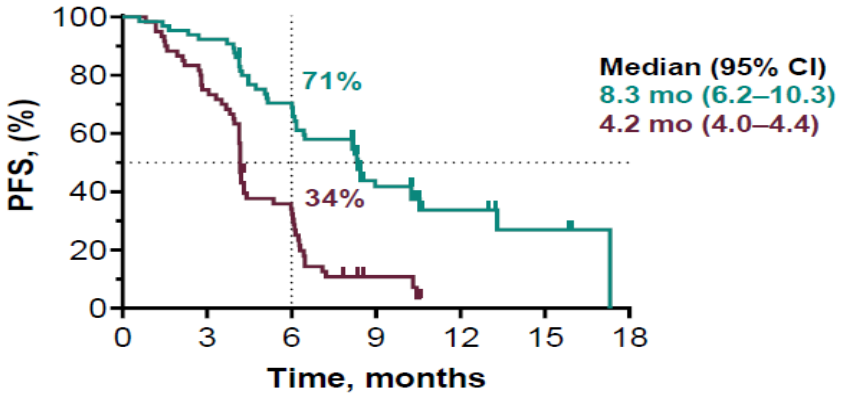
# Progression-Free Survival[a]

## KEYNOTE-407 Global Study[1]




| | Events, n (%) | HR (95% CI) |
|---|---|---|
| Pembro + Chemo | 217 (78.1) | 0.57 (0.47–0.69) |
| Control | 252 (89.7) | |

## KEYNOTE-407 China Extension Study




| | Events, n (%) | HR (95% CI) |
|---|---|---|
| | 41 (63.1) | 0.32 (0.21–0.49) |
| | 54 (90.0) | |

[a]Response assessed per RECIST version 1.1 by blinded, independent central review.
1. Paz-Ares L, et al. ESMO 2019, September 27–October 1, 2019, Barcelona, Spain (LBA852).
Data cutoff date: May 9, 2019 (both global and extension study).


1.L. Paz-Ares et al; Pembrolizumab plus Chemotherapy for Squamous Non–Small-Cell Lung Cancer; DOI: 10.1056/NEJMoa1810865

2.Y Cheng et al; Keynote-407 China Extension study: Pembrolizumab (pembro) plus chemotherapy in Chinese patients with metastatic squamous NSCLC; https://doi.org/10.1093/annonc/mdz446.019

- Maki Kobayashi et al(ESMO 2021) retrospective study of 300 recruited patients who had tumors with high PD-L1 expression (PD-L1 ≥50%) treated from 12/2018 to 1/2020
- Study design with 2 arms: monotherapy pembrolizumab(n=166) versus combination pembrolizumab and chemotherapy(n=134).

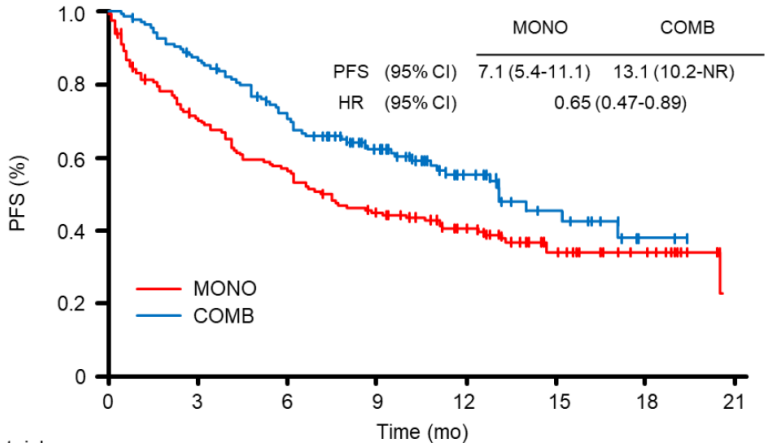
➢ Combination arm achieved ORR 67,9% (CR 3%), mPFS 13,1 months. Combination regimen demonstrated significant increase effectiveness in very high PD-L1 expression population.

➢ mOS not reach

➢ Patients with PS=2 had shorter PFS when receive combination

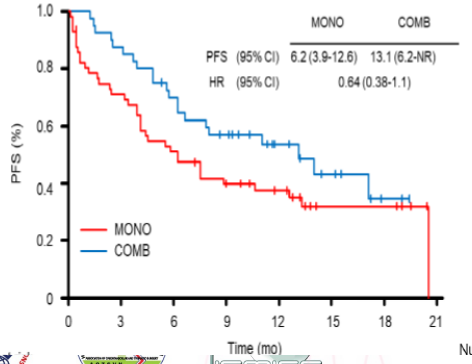
➢ Safety profile was similar  in both.

# PFS in ITT

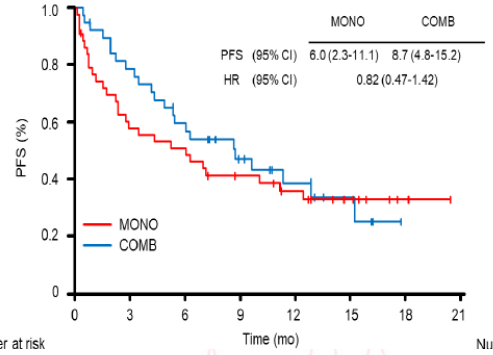



## PD-L1

**50-74%**

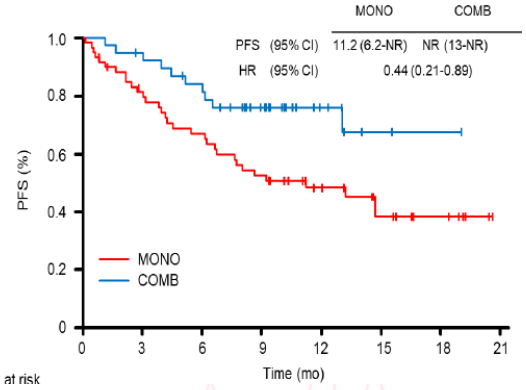



**75-89%**




Number at risk

**≥90%**

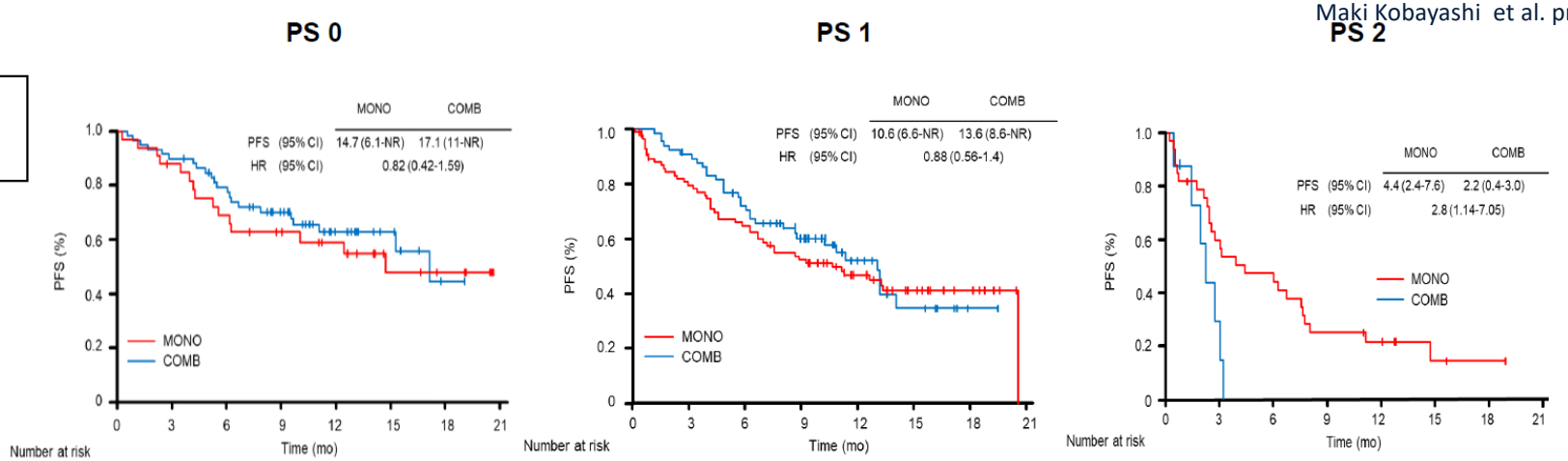



Number at risk

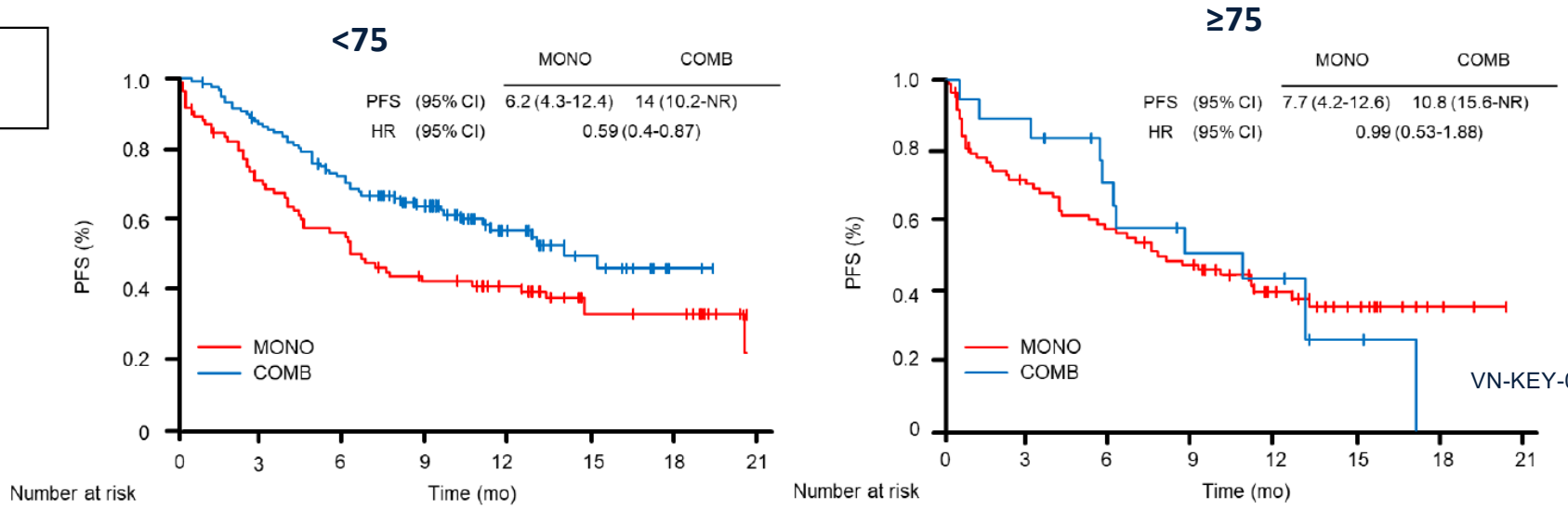
# PFS in subgroup by ECOG & Ages

Maki Kobayashi et al. presented in WCLC 2021

## ECOG




## Ages

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# Objective response rate & Safety profile

## ORR

| Variable | monotherapy | combination therapy |
|---|---|---|
| Tumor Response- no. (%) | (n=166) | (n=134) |
| ORR | 70(42.2) | 91(67.9) |
| DCR | 109(65.7) | 117(87.3) |
| Best overall response | | |
| CR | 5(3.0) | 3(2.2) |
| PR | 65(39.2) | 88(65.7) |
| SD | 39(23.5) | 26(19.4) |
| PD | 46(27.7) | 15(11.1) |
| NE | 11(6.6) | 2(1.5) |

## Safety profile

| monotherapy(n=166) | | combination therapy(n=134) | |
|---|---|---|---|
| AE ≥ G3 | AE leading to discontinuation | AE ≥ G3 | AE leading to discontinuation |
| 36(21.6) | 36(21.6) | 33(24.6) | 28(20.9) |

# RESULT: ORR

| | | | This study | Thuận An's study | Tiến Sơn's study | Hidehito's study | Y Cheng's study | Maki Kobayashi's study |
|---|---|---|---|---|---|---|---|---|
| ORR(%) | Total (CR) | | 45,5(6) | 10,2(3,4) | 60,7(10,7) | | | 67,9(2) |
| | Adenocarcinoma | | 48,15(7,41) | 13,0(4,3) | 72,7 | 56,0(4) | | |
| | Squamous | | 33,33 | 0 | 55,2 | | 78,5 | |
| | PD-L1(%) | <1 | 41,6 | 0 | 66,7 | | | |
| | | 1-49% | 53,3(6,67) | 0 | 60,0 | | | |
| | | ≥50 | 33,3(16,67) | 37,5(12,5) | 70,6 | | | |
| | Line | 1st | 52,0(8,0) | | | | | |
| | | Post | 00 | | | | | |

# RESULT: TTF

| | | | This study | Thuận An's study | Tiến Sơn's study | Hidehito 's study | Y Cheng's study | Maki Kobayashi's study |
|---|---|---|---|---|---|---|---|---|
| TTF(PFS) months | Total | | 9,0 | 9,0 | 8,6 | | | 13,1 |
| | Adenocarcinoma | | 12,0 | 9,7 | | 16,5 | | |
| | Squamous | | 6,0 | 5,0 | | | 8,3 | |
| | PD-L1(%) | <1 | 8 | 4,5 | | | | |
| | | 1-49 | 12 | 9 | | | | |
| | | ≥50 | NR | 9,7 | | | | |
| | Line | 1 | 26,0 | | | | | |
| | | Post | 6,0 | | | | | |

# RESULT: OS

| | | | This study | Thuận An's study | Tiến Sơn's study | Hidehito's study | Y Cheng's study | Maki Kobayashi's study |
|---|---|---|---|---|---|---|---|---|
| OS | Total | | 21,0 | 12,5 | | | | NR |
| | Adenocarcinoma | | 23,0 | 13,75 | | NR | | |
| | Squamous | | 12,0 | 10,0 | | | 30,1 | |
| | PD-L1(%) | <1 | 12,0 | 8,5 | | | | |
| | | 1-49 | 23,0 | 12,5 | | | | |
| | | ≥50 | 13,0 | 16 | | | | |
| | Line | 1 | 21,0 | 12,5 | | | | |
| | | Post | 6,0 | | | | | |

# DISCUSSION

- The slight variation was due to difference in histopathology, age, PS, PD-L1 expression. Besides, geographic regional, site of studies, timepoint might affected.

# Toxicities Associated With Immune Checkpoint Inhibitors

| | Chemotherapy | Immunotherapy |
|---|---|---|
| Incidence (moderate/severe AEs) | Almost all patients | Majority without |
| AE profile | Well described | Variable |
| Affected systems/organs | Few organs affected | Any organ |
| Time course | Well established | Variable (even after end of Tx) |
| | Predictable | Relatively unpredictable |

Slide credit: clinicaloptions.com

# TOXICITY

- Interstitial pneumonia: 1 patient
  - First symptoms of Interstitial pneumonia appeared after Cycle 3
  - Non specific CT-scan, no progression recorded
  - Responded well clinically to corticosteroid treatment and oxygen therapy after 2 days
  - Withdrawal oxygen and corticoid after 1 month
  - From there on, the patient were no longer receive tumor specific treatment and died in 4 months

# TOXICITY

- Hyper transaminasemia: 2 cases, after cycle 3 and cycle 6 respectively
  - 1 case: grade 4, transaminases level was as 20 times as much upper limit of normal, bilirubin level did not increase
  - Another patient had transaminases level as 5 times as much ULN
  - Both patients were asymptomatic
  - transaminases levels returned to normal limits after discontinuation of pembrolizumab

# TOXICITY (OTHERS)

- Anemia grade 1 – grade 2 accounted for 64,6%
- Leukopenia:  no recorded
- Thrombocytopenia grade 2: 1/33 patient accounted for 2%
- Hyperglycemia: 1 case was recorded, well-controlled with metformin
- Pruritus: 1 case was recorded at moderate, well response to corticoid
- Other adverse events such as infusion-related reaction, nausea, vomit, hypothyroidism…were not recorded

# TOXICITY

- All toxicity occurred in this study were already reported and well managed
- There were no un-reported adverse events,
- No grade 5 AE.

# CONCLUSION

- By conducted retrospective study of 33 cases treated in Oncology department Thong Nhat Hospital:
  - Treatment of stage IV NSCLC with combination regimen chemotherapy and pembrolizumab is consistent in results with previous studies, regardless PD-L1 expression;
  - Manageable toxicity profile, no arise unreported AE.
  - There were no deaths due to toxicity.
- Even though sample size of this study is still limited and this is a retrospective study in multiple lines, this is premise for further research with larger sample size.

# SUGGESTION

- Combination treatment of NSCLC stage IV by chemotherapy and pembrolizumab:
  - Combination is recommended at early approach when the patient's general condition is good could be resulted in the best response, especially in the patient with aggressive progression
  - For patients with PS ≥2, PD-L1≥50% combination is not strongly recommended
- PD-L1 testing should be performed routinely.

# THANK YOU
# FOR YOUR ATTENTION