IMMUNOTHERAPY IN LUNG CANCER

DR DEEPAK SUNDRIYAL
DEPARTMENT OF MEDICAL ONCOLOGY &
HEMATOLOGY
IMMUNOTHERAPY IN LUNG CANCER

- Introduction, challenges, epidemiology, evolution, personalized medicine
- Era of immunotherapy
- Early approvals
- When to use
- Indications in metastatic, adjuvant, and neoadjuvant setting
- Biomarkers
- Immuno-toxicities
- Future prospects
CHALLENGES IN TREATING CANCER

- EVERY TUMOR IS DIFFERENT
- EVERY PATIENT IS DIFFERENT
- PERSONALISED DIAGNOSIS
- PERSONALISED THERAPY

ONE SIZE DOESN’T FIT ALL
EPIDEMIOLOGY OF NSCLC

- NSCLC divided into squamous (~30%) and nonsquamous (~70%)
- Nonsquamous includes
  - Adenocarcinoma: most common form; originates from mucus-secreting cells
  - Large cell carcinoma: heterogeneous group of undifferentiated epithelial neoplasms
- More than one half of patients diagnosed with lung cancer succumb to their disease within 1 year of diagnosis

Prevalence of NSCLC Subtypes

- Squamous cell carcinoma: ~10%
- Adenocarcinoma: ~40%
- Large cell carcinoma: ~15%
- Other: ~30%

EPIDEMIOLOGY OF NSCLC

- AMONGST TOP 5 CANCER KILLERS
- 5 YEAR SURVIVAL RATES
  - OVERALL : 18-20%
  - METASTATIC : <5%
PERSONALIZED THERAPY EVOLUTION

1970s - today
Chemotherapy
Histologic subtype

2000s - today
Targeted TKI Therapy
EGFR mutations
ALK, ROS1 rearrangements

2015 - today
Immunotherapy
Anti–PD-1
Anti–PD-L1
DECISION MAKING IN LUNG CANCER: INTERLINKS

Histologic Subtyping ↔ Genotyping for Predictive Biomarkers

Therapeutic Decision Making

These factors are interlinked and not independent.
IMMUNOTHERAPY

THE IMMUNOLOGICAL BASIS OF IMMUNE THERAPEUTIC AGENTS
PD-1 & PDL-1

Inhibition

Activation

Anti-PD1

Anti-PDL1

Anti-PD1

PD1

PDL1

PDL2

PD1

PD1

PDL1

PDL1

Tumor cells

Tumor-infiltrating immune cells

Killing

IFNγ

Upregulation
IMMUNOTHERAPY: MECHANISM OF ACTION

PD-1 inhibitors
- Nivolumab
- Pembrolizumab

CTLA-4 inhibitors
- Ipilimumab
- Tremelimumab

PD-L1 inhibitors
- Atezolizumab
- Durvalumab
PD-1/PD-L1 AS A TARGET IN CANCER THERAPY

- Activated T-Cell
  - Initial immune response
  - Cytokines
  - Proliferation
  - Activation

- Tumor

- Exhausted T-Cell
  - Persistent antigen stimulation

- Tumor

- Nivolumab
- Pembrolizumab

- Atezolizumab
- Durvalumab
- Avelumab
**IMMUNOTHERAPY**

- Immune checkpoint inhibition removes tumor repression of the immune system and activates potency of immune cells against tumor cells.

- In stage IV NSCLC, immune checkpoint inhibition achieved durable and prolonged responses in some patients.
  - Median OS ranges from 15 to 27 mos.
IMMUNOTHERAPY RELATED ADVERSE EVENTS

**Skin**
- Dermatitis
- Erythema multiforme
- Stevens-Johnson syndrome
- Toxic epidermal necrolysis
- Vitiligo
- Alopecia

**Eye**
- Uveitis
- Iritis

**Endocrine**
- Hypothyroidism
- Hyperthyroidism
- Adrenal insufficiency
- Hypophysitis

**Pulmonary**
- Pneumonitis
- Interstitial lung disease
- Acute interstitial pneumonitis

**Gastrointestinal**
- Colitis
- Enterocolitis
- Necrotizing colitis
- GI perforation

**Neurologic**
- Autoimmune neuropathy
- Demyelinating polyneuropathy
- Guillain-Barré
- Myasthenia gravis-like syndrome

**Hepatic**
- Hepatitis, autoimmune

**Renal**
- Nephritis, autoimmune
- Renal failure

*If not vigilant, may result in more serious immune-related AEs*
NOBEL PRIZE (MEDICINE) 2018

JAMES ALLISON

TASUKO HONJO
WHEN TO USE

- NOT RECOMMENDED
- 1. C/I – ACTIVE OR PREVIOUSLY DOCUMENTED AUTO-IMMUNE DISORDER
- CURRENT USE OF IMMUNOSUPPRESSIVE DRUGS
- PRESENCE OF A TARGET THAT PRECLUDE LACK OF BENEFIT (BASED ON DATA FROM EARLIEST STUDY OF io in patients with a targetable mutation)- EXCESS TOXICITIES WITHOUT ANY CLINICAL BENEFIT
- FINANCIAL TOXICITIES
## RESPONSE RATE

<table>
<thead>
<tr>
<th></th>
<th>EGFR</th>
<th>ALK</th>
<th>ROS1</th>
<th>BRAF</th>
<th>HER2</th>
<th>MET</th>
<th>RET</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TARGETED THERAPY</strong></td>
<td>80%</td>
<td>83%</td>
<td>77%</td>
<td>64%</td>
<td>55%</td>
<td>71%</td>
<td>68%</td>
</tr>
<tr>
<td><strong>IO</strong></td>
<td>11%</td>
<td>4%</td>
<td>14%</td>
<td>24%</td>
<td>15%</td>
<td>23%</td>
<td>11%</td>
</tr>
<tr>
<td><strong>IO + TARGETED</strong></td>
<td>75%</td>
<td>81% (increased toxicities)</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td><strong>CHEMO+IO</strong></td>
<td>81%</td>
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</tr>
</tbody>
</table>
- Testing for driver mutations (NGS/individually)
- Testing for PDL1
IMMUNOTHERAPY (METASTATIC SETTING)

SECOND LINE

• CHECKMATE 017 TRIAL
• Phase III, randomized, open-label study (n=272), nivolumab vs. docetaxel; metastatic squamous NSCLC, disease progression during or after one prior platinum doublet based chemotherapy
  • Median Overall Survival (OS) = 9.2 months on nivolumab (n=132) vs. 6.0 months on docetaxel (n=137)

CHECKMATE 057 TRIAL
Phase III randomized, metastatic non-squamous NSCLC nivolumab vs docetaxel in second or later lines of therapy
• Median Overall Survival (OS) = 12.2 months on nivolumab vs. 9.5 months on docetaxel
• Response rates around 20% for nivolumab vs 9-12% for docetaxel in both the trials
SECOND LINE

KEYNOTE010

RANDOMIZED 1:1:1 PEMBROLIZUMAB 2MG/KG VS 10 MG/KG VS DOCE TAXEL, IN SECOND OR LATER LINES FOR SQ/NON SQ HISTOLOGY

OS 10.4 VS 12.7 VS 8.5 MONTHS, SHOWING GREATEST BENEFIT FOR TUMORS PDL-1>50%
- SECOND LINE
- OAK TRIAL: PHASE 3 TRIAL ATEZOLIZUMAB VS DOCETAXEL IN SECOND OR LATER LINES IN SQ/NONSQ.
- OS 13.8 VS 9.6 MONTHS IRRESPECTIVE OF PDL1 EXPRESSION
<table>
<thead>
<tr>
<th>Study name</th>
<th>Phase</th>
<th>Histology, PD-L1</th>
<th>Line of treatment</th>
<th>Study design</th>
<th>Control arm outcome</th>
<th>Experimental arm outcome</th>
<th>Hazard ratio (95% Confidence Interval, p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Later-line ICI</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>CheckMate017</td>
<td>III</td>
<td>Squamous</td>
<td>Second or later</td>
<td>Nivolumab vs. docetaxel</td>
<td>mos 6.0 months</td>
<td>mos 9.2 months</td>
<td>0.62 (0.47–0.80)</td>
</tr>
<tr>
<td>CheckMate057</td>
<td>III</td>
<td>Nonsquamous</td>
<td>Second or later</td>
<td>Nivolumab vs. docetaxel</td>
<td>mos 12.2 months</td>
<td>mos 9.5 months</td>
<td>0.75 (0.63–0.91)</td>
</tr>
<tr>
<td>KEYNOTE-010</td>
<td>II/III</td>
<td>NSCLC, PD-L1 TPS≥1%</td>
<td>Second or later</td>
<td>Pembrolizumab 2 mg/kg or 10 mg/kg vs. docetaxel</td>
<td>mos 8.5 months 2 mg/kg: mos 10.4 months</td>
<td>2 mg/kg: 0.71, p=0.0008 10 mg/kg: mos 12.7 months</td>
<td>10 mg/kg: 0.61, p&lt;0.0001</td>
</tr>
<tr>
<td>OAK</td>
<td>III</td>
<td>NSCLC</td>
<td>Second or later</td>
<td>Atezolizumab vs. docetaxel</td>
<td>mos 9.6 months</td>
<td>mos 13.8 months</td>
<td>0.73 (0.62–0.87), p=0.0003</td>
</tr>
</tbody>
</table>
IMMUNOTHERAPY (2ND AND SUBSEQUENT LINE)

- Consistent improvement in OS, ORR with immunotherapy
- Lesser toxicity as compared to chemotherapy
- Cut-offs for PDL1 not defined
- Diagnostic methods for PDL1 testing not defined
- Unclear whether PDL1 testing should be done for second line therapy or not
IMMUNOTHERAPY IN UNTREATED NSCLC(METASTATIC)

- **Keynote 024; PHASE III, nsclc(sq/nonsq) qwith PDL-1 50% OR MORE(tps) PEMBROLIZUMAB WITH STANDARD [PLATINUM DOUBLET. PFS 10.3 VS 6.0 MONTHS**

- **KEYNOTE 042: SIMILAR TRIAL BUT PDL-1 >1% WERE ELIGIBLE. OS BENEFIT WAS GREATEST IN TPS >50% AND NOT PRESENT IN LOWER SCORE**
IMMUNOTHERAPY IN UNTREATED NSCLC(METASTATIC)

- CHECKMATE 026 PHASE III, NIVOLUMAB VS PLATINUM DOUBLET IN NSCLC, PDL-1 TPS ≥ 1%.

- NO BENEFIT IN PFS OR OS, SUBGROUP ANALYSIS ALSO FUTILE.

- HOWEVER, A TMB ANALYSIS REVEALED AN INCREASED RR(47 VS 28%) AND PFS(9.7 MONTHS VS 5.8), BUT NO DIFFERENCE IN OS.
IMMUNOTHERAPY IN UNTREATED NSCLC (METASTATIC)

- MYSTIC TRIAL. DURVALUMAB VS DURVA + TREMELIMUMAB VS PLATINUM DOUBLET.
  - DID NOT MEET ENDPOINT (pfs)

- IMPOWER 110: PHAE III ATEZOLIZUMAB VS PLATINUM DOUBLET IN NSCLC
  - OS 20.2 MONTHS VS 11.0 MONTHS
## IMMUNOTHERAPY IN UNTREATED NSCLC (METASTATIC)

<table>
<thead>
<tr>
<th>Study name</th>
<th>Phase</th>
<th>Histology, PD-L1</th>
<th>Line of treatment</th>
<th>Study design</th>
<th>Control arm outcome</th>
<th>Experimental arm outcome</th>
<th>Hazard ratio (95% Confidence interval, p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-line ICI only</strong></td>
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</tr>
<tr>
<td>KEYNOTE-024</td>
<td>III</td>
<td>NSCLC, PD-L1 TPS≥50%</td>
<td>Treatment-naïve</td>
<td>Pembrolizumab vs. chemotherapy</td>
<td>mOS 14.2 months</td>
<td>mOS 30.0 months</td>
<td>0.63 (0.47–0.86), p=0.002</td>
</tr>
<tr>
<td>KEYNOTE-042</td>
<td>III</td>
<td>NSCLC, PD-L1 TPS≥1%</td>
<td>Treatment-naïve</td>
<td>Pembrolizumab vs. chemotherapy</td>
<td>mOS 12.1 months</td>
<td>mOS 16.7 months</td>
<td>0.85 (0.71–0.93), p=0.0018</td>
</tr>
<tr>
<td>CheckMate026</td>
<td>III</td>
<td>NSCLC, PD-L1 TPS≥1%</td>
<td>Treatment-naïve</td>
<td>Nivolumab vs. chemotherapy</td>
<td>mOS 13.2 months</td>
<td>mOS 14.4 months</td>
<td>1.02 (0.80–1.30), p=NS</td>
</tr>
<tr>
<td>MYSTIC</td>
<td>III</td>
<td>NSCLC</td>
<td>Treatment-naïve</td>
<td>D vs. D+Tr vs. chemotherapy</td>
<td>mOS 12.9 months</td>
<td>mOS 16.3 months (D)</td>
<td>D vs. Chemotherapy: 0.76 (0.56–1.02), p=NS</td>
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<td>D+Tr vs. Chemotherapy: 0.85 (0.61–1.17), p=NS</td>
</tr>
</tbody>
</table>
CONCLUSION

PDL1 OR TMB ARE NOT A CONSISTENT BIOMARKER TO PREDICT EFFICACY ACROSS VARIOUS ICI.

PEMBROLIZUMAB, ATEZOLIZUMAB, CEMIPLIMAB-rwlc REMIANS THE ONLY APPROVED ICI IN FIRST LINE SETTING IN ADVANCED NSCLC PATIENTS (tps >50%).
IMMUNOTHERAPY IN COMBINATION WITH CHEMOTHERAPY NSCLC (METASTATIC)

- **NEED?**
  - patients with a tumor proportion score of 50% or greater represent a minority of those with NSCLC
  - less than one half of patients ever receive second-line therapy.
HYPOTHESIS

Modulation of the immune response through PD-1 inhibition may be enhanced by the potential immunogenic effects of cytotoxic chemotherapy
IMMUNOTHERAPY IN COMBINATION WITH CHEMOTHERAPY NSCLC(METASTATIC)

- KEYNOTE-189 PHASE III, FIRSTLINE SETTING, NONSQ NSCLC, PEM + PLATINUM + PEMBRO VS PEM + PLATINUM
- ORR 47.6% VS 18.9%
- 3 YEAR OS 31.3% VS 17.4% (SEEN IRRESPECTIVE OF PDL-1 STATUS)
IMMUNOTHERAPY IN COMBINATION WITH CHEMOTHERAPY NSCLC(METASTATIC)

- Impower 150/Impower 132: PHASE III ATEZOLIZUMAB +CHEMOTHERAPY, in nonsquamous nsclc, favourable result irrespective of pdl-1 expression

- Keynote-407 impower 131 phase III TRIAL OF PEMBROLIZUMAB AND ATEZOLIZUMAB RESPECTIVELY, IN CONBINATION WITH CHEMOTHERAPY IN ADVANCED SQUAMOUS NSCLC, WITH FAVOURABLE RESULTS.
<table>
<thead>
<tr>
<th>Study</th>
<th>Phase</th>
<th>Tumor Type</th>
<th>Treatment-naïve</th>
<th>Treatment-naïve Vs.</th>
<th>12-month OS</th>
<th>12-month OS 69.2%</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>KEYNOTE-189</td>
<td>III</td>
<td>Nonsquamous</td>
<td>Treatment-naïve</td>
<td>Pem/C+pembrolizumab vs. placebo</td>
<td>49.4%</td>
<td>0.49 (0.38–0.64), p&lt;0.001</td>
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<td></td>
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<td></td>
<td>B/Pac/C+atezolizumab</td>
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<tr>
<td>IMpower150</td>
<td>III</td>
<td>Nonsquamous, including EGFR/ALK+</td>
<td>Treatment-naïve</td>
<td></td>
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</tr>
<tr>
<td>IMpower132</td>
<td>III</td>
<td>Nonsquamous</td>
<td>Treatment-naïve</td>
<td>Pem/P+atezolizumab</td>
<td>mPFS 5.2 months</td>
<td>0.60 (0.49–0.73), p&lt;0.0001</td>
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<tr>
<td>KEYNOTE-407</td>
<td>III</td>
<td>Squamous</td>
<td>Treatment-naïve</td>
<td>T/C+pembrolizumab</td>
<td>mOS 11.3 months</td>
<td>0.64 (0.49–0.85), p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>IMpower131</td>
<td>III</td>
<td>Squamous</td>
<td>Treatment-naïve</td>
<td>Nab/C+atezolizumab</td>
<td>mPFS 5.6 months</td>
<td>0.715 (0.603–0.848), p&lt;0.0001</td>
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</tbody>
</table>
Combination immunotherapy in first line setting

- Nivolumab + ipilimumab (irrespective of pdl1 status)
IMMUNOTHERAPY IN ADJUVANT SETTING
IMMUNE-BIOMARKERS

- NIVO/PEMBRO/CEMIP-rwlc
- PD-1
- ATEZO/DURVA PDL-1
PDL-1 : NOT AN OPTIMAL BIOMARKER?

- Expression is dynamic/variable/temporal: difficult to define a cut off
- Each drug trial used different antibody clones/assays (Dako 28-8, Dako 22C3, Ventana SP142, Ventana SP263 for nivolumab, pembrolizumab, atezolizumab and durvalumab, respectively)
- Cross compatibility of various platforms have failed to provide a uniform result
- Moreover, even PD-L1 negative patients may respond to anti-PD-1/PD-L1 inhibitor
- while some PD-L1 highly positive patients do not show response
PDL-1: NOT AN OPTIMAL BIOMARKER?

- Multiple studies have shown an absence of association between PD-L1 expression and OS in ICI therapy
GOLDIE-COLDMAN HYPOTHESIS

As tumor grows, genetic alterations/mutations accumulate

- The number of genetic alterations within a tumor genome is considered correlative with mutant protein burden
- Higher the mutations, more the mutant protein and hence immunogenicity - more likelihood of response to IO
However, the relationship between TMB and response to immune checkpoint inhibitors is imperfect across and within tumor types.

Imperfect correlation between OS, RR and TMB across various studies with IO.

TMB does not identify patients who will respond to immun chemotherapy.

determination of TMB and the TMB thresholds predicting response to immune checkpoint blockade have been developed independently in each tumor type, they are likely to differ across tumor types,
- and also across testing platforms (e.g., blood versus tumor tissue)
- So, a lack of agreement on a cut-off value
- Lack of standardization of TMB across labs
- Time consuming
- In 2020 NCCN panel removed TMB as an emerging biomarker for patients with NSCLC and do not recommend TMB measurement before deciding for IO
OTHER BIOMARKERS

- MMR/MSI
- TUMOR INFILTRATING LYMPHO CYTES
- GENE EXPRESSION PROFILE
- Treg

- None approved as companion diagnostic for the use of IO in lung cancer
A. (A) Intratumoral (and intrapersonal) cellular heterogeneity. Further dynamic alterations in clonal composition under the pressure of time (1) and therapy (2) prohibit pretreatment biomarker accuracy.

B. Patient host immunity & tumor microenvironment remain highly individualized and responsive to progressive cytokine (1) and/or treatment (2) exposure.
retrospective analysis of clinical trials (2011–2019) prompting FDA approval of checkpoint inhibitor regimens identified PD-L1 as a predictive biomarker in only 28.9% of cases.

Second-Line & Beyond Treatment

Non-Squamous NSCLC**

Squamous NSCLC*

Nivolumab (CheckMate 017* & 057**)
  Atezolizumab (OAK & POPLAR)
  Pembrolizumab (KEYNOTE-010)
Non-squamous

PD-L1 ≤1%
- High TMB (≥10 mut/Mb)
  - Nivolumab + Ipilimumab (CM227)
  - Pembrolizumab + platinum-pemetrexed (KN-189)
  - Atezolizumab + platinum-pemetrexed (IMP-132)
  - Atezolizumab + carboplatin-Nab-paclitaxel (IMP-130)
  - Atezolizumab + bevacizumab-carboplatin-paclitaxel (IMP-150)

PD-L1 1%–49%
- Pembrolizumab (KN-024)

PD-L1 ≥50%

Squamous

PD-L1 ≤1%
- High TMB (≥10 mut/Mb)
  - Nivolumab + Ipilimumab (CM227)

PD-L1 1%–49%

Pembrolizumab + carboplatin-paclitaxel (KN-407)
- Atezolizumab + carboplatin-Nab-paclitaxel (IMP-131)
### TIMELINE: FDA APPROVAL FOR LUNG CA

<table>
<thead>
<tr>
<th>Drug</th>
<th>Manufacturer</th>
<th>FDA approval</th>
<th>Indication</th>
<th>Companion diagnostic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivolumab</td>
<td>Bristol-Myers Squibb (Princeton, New Jersey)</td>
<td>March 2015</td>
<td>Second-line advanced stage NSCLC (squamous cell carcinoma)</td>
<td>None required</td>
</tr>
<tr>
<td>Nivolumab</td>
<td>Bristol-Myers Squibb</td>
<td>October 2015</td>
<td>Second-line advanced stage NSCLC (nonsquamous cell carcinoma)</td>
<td>None required</td>
</tr>
<tr>
<td>Pembrolizumab</td>
<td>Merck (Kenilworth, New Jersey)</td>
<td>October 2015</td>
<td>Second-line advanced stage NSCLC</td>
<td>PD-L1 IHC &gt;1% TPS*</td>
</tr>
<tr>
<td>Atezolizumab</td>
<td>Genentech/Roche (San Francisco, California)</td>
<td>April 2016</td>
<td>Second-line advanced stage NSCLC</td>
<td>None required</td>
</tr>
<tr>
<td>Pembrolizumab</td>
<td>Merck</td>
<td>October 2016</td>
<td>First-line advanced stage NSCLC</td>
<td>PD-L1 IHC &gt;50% TPS</td>
</tr>
<tr>
<td>Pembrolizumab with carboplatin/pemetrexed</td>
<td>Merck</td>
<td>May 2017</td>
<td>First-line advanced stage NSCLC (nonsquamous cell carcinoma)</td>
<td>None required</td>
</tr>
</tbody>
</table>

FDA, US Food and Drug Administration; IHC, immunohistochemistry; NSCLC, non-small cell lung cancer; PD-1, programmed cell death 1; PD-L1 programmed cell death ligand 1; TPS, tumor proportion score.
# Summary of PD-1/PD-L1 Immune Checkpoint Inhibitors Approved for Advanced NSCLC

<table>
<thead>
<tr>
<th>Dose/schedule</th>
<th>Nivolumab(^1) (Anti–PD-1)</th>
<th>Pembrolizumab(^2) (Anti–PD-1)</th>
<th>Atezolizumab(^3) (Anti–PD-L1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>240 mg every 2 wks; 480 mg every 4 wks</td>
<td>200 mg every 3 wks</td>
<td>1200 mg every 3 wks</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Requirement for PD-L1 expression/approved settings</th>
<th>Nivolumab</th>
<th>Pembrolizumab</th>
<th>Atezolizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>No; second line or later</td>
<td>▪ First-line monotherapy if ≥ 50% PD-L1 expression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ First line in combination with chemotherapy*</td>
<td>▪ After chemotherapy if ≥ 1% PD-L1 expression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ After chemotherapy if ≥ 1% PD-L1 expression</td>
<td>No; second line or later</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PD-L1 IHC assay</th>
<th>Nivolumab</th>
<th>Pembrolizumab</th>
<th>Atezolizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dako 28-8(^4)</td>
<td>Dako 22C3(^5)</td>
<td>Ventana SP142(^6)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Definition of PD-L1 positive</th>
<th>Nivolumab</th>
<th>Pembrolizumab</th>
<th>Atezolizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-L1(+) ≥ 1%</td>
<td>PD-L1(+) ≥ 1%</td>
<td>PD-L1(+) ≥ 50% TC or ≥ 10% IC</td>
<td></td>
</tr>
<tr>
<td>Strong(+) ≥ 5%</td>
<td>Strong(+) ≥ 50%</td>
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<td></td>
</tr>
</tbody>
</table>
"THERE ARE NO SUCH THINGS AS INCURABLE, THERE ARE ONLY THINGS FOR WHICH MAN HAS NOT FOUND A CURE."

Everything is Curable!